CHEMICAL REVIEWS

Review

pubs.acs.org/CR

Constituents from *Salvia* Species and Their Biological Activities

Yi-Bing Wu,[†] Zhi-Yu Ni,[†] Qing-Wen Shi,*[,†] Mei Dong,[‡] Hiromasa Kiyota,*[,§] Yu-Cheng Gu,[†,∥] and Bin Cong*[,‡]

[†]School of Pharmaceutical Sciences, Hebei Key Laboratory of Forensic Medicine, Hebei Medical University, Shijiazhuang, Hebei Province 050017, China

[‡]Department of Forensic Medicine, Hebei Medical University, Hebei Key Laboratory of Forensic Medicine, Shijiazhuang, Hebei Province 050017, China

[§]Department of Bioscience and Biotechnology for Future Bioindustry, Graduate School of Agricultural Science, Tohoku University, 1-1 Tsutsumidori-Amamiya, Aoba-ku, Sendai 981-8555, Japan

[∥]Syngenta Jealott's Hill International Research Centre, Berkshire RG42 6EY, United Kingdom

CONTENTS

1. INTRODUCTION

The Lamiaceae (formerly Labiatae), a widespread family, comprises 220 genera and 4000 species distributed throughout most of the world as annuals and perennial plants. The increasing number of commonly known crops in this family reflects the intensification of taxonomical and ethnobotanical research in this field. The chemistry of the Lamiaceae is very extensive and dominated by reports concerning the volatile oils (mainly monoterpenes and sesquiterpenes) found in genera of economic importance, but chemical constituents such as diterpenes (mainly abietane and clerodane diterpenes) and triterpenes, phenolics, and others may offer great significance as taxonomic characters and biologically active compounds with a potential ecological role. *Salvia* L., one of the largest genera of the family, is represented by over 1000 species, organized in five subgenera (Sclarea, Audibertia, Jungia, Leonia, and Salvia) as herbaceous, suffruticose, or shrubby perennial plants, of which 78 species, 24 varieties, and 8 forms are distributed in China, especially in the southwest.[1,2] The name *Salvia* is derived from the Latin "salvare" meaning "to heal or to be safe and unharmed", which sums up the folkloric belief of its "magical" therapeutic properties for many kinds of ailments and its popularity in traditional medicine, and it is also known by the common name sauge (sage) in French and sawge in old English.[3] The genus *Salvia* is widely distributed in various regions of the world including the temperate and warmer zones of the world such as the Mediterranean, Central Asia, the Pacific Islands, tropical Africa, and America.[4,5] The genus *Salvia* has a subcosmopolitan distribution, which is largely absent in

Received: February 18, 2011
Published: September 11, 2012

   dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Figure 1. (a, b) The flowers and (c) the roots of *S. miltiorrhiza* and (d) commercial tablets of Danshen (taken by Q.-W. Shi).

the North and most of the low-lying tropical areas of the world such as the Amazon basin and central and west Africa. Mexico has the largest number of species (about 300). There are about 90 *Salvia* species growing naturally in Turkey; half of the plants are endemic.[6] Sixty species are found in Iran, of which 17 are endemic.[7] In Africa, the greatest number of species (ca. 30) is found in the northwest and the southern parts. The genus is absent from most of western and central tropical Africa.[8] Many species in the genus *Salvia* L. are noted for their brightly colored flowers, which are typically pink to red or purple to blue. *S. uliyinosa* Benth., a perennial herb native to South America, was first cultivated at the Royal Botanic Gardens, Kew, as long ago as 1913 because of its beautiful sky-blue flowers.[9] Some members of this genus have economic importance because they have been used as flavoring agents in perfumery and cosmetics. For example, clary sage (*S. sclarea*) is commercially cultivated, and its essential oil is widely used as a flavoring. Meadow sage (*S. pratensis*) is used in cosmetics and has some medicinal properties.[7] Since ancient times *Salvia* species have been used in folk medicine all around the world because of their diverse biological activities, including antibacterial, spasmolytic, hemostatic, and many others.[3] Some species of *Salvia* have been cultivated worldwide for culinary purposes.

Of 1000 *Salvia* species, about 134 of them have been studied. For example, the dried root of *S. miltiorrhiza* (Danshen or Tanshen in Chinese) is one of the most popular herbal traditional medicines in Asian countries and has been used extensively for the treatment of coronary artery diseases, angina pectoris, myocardial infarction, cerebrovascular diseases, and various types of hepatitis, chronic renal failure, and dysmenorrhea (Figure 1). There are about 40 *Salvia* species that were used for the treatment of coronary heart disease, and more than 700 pharmaceutical companies produce preparations of Danshen in China. In the United States and Europe, Danshen products have been widely used for the treatment of cardiovascular and cerebrovascular diseases; in China Danshen ranked as a "Supergrade" medicine in Shen-Nung's Pen-Ts'ao, and the specific clinical use is to treat particularly angina pectoris and myocardial infarction.[10] It has also been indicated for hemorrhage, dysmenorrhea, miscarriage, swelling, and insomnia, as well as inflammatory diseases such as edema, arthritis, and endangitiis. Chronic hepatitis and liver fibrosis have also been treated with Tanshen for centuries. Fufang Danshen tablet, a combined prescription mainly derived from the rhizome of *S. miltiorrhiza* and Panaxnotoginseng, is a common traditional Chinese medicine used for the treatment of cardiovascular disease in China for over 30 years. It has been documented in the Pharmacopoeia of the People's Republic of China from the 1977 edition to the 2010 edition (The Pharmacopoeia Committee of China, 2010). It was reported that Fufang Danshen tablet showed effects by activating blood circulation, dilating coronary artery, and antagonizing myocardial ischemia, and it was very effective for treating coronary heart disease, cardiac angina, and atherosclerosis in clinic. The product of Danshen, Fufang Danshen Diwan, by extracting curative ingredients mainly from the plant, is now available in 16 countries and became the first Chinese herbal medicine approved by the Food and Drug Administration for clinical tests in the United States.[11] In Japan, Danshen products are used to promote circulation and improve blood flow.[12] The chemical composition of Danshen has been studied extensively

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

over the last 50 years. The alcohol extract of Danshen is particularly rich in abietanoids and diterpene quinone pigments.[13] Tanshinone IIA (**255**), as one of the major active components of this Chinese medicine, has been shown to be effective against atherosclerotic calcification, as well as apoptosis through antioxidative damage. Tanshinone IIA (**255**) was also reported to dilate coronary arteries and increase coronary flow by activating potassium channels. Additionally, **255** was found to have anti-inflammatory properties. The present studies by Ren et al. demonstrated that **255** exerted its cardioprotective effect by attenuating inflammatory responses following myocardial infarction. **255** could reduce MCP-1 expression and macrophage infiltration, as well as inhibit the expression of TGF-β_1 especially in cardiac fibroblasts.[14] **255** is one of the potential anticancer components, despite the fact that its traditional application was in the treatment of cardiovascular diseases in China. Experiments have shown that **255** exerted cytotoxic effect on a number of human tumor cell lines. Studies revealed that induction of apoptosis was the key factor in contributing to the cytotoxic property of **255**.[15]

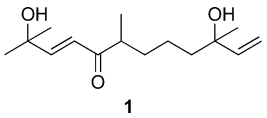
S. yunnanensis is used as a resource of Danshen in Yunnan province, China. The water-soluble extracts of *S. yunnanensis* were found to have a potent effect against human immunodeficiency virus type 1 (HIV-1) and hepatitis B virus (HBV).[16] *S. przewalskii* was a traditional medicinal plant used as the surrogate of *S. miltiorrhhiza* (Danshen) for the treatment of various cardiovascular diseases.[17] There is also a large number of species mentioned in the handbook of Xinhua Bencao.

S. officinalis is one of the most widespread species, and since ancient times it has been used in the treatment of various disorders, such as tuberculosis, psoriasis, and seborrhoeic eczemas. It has shown strong antibacterial and antifungal activities.[18] *S. divinorum*, also referred to as "diviner's sage", "magic mint", or "holey mint", is a psychotropic plant first described in the 1960s, contains the neo-clerodane diterpene salvinorin A (**465**) as a hallucinogenic active constituent.[19−21] *S. parryi* is endemic in Northern Mexico and in Arizona. Local people use its aqueous root extract to cure stomach disorders.[5] The Canary sage (*S. canariensis* L.) is a protected endemism widely used in the popular medicine of the Canary Archipelago because of its anti-inflammatory, wound healing, and antiseptic properties, with its infusion being particularly recommended for all kinds of stomach complaints. In contrast, with other species of genus *Salvia*, the Canary sage is a shrub that can grow up to 2 m high and whose long branches with long lanceolate leaves show a characteristic dense arrangement. Therefore, this species has been considered as a likely link between Old and New World sages.[2] A mixture of leaves of *S. fulgens* Cav. and *S. microphylla* Kunth is a traditional Mexican medicine—called "mirto"—for stomach ailments in Mexico.[22] *S. cavaleriei* is used for the treatment of dysentery, boils, and fall injuries; *S. desoleria* is used for the treatment of menstrual, digestive, and central nervous system diseases; and *S. bucharica* is used as a traditional medicine for the treatment of hepatic problems.[23] *S. aegyptiaca* L. (English name, Egyptian sage; vernacular names, Shajarat al ghazal, Ghabeisha; family Labiatae) is a green dwarf shrub that grows in various locations in the Arabian Peninsula, Egypt, Israel, Palestine, Iran, and Afghanistan. It is commonly used in local folk medical practices and in cosmetics. For example, the seeds are used as a demulcent for diarrhea and for piles, and the whole plant is used in diarrhea, gonorrhea and hemorrhoids, and eye diseases, and as an antiseptic, antispasmodic, and stomachic. The plant is also used in cases of nervous disorders, dizziness, and trembling.[24] *S. moorcroftiana*, commonly known in Pakistan as "kallijari", is used as a folk medicine for the guinea worm and itch and is applied in the form of a poultice to wounds.[25]

This group of plants has been characterized from a phytochemical standpoint by the production of monoterpenoids, mainly diterpenoids with an abietane or clerodane skeleton, triterpenoids, and flavonoids. Many diterpenoids isolated from *Salvia* species have shown antioxidant, antifeedant, antibacterial, antimutagenic, anti-inflammatory, and antiplatelet aggregation activities or cytotoxic properties.[26] Several authors have given reviews about the structures, synthesis, and biological activities of diterpenoids from *Salvia* species.[8,27−40] However, no a comprehensive review has been published so far. Considering the recent flurry of reports in this area, here we review systematically all the papers that have published in the literature from 1934 until the beginning of 2011, concerning the isolation, structural elucidation, and biological evaluations of *Salvia* plant constituents.

2. CHEMICAL CONSTITUENTS

Investigated *Salvia* plants have produced an array of secondary metabolites. Some of them have attracted considerable attention from the chemical and biological communities for their broad spectrum of biological activities and novel structure; for example, salvinorin A and tanshinone IIA delayed a variety of significant bioactivities. Until the beginning of 2011, a total of 773 compounds were isolated from 134 *Salvia* species. We classify the constituents into seven groups: sesquiterpenoids, diterpenoids, sesterterpenoids, triterpenoids, steroids, polyphenols, and others. Their structures are shown in Figures 2−54, and their names, the corresponding plant sources, and references are collected in Tables 1−5.



1

Figure 2. Aliphatic sesquiterpenoid.

2.1. Sesquiterpenoids

Sesquiterpenes are a wide variety of 15-carbon skeletons derived from the coupling of three isoprene subunits, and the majority of sesquiterpenes arise directly from farnesyl diphosphate (FPP), a key C15 diphosphorylated intermediate of the mevalonate (MVA) biosynthetic pathway. The number of natural sesquiterpenoids from *Salvia* species reported by April of 2010 is 46. This group is distributed in 15 *Salvia* species and can be divided into six subgroups: aliphatic sesquiterpene, germacrane sesquiterpenes, carotane sesquiterpenes, caryophyllane sesquiterpenes, guaiane sesquiterpenes, and other sesquiterpenes (Table 1).

2.1.1. Aliphatic Sesquiterpene. In this subgroup, only one compound, salvinine (**1**), has been found in *S. divaricata*.[41]

2.1.2. Germacranes. Germacrane sesquiterpenoids are a group of sesquiterpenes with a 10-membered ring system with different arrangements in functionality. Salviadienol A (**2**) and salviadienol B (**6**) were the first germacrane sesquiterpenes obtained from *S. chinensis*. Compounds **2** and **6** were highly acetylated members with oxy-isovaleryl groups being the most unusual ones.[42] From the whole plant of *S. roborowskii*, four new germacrane sesquiterpene esters, **3**, **4**, **5**, and **16**, were

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Table 1. Sesquiterpenoids 1−46

no.	name	plant	ref	no.	name	plant	ref
1	salvinine	*S. divaricata*	41, 397	**24**	(1*R*,5*R*)-1,5-epoxysalvial-4(14)-ene	*S. sclarea*	49
2	salviadienol A	*S. chinensis*	42	**25**	(2*R*,5*E*)-2,12-epoxycaryophyll-5-ene	*S. sclarea*	49
3	3*β*,6*β*,8a-triacetoxy-4*β*,5*α*-epoxy-1-oxogermacr-10(14)-ene	*S. roborowskii*	43	**26**	(2*R*,5*E*)-caryophyll-5-en-12-al	*S. sclarea*	49
4	3*β*,6*β*,8a-triacetoxy-4*β*,5*α*-epoxygermacr-1(10)*E*-ene	*S. roborowskii*	43	**27**	(2*S*,5*E*)-caryophyll-5-en-12-al	*S. sclarea*	49
5	3*β*,6*β*,8a-triacetoxy-4*β*,5*α*:1*α*,10*β*-diepoxygermacrane	*S. roborowskii*	43	**28**	caryophyllene oxide	*S. sclarea*	51, 47
6	salviadienol B	*S. chinensis*	42			*S. palaefolia*	50
7	trijugin A	*S. trijuga*	45	**29**	4,10-epoxy-6*α*-hydroxyguaiane (= buchariol)	*S. bucharica*	343
8	trijugin B	*S. trijuga*	45	**30**	isospathulenol	*S. sclarea*	49
9	trijugin C	*S. trijuga*	45	**31**	(1*β*,3*β*,4*α*,5*α*,6*α*,8*α*)-guai-10(14)-ene-3,4,6,8-tetrol 3,6,8-triacetate	*S. roborowskii*	48
10	trijugin D	*S. trijuga*	45	**32**	spathulenol	*S. eupatorium*	361
11	trijugin E	*S. trijuga*	45			*S. sclarea*	51
12	trijugin F	*S. trijuga*	45	**33**	nubiol	*S. nubicola*	23
13	trijugin G	*S. trijuga*	45	**34**	nubenolide	*S. nubicola*	52
14	trijugin H	*S. trijuga*	45	**35**	nubenolideacetate	*S. nubicola*	52
15	trijugin I	*S. trijuga*	45	**36**	bisnubidiol	*S. nubicola*	23
16	(1a*S**,6*R**,6a*S**,7a*R**,9a*R**)-1a,2,6,6a,7a,8,9,9a-octahydro-1a,5,7a-trimethylbisoxireno[4,5:8,9]cyclodeca[1,2-*b*]furan-6-yl acetate (= castanin B)	*S. castanea*	44	**37**	bisnubenolide	*S. nubicola*	52
	6-acetoxyglechomafuran	*S. roborowskii*	43	**38**	1*α*,9*β*-dibenzoyloxy-2*β*,3*β*,4*β*-trihydroxydihydro-*β*-agarofuran	*S. palaefolia*	50
17	glechomafuran	*S. palaefolia*	47	**39**	l*α*-acetoxy-11-hydroxy-2,8-dioxo-eudesman-3-en-12-oic acid methyl ester	*S. palaefolia*	53
18	castanin C	*S. castanea*	46	**40**	11-hydroxy-3,8-dioxo-eudesman-1,4-dien-12-oic acid methyl ester	*S. palaefolia*	53
19	castanin D	*S. castanea*	46	**41**	*β*-eudesmol	*S. microphylla*	55
20	castanin E	*S. castanea*	46	**42**	8*α*-hydroxy-*β*-eudesmol	*S. microphylla*	55
21	castanin F	*S. castanea*	46	**43**	1*α*-acetoxy-2-oxoeudesman-3,7(11)-dien-8*β*,12-olide	*S. palaefolia*	53
22	(4*R**,5*R**,5a*S**,8*S**,8a*R**,8b*R**)-8-formyl-4,5,5a,6,7,8,8a,8b-octahydro-5,8b-dihydroxy-3,5a,8-trimethyl-2-oxo-2*H*-indeno[4,5-*b*]furan-4-yl acetate (= castanin A)	*S. castanea*	44	**44**	1*α*-hydroxy-2-oxoeudesman-3,7(11)-dien-8*β*,12-olide	*S. palaefolia*	53
23	(3*β*,4*α*,6*α*,8*β*,9*β*,10*α*)-8-(acetyloxy)-3,4:9,10-diepoxygermacr-7(11)-eno-12,6-lactone	*S. roborowskii*	48	**45**	1*α*,8*α*-dihydroxy-2-oxoeudesman-3,7(11)-dien-8*β*,12-olide	*S. palaefolia*	53, 54
				46	1*α*-acetoxy-8*α*-hydroxy-2-oxoeudesman-3,7(11)-dien-8,12-olide	*S. palaefolia*	54

isolated in 2003.[43] In 2005, the same compound **16** was isolated from *S. castanea* Diels f. tomentosa Stib again and given another name: castanin B (**16**).[44] Trijugins A−I (**7**−**15**) were all isolated from *S. trijuga,* and the structure of **7** was confirmed by X-ray analysis. Compound **15** exhibited moderate toxicity against HL-60, SMMC-7721, and SW480 with IC_{50} values of 17.9, 34.5, and 24.88 μM, respectively.[45] Six germacrane sesquiterpenes, castanin A (**22**),[44] castanin B (**16**),[44] and castanins C−F (**18**−**21**),[46] were isolated from *S. castanea* Diels f. tomentosa Stib. Among them, castanin A (**22**) represents a novel germacrane sesquiterpene, with a contracted ring A, derived from eudesmanolide. The structural determination of **18**−**21** was complex because they existed as two mixtures of interconvertible isomers. The computational study explained that the ratios of **18** and **19**, **20** and **21**, in the mixtures were 1:1 and 1:2, respectively. In addition, the semisynthesis of **18** and **19** was conducted by the photooxidation of **16**, the major constituent of this plant. The other two members belonging to germacrane sesquiterpenes, compounds **17**[47] and **23**,[48] were obtained from *S. palaefolia* and *S. roborowskii* Maxim, respectively.

2.1.3. Carotanes. Carotane sesquiterpenes are also called daucane sesquiterpenes. The daucane class of sesquiterpenes is a relatively small group of compounds that, for a long time, seemed to be restricted to members of the plant family Umbelliferae. In recent years, daucane derivatives have also been found in the Compositae, Rosaceae, Bryophyta, fungal, and marine sources. Only one carotane sesquiterpene, **24**, was discovered from *Salvia sclarea* (Figure 3).[49] Compounds **24** had a structural feature with a C_1-O-C_5 6-membered oxygen bridge.

2.1.4. Caryophyllanes. Caryophyllane sesquiterpenes are a group of natural bicyclic sesquiterpenes with a 4/9-ring system. Three compounds (**25**−**27**) were reported from *S. sclarea* L. Their structures were very similar, in which every molecule had a different group at C-2. Rearrangement of epoxide **25** using $MgBr_2$ in ether gave an epimeric mixture of the two aldehydes **26** and **27**.[49] Caryophyllene oxide (**28**) was obtained from *S. palaefolia* and *S. sclarea* by three research groups.[47,50,51]

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

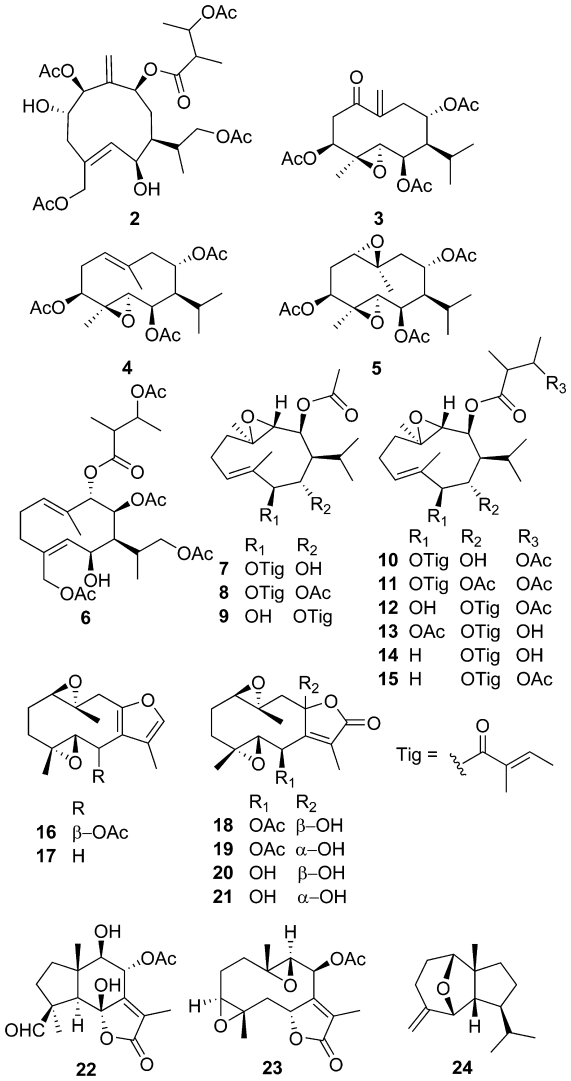


Figure 3. Germacranes and a carotane.

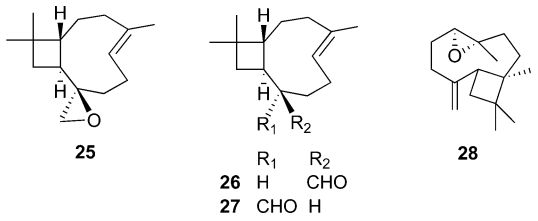


Figure 4. Caryophyllanes.

2.1.5. Guaianes. Nine guaiane sesquiterpenes (**29**–**37**) were obtained from this species. In the studies carried out by Ali et al., nubiol (**33**), nubenolide (**34**), nubenolideacetate (**35**), bisnubidiol (**36**), and bisnubenolide (**37**) were identified from *S. nubicola*.[23,52] The structures of **33** and **34** were finally confirmed via the single-crystal X-ray diffraction, which was found to be moderately active against *Pseudomonas aeruginosa*. Compounds **36** and **37** were two dimers of **33** and **34**, respectively.

2.1.6. Other Sesquiterpenoids. Compound **38** was a *β*-agarofuran sesquiterpene dibenzoate isolated from the aerial part of *S. palaefolia*.[50] Further investigation on the same species collected in Colombia was undertaken, and compounds **39**, **40**, and **43**–**46** were isolated. Among them, **43**–**46** were four

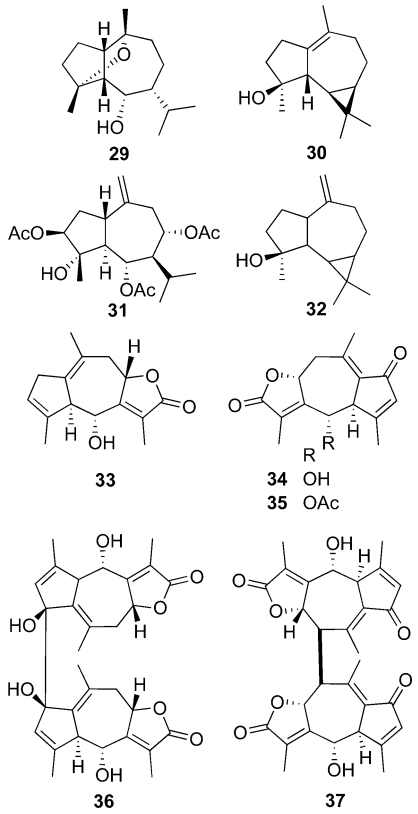


Figure 5. Guaianes.

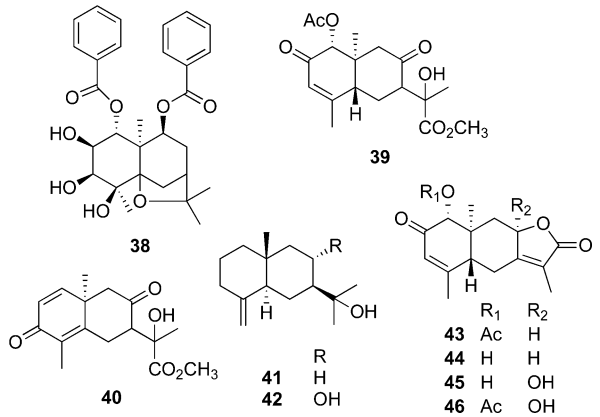


Figure 6. Other sesquiterpenoids.

eudesmanolides with a five-membered *α*,*β*-unsaturated lactone ring.[53,54] **41** and **42** were two sesquiterpenes isolated from the acetone extract of *S. microphylla*.[55]

2.2. Diterpenoids

Diterpenes are one class of natural compounds that possess a core skeleton of 20 carbons. Their formation can be rationalized by considering the different types of cyclization of geranylgeranyl diphosphate (GGPP), and they are found in many different plant families and some animals. They are biosynthesized by two different pathways, the mevalonic acid pathway (MVA) or the deoxyxylulose phosphate pathway (DOXP). Cyclization is an important and interesting process, from the perspective of the formation of a variety of diterpene carbon skeletons, and is a major branch of the biosynthesis of cyclic diterpenes. Diterpenes are of interest as many have been

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Table 2. Diterpenoids 47−591

no.	name	plant	ref
47	*O*-methylpisiferic acid methyl ester	*S. blepharochlaena*	73
48	pisiferic acid	*S. blepharochlaena*	73
49	*O*-methylpisiferic acid	*S. blepharochlaena*	73
50	ferruginol	*S. blepharochlaena*	73
		S. candidissima	82
		S. apiana	64
		S. argentea	66
		S. broussonetii	58
		S. cilicica	57
		S. miltiorrhiza	61
		S. montbretii	59
		S. przewalskii	60
		S. sclarea	51
		S. tiliaefolia	62
		S. wiedemannii	65
		S. potentillifolia	401
		S. mellifera	347
		S. syriaca	345
		S. cyanescens	154
		S. napifolia	83
		S. microstegia	76
		S. candidissima	82
		S. eriophora	3
		S. hypargeia	399
		S. bracteata	6
		S. viridis	84
		S. multicaulis	80
51	candelabrone	*S. palaestina*	140
		S. candelabrum	365
52	12-*O*-methylcandelabrone	*S. palaestina*	140
53	forskalinone	*S. forskahlei*	79
54	20-norinuroyleanol	*S. semiatrata*	74
55	1-isopropyl-4b,8,8-trimethyl-9-oxo-4b,5,6,7,8,8a,9,10-octahydrophenanthrene-2,3,10-triyl triacetate	*S. melissodora*	74
56	14-hydroxy-12-methoxy-abieta-8,11,13-trien-3-one	*S. multicaulis*	80
57	12-peroxyabieta-8,11,13-trien-6-one	*S. multicaulis*	80
58	1-oxoferruginol	*S. napifolia*	83
59	6-oxoferruginol	*S. napifolia*	83
60	1-oxo-5-hydroxyabieta-8,11,13-trien-18-oic acid	*S. candidissima*	81
61	abieta-9,12,14-trien-7-one	*S. amplexicaulis*	263
62	salviviridinol	*S. viridis*	84
63	iguestol	*S. broussonetii.*	58
64	sugiol	*S. miltiorrhiza*	13, 61
		S. tomentosa	67
		S. broussonetii	58
		S. canariensis	69
		S. pachystachys	68
		S. przewalskii	60
65	hypargenin A (= 6*β*,12-dihydroxyabieta-8,11,13-triene-1,7-dione)	*S. hypargeia*	72
66	hypargenin B (= 12,15-dihydroxyabieta-8,11,13-trien-7-one)	*S. hypargeia*	72
67	hypargenin C (= 12-hydroxyabieta-8,11,13-triene-6,7-dione)	*S. hypargeia*	72
68	hypargenin E (= 6*β*,14-dihydroxyabieta-8,11,13-trien-1-one)	*S. hypargeia*	72
69	euphraticol	*S. euphratica*	85
70	euphracal	*S. euphratica*	85
71	2*α*-hydroxyferruginyl-2,12-dimethyl ether	*S. pachystachys*	68
72	14-hydroxyferruginol	*S. montbretii*	59
73	(3*S*,4a*S*,10a*S*)-1,2,3,4,4a,9,10,10aoctahydro-6-hydroxy-7-isopropyl-1,1,4a-trimethyl-9-oxophenanthren-3-yl acetate (= 2*α*-acetoxysugiol)	*S. miltiorrhiza*	61
74	16-hydroxycarnosic acid	*S. mellifera*	75

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Table 2. continued

no.	name	plant	ref
		S. apiana	362
		S. chinopeplica	26
75	16-acetoxycarnosic acid	*S. mellifera*	75
76	abieta-8,11,13-triene-11,12,16,20-tetraol	*S. mellifera*	75
77	12-methoxyabieta-8,11,13-trien-11-ol	*S. candidissima*	82
78	pomiferin A	*S. pomifera*	71
79	pomiferin B	*S. pomifera*	71
80	pomiferin C	*S. pomifera*	71
81	pomiferin D	*S. pomifera*	71
82	pomiferin E	*S. pomifera*	71
83	10-acetylferruginol	*S. microstegia*	76
84	abieta-8,11,13-triene-5,11,12-triol	*S. microstegia*	76
85	abieta-8,11,13-trien-3-one	*S. wiedemannii*	65
86	2α-hydroxysugiol diacetate	*S. cardiophylla*	86
87	2α-hydroxysugiol	*S. cardiophylla*	86
88	salviol	*S. cardiophylla*	86
		S. tomentosa	67
89	7-oxocarnosic acid diacetate	*S. canariensis*	87
90	6-oxo-7β-hydroxycarnosic acid diacetate	*S. canariensis*	87
91	6-oxo-7α-hydroxycarnosic acid diacetate	*S. canariensis*	87
92	12-methoxycarnosic acid	*S. lanigera*	77
		S. tomentosa	67
		S. officinalis	104
93	abietatriene-7β,15-diol	*S. sapinae*	367
94	methyl carnosoate	*S. lanigera*	78
		S. officinalis	104
95	12-methoxy-11,7-dihydroxy-dehydroabietane	*S. bicolor*	369
96	20-oxoinuroyleanol	*S. coulteri*	372
97	3β-hydroxydehydroabietic acid	*S. oxyodon*	129
98	pomiferin F	*S. pomifera*	70
99	pomiferin G	*S. pomifera*	70
100	7-oxoferruginol-18-al	*S. sclarea*	51
101	methyl 12-*O*-methylcarnosoate	*S. africana-lutea*	286
102	cryptojaponol	*S. barrelieri*	111
103	inuroyleanol	*S. barrelieri*	111
104	carnosic acid	*S. mellifera*	75
105	demethylcryptojaponol	*S. phlomoides*	94
106	nemorosin	*S. nemorosa*	402
107	abieta-8,11,13-triene-11,12,20-triol	*S. mellifera*	403
108	11,12,16-trihydroxyabieta-8,11,13-trien-20-al	*S. mellifera*	403
109	3β-hydroxydemethylcryptojaponol	*S. pubescens*	404
110	15-hydroxyabieta-8,11,13-trien-7-one	*S. albocaerulea*	405
111	trilobinone	*S. triloba*	406
112	safficinolide	*S. officinalis*	63
113	salvidorol	*S. dorrii*	88
114	salvirecognone	*S. recognita*	89
115	salvirecognine	*S. recognita*	89
116	16-hydroxy-6,7-didehydroferruginol	*S. apiana*	64
117	6,7-dehydrosempervirol	*S. apiana*	64
118	abieta-6,8,11,13-tetraene-6,12,14-triol	*S. napifolia*	83
119	hypargenin D (= 12-hydroxyabieta-6,8,11,13-tetraen-3-one)	*S. hypargeia*	72
120	6,7-didehydroferruginol	*S. apiana*	64
121	11,12-dimethoxyabieta-6,8,11,13-tetraen-20-oic acid methyl ester	*S. canariensis*	87
122	cryptanol	*S. cryptantha*	90
		S. cilicica	57
		S. euphratica	85
		S. pachystachys	68
		S. wiedemannii	65
123	trilobinol	*S. triloba*	406
124	20(10→5)abeoabieta-1(10),6,8,11,13-pentaene-11,12,16-triol	*S. apiana*	64
125	19(4→3)abeo-*O*-demethylcryptojaponol	*S. pubescens*	404

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Table 2. continued

no.	name	plant	ref
126	2-oxocandesalvone A	*S. palaestina*	140
127	12-*O*-methyl-2-oxocandesalvone A	*S. palaestina*	140
128	12-*O*-*m*ethylcandesalvone A	*S. palaestina*	140
129	candesalvone A	*S. candelabrum*	407
130	blephaein	*S. blepharochlaena*	73
131	6,12-dihydroxyabieta-5,8,11,13-tetraen-7-one (= montbretol)	*S. miltiorrhiza*	91
		S. montbretii	59
132	salvitchihatine	*S. tchihatcheffii*	92
133	7-oxo-11,12,14-trihydroxy-20-methoxyabieta-5,8,11,13-tetraene	*S. candidissima*	81
134	salvinolone	*S. prionitis*	408
135	montbretyl 12-methyl ether (= 6-hydroxy-12-methoxyabieta-5,8,11,13-tetraen-7-one)	*S. montbretii*	59
136	6-hydroxysalvinolone	*S. montbretii*	93
	14-deoxycoleon U	*S. phlomoides*	94
137	6,11-dihydroxy-12-methoxyabieta-5,8,11,13-tetraen-7-one	*S. phlomoides*	409
138	multicaulin	*S. blepharochlaena*	73
		S. multicaulis	95
139	7,8-dimethyl-2-(1-methylethy)phenanthren-3-ol	*S. hydrangea*	96
		S. multicaulis	95
140	11,12-dihydroxy-20-nor-5(10),6,8,11,13-abietapentaen-1-one (= arucadiol)	*S. anastomosans*	74
		S. prionitis	410
		S. argentea	66
141	1,2,3,4-tetrahydro-5-hydroxy-7-isopropyl-1,1-dimethyl-4-oxophenanthren-6-yl palmitate	*S. miltiorrhiza*	61
142	3β-hydroxy-8,11,13(14),15-abietatetraen-18-oic acid	*S.tomentosa*	56
143	sageone	*S. officinalis*	63, 104
		S. mellifera	357
144	11,12,16-trihydroxy-20-norabieta-5(10),8,11,13-tetraen-1-one	*S. mellifera*	97
145	9,10-dihydro-7,8-dimethyl-2-(1-methylethyl)phenanthren-3-ol	*S. hydrangea*	96
146	maytenoquinone	*S. melissodora*	74
147	viridinol	*S. viridis*	84
148	2α,7,11-trihydroxy-7,9(11),13-abietatrien-12-one	*S. texana*	99
149	2-oxotaxodione	*S. texana*	99
150	7-hydroxytaxodione	*S. montbretii*	93
151	2α-hydroxytaxodione	*S. texana*	98
152	2α-hydroxytaxodone	*S. texana*	98
153	2α,7-dihydroxytaxodone	*S. texana*	98
154	fruticulin B	*S. fruticulosa*	110, 411
155	2α,10β-dihydroxy-12-oxo-norabieta-9(11),13-dien (= salvipiliferol)	*S. pilifera*	128
156	viridone	*S. viridis*	84
157	2α,11-dihydroxy-5,7,9(11),13-abietatetraen-12-one	*S. texana*	99
158	5,6-dehydro-2α,7-dihydroxytaxodone	*S. texana*	101
159	5,6-didehydro-7-hydroxytaxodone	*S. munzii.*	166
160	15-deoxyfuerstione (= 11-hydroxy-5,7,9(11),13-abietatetraen-12-one)	*S. moorcraftiana*	100
161	7-hydroxy-12-methoxy-20-norabieta-1,5(10),7,9,12-pentaene-6,14-dione	*S. cilicica*	57
162	horminone	*S. blepharochlaena*	73
		S. anastomosans	74
		S. barrelieri	111
		S. tomentosa	67
		S. candidissima	82
		S. cryptantha.	90
		S. pachystachys	68
		S. sahendica	106
		S. wiedemannii	65
		S. lanata	391
		S. verbenaca	412
163	7-acetylhorminone	*S. blepharochlaena*	73
		S. candidissima	82
		S. cryptantha	90
		S. wiedemannii	65

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Table 2. continued

no.	name	plant	ref
164	19-hydroxyroyleanone	*S. chinopeplica*	26
165	abieta-8,12-diene-11,14-dione	*S. cilicica*	57
166	royleanone	*S. anastomosans*	74
		S. fruticulosa	110
		S. nutans	108
		S. pachystachys	68
		S. tomentosa	105
		S. pratensis	413
		S. ringens	414
167	deacetylnemorone	*S. anastomosans*	74
168	deacetoxynemorone	*S. anastomosans*	74
169	royleanonic acid	*S. plebeia*	337
170	trilobic acid	*S. triloba*	339
171	candelabroquinone	*S. candelabrum*	145
172	6-oxoroyleanone-18-oic acid	*S. divaricata*	41
173	6-oxo-12-methylroyleanone-18-oic acid	*S. divaricata*	41
174	horminone-18-oic acid	*S. divaricata*	41
175	12-deoxy-7,7-dimethoxy-6-oxoroyleanone	*S. nutans*	108
176	16-hydroxyroyleanone	*S. apiana*	64
177	2β-hydroxyroyleanone	*S. cryptantha*	90
178	19-hydroxy-7α-acetoxyroyleanone	*S. regla*	366
179	7α-ethoxyroyleanone	*S. lavandulaefolia*	368
180	7α-ethoxy-12-*O*-methyl-royleanone	*S. lavandulaefolia*	368
181	7,12-diacetylhorminon-18-al	*S. candicans*	122
182	20-hydroxy-7α-acetoxyroyleanone	*S. lanata*	374
183	7-oxoroyleanone-12-methyl ether	*S. barrelieri*	111
184	virgatol (= 12,16,17-trihydroxy-8,12-abietadiene-11,14-dione)	*S. virgata*	415
185	bractealine	*S. bracteata*	6
186	12-methyl-5-dehydrohorminone	*S. multicaulis*	95
187	12-methyl-5-dehydroacetylhorminone	*S. multicaulis*	95
188	neocryptotanshinone II	*S. miltiorrhiza*	91
189	kronenquinone	*S. kronenburgii*	247
190	12-deoxydanshenxinkun B	*S. glutinosa*	105
191	danshenxinkun B	*S. glutinosa*	105
		S. miltiorrhiza	61
192	(−)-danshexinkun A	*S. miltiorrhiza*	360
		S. trijuga	45
193	trilobiol	*S. triloba*	339
194	oleoyl neocryptotanshinone	*S. miltiorrhiza*	350
195	miltionone I	*S. miltiorrhiza*	416
196	oleoyl danshenxinkun A	*S. miltiorrhiza*	350
197	hypargenin F (= 5,12-dihydroxyabieta-6,8,12-triene-11,14-dione)	*S. hypargeia*	72
		S. montbretii	59
198	12-deoxy-6,7-dehydroroyleanone	*S. nutans*	108
199	12-deoxy-6-hydroxy-6,7-dehydroroyleanone	*S. nutans*	108
200	6,7-dehydroroyleanone	*S. aegyptiaca*	112
		S. moorcraftiana	417
201	6α-hydroxy-11,12-dioxo-8,13-abieta-diene	*S. recognita*	89
202	11,12,-dioxoabieta-8,13-dien (= miltirone)	*S. napifolia*	83
		S. miltiorrhiza	418
203	7β-hydroxy-8,13-abietadiene-11,12-dione	*S. miltiorrhiza*	13
204	salviphlomone	*S. phlomoides*	94
205	1*R*-hydroxy-20-nor-5(10),6,8,13-abietatetraene-11,12-dione (= 1*R*-hydroxymiltirone)	*S. argentea*	66
206	4-methylenemiltirone	*S. miltiorrhiza*	13
207	multiorthoquinone	*S. blepharochlaena*	73
		S. multicaulis	95
208	demethylmultiorthoquinone	*S. blepharochlaena*	73
		S. multicaulis	95
209	18,20-dinor-1,3,5(10),6,8,13-abietahexaene-11,12-dione	*S. glutinosa*	105

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Table 2. continued

no.	name	plant	ref
210	carnosol	*S. rubescens*	116
		S. canariensis	87
		S. chinopeplica	26
		S. officinalis	104
211	11,12-di-*O*-methylcarnosol	*S. rubescens*	116
212	16-hydroxicarnosol	*S. rubescens*	116
		S. chinopeplica	26
		S. mellifera	97
213	6-*epi*-demethylesquirolin D	*S. anastomosans*	74
		S. aspera	162
214	salvibracteone	*S. bracteata*	6
215	12-*O*-methylcarnosol	*S. officinalis*	107
216	16-hydroxyisorosmanol	*S. mellifera*	75
217	16-hydroxy-20-deoxocarnosol	*S. mellifera*	75
218	16-acetoxycarnosol	*S. canariensis*	356
219	isogaldosol	*S. mellifera*	357
220	przewalskin	*S. przewalskii*	60, 359
221	deoxocarnosol 12-methyl ether	*S. canariensis*	69
222	isocarnosol	*S. lanigera*	113
223	przewalskin F	*S. przewalskii*	381
224	6α,12,19-trihydroxy-11,14-dioxo-8,12-abietadien-20,7β-olide	*S. gilliessi*	124
225	przewalskin G	*S. przewalskii*	381
226	yunnannin A	*S. yunnanensis*	132
227	7,20-epoxyroyleanone	*S. napifolia*	83
228	12-hydroxyabieta-11,14-quinone-(20→7)-lactone	*S. columbariae*	115
229	rosmanol	*S. rubescens*	116
		S. tomentosa	67
		S. canariensis	87, 118
		S. officinalis	104, 107
		S. pachyphylla	117
230	16-hydroxy-7-methoxyrosmanol	*S. rubescens*	116
		S. munzii	119
231	6,7-dimethoxy-7-*epi*-rosmanol	*S. officinalis*	120
232	16-hydroxyrosmanol	*S. mellifera*	75
233	16-hydroxy-*epi*-rosmanol	*S. mellifera*	75
234	7α,11,12-trihydroxyabieta-8,11,13-trien-20-oic acid-20,6-lactone	*S. canariensis*	118
235	7α-methoxyrosmanol	*S. dorrii*	88
		S. chinopeplica	26
236	7β-methoxyrosmanol	*S. dorrii*	88
237	galdosol	*S. mellifera*	357
238	sagequinone methide A	*S. officinalis*	120
239	12-hydroxy-11,14-dioxo-6,8,12-abietatrien-19,20-olide	*S. gilliessi*	124
240	12-acetoxy-11,14-dioxo-6,8,12-abietatrien-19,20-olide	*S. gilliessi*	124
241	sessein	*S. regla*	125
		S. sessei	126
242	deacetylsessein	*S. regla*	125, 366
243	7α-hydroxy-12,19-dihydroxyabieta-8,12-diene-11,14-dione-19,20-δ-lactone	*S. candicans*	122
244	7α-hydroxy-12-dihydroxy-19-methylabieta-8,12-diene-11,14-dione-19,20-δ-lactone	*S. candicans*	122
245	conacytone	*S. ballotaeflora*	121
		S. candicans	122
246	8-hydroxy-12-oxoabieta-9(11),13-dien-20-oic acid 8,20-lactone	*S. wiedemannii*	127
247	2α,8-dihydroxy-12-oxoabieta-9(11),13-dien-20-oic acid-8,20-lactone (= piliferalactone)	*S. pilifera*	128
248	2α,20-dihydroxy-12-oxoabieta-9(11),13-dien-8,20-ether (= piliferol)	*S. pilifera*	128
249	pachyphyllone	*S. pachyphylla*	117
250	3β-acetoxyabiet-8(14)-en-18-oic acid 9α,13α-endoperoxide	*S. oxyodon*	129
251	3β-hydroxyabiet-8(14)-en-18-oic acid 9α,13α-endoperoxide	*S. oxyodon*	129
252	methylenedihydrotanshinquinone	*S. miltiorrhiza*	13
		S. trijuga	45
253	1,2,5,6-tetrahydrotanshinone I	*S. miltiorrhiza*	13
	trijuganone B	*S. trijuga*	419
254	methylenetanshiquinone	*S. miltiorrhiza*	61, 338

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Table 2. continued

no.	name	plant	ref
		S. trijuga	45
255	tanshinone IIA	*S. glutinosa*	105
		S. miltiorrhiza	61
		S. przewalskii	60, 359
256	3α,17-dihydroxytanshinone II	*S. hians*	352
257	tanshindiol A	*S. miltiorrhiza*	130
258	tanshindiol B	*S. miltiorrhiza*	130
259	tanshindiol C	*S. miltiorrhiza*	130
260	3⟨-hydroxytanshinone IIA	*S. miltiorrhiza*	130
261	tanshinone IIB	*S. miltiorrhiza*	383
262	nortanshinone	*S. miltiorrhiza*	130
263	15,16-dihydrotanshinone I	*S. glutinosa*	105
		S. miltiorrhiza	61
		S. trijuga	45
		S. nipponica	420
264	tanshinone I	*S. glutinosa*	105
		S. miltiorrhiza	61
		S. przewalskii	60, 359
		S. trijuga	45
265	formyltanshinone	*S. miltiorrhiza*	13
266	cryptotanshinone	*S. ballotaeflora*	131
		S. apiana	64
		S. glutinosa	105
		S. mellifera	97
		S. miltiorrhiza	61
		S. munzii	119
		S. przewalskii	60
		S. trijuga	45
267	6-methylcryptotanshinone	*S. aegyptiaca*	168
268	17-hydroxycryptotanshinone	*S. munzii*	166
269	6-deoxo-5,6-didehydrolanugon Q	*S. apiana*	64
270	miltionone II	*S. miltiorrhiza*	416
271	danshenol A	*S. glutinosa*	105, 335
272	15-*epi*-danshenol A	*S. glutinosa*	335
		S. glutinosa	105
273	danshenol C	*S. yunnanensis*	132
		S. trijuga	45
274	neotanshinlactone	*S. miltiorrhiza*	133
275	dihydroisotanshinone I	*S. glutinosa*	105
		S. miltiorrhiza	61
276	trijuganone A	*S. trijuga*	419
277	isotanshinone I	*S. glutinosa*	105
278	isotanshinone II	*S. glutinosa*	105
279	dihydroisotanshinone II	*S. glutinosa*	105
280	derivative of tanshinone IIA	*S. miltiorrhiza*	13
281	derivative of tanshinone IIA	*S. miltiorrhiza*	13
282	derivative of tanshinone IIA	*S. miltiorrhiza*	13
283	salviamine E	*S. yunnanensis*	137
284	salviamine F	*S. yunnanensis*	137
285	salviamine B	*S. yunnanensis*	137
286	salviamine C	*S. yunnanensis*	137
287	salviamine D	*S. yunnanensis*	137
288	isosalviamine E	*S. yunnanensis*	137
289	salvianan	*S. miltiorrhiza*	136
290	neosalvianen	*S. miltiorrhiza*	136
291	salvianen	*S. miltiorrhiza*	136
292	salviamine A	*S. yunnanensis*	137
293	isosalviamine C	*S. yunnanensis*	137
294	isosalviamine D	*S. yunnanensis*	137
295	isosalviamine A	*S. trijuga*	138
296	isosalviamine B	*S. trijuga*	138

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Table 2. continued

no.	name	plant	ref
297	salviadione	*S. miltiorrhiza*	136
298	prioline	*S. prionitis*	147
299	salvigerone	*S. lanigera*	139
300	salvipalestinoic acid	*S. palaestina*	140
301	methyl 12-*O*-methylsalvipalestinoate	*S. palaestina*	140
302	candesalvolactone	*S. candelabrum*	141
303	3,4-secoisopimara-4(18),7,15-triene-3-oic acid	*S. cinnabarina*	142−144
304	candesalvoquinone	*S. candelabrum*	145
305	12-*O*-methylcandesalvone B	*S. candelabrum*	145
306	candesalvones B	*S. candelabrum*	407
307	candesalvone B methyl ester	*S. candelabrum*	145
308	limbinol	*S. limbata*	152
309	acetyllimbinol	*S. limbata*	149
310	salvilimbinol	*S. limbata*	152
311	4-dehydrosalvilimbinol	*S. limbata*	152
312	sclareapinone	*S. sclarea*	148
		S. prionitis	146
313	4,14-dihydroxysaprorthoquinone	*S. eriophora*	3
314	salvisyrianone	*S. syriaca*	345
315	prionoid D	*S. prionitis*	150
316	4-hydroxysaprorthoquinone	*S. prionitis*	146
317	prionoid E	*S. prionitis*	150
318	2-hydroxysaprorthoquinone	*S. limbata*	152
319	saprorthoquinone	*S. prionitis*	157
320	4.5-seoo-5,10-*friedo*-abieta-4(18),5(10),6,8,13-pentaene-1,11,12-trione (= 1-oxoaethiopinone)	*S. argentea*	66
321	4,5-seco-5,10-*friedo*-abieta-4(18),5,6,8,13-pentaene-11,12-dione	*S. aethiopis*	151
322	prionoid F	*S. prionitis*	150
323	3-oxosapriparaquinone	*S. prionitis*	421
324	12-hydroxy-sapriparaquinone	*S. limbata*	152
		S. prionitis	382
325	sahandinone	*S. sahendica*	106
326	limbinal	*S. limbata*	149
327	3,12-dihydroxysapriparaquinon-1-ene	*S. limbata*	152
328	prineoparaquinone	*S. prionitis*	147
329	2,3-dehydrosalvipisone	*S. sclarea*	51
330	acetylsalvipisone	*S. sclarea*	148
331	12-isopentenyl-3-oxosalvipisone	*S. cyanescens*	154
332	1,4-dihydro-6-methyl-2-(1-methylethyl)-5-(4-methylpent-4-enyl)naphthalene-1,4-dione	*S. sahendica*	106
333	1-oxosalvipisone	*S. candidissima*	82
334	12-hydroxy-4,5-seco-5,10-*friedo*-4(18),5(10),6,8,12-abietapentaene-11,14-dione	*S. aethiopis*	153
335	saprionide	*S. prionitis*	146
336	saprirearine	*S. prionitis*	146
337	prionoid A	*S. prionitis*	150
338	salvonitin	*S. prionitis*	364
339	sapriolactone	*S. prionitis*	422
340	de-*O*-ethylsalvonitin	*S. prionitis*	342
341	prionoid B	*S. prionitis*	150
342	salvibretol	*S. montbretii*	93
343	microstegiol	*S. microstegia*	156
		S. prionitis	147
344	1-oxosalvibretol	*S. montbretii*	93
345	candidissiol	*S. condidissima*	155
		S. sclarea	51
346	sahandone	*S. sahendica*	106
347	prionoid C	*S. prionitis*	150
348	cariocal	*S. anastomosans*	74
349	16-hydroxyrosmadial	*S. mellifera*	75
350	7,8-seco-*para*-ferruginone	*S. prionitis*	146
351	rosmanoyl carnosate	*S. canariensis*	87
352	7,7′-bistaxodione	*S. montbretii*	93
353	11,11′-didehydroxy-7,7′-dihydroxytaxodione	*S. montbretii*	93

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Table 2. continued

no.	name	plant	ref
354	hongencaotone	*S. prionitis*	158
355	bisprioterone B	*S. prionitis*	159
356	bisprioterone A	*S. prionitis*	159
357	bisprioterone C	*S. prionitis*	159
358	salvicanol	*S. apiana*	64
		S. canariensis	69
		S. przewalskii	60
359	10,11,14-trihydroxy-12-methoxy-9(10→20)abeoabieta-8,11,13-trien-7-one	*S. coulteri*	372
360	demethylsalvicanol	*S. broussonetii*	58
361	przewalskin C	*S. przewalskii*	60
362	przewalskin D	*S. przewalskii*	60
363	fruticulin A	*S. fruticulosa*	110
364	1(10)-seco-2(10)-cycloicetexane (= salvimultine)	*S. multicaulis*	354
365	19-deoxyicetexone	*S. ballotaeflora*	131
366	5-*epi*-icetexone	*S. gilliessi*	161
367	icetexone	*S. gilliessi*	124
		S. ballotaeflora	121, 123, 160
		S. candicans	122
368	19-deoxyisoicetexone	*S. ballotaeflora*	131
369	5,6-dihydro-6α-hydroxysalviasperanol	*S. aspera*	162
370	brussonol	*S. broussonetii*	58
371	salviasperanol	*S. aspera*	162
372	3,11,11a,11b-tetrahydro-8,11-dihydroxy-2a-methyl-9-(1-methylethyl)benzo[5,6]cyclohept[1,2,3-cd]isobenzofuran-2,7,10(2aH)-trione	*S. candicans*	122
373	7,20-dihydroanastomosine	*S. ballotaeflora*	131
374	anastomosine	*S. anastomosans*	423
375	przewalskin E	*S. przewalskii*	381
376	tilifolidione	*S. semiatrata*	74
		S. tiliaefolia	62
		S. thymoides	424
377	3-oxo-tilifolidione	*S. thymoides*	424
378	3-hydroxytilifolidione	*S. thymoides*	424
379	aegyptinone B	*S. aegyptiaca*	112
380	5-nor-3-oxo-tilifolidione	*S. thymoides*	424
381	aegyptinone A	*S. aegyptiaca*	112
382	dichroanal B	*S. dichroantha*	67
383	dichroanal A	*S. dichroantha*	67
384	derivatives of **353**	*S. dichroantha*	67
385	derivatives of **353**	*S. dichroantha*	67
386	dichroanone	*S. dichroantha*	67
387	2α-hydroxysalvicanaric acid	*S. texana*	101
388	salvicanaraldehyde	*S. munzii*	166
389	salvicanaric acid	*S. canariensis*	165
		S. munzii	166
390	paramiltioic acid	*S. paramiltiorrhiza*	169
391	*epi*-cryptoacetalide	*S. miltiorrhiza*	171
392	6-methyl-*epi*-cryptoacetalide	*S. aegyptiaca*	168
393	cryptoacetalide	*S. miltiorrhiza*	171
394	6-methylcryptoacetalide	*S. aegyptiaca*	168
395	*epi*-danshenspiroketallactone	*S. glutinosa*	105
		S. przewalskii	60
396	danshenspiroketallactone	*S. glutinosa*	105
		S. miltiorrhiza	61, 167, 170
		S. przewalskii	60
397	4,8-dimethyl-8,9-dihydro-10,12-dioxa-benzo[*a*]anthracene-7,11-dione (= salviamone)	*S. miltiorrhiza*	61
398	salprionin	*S. prionitis*	342
399	przewalskin B	*S. przewalskii*	17
400	12-methoxy-8,11,13-abietatrien-20,11-olide	*S. officinalis*	172
401	9-isopropyl-2,2,5-trimethyl-8*H*-phenaleno[1,9*bc*]furan-8-one (= salvilenone)	*S. miltiorrhiza*	370
402	3-hydroxysalvilenone	*S. prionitis*	421

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Table 2. continued

no.	name	plant	ref
403	prionitin	*S. sahendica*	106
404	pachystazone (abiet-5-en-7-one)	*S. pachystachys*	68
		S. condidissima	155
405	wiedemannic acid	*S. wiedemannii*	65
406	heldrichinic acid	*S. heldrichiana*	341
407	lanigerone	*S. lanigera*	139
408	salvinolactone	*S. prionitis*	408
409	miltipolone	*S. castanea*	164
410	castanolide	*S. castanea*	164
411	*epi*-castanolide	*S. castanea*	164
412	salvigreside A	*S. greggii*	174
413	salvigreside B	*S. greggii*	174
414	salvigreside C	*S. greggii*	174
415	19-*O*-acetoxy-15,16-epoxy-*ent*-cleroda-3,13(16),14-triene-6,18-diol	*S. fulgens*	22
416	19-acetoxy-15,16-epoxy-6-hydroxy-*ent*-cleroda-3,13(16),14trien-18-al	*S. fulgens*	22
417	hardwickiic acid	*S. regla*	125
418	divinatorin A	*S. divinorum*	175
419	divinatorin B	*S. divinorum*	175
420	divinatorin C	*S. divinorum*	175
421	divinorin F	*S. divinorum*	20
422	divinatorin D	*S. divinorum*	176
423	divinatorin E	*S. divinorum*	176
424	kerlinic acid	*S. keerlii*	102
425	thymonin	*S. thymoides*	177
426	derivative of **392**	*S. thymoides*	177
427	derivative of **392**	*S. thymoides*	177
428	7β-hydroxythymonin	*S. thymoides*	177
429	derivative of **395**	*S. thymoides*	177
430	derivative of **395**	*S. thymoides*	177
431	clerodermic acids	*S. regla*	125
432	7β-18,19-trihydroxy-*ent*-cleroda-3,13-dien-16,15-olide	*S. melissodora*	178
433	lasianthin	*S. lasiantha*	179
434	salvidivin D	*S. divinorum*	20
435	salvigreside D	*S. greggii*	174
436	salvidivin C	*S. divinorum*	20
437	brevifloralactone	*S. melissodora*	182
		S. breviflora	180
438	brevifloralactone acetate	*S. breviflora*	180
439	salvimadrensinone	*S. madrensis*	181
440	salvimadrensinol	*S. madrensis*	181
441	salvimadrensin	*S. madrensis*	181
442	portulide C	*S. melissodora*	182
443	7α-hydroxyneoclerodane-3,13-diene-18,19:15,16-diolide	*S. microphylla*	183
		S. melissodora	182
		S. thymoides	177
444	semiatrin	*S. semiatratha*	184
445	7-acetoxy-12(*R*)-hydroxyneocleroda-3,13-diene-18,19:15,16-diolide (= kerlinolide)	*S. keerlii*	185
446	7α-oxo-neocleroda-3,13-diene-18,19:15,16 diolide	*S. thymoides*	177
447	salvigresin	*S. greggii*	186
448	1(10)-dehydrosalviarin	*S. sousae*	187
449	15,16-epoxy-2β-*O*-β-D-glucopyranosylneocleroda-3,13(16),14-trien-18,19-olide	*S. amarissima*	188
450	15,16-epoxy-2β-*O*-tetraacetyl-β-D-glucopyranosylneocleroda-3,13(16),14-trien-18,19-olide	*S. amarissima*	188
451	neocleroda-3,13(16),14-trien-15,16-epoxy-18,19-olide	*S. amarissima*	188
452	salvisplendin C	*S. splendens*	189
453	(5*R*,9*R*,10*S*)-7*S*-acetoxy-15,16-epoxy-1*S*,2*S*,12-trihydroxy-*ent*-cleroda-3,13(16),14-trien-18,19-olide	*S. haenkei*	190
454	7α-acetoxy-2β-hydroxy-*ent*-cleroda-3,13-diene-l8,19:16,15-diolide	*S. melissodora*	178
455	7β-hydroxy-*ent*-cleroda-3,13-diene-18,19:16,15-diolide	*S. melissodora*	178
456	7α-acetoxy-*ent*-cleroda-3,13-diene-18,19:16,15-diolide	*S. melissodora*	178
457	2β,7α-dihydroxy-*ent*-cleroda-3,13-diene-18,19:16,15-diolide	*S. melissodora*	178
458	2β-acetoxy-7α-hydroxy-*ent*-cleroda-3,13-diene-18,19:16,15-diolide	*S. melissodora*	178
459	7-oxo-*ent*-cleroda-3,13-dien-18,19:16,15-diolide	*S. melissodora*	178

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Table 2. continued

no.	name	plant	ref
460	2β-hydroxy-*ent*-cleroda-3,13-diene-18,19:16,15-diolide	*S. melissodora*	178
461	2β-hydroxy-7-oxo-*ent*-cleroda-3,13-diene-18,19:16,15-diolide	*S. melissodora*	178
462	7α-hydroxy-*ent*-cleroda-3,13-diene-18,19:16,15-diolide	*S. melissodora*	182
463	salvinicin A	*S. divinorum*	195
464	salvinicin B	*S. divinorum*	195
465	salvinorin A	*S. divinorum*	19, 20, 176, 194
466	divinorin B	*S. divinorum*	191
467	salvinorin C	*S. divinorum*	20, 175, 176, 193
468	salvinorin D	*S. divinorum*	20, 175, 176, 192
469	salvinorin E	*S. divinorum*	20, 175, 176, 192
470	salvinorin F	*S. divinorum*	20, 175, 176, 192
471	salvinorin G	*S. divinorum*	176
472	salvinorin H	*S. divinorum*	20
473	1-deacetoxy-8-*epi*-salvinorin G	*S. divinorum*	196
474	salvidivin A	*S. divinorum*	20
475	salvidivin B	*S. divinorum*	20
476	salvinorin I	*S. divinorum*	20
477	17β-salvinorin J	*S. divinorum*	197
478	17α-salvinorin J	*S. divinorum*	197
479	linearolactone (= linearifoline)	*S. polystachya*	201
		S. lineata	204
480	(5*R*,9*R*)-l5,16-epoxy-10*S*-hydroxy-*ent*-cleroda-3,13(16),14-triene-17,12*S*:18,19-diolide	*S. haenkei*	190
481	(5*R*,9*R*)-15,16-epoxy-*ent*-cleroda-3,7,13(16),14-tetraene-17,12*S*:18,19-diolide	*S. wagneriana*	220
482	(5*R*,9*R*)-15,16-epoxy-10*S*-hydroxy-*ent*-cleroda-3,7,13(16),14-tetraene-17,12*S*:18,19-diolide	*S. haenkei*	190
483	15,16-epoxy-4β, 8α,10β-trihydroxyneocleroda-1,13(16),14-triene-17,12*R*:18,19-diolide	*S. infuscata*	348
484	splendidin	*S. splendens*	19, 198
485	salviarin	*S. greggii*	186
		S. splendens	19, 425
		S. rhyacophila	199
486	splenolide B	*S. splendens*	19
487	splenolide A	*S. splendens*	200
488	1-*O*-acetylspenolide A	*S. splendens*	398
489	salvisplendin A	*S. splendens*	189
490	15,16-epoxy-8α-hydroxyneocleroda-2,13(16),14-triene-17,12*R*:18,19-diolide	*S. reflexa*	216
491	6β-hydroxy salviarin	*S. rhyacophila*	199
492	6β-acetoxy salviarin	*S. rhyacophila*	199
493	10β-acetoxy salviarin	*S. rhyacophila*	199
494	7,8β-dihydrosalviacoccin	*S. greggii*	226
495	salvisplendin B	*S. splendens*	189
496	salviacoccin	*S. coccinea*	375
497	splenolide C	*S. splendens*	200
498	(4*S*,5*R*,9*S*,10*R*)-15,16-epoxy-*ent*-cleroda-1,13 (16),14-triene-17,12*S*:18,19-diolide	*S. haenkei*	190
499	polystachyne D	*S. polystachya*	201
500	polystachyne E	*S. polystachya*	201
501	1α,2α-epoxy-3,4α-dihydrolinearolactone	*S. reptans*	202
502	1α,10α-epoxysalviarin	*S. lineata*	204
503	2β,3β:15,16-diepoxy-10β-hydroxyneocleroda-7,13(16),14-triene-17,12*R*:18,l9-diolide (= epoxysalviacoccin)	*S. plebeia*	205
504	1,2-dihydro-6α,7α-epoxylinearifoline	*S. sousae*	203
505	8,12(*R*)-epoxyneocleroda-3,13(14)-diene-18,19:15,16-diolide (= kerlin)	*S. keerlii*	185
506	dehydrokerlin	*S. polystachya*	201
		S. rhyacophila	199
507	salvisplendin D	*S. splendens*	189
508	salvifolin	*S. tiliaefolia*	349
		S. dugesii	208
509	polystachyne A	*S. polystachya*	201
510	polystachyne B	*S. polystachya*	201
511	polystachyne C	*S. polystachya*	201
512	salvifarin	*S. farinacea*	19, 206, 207

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Table 2. continued

no.	name	plant	ref
513	salvifaricin	*S. farinacea*	19, 207, 426
		S. dugesii	208
		S. leucantha	209
514	*trans*-1,2-dihydrosalvifaricin	*S. fulgens*	22
515	salvixalapoxide	*S. xalapensis*	213
516	2α-hydroxy-7-*epi*-8β,17-dihydrolanguiduline	*S. tonalensis*	212
		S. miltiorrhiza	13
		S. sousae	203
517	tonalenin	*S. tonalensis*	212
518	isosalvisousolide	*S. sousae*	187
519	7-*epi*-languiduline	*S. tonalensis*	212
520	salvilanguiduline A	*S. languidula*	214
521	salvilanguiduline B	*S. languidula*	214
522	salvilanguiduline C	*S. languidula*	214
523	salvilanguiduline D	*S. languidula*	214
524	salvifulgenolide	*S. fulgens*	22
525	salvixalapadiene	*S. xalapensis*	213
526	isosalvixalapadiene	*S. xalapensis*	213
527	salvianduline C	*S. lavanduloides*	215
528	salvireptanolide	*S. reptans*	202
529	rhyacophiline	*S. rhyacophila*	199
530	7-*epi*-rhyacophiline	*S. rhyacophila*	427
531	7,8-didehydrorhyacophiline	*S. reflexa*	216
532	cardiophyllidin	*S. cardiophylla*	86, 217
533	polystachyne F	*S. polystachya*	218
534	salvianduline A	*S. lavanduloides*	219
535	salvianduline B	*S. lavanduloides*	219
536	derivative of **535**	*S. lavanduloides*	219
537	bisditerpenoid derivative	*S. wagneriana*	220
538	bisditerpenoid derivative	*S. wagneriana*	220
539	blepharolide A	*S. blepharophylla*	221
540	salvianduline D	*S. lavanduloides*	222
541	spiroleucantholide	*S. leucantha*	209
542	salvileucalin B	*S. leucantha*	223
543	salvigenolide	*S. fulgens*	183, 392
544	2β-hydroxysalvigenolide	*S. xalapensis*	213
545	blepharolide B	*S. blepharophylla*	221
546	dugesin B	*S. dugesii*	208
547	salvileucantholide	*S. leucantha*	224
548	salviandulin E	*S. leucantha*	224
		S. leucantha	209
549	dugesin A	*S. dugesii*	208
550	(−)-isopimara-8(14),15-diene	*S. parryi*	5
551	7α-hydroxyisopimara-8(14),15-diene	*S. parryi*	5
552	isopimara-8(14),15-dien-7-one	*S. parryi*	5
553	sandaracopimaric acid	*S. fulgens*	183
554	7α-hydroxysandaracopimaric acid	*S. microphylla*	183
555	methyl 7α-hydroxysandaracopimarate	*S. microphylla*	183
556	7-oxo-sandaracopimarate	*S. microphylla*	183
557	7-oxo-sandaracopimaric acid	*S. microphylla*	183
558	salvipimarone	*S. multicaulis*	95
559	7α-acetoxyisopimara-8(14),15-diene-18-oic acid	*S. microphylla*	428
560	isopimaric acid	*S. greggii*	186, 226
		S. wiedemannii	65
561	14α-hydroxy-7,15-isopimaradien-18-oic acid	*S. greggii*	186, 226
562	14α-hydroxyisopimara-7,15-diene	*S. parryi*	5
563	14α,18-dihydroxy-7,15-isopimaradiene	*S. greggii*	226
564	3β-hydroxy-7,l5-isopimaradien-18-oic acid methyl ester	*S. greggii*	226
565	14-oxo-pimaric acid	*S. wiedemannii*	109
566	11β-hydroxymanoyl oxide	*S. candidissima*	340
567	isopimara-8,15-dien-7-one	*S. parryi*	5

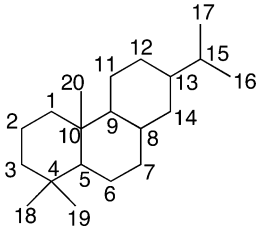
dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Table 2. continued

no.	name	plant	ref
568	isopimara-6,8(14),15-triene	*S. parryi*	5
569	parryin	*S. parryi*	5
570	7α-hydroxy-labd-8(17)-en-15-oic (= salvic acid)	*S. eupatorium*	361
571	8(17)-labdene-3α,7β-diacetoxy-15-oic acid	*S. eupatorium*	361
572	7α-hydroxy-14,15-dinor-13-oxo-8(17)-labdene	*S. eupatorium*	361
573	sclareol	*S. sclarea*	51
574	manool	*S. sclarea*	51
		S. officinalis	172
575	8(17),12*E*,14-labdatrien-6,19-olide	*S. leriaefolia*	289
576	2α-hydroxyambreinolide	*S. palaestina*	227
577	ambreinolide-18-oic acid	*S. palaestina*	227
578	13-*epi*-manoyloxide-15,18-dioic acid	*S. palaestina*	227
579	15-normanoyloxide-14,18-dioic acid	*S. palaestina*	227
580	8α-acetoxy-14,15,16-trinorlabdan-13-oic acid	*S. palaestina*	227
581	6α-hydroxy-8α-acetoxy-13,14,15,16-tetranorlabdan-12-oic acid	*S. yosgadensis*	228
582	methyl 3α-hydroxy-8α-acetoxy-13,14,15,16-tetranorlabdan-12-oate	*S. aethiopis*	229
583	6α-hydroxynorambreinolide	*S. yosgadensis*	228
584	3α-hydroxynorambreinolide	*S. aethiopis*	229
585	6α-hydroxyambreinolide	*S. yosgadensis*	228
586	norambreinolide-18,6α-olide	*S. sahendica*	429
587	8-acetoxy-13,14,15,16-tetranorlabdan-12-oic acid-18,6α-olide	*S. sahendica*	429
588	2,6-dimethyl-10-(*p*-tolyl)undeca-2,6-diene	*S. dorisiana*	230
589	salviolone	*S. miltiorrhiza*	13, 231
590	salviatalin A	*S. digitaloides*	232
591	salvitrijudin A	*S. digitaloides*	232

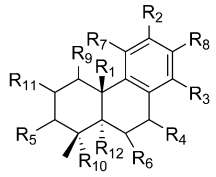
found to have biological activity; for example, taxol, cafestol, and kahweol all display anticancer properties. Diterpenes isolated from *Salvia* spp. are the largest group, comprising 545 of the 791 *Salvia* constituents (Table 2). According to their structure, this group is further classified into five subgroups: abietane diterpenoids, clerodane diterpenoids, pimarane diterpenoids, labdane diterpenoids, and other diterpenoids.

2.2.1. Abietanes. Abietanes and rearranged abietanes are a family of naturally occurring diterpenoids that have been isolated from a variety of terrestrial plant sources. These compounds exhibit an array of interesting biological activities, which has generated significant interest from the pharmacological community. Abietanes and rearranged abietane comprised the largest group of components of *Salvia* plants. Of 545 known *Salvia* diterpenoids, 365 found in *Salvia* species belong to the abietane diterpenoids and have been identified since 1976. This is the largest group of known *Salvia* diterpenoids, appears to be the most widely distributed, and can be divided into 19 subgroups.



2.2.1.1. Abieta-8,11,13-trienes. Compounds **47**−**145** have an aromatic C ring and differ in the functionalities at C-1, 2, 3, 6, 7, 11−14, 18, and 20. The first aromatic C ring abietane found in *Salvia* species was 3β-hydroxy-8,11,13(14),15-abietatetraen-18-oic acid (**142**) isolated from *S. tomentosa* in 1981.[56] Two of the aromatic C ring abietanes, ferruginol (**50**) and iguestol (**63**), are typical compounds in this group and have been isolated from several species.[51,57−69] Investigation of *S. pomifera* gave seven new aromatic C ring abietanes: pomiferin A−G (**78**−**82**, **98**, and **99**).[70,71] Extraction of the roots of *S. hypargeia* from Turkey afforded four new diterpenoids, hypargenins A−C and E (**65**−**68**).[72] Pomiferins E and F and hypargenins A−C, having an α,β-unsaturated keto group in the B ring, differ in the functionalities at C-2, 6, and 15. Only three compounds (**47**−**49**), along with two known ones, salviol (**88**) and 12-methoxycarnosic acid (**92**), were reported from *S. blepharochlaena*[73] and *S. tomentosa*.[67] Their structures are very similar, in which every molecule has a carboxy group at C-10 (except **88**). The plants of *S. lanigera*, *S. melissodora*, *S. mellifera*, and *S. microstegia* were systematically investigated by many groups. Seven diterpenes, 16-hydroxycarnosic acid (**74**), 16-acetoxycarnosic acid (**75**), 11,12,16,20-tetrahydroxyabieta-8,11,13-triene (**76**), 10-acetylferruginol (**83**), **84**, 12-methoxycarnosic acid (**92**), and methyl carnosoate (**94**), were isolated.[61,72,74−78] Their structures were determined mainly by spectroscopic means. Ulubelon and co-workers published 14 papers on several *Salvia* species during the period 1988−2001, reporting the isolation and identification of forskalinone (**53**),[79] compounds **56**,[80] **57**,[80] **60**,[81] **71**,[68] **72**,[59] **77**,[82] **85**,[65] and **100**,[51] 1-oxoferruginol (**58**),[83] 6-oxoferruginol (**59**),[83] salviviridinol (**62**),[84] euphraticol (**69**),[85] and euphracal (**70**).[85] González and co-workers obtained four compounds (**87** and **89**−**91**) from *S. cardiophylla* and the flowers of *S. canariensis*.[86,87] Salvidorol (**113**), salvirecognone (**114**), and salvirecognine (**115**) were three 20-norditerpenoids that were isolated from *S. dorrii*[88] and *S. recognita*.[89] Cryptanol (**122**), as one of the chief constituents of five *Salvia* species (*S. cilicica*, *S. euphratica*, *S. pachystachys*, *S. wiedemannii*, and *S. cryptantha*), was first isolated from *S. cryptantha* in 1987. Investigation of *S. apiana* gave three new abietanes: **116**, **117**, and **124**.

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026



	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9	R_{10}	R_{11}	R_{12}
47	CO_2CH_3	OCH_3	H	H	H	H	H	*i*-Pr	H	CH_3	H	H
48	CO_2H	OH	H	H	H	H	H	*i*-Pr	H	CH_3	H	H
49	CO_2H	OCH_3	H	H	H	H	H	*i*-Pr	H	CH_3	H	H
50	CH_3	OH	H	H	H	H	H	*i*-Pr	H	CH_3	H	H
51	CH_3	OH	OH	O	O	H	OH	*i*-Pr	H	CH_3	H	H
52	CH_3	OCH_3	OH	O	O	H	OH	*i*-Pr	H	CH_3	H	H
53	CH_2OH	OCH_3	OH	O	H	O	OH	*i*-Pr	H	CH_3	H	H
54	H	OCH_3	OH	O	H	H	OH	*i*-Pr	H	CH_3	H	H
55	CH_3	OAc	*i*-Pr	OAc	H	O	H	OAc	H	CH_3	H	H
56	CH_3	OCH_3	OH	H	O	H	H	*i*-Pr	H	CH_3	H	H
57	CH_3	OOH	H	H	H	O	H	*i*-Pr	H	CH_3	H	H
58	CH_3	OH	H	H	H	H	H	*i*-Pr	O	CH_3	H	H
59	CH_3	OH	H	H	H	O	H	*i*-Pr	H	CH_3	H	H
60	CH_3	H	H	H	H	H	H	*i*-Pr	O	CO_2H	H	H
61	CH_3	H	H	O	H	H	H	*i*-Pr	H	CH_3	H	O
62	CH_3	OCH_3	H	β–OH	H	α–OH	OH	*i*-Pr	H	CH_3	H	H
63	CH_3	OCH_3	H	H	H	α–OH	OH	*i*-Pr	H	CH_3	H	H
64	CH_3	OH	H	O	H	H	H	*i*-Pr	H	CH_3	H	H
65	CH_3	OH	H	O	H	β–OH	H	*i*-Pr	O	CH_3	H	H
66	CH_3	OH	H	O	H	H	H	$C(CH_3)_2OH$	H	CH_3	H	H
67	CH_3	OH	H	O	H	O	H	*i*-Pr	H	CH_3	H	H
68	CH_3	H	OH	H	H	β–OH	H	*i*-Pr	O	CH_3	H	H
69	CH_3	OH	H	H	H	H	OH	*i*-Pr	H	CH_3	α–OH	H
70	CHO	OH	H	H	H	H	OH	$C(CH_3)_2OH$	H	CH_3	H	H
71	CH_3	OCH_3	H	H	H	H	H	*i*-Pr	H	CH_3	α–OCH_3	H
72	CH_3	OH	OH	H	H	H	H	*i*-Pr	H	CH_3	H	H
73	CH_3	OH	H	O	H	H	H	*i*-Pr	H	CH_3	α–$OCOCH_3$	H
74	CO_2H	OH	H	H	H	H	OH	$CH(CH_3)CH_2OH$	H	CH_3	H	H
75	CO_2H	OH	H	H	H	H	OH	$CH(CH_3)CH_2OAc$	H	CH_3	H	H
76	CH_2OH	OH	H	H	H	H	OH	$CH(CH_3)CH_2OH$	H	CH_3	H	H
77	CH_3	OCH_3	H	H	H	H	OH	*i*-Pr	H	CH_3	H	H
78	CH_3	H	H	H	H	H	H	*i*-Pr	H	CH_2OH	H	H
79	CH_3	OH	H	H	H	H	H	*i*-Pr	H	CH_2OAc	H	H
80	CH_3	OCH_3	H	H	H	H	OH	*i*-Pr	O	CO_2H	H	H
81	CH_3	H	H	H	H	H	H	*i*-Pr	H	CH_3	α–OH	H
82	CH_3	H	H	O	H	H	H	*i*-Pr	H	CH_3	α–OH	H
83	$COCH_3$	OH	H	H	H	H	H	*i*-Pr	H	CH_3	H	H
84	CH_3	OH	H	H	H	H	OH	*i*-Pr	H	CH_3	H	H
85	CH_3	H	H	H	O	H	H	*i*-Pr	H	CH_3	H	H
86	CH_3	OAc	H	O	H	H	H	*i*-Pr	H	CH_3	OAc	O
87	CH_3	OH	H	O	H	H	H	*i*-Pr	H	CH_3	OH	H
88	CH_3	OH	H	H	H	H	H	*i*-Pr	H	CH_3	OH	H
89	CO_2CH_3	OAc	H	O	H	H	OAc	*i*-Pr	H	CH_3	H	H
90	CO_2CH_3	OAc	H	β–OH	H	O	OAc	*i*-Pr	H	CH_3	H	H
91	CO_2CH_3	OAc	H	α–OH	H	O	OAc	*i*-Pr	H	CH_3	H	H
92	CO_2H	OCH_3	H	H	H	H	OH	*i*-Pr	H	CH_3	H	H
93	CH_3	H	H	β–OH	H	H	H	$C(CH_3)_2OH$	H	CH_3	H	H
94	CO_2CH_3	OH	H	H	H	H	OH	*i*-Pr	H	CH_3	H	H
95	CH_3	OCH_3	H	α–OH	H	H	OH	*i*-Pr	H	CH_3	H	H
96	CHO	OCH_3	OH	O	H	H	OH	*i*-Pr	H	CH_3	H	H
97	CH_3	H	H	H	OH	H	H	*i*-Pr	H	CO_2H	H	H
98	CH_3	H	H	O	H	H	H	$C(CH_3)_2OH$	H	CH_3	OH	H
99	CH_3	H	H	H	H	H	H	*i*-Pr	H	CH_2OAc	H	H
100	CH_3	OH	H	O	H	H	H	*i*-Pr	H	CHO	H	H
101	CO_2CH_3	OCH_3	H	H	H	H	OH	*i*-Pr	H	CH_3	H	H
102	CH_3	OCH_3	H	O	H	H	OH	*i*-Pr	H	CH_3	H	H
103	CH_3	OCH_3	OH	O	H	H	OH	*i*-Pr	H	CH_3	H	H
104	CO_2H	OH	H	H	H	H	OH	$CH(CH_3)CH_2OH$	H	CH_3	H	H
105	CH_3	OH	H	O	H	H	OH	*i*-Pr	H	CH_3	H	H
106	CH_3	H	OH	H	H	H	H	*i*-Pr	H	CO_2H	α–OH	H
107	CH_2OH	OH	H	H	H	H	OH	*i*-Pr	H	CH_3	H	H
108	CHO	OH	H	H	H	H	OH	$CH(CH_3)CH_2OH$	H	CH_3	H	H
109	CH_3	OH	H	O	OH	H	OH	*i*-Pr	H	CH_3	H	H
110	CH_3	H	H	O	H	H	H	$C(CH_3)_2OH$	H	CH_3	H	H
111	CH_3	OH	H	OH	H	O	H	*i*-Pr	H	CH_3	H	H

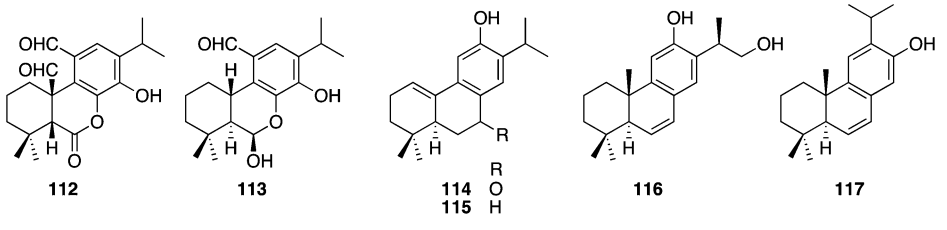


Figure 7. continued

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

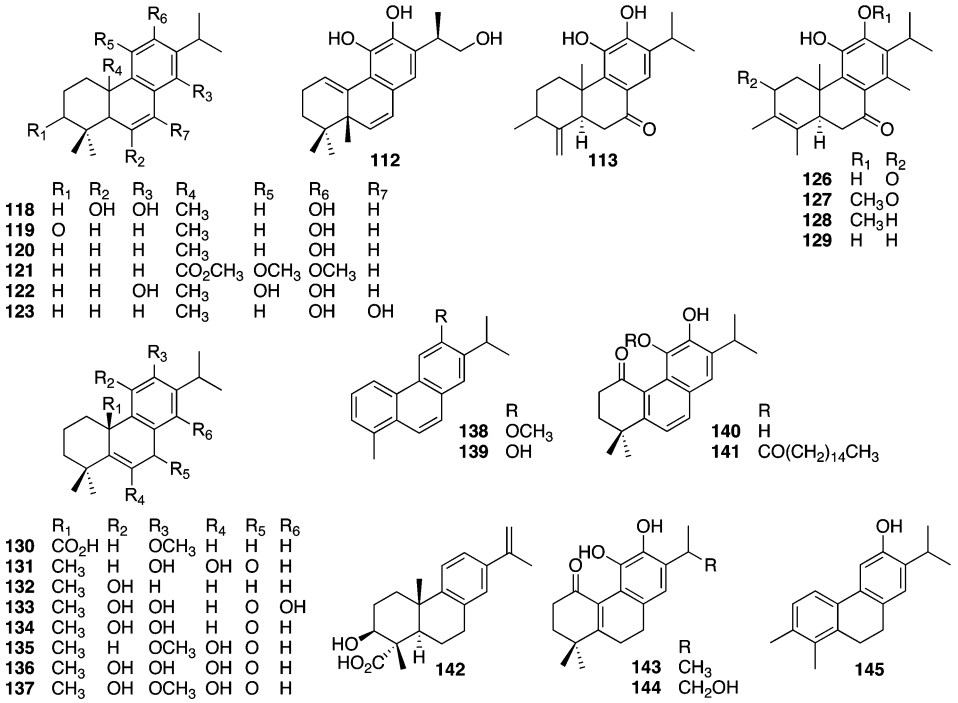


Figure 7. Abieta-8,11,13-trienes.

Compounds **117**−**124** bear the same structural features: an aromatic C ring and a double bond between C-6 and C-7. **124** has another unusual double bond between C-1 and C-10. The differences among them are the substituents at carbons C-3, 6, 11, 12, 14, and 20.[57,64,65,68,85,89,90] **130**−**136** also have an aromatic C ring but have a double bond between C-5 and C-6. The positions C-6, C-11, and C-12 are commonly functionalized by a hydroxy group or methoxy group, and carbon C-7 is always a keto group.[59,73,81,91−93] 14-Deoxycoleon U (**136**) was first isolated from *S. phlomoides* in 1983.[94] The same compound was obtained from *S. montbretii* in 1996 and given another name: 6-hydroxysalvinolone.[93] Multicaulin (**138**),[73,95] **139**,[95,96] and **145**[97] were three other aromatic C ring abietanes with an aromatic A ring in their structures. **140**−**144** bear the same structural features: a C-1 keto group and a C-11 hydroxy group. Of them, **140**[66,74] and **141**[61] have an aromatic B ring and **144**[97] has a hydroxy group at C-15.

2.2.1.2. Abietan-12-ones. Compounds **148**, **149**, and **151**−**153**, isolated from *S. texana*, have a keto group at C-12 and three double bonds between C-7 and C-8, C-9 and C-11, and C-13 and C-14. Among them, **149** and **151** have a keto group at C-6, and **153** has a hydroxy group at C-7.[98,99] **156**−**160**, obtained from four *Salvia* species, bear the same structural features: a keto group at C-12 and four double bonds between C-5 and C-6, C-7 and C-8, C-9 and C-11, and C-13 and C-14.[84,87,100−102]

2.2.1.3. Abietane-11,14-diones. The genus *Salvia* is rich in tanshinones, which have a furo-1,2- or a furo-1,4-naphthoquinone chromophore, first isolated from *Salvia miltiorrhiza* Bunge, a traditional Chinese medicinal herb, by Nakao and Fukushima in 1934.[103] This group of secondary metabolites is interesting to organic chemists, pharmacologists, and phytochemists not only for chemical reasons as challenging synthetic targets but also for their remarkable biological properties.

Horminone (**162**), 7-acetylhorminone (**163**), and royleanone (**166**) are typical compounds in this subgroup and have

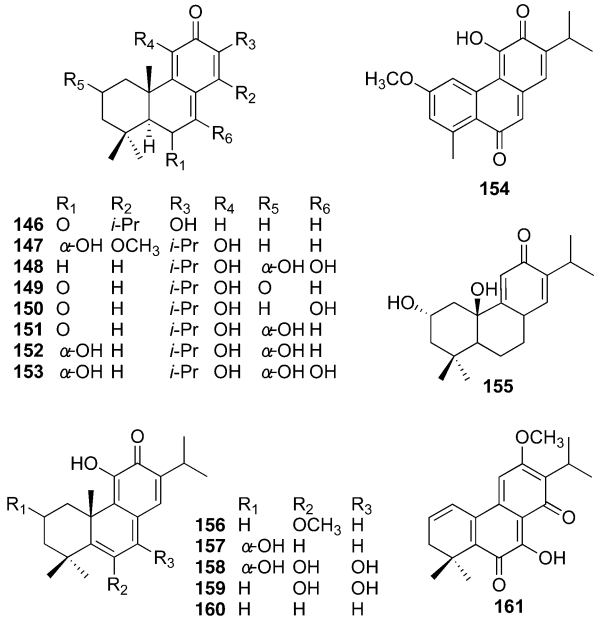


Figure 8. Abietan-12-ones.

been isolated from 14 *Salvia* species.[26,57,65,67,68,73,74,82,90,104−110] They have the same C ring: two keto groups at C-11 and C-14 and two double bonds between C-8 and C-9, C-12, and C-13. Recently, a new natural abietane diterpenoid 7-oxoroyleanone-12-methyl ether (**183**) and six known diterpenoids 7*α*-acetoxyroyleanone-12-methyl ether, cryptojaponol (**102**), inuroyleanol (**103**), horminone (**162**), 7-acetylhorminone (**163**), and royleanone (**166**) were isolated from the root of *S. barrelieri* Ettling. Among the diterpenoids, the new diterpenoid **183** showed the highest superoxide anion scavenging activity whereas **103** showed both the highest 1,1-diphenyl-2-picrylhydrazyl (DPPH) scavenging activity and inhibition of lipid peroxidation in the *β*-carotene−linoleic acid system. These

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

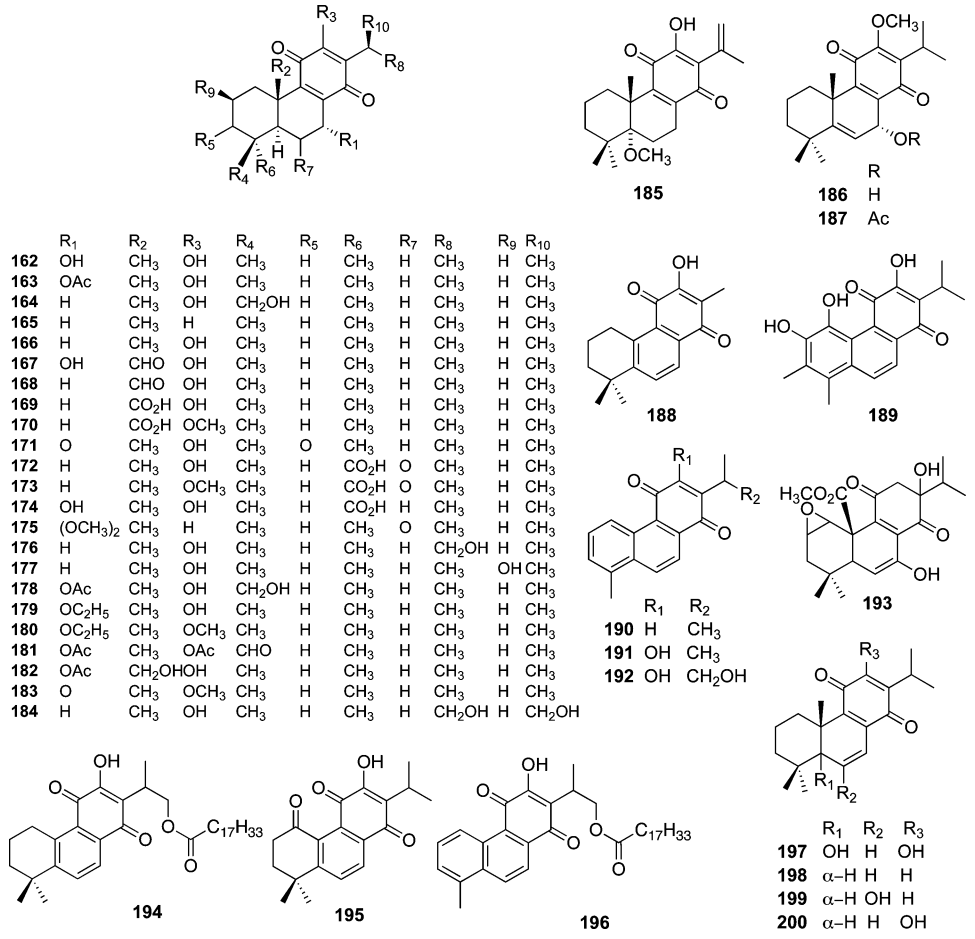


Figure 9. Abietane-11,14-diones.

findings indicate that *S. barrelieri* extract as well as isolated abietane diterpenes, particularly **103**, are promising antioxidants that can be used as food additives.[111] **185**−**200** were sixteen C-11, C-14 keto abietanes that were isolated from *Salvia* species. Of them, bractealine (**185**)[6] has a double ring between C-15 and C-16, **186** and **187**[95] have one between C-5 and C-6, and **197**−**200**[59,72,108,112] have one between C-6 and C-7.

2.2.1.4. Abietane-11,12-diones. In this subgroup, nine compounds have been found in eight *Salvia* species, with similar structures: two keto groups at C-11 and C-12 and two double bonds between C-8 and C-9, C-13 and C-14. **201**−**204** were four C-11, C-12 keto abietanes that were isolated from *S. recognita*, *S. napifolia*, *S. miltiorrhiza*, and *S. phlomoides*, respectively.[13,83,89,94] **205**−**209** are 20-norabietanes, and **206** has an unusual double bond between C-4 and C-18.[13,66,73,83,89,95,105]

2.2.1.5. 7,20-Epoxyabietanes. Isocarnosol (**222**), as one of the major constituents of *S. lanigera*, was first isolated in 1984. Its structure was established mainly by analysis of NMR data.[113] A series of derivatives of isocarnosol, **210**−**223**, were then isolated by repeated phytochemical investigations on many *Salvia* species. Abietanes in which the C ring is aromatic, carbon C-20 is a keto group, and carbons C-11 and C-12 are hydroxy groups are the most common substitutional pattern of 7,20-epoxyabietanes, and this group of abietanes are exemplified by **210**−**212**, **215**, **216**, **218**, and **219**. Among them, 16-hydroxycarnosol (**212**) was the major diterpene isolated from *Salvia* species and showed anticancer activities against A2780 (ovarian) and HBL-100 (breast) cancer cell lines ($GI_{50} \approx 3.6$ μM). Diterpenes such as 12,16-epoxycarnosol, isotanshinone II (**278**), (+)-neocryptotanshinone, and seven new semisynthetic diterpene analogues were obtained by partial synthesis from **212**.[114] **224**−**228** were five 7,20-epoxyabietanes, with one or two keto groups in C ring. Investigation of *S. miltiorrhiza*, *S. napifolia*, and *S. columbariae* gave three new 7,20-epoxyabietanes: **224**, **227**, and **228**.[83,91,115]

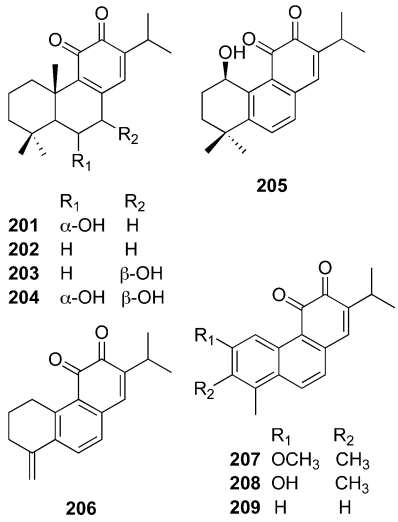
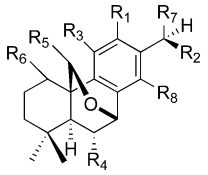
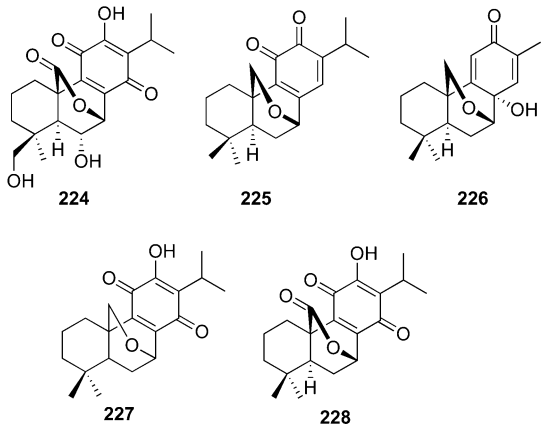


Figure 10. Abietane-11,12-diones.

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026



	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8
210	OH	CH_3	OH	H	O	H	CH_3	H
211	OCH_3	CH_3	OCH_3	H	O	H	CH_3	H
212	OH	CH_2OH	OH	H	O	H	CH_3	H
213	OH	CH_3	OH	OH	OH	H	CH_3	H
214	OCH_3	CH_3	H	H	H	O	CH_3	H
215	OCH_3	CH_3	OH	H	O	H	CH_3	H
216	OH	CH_2OH	OH	OH	O	H	CH_3	H
217	OH	CH_2OH	OH	H	H	H	CH_3	H
218	OH	CH_2OAc	OH	H	O	H	CH_3	H
219	OH	CH_3	OH	O	O	H	CH_3	H
220	OH	H	H	H	H	H	H	H
221	OCH_3	CH_3	OH	H	H	H	CH_3	H
222	H	CH_3	OH	H	O	H	CH_3	OH
223	OH	H	H	H	H	H	CHO	H



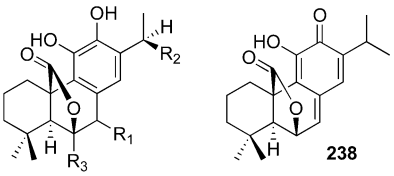
224 **225** **226**

227 **228**

Figure 11. 7,20-Epoxyabietanes.

2.2.1.6. 6,20-Epoxyabietanes. Rosmanol (**229**), the typical one belonging to this 6,20-epoxyabietane subgroup, was obtained repeatedly from five *Salvia* species: *S. rubescens*, *S. blepharochlaena*, *S. canariensis*, *S. officinalis*, and *S. pachyphylla*.[67,87,104,107,116−118] Following that, four analogues, **230**, **231**, **235**, and **236**, have been reported.[88,116,119] Of them, the structure of **235** was established by X-ray analysis.[88] Sagequinone methide A (**238**) was isolated from *S. officinalis* with a keto group at C-12 and a hydroxy group at C-11.[120]

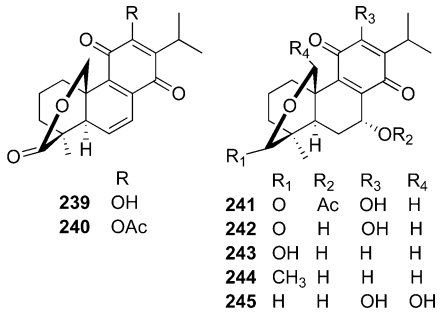
2.2.1.7. 19,20-Epoxyabietanes. Conacytone (**245**), the first one belonging to this subgroup, was obtained from the aerial parts of *S. ballotaeflora* Benth in 1976.[121] Then, in 1995, it was also isolated from *S. candicans*.[122] The structure and relative stereochemistry were elucidated by single-crystal X-ray diffraction techniques.[123] **239** was isolated from the aerial parts of *S. gilliesii*, and **240** was an acetyl derivative of **239**.[124] **241** was obtained from two *Salvia* species: *S. regla*[125] and *S. sessei*.[126] Investigation of *S. candicans* gave two other 19,20-epoxyabietanes: **243** and **244**.[122]



	R_1	R_2	R_3
229	OH	CH_3	H
230	OCH_3	CH_2OH	H
231	OCH_3	CH_3	OCH_3
232	α-OH	CH_2OH	H
233	β-OH	CH_2OH	H
234	α-OH	CH_3	H
235	α-OCH_3	CH_3	H
236	β-OCH_3	CH_3	H
237	O	CH_3	H

238

Figure 12. 6,20-Epoxyabietanes.

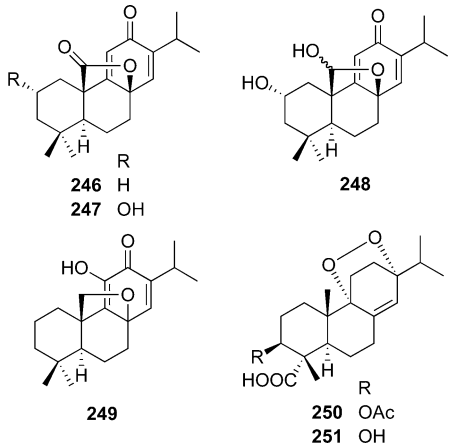


	R
239	OH
240	OAc

	R_1	R_2	R_3	R_4
241	O	Ac	OH	H
242	O	H	OH	H
243	OH	H	H	H
244	CH_3	H	H	H
245	H	H	OH	OH

Figure 13. 19,20-Epoxyabietanes.

2.2.1.8. 8,20-Epoxy- and 9,13-Epoxyabietanes. Only four compounds (**246**−**249**) belonging to 8,20-epoxyabietane have been found in three different species.[117,127,128] Investigation of *S. oxyodon* led to the isolation of two new 9,13-epoxyabietanes: **250** and **251**.[129]



	R
246	H
247	OH

248

249

	R
250	OAc
251	OH

Figure 14. 8,20-Epoxy- and 9,13-epoxyabietanes.

2.2.1.9. 11,17-Epoxy-, 12,17-Epoxy-, and 14,17-Epoxyabietanes. Nakao and Fukushima first extracted the tanshinones from traditional Chinese medicine Danshen *S. miltiorrhiza* in 1934. Subsequently, it was shown that the broad spectrum biological activity of Danshen was due to the presence of a number of interesting abietane diterpenoid quinones. A number of abietane diterpenoid quinones were subsequently isolated.

In this subgroup, 31 diterpenoids with four rings structures, compounds (**252**−**282**), were isolated by several research groups during 1985−2010. All of these diterpenoids consist of four characteristic rings, with ring C being an *ortho*-quinone or a *para*-quinone and ring D being a dihydrofuran or a furan. The most representative species that produced this type of diterpenoid is *S. miltiorrhiza*. In 1985, investigation of the root of *S. miltiorrhiza* from China gave five new 14,17-epoxyabietanes: tanshindiols A−C (**257**−**259**), 3α-hydroxytanshinone A (**260**), and nortanshinone (**262**). Their relative

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

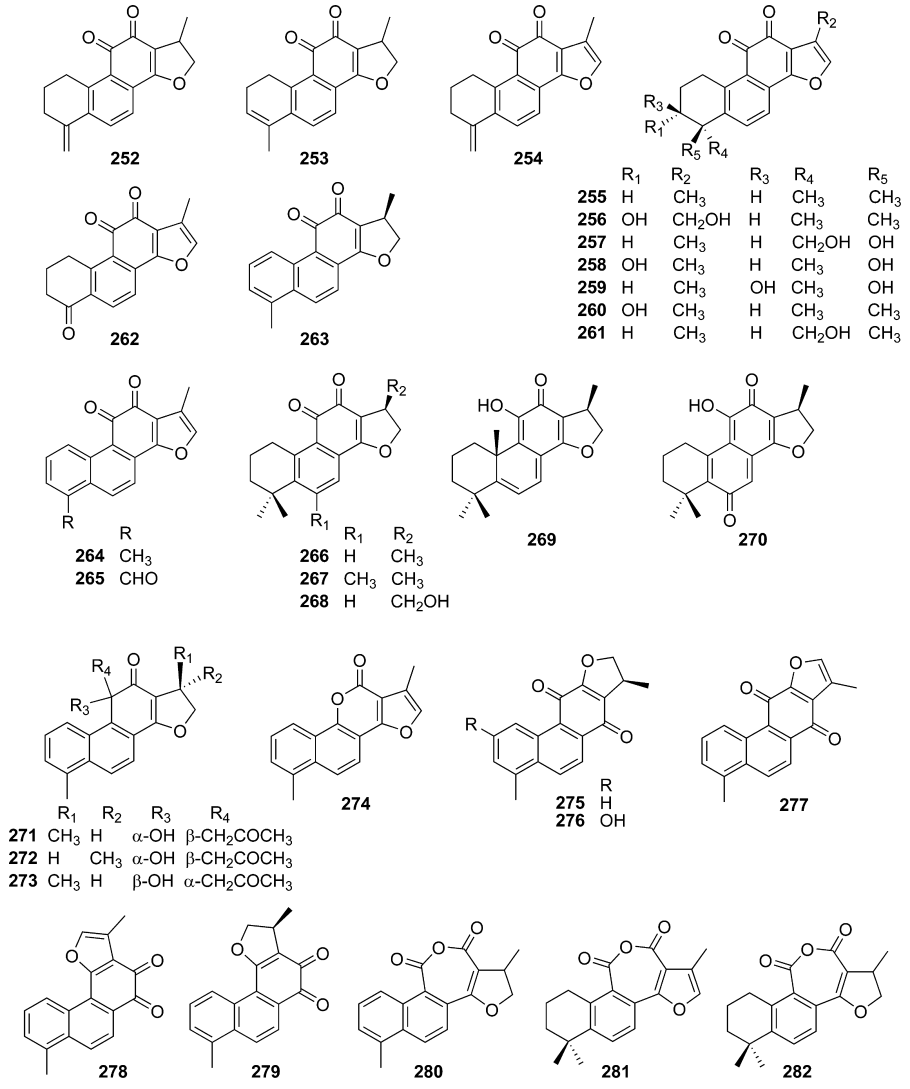


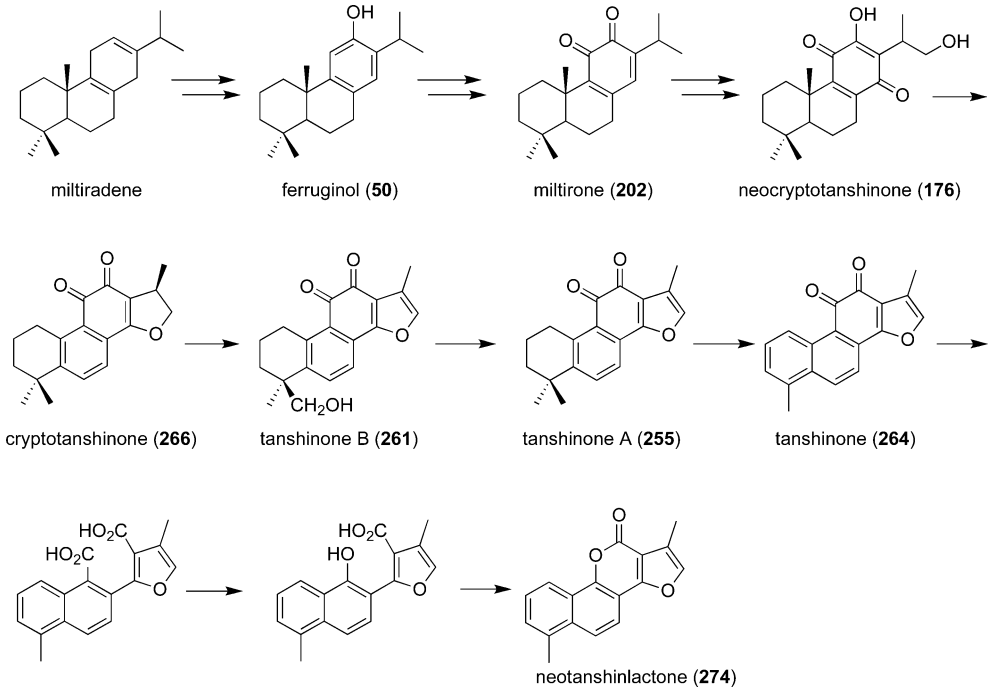
Figure 15. 11,17-Epoxy-, 12,17-epoxy-, and 14,17-epoxyabietanes.

stereochemistries have been established on the basis of spectral and chemical evidence.[130] **280**−**282** were isolated from the same plant with a 6/6/7/5-membered ring system.[13] 20-Norabietane cryptotanshinone (**266**) was the sole diterpenoid isolated from both aerial parts and roots of *S. axillaris*.[131] Extraction of the aerial part of *S. yunnanensis* from China afforded two diterpenoids, danshenols A (**271**) and C (**273**). It is interesting that the cytotoxic activities of **271** and **273**, being stereoisomers of each other, differed significantly. **271** showed potential inhibitive activity to K562 (IC_{50} = 0.53 μg/mL), T-24 (IC_{50} = 7.94 μg/mL), and Me180 (IC_{50} = 6.89 μg/mL) cell lines whereas **273** was inactive.[132] Recently, neo-tanshinlactone (**274**), having an α,β-unsaturated lactone in the C ring, was isolated from this plant, and was also synthesized for the first time. It showed significant inhibition against two ER human breast cancer cell lines.[133] Investigation of the roots of *S. glutinosa* gave five 12,17-epoxyabietanes: danshenol A (**271**), dihydroisotanshinone I (**275**), isotanshinone I (**277**), isotanshinone II (**278**), and dihydroisotanshinone II (**279**).[105] Because the cyclohexan-1,4-diene is relatively unstable, the authors proposed that miltiradiene may undergo aromatization to ferruginol (**50**), followed by further installation of different groups to give miltirone (**202**) and neocryptotanshinone (**176**). **176** can be converted stepwise to **266**, **261**, **255**, and **264** (Scheme 1).[134] In addition, Luo et al. proposed that tanshinlactone may be produced biologically from **264** through three intermediates, carboxylic acid, β-ketocarboxylic acid, and ketone (Scheme 1).[135]

2.2.1.10. Abietane Alkaloids. In 2005 and 2006, 16 abietane alkaloids, compounds **283**−**298**, were found from *S. yunnanensis*, *S. miltiorrhiza*, and *S. trijuga*. Most of them have an oxazole ring between C-11 and C-12 (except **297** and **298**), and some of them also have a dihydrofuran or furan ring between C-14 and C-15. Four new N-containing compounds, salvianan (**289**), neosalvianen (**290**), salvianen (**291**), and salviadione (**297**), were isolated from *S. miltiorrhiza*. Their structures were mainly established by spectroscopic methods. Compound **290** was prepared by treatment of tanshinone IIA (**255**) in EtOH with aqueous ethylamine solution (Scheme 2). Among these components, **291** exhibited the most potent cytotoxicity with a CD_{50} (cytotoxic dose) range of 30.4−39.5 μM against HeLa (cervical epitheloid carcinoma), HepG2 (hepatocellular carcinoma), and OVCAR-3 (ovarian adenocarcinoma) cell lines in a dose-dependent manner.[136] Eleven new abietane diterpene alkaloids containing an oxazole ring, salviamines A−F (**292** and **283**−**287**) and isosalviamines A−

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Scheme 1. Biogenetic Pathway Proposed for Neotanshinlactone (274) and Derivatives



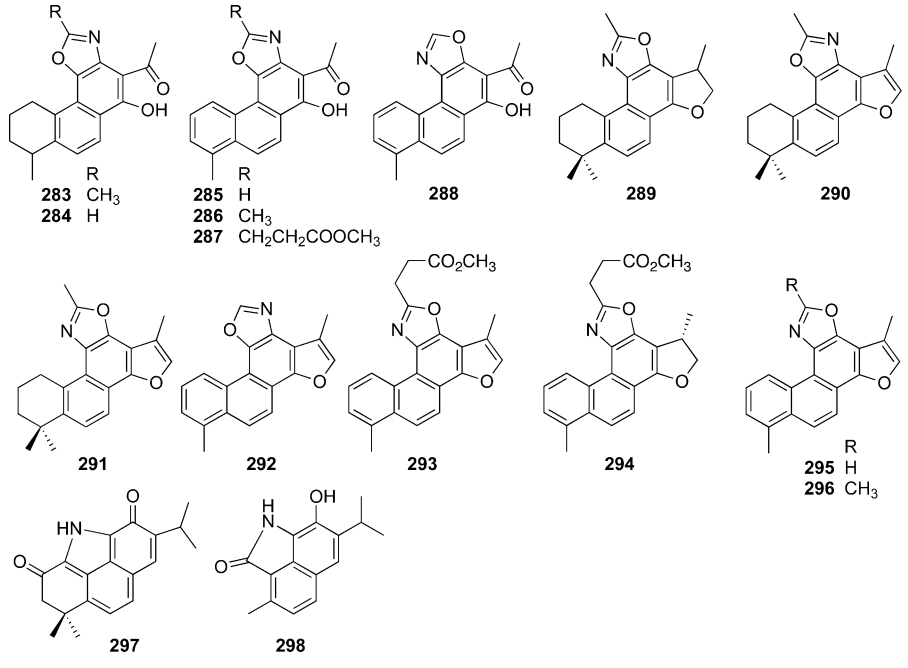
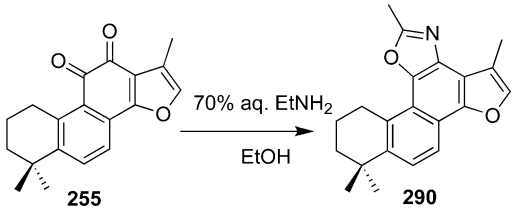


Figure 16. Abietane alkaloids.

Scheme 2. Conversion of 255 to 290

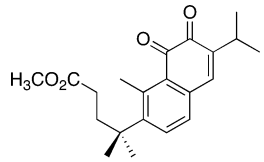


E (**293**–**296** and **288**), were isolated and characterized from the roots of *S. yunnanensis* and *S. trijuga*.[137,138]

2.2.1.11. 1,2-Seco-abietanes. Compound **299** was the only example reported so far belonging to 1,2-seco-abietane-type diterpene, isolated from *S. lanigera*.[139]

2.2.1.12. 2,3-Seco-abietanes. Salvipalestinoic acid (**300**), one example of 2,3-seco-abietanes, was obtained from *S. palaestina*. The impure **300** was purified as its *O*-methyl derivative (**301**) after treatment with ethereal CH_2N_2. **300** could arise biogenetically from the normal abietane candelabrone (**51** co-occurring in the plant) by a rupture of the C-2 and C-3 bond.[140] Candesalvolactone (**302**), isolated from the aerial parts of *S. candelabrum*, is another example in this subgroup

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026



299

Figure 17. 1,2-Seco-abietane.

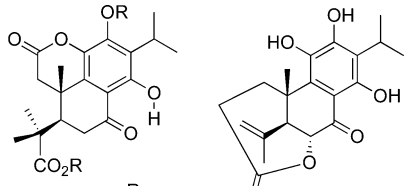


Figure 18. 2,3-Seco-abietanes.

that exhibited pronounced antioxidant effects in both enzyme-dependent and enzyme-independent anti-LPO systems.[141]

2.2.1.13. 3,4-Seco-abietanes. Compound **303** was obtained from *S. cinnabarina* by three research groups.[142−144] The new 3,4-seco-abietanes, candesalvoquinone (**304**), 12-*O*-methylcandesalvone B (**305**), and candesalvone B methyl ester (**307**), were isolated from *S. candelabrum*.[145]

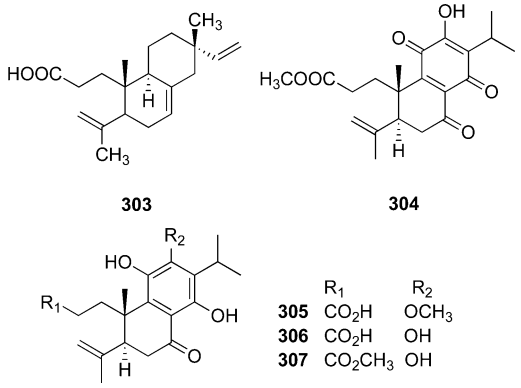


Figure 19. 3,4-Seco-abietanes.

2.2.1.14. 4,5-Seco-abietanes. Twenty-seven 4,5-seco-bicyclo-abietanes (**308−334**) have been isolated since 1981.[3,51,57,66,82,106,146−154] Among them, sclareapinone (**312**), prionoid D (**315**), prionoid E (**317**), and prionoid F (**322**), isolated from the roots of *S. prionitis* Hance, showed significant cytotoxic activity against P-388 (**315**, IC_{50} = 0.41 μM), A-549 (**317**, IC_{50} = 0.72 μM), HL-60 human leukemia (**312**, IC_{50} = 4.6 μM), SGC-7901 (**312**, IC_{50} = 0.2 μM), and MKN-28 stomach cancer (**312**, IC_{50} = 0.3 μM) cell lines. The results indicated that *ortho*-quinone diterpenoids were more cytotoxic than *para*-quinone diterpenoids in *S. prionitis*.[146,150] In addition, 4-hydroxysaprorthoquinone (**316**), also discovered from this species, exhibited significant inhibition against topoisomerase with an IC_{50} value of 0.8 μM.[146,148]

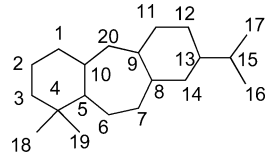
Thirteen 4,5-seco-tricyclo-abietanes (**335−347**) have been obtained from eight species. Salvibretol (**342**), microstegiol (**343**), 1-oxosalvibretol (**344**), and candidissiol (**345**) were four rearranged 4,5-seco-abietanes with seven- or eight-membered ring skeletons. The possible mechanisms of these rearrangements were considered as shown in Schemes 3 and 4, respectively.[93,147,155,156] Prionoid A (**337**) was the first rearranged tetracyclic diterpenoid with an epoxy group isolated from *S. prionitis*. Its structure was elucidated using spectroscopic analysis and further confirmed by a single-crystal X-ray diffraction determination.[150] A plausible origin of 4,5-seco-abietanes can be rationalized biogenetically from saprorthoquinone (**319**),[157] as shown in Scheme 5.[146,150]

2.2.1.15. 6,7-Seco-abietanes. Cariocal (**348**), obtained from *S. anastomosans* collected in Mexico, was one of the compounds belonging to the 6,7-seco-abietane group.[74] 16-Hydroxyrosmadial (**349**), isolated from the aerial parts of *S. mellifera*, is the other example in this subgroup, with ring B being a 10,11-lactone.[75]

2.2.1.16. 7,8-Seco-abietane. Compound **350** was the sole example reported so far belonging to 7,8-seco-abietane, which was isolated from *S. prionitis*, which is used in Chinese folk medicine as an antiphlogistic, antibacterial, and antitubercular drug. **350** showed antimicrobial activities against two Gram-positive organisms, *Staphylococcus aureus* and *Micrococcus luteus*, with MIC values of 20.0 and 15.0 μM, respectively.[146]

2.2.1.17. Abietane Dimers. Rosmanoyl carnosate (**351**), obtained from the flowers of *S. canariensis*, was the first abietane dimer consisting of rosmanol triacetate and carnosic acid diacetate, which were bonded together by an ester bond.[87] Two novel abietane dimers, 7,7′-bistaxodione (**352**) and 11,11′-didehydroxy-7,7′-dihydroxytaxodione (**353**), were isolated from the roots of *S. montbretii*. They consisted of two 7-hydroxytaxodiones (**150**), which were joined together at C-7−C-7′ and C-11−C-11′.[93] One other novel dimeric abietane diterpene, hongencaotone (**354**), has been isolated from the roots of *S. prionitis*, and its structure was determined by spectral data interpretation and X-ray analysis. **354** is the first ether-linked heterodimeric diterpene to have been isolated from the genus *Salvia*.[158] More recently, three abietane diterpenoid dimers, bisprioterones A−C (**355−357**), were isolated from roots of the Chinese folk medicinal plant *S. prionitis* Hance. They possessed two different abietane diterpenoid skeletons, which were linked via either a C−C single bond (**355** and **356**) or an ether bridge (**357**). Their structures were elucidated by analysis of 1D and 2D NMR spectroscopic data. The structure of **355** was further confirmed by a single-crystal X-ray diffraction determination.[159]

2.2.1.18. Icetexanes. The icetexanes are a family of diterpenoid natural products that have been isolated from a variety of terrestrial plant sources. The compounds in this family exhibit an array of interesting biological activities that, coupled with their unique structural features, have generated significant interest from the synthetic community. Icetexane diterpenoids are biosynthetically believed to arise from a rearrangement of the more common abietane and chemically belong to 9(10→20)*abeo*abietane skeleton with a 6/7/6-membered ring system.



In 1976, the isolation and structural determination of icetexone (**367**), a rearranged abietane quinone isolated from

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

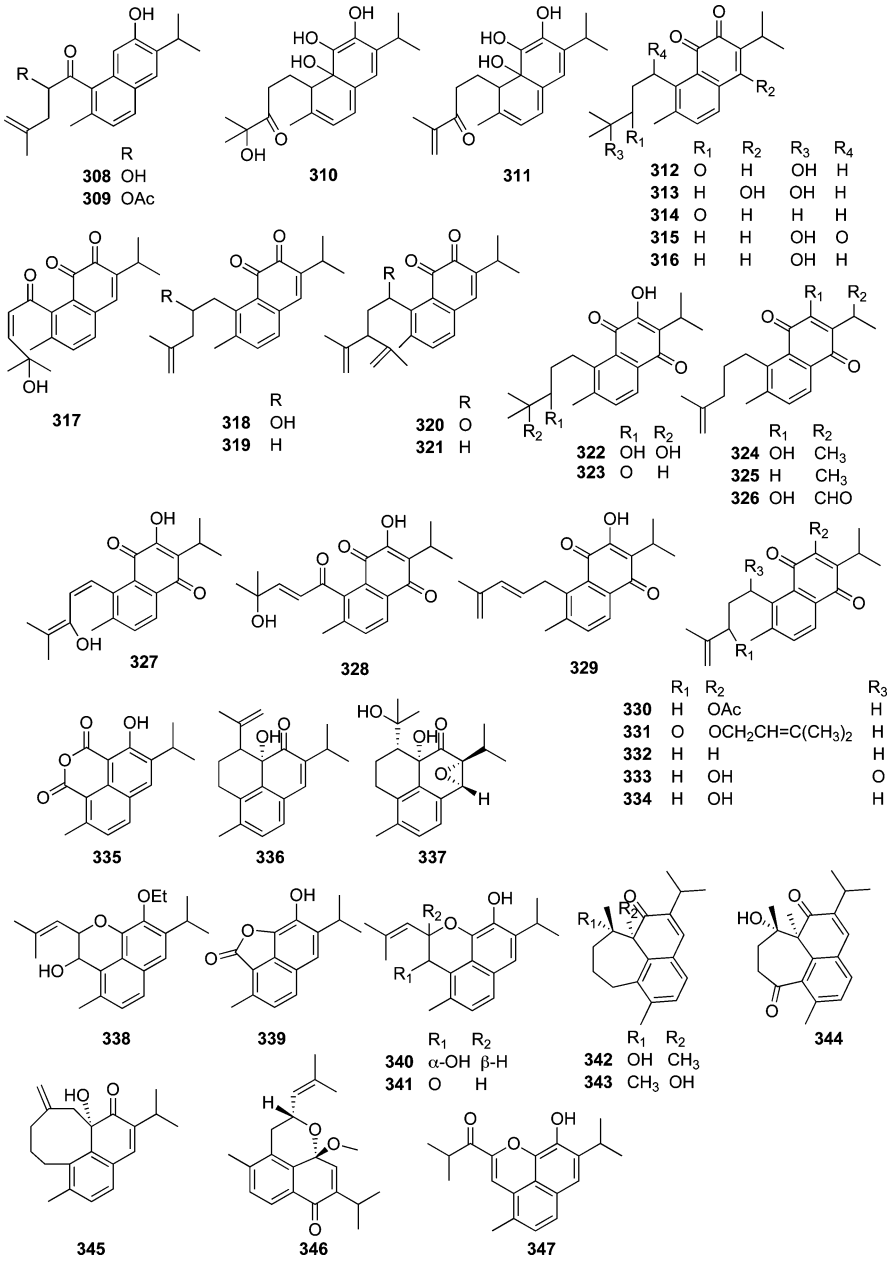


Figure 20. 4,5-Seco-abietanes.

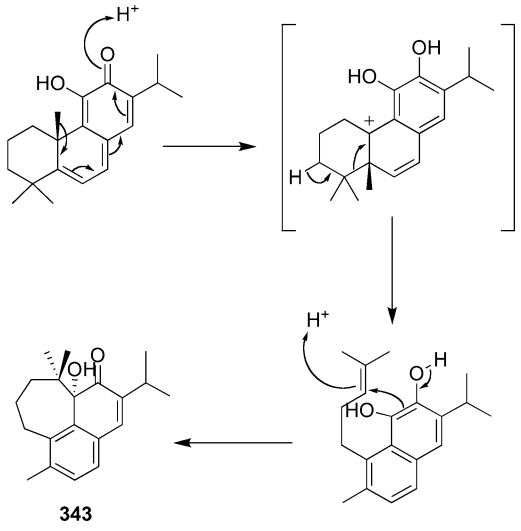
S. ballotaeflora, was described.[160] Following that, 18 analogues (**358**−**375**) from 12 *Salvia* species have been reported. 19-Deoxyicetexone (**365**), 5-*epi*-icetexone (**366**), **367**, and 19-deoxyisoicetexone (**368**) were four icetexane diterpenoids with a 10,19-epoxy-icetexane core.[122−124,131,160,161] Four 7,10-epoxy-icetexane diterpenoids, **369**, brussonol (**370**), salviasperanol (**371**), and przewalskin E (**375**), were obtained from *Salvia* species. A plausible biogenetic relation is given in Scheme 6 for the formation of compounds **370**, demethylsalvicanol (**360**), **369**, and **371**, all found in *Salvia* species.[58,162,163]

2.2.1.19. Other Abietanes. This group includes all of the *Salvia* abietane diterpenoids that do not belong in any of the above-mentioned groups. Thirty-three diterpenoids are included in this group.

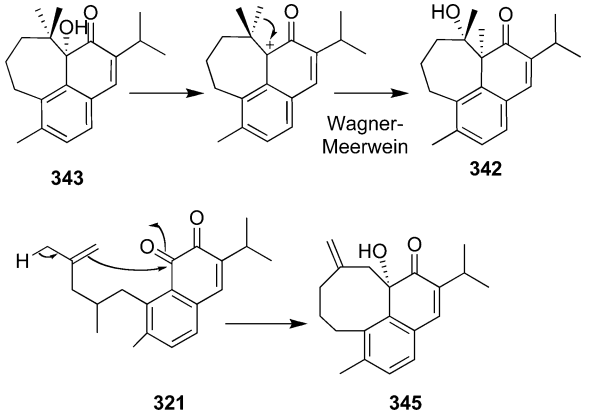
Castanolide (**410**) and *epi*-castanolide (**411**), two novel diterpenoids possessing a unique seco-norabietane skeleton, which features a six-membered α,β-unsaturated lactone ring and a five-membered α-methyl-α,β-unsaturated γ-spirolactone moiety, were isolated from *S. castanea* Diels f. pubescens Stib. Their structures and relative stereochemistry were elucidated by extensive NMR analysis and confirmed by a single-crystal X-ray diffraction study. A possible biosynthetic pathway of these two compounds from miltipolone (**409**) was also proposed (Scheme 7).[164] Tilifolidione (**376**), a salvifolane (9→20,10→6)-diabeoabietane, possessed a cycloheptanenaphthoquinone skeleton and was isolated from the roots of *S. tiliaefolia* and *S. semiatrata*.[62,74] It could be biogenetically derived from an abietanic diterpene as indicated in Scheme 8.[62] Two novel diterpene quinones with rearranged abietane skeletons, aegyptinones A (**381**) and B (**379**), have been isolated from the roots of *S. aegyptiaca*. Their structures have been established primarily by interpretation of detailed NMR data. The structure of **381** was further confirmed by single-crystal X-ray analysis. Biosynthetically, the novel carbon skeleton of **381**

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Scheme 3. Biogenetic Pathway Proposed for 343

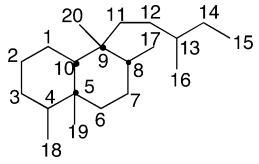


Scheme 4. Biogenetic Pathway Proposed for 4,5-Seco-abietanes



and **379** may arise from 6,7-dehydroroyleanone (**200**) (commonly found in *Salvia*) as shown in Scheme 9.[112] The six-five-six-membered ring system is a unique skeleton, and only six compounds with this structure have been reported from *Salvia* species. Among them, dichroanal A (**383**), dichroanal B (**382**), and dichroanone (**386**) were isolated from the roots of *S. dichroantha*.[67] The other three, salvicanaric acid (**389**), 2α-hydroxysalvicanaric acid (**387**), and salvicanaraldehyde (**388**), were obtained from *S. canariensis*, *S. texana* Torrand, and *S. munzii*, respectively. **389** and **388** could be biogenetically derived from abietanic diterpenes **159** and **120** as indicated in Schemes 10 and 11, respectively.[101,165,166] Paramiltioic acid (**390**), *epi*-cryptoacetalide (**391**), 6-methyl-*epi*-cryptoacetalide (**392**), cryptoacetalide (**393**), 6-methylcryptoacetalide (**394**), *epi*-danshenspiroketallactone (**395**), and danshenspiroketallactone (**396**) were seven spirolactones isolated from many *Salvia* species.[60,61,105,167−171] Biogenetically, the 6-methyl groups of 6-methyl-*epi*-cryptoacetalide (**392**) and 6-methylcryptoacetalide (**394**), isolated from whole plant of *S. aegyptiaca*, might arise by a series of methyl group shifts from C-10 to C-5 and then C-6. Przewalskin B (**399**), a novel diterpenoid possessing a unique skeleton, was isolated from a Chinese medicinal plant *S. przewalskii*. Its structure and relative stereochemistry were elucidated by extensive NMR analysis and a single-crystal X-ray study. Compound **431** exhibited modest anti-HIV-1 activity with EC_{50} = 30 μg/mL.[17] A new oxygenated diterpene γ-lactone, compound **400**, was isolated from the aerial parts of *S. officinalis*. The structure was established by spectroscopic data and substantiated by X-ray diffraction.[172] **405** and **406** were two abietane diterpenes, isolated from *S. wiedemannii* and *S. heldrichiana*, with a double bond between C-15 and C-16.[56,65,92]

2.2.2. Clerodanes. The structure and stereochemistry (apart from absolute configuration) of clerodin, a group of diterpenoids as bitter principle first isolated from the Indian bhat tree *Clerodendron infortunatum* (Verbenaceae), were established using X-ray analysis of a bromolactone derivative.[173] The parent hydrocarbon skeleton has been known as clerodane ever since. Clerodanes are found in many different plant families and contain four contiguous stereocenters contained in a *cis*- or *trans*-decalin. Biosynthetically, the clerodanes appear to be related to the labdanes, via a series of methyl and hydride shifts. The best-known and most extensively studied biological property of clerodane diterpenoids is insect antifeedant activity. A total of 138 clerodane diterpenoids, compounds **412**−**549**, isolated from *Salvia* species displayed biological activity. According to their structure, this group is further classified into 15 subgroups.



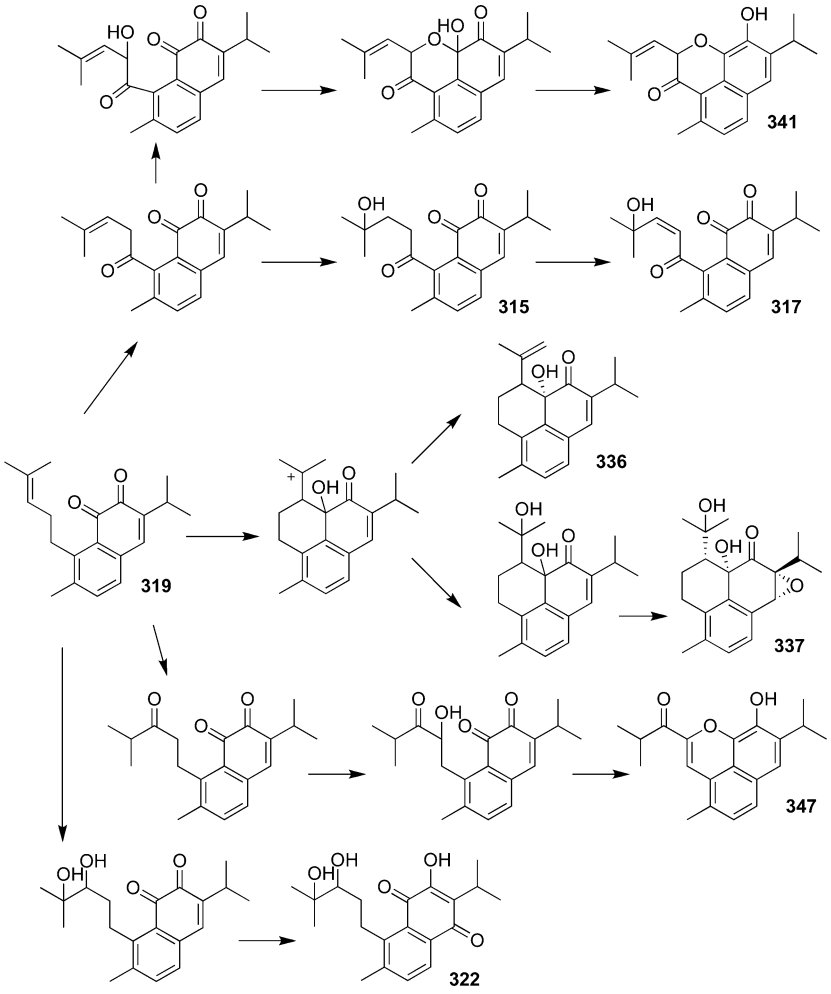
2.2.2.1. Clerodane-15,16-diols. In this subgroup, only three examples, salvigresides A−C (**412**−**414**), were obtained from the aerial parts of *S. greggii*, with two hydroxys at C-15 and C-16 and a β-D-glucopyranoside at C-6.[174] Among the members of the genus *Salvia*, *S. greggii* is considered to be abundant in neoclerodane diterpenoid glucosides.

2.2.2.2. 15,16-Epoxyclerodanes. Twenty-two 15,16-epoxy-clerodanes, compounds (**415**−**436**), were isolated from *Salvia* species. Most of them have a double bond between C-3 and C-4 (except **434**) and a β-substituted furan ring or an α,β-unsaturated lactone ring at C-12. **415**, **416**, and hardwickiic acid (**417**) were three 15,16-epoxyclerodanes that were isolated from *S. fulgens*[22] and *S. regal*.[125] Six new 15,16-epoxyclerodanes, divinatorins A−E (**418**−**420**, **422**, and **423**) and divinorin F (**421**), were obtained from the leaves of *S. divinorum*.[20,175,176] Further investigation on the same species collected in Japan was undertaken, and salvidivins C (**436**) and D (**434**) were isolated. **436** and **434** were neoclerodane diterpenes that possess an γ-hydroxy-α,β-unsaturated γ-lactone moiety.[20] Kerlinic acid (**424**) was isolated from *S. keerlii* with a carboxy group at C-5.[102] Thymonin (**425**) and 7β-hydroxythymonin (**428**) were two diterpenes that were isolated from *S. thymoides*, and **426** was an acetyl derivative of **425**; allylic oxidation of **425** gave the α,β-unsaturated aldehyde **427**, and **429** and **430** were acetyl derivatives of **428**.[177] **431**−**433** were examples from three *Salvia* species: *S. regal*,[125] *S. melissodora*,[178] and *S. lasiantha*.[179] Salvigreside D (**435**), a diterpenoid glucoside, isolated from the aerial parts of *S. greggii*, showed antibacterial activity against *Bacillus subtilis* ATCC6633 in the agar diffusion paper disk method at 8 μg/disk.[174]

2.2.2.3. 2,19-Epoxyclerodan-16,15-olides. This subgroup is rare in genus *Salvia*; only brevifloralactone (**437**) and

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Scheme 5. Biogenetic Pathway Proposed for 4,5-Seco-abietanes



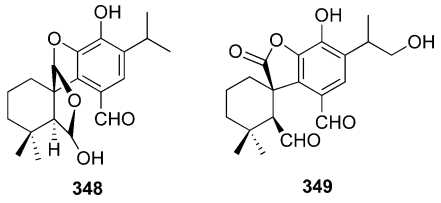


Figure 21. 6,7-Seco-abietanes.

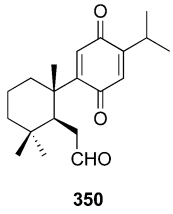


Figure 22. 7,8-Seco-abietane.

brevifloralactone acetate (**438**) have been isolated from *S. brevifl ora*.[180]

2.2.2.4. Clerodane-17,19:16,15-diolides. In this subgroup, only three compounds, salvimadrensinone (**439**), salvimadrensinol (**440**), salvimadrensin (**441**), have been found in *S. madrensis*.[181]

2.2.2.5. Clerodan-18,19-olides. Portulide C (**442**) was one example in this subgroup, isolated from *S. melissodora*, with two hydroxys at C-15 and C-16. Its structure was established by spectroscopic and chemical means.[182] **443**−**446** were four clerodane-18,19:15,16-diolides obtained from genus *Salvia*, with an α,β-unsaturated γ-lactone ring at C-12.[177,183−185] **447**−**453** were seven clerodan-18,19-olides, with a β-substituted furan ring at C-12.[186−190] Among them, salvisplendin C (**452**), from an acetone extract of the flowers of *S. splendens*, has an acetoxy group at the C-12 position. From the aerial parts of *S. melissodora*, nine *ent*-clerodane-18,19:16,15-diolides were isolated. The presence of an α-substituted butenolide is a common feature in all the diterpenoids isolated from this population of *S. melissodora*.[178] Investigation of *S. melissodora* gave six clerodane-18,19-olides: **455**, **457**, **459**−**461**,[178] and **462**[182] with an α-substituted lactone group at C-12. **454** and **458** were acetyl derivatives of **457**, and **456** was an acetyl derivative of **455**.

2.2.2.6. Clerodan-17,12-olides. In this subgroup, 13 examples were all isolated from *S. divinorum*. Salvinicins A (**463**) and B (**464**), salvinorin A (**465**), divinorin B (**466**),[191] and salvinorins C−H (**467**−**472**)[20,175,176,192,193] were 10 clerodan-17,12-olides, isolated from the hallucinogenic sage *S. divinorum*. Salvinorin A (**465**), first isolated from this plant in 1982,[194] the main active component of the psychotropic herb *S. divinorum*, has been reported to be a potent agonist at the κ-opioid receptor.[19,20,175,176] Two new neoclerodane diterpenes, **463** and **464**, were isolated from the dried leaves of this plant. The structures of these compounds were elucidated by

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

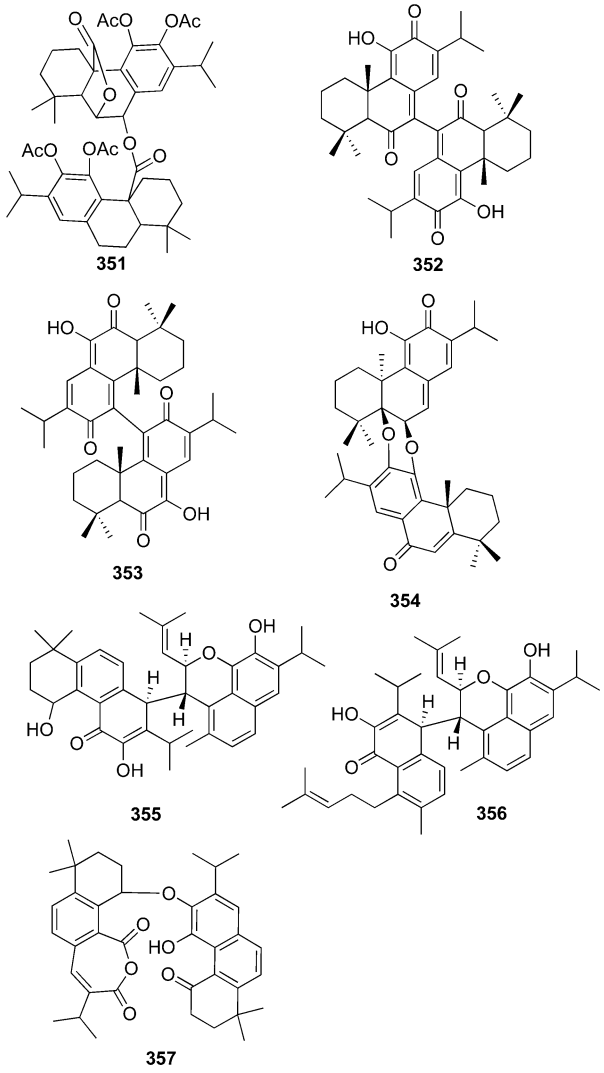
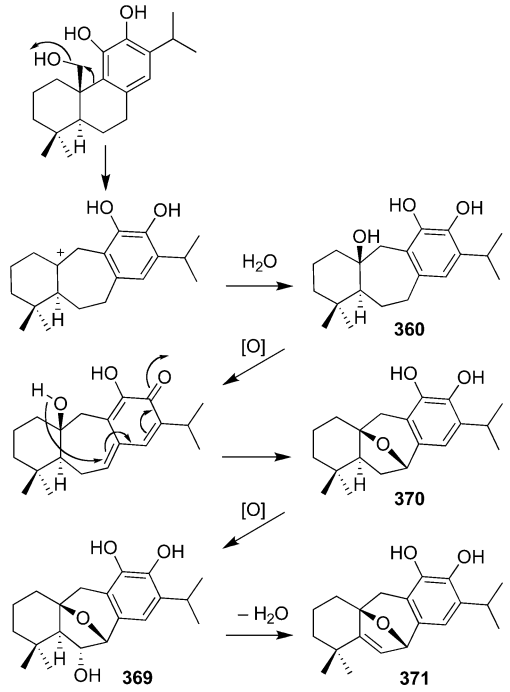


Figure 23. Abietane dimers.

Scheme 6. Biogenetic Pathway Proposed for 360 and 369–371



spectroscopic techniques. The absolute stereochemistry of these compounds was assigned on the basis of single-crystal X-ray crystallographic analysis of **463**. This is the first report of this highly oxygenated tetrahydrofuran ring system in compounds isolated from the *Salvia* genus. Further work indicated that **463** exhibited partial κ-agonist activity and **464** exhibited antagonist activity at μ-receptors.[195] 1-Deacetoxy-8-*epi*-salvinorin G (**473**), salvidivin A (**474**), and salvidivin B (**475**) were other examples from this plant.[20,196]

2.2.2.7. 12,17-Epoxyclerodane. This subgroup is rare in genus *Salvia*; only salvinorin I (**476**), 17β-salvinorin J (**477**), and 17α-salvinorin J (**478**) have been isolated from *S. divinorum*.[20,197]

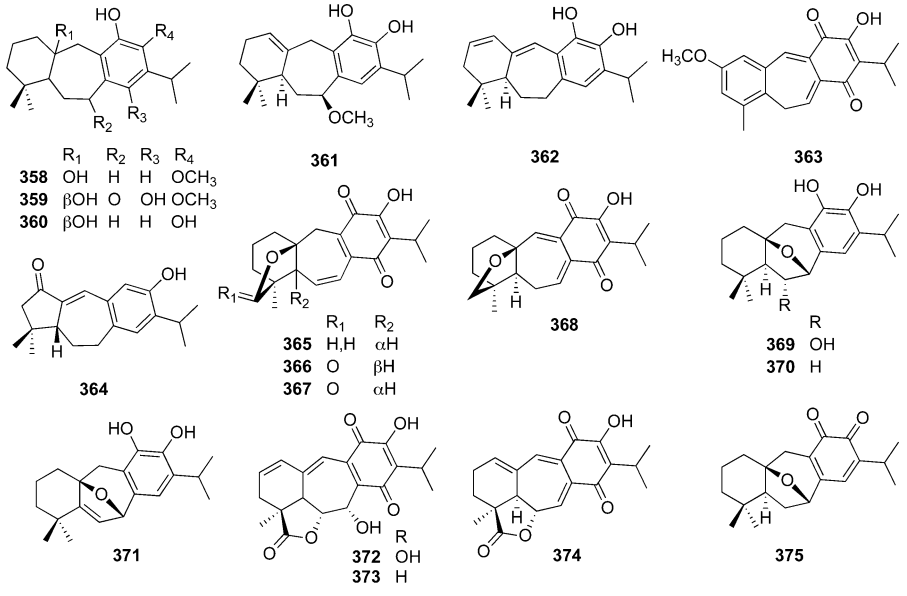


Figure 24. Icetexanes.

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

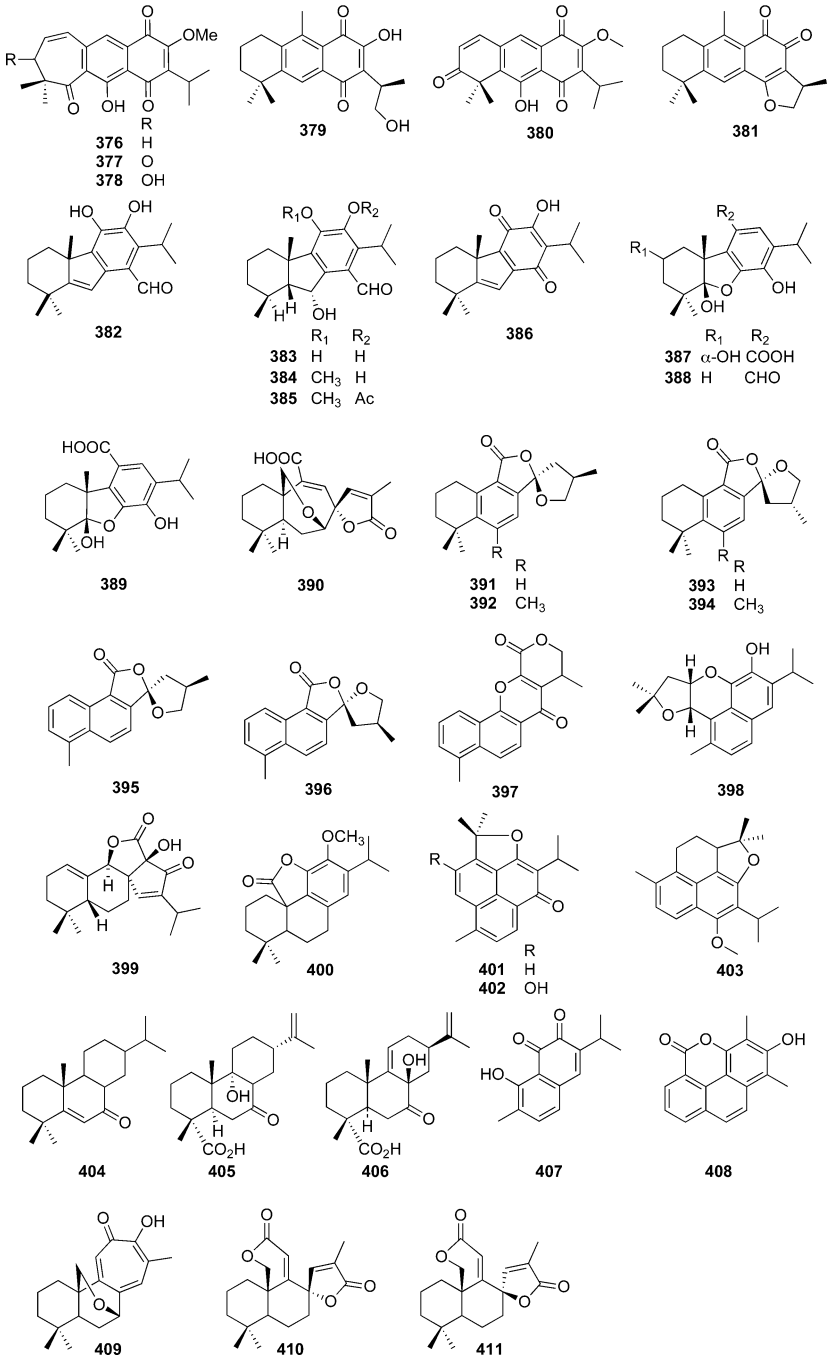


Figure 25. Other abietanes.

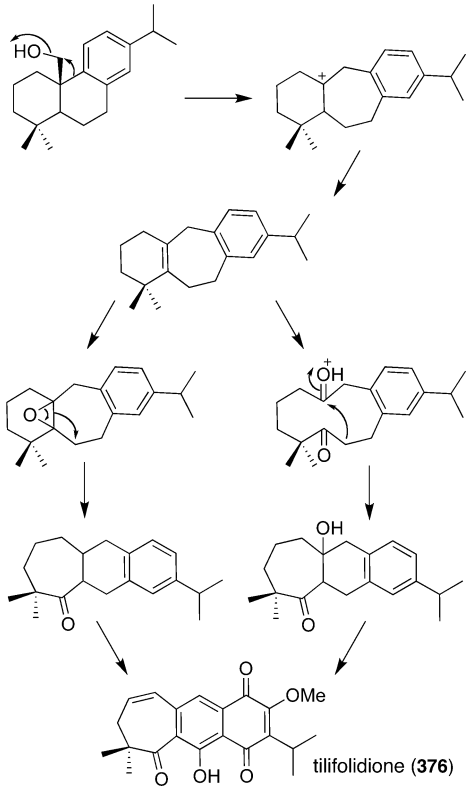
2.2.2.8. Clerodane-17,12:18,19-diolides. Twenty-six clerodane-17,12:18,19-diolides, **479**−**504**, have been isolated from genus *Salvia*. All of these diterpenoids share very similar structures with two lactone rings and a furan ring at C-12 (except **497**). Splendidin (**484**) and splenolide B (**486**) were isolated from *S. splendens*.[19,198] Salviarin (**485**) was isolated from three *Salvia* species: *S. divinorum*,[19] *S. greggii*,[186] and *S. rhyacophila*.[199] Investigation of the plant of *S. splendens* gave three new clerodane-17,12:18,19-diolides: salvisplendins A (**489**) and B (**495**) and splenolide C (**497**).[189,200] Polystachynes D (**499**) and E (**500**) and **501**, isolated from *S. polystachya* and *S. reptans*, have an epoxy ring between C-1 and C-2.[201,202] The structures were established by spectroscopic methods, including the X-ray analysis of **499**. **502**, **503**, and **504** have a 1,10-epoxy, 2,3-epoxy, and 6,7-epoxy ring, respectively.[203−205]

2.2.2.9. 8,12-Epoxyclerodan-18,19-olides. Kerlin (**505**) was one example in this subgroup, isolated from *S. keerlii*, with an epoxy ring between C-8 and C-12 and a *β*-substituted butenolide ring at C-12.[185] The other compounds belonging to this subgroup were dehydrokerlin (**506**) and salvisplendin D (**507**), both with a *β*-substituted furan ring at C-12.[189,199,201]

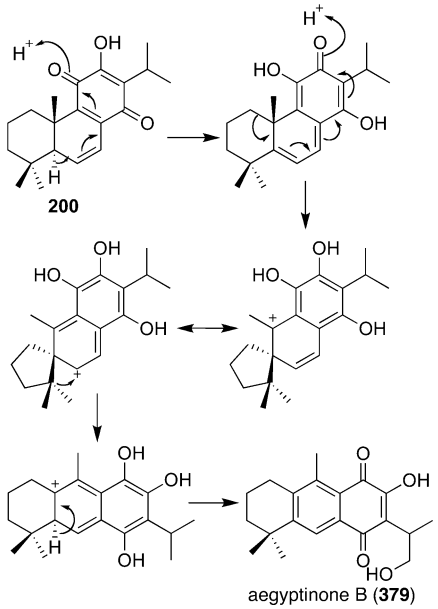
2.2.2.10. C-9 Spiroclerodanes. In this subgroup, seven compounds (**508**−**514**) were reported from *Salvia* species. They share similar structural characteristics: an epoxy ring between C-12 and C-20, an epoxy ring between C-7 and C-20 (except **508**), a lactone ring attached to ring A, and a *β*-substituted furan ring at C-12. From the aerial parts of *S.*

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

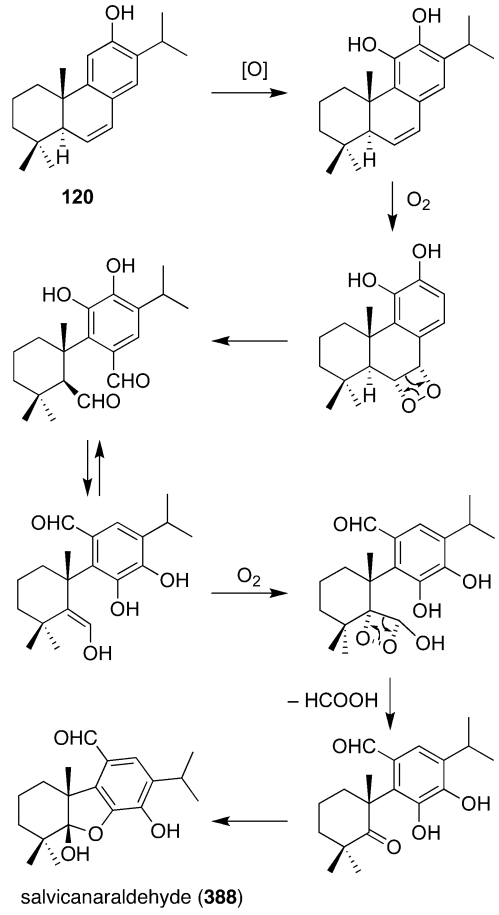
Scheme 7. Biogenetic Pathway Proposed from Miltipolone (409) to Catanolide (410) and *epi*-Castanolide (411)



Scheme 8. Biogenetic Pathway Proposed for 376



Scheme 9. Biogenetic Pathway Proposed for 379



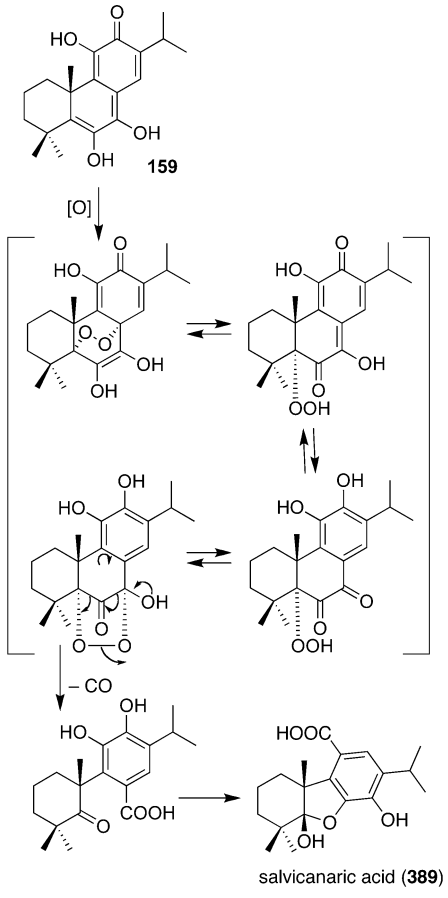
polystachya, three new neoclerodane diterpenoids, polystachynes A–C (**509**–**511**), have been isolated. The structures were established by spectroscopic methods, including the X-ray analysis of **511**. The structures of **510** and **511** were quite similar to that of **509** except the C-1,2-epoxy ring. Salvifarin (**512**) has been isolated from *S. farinacea* by three groups.[19,206,207] Salvifaricin (**513**) was obtained from three *Salvia* species: *S. farinacea*,[19,207] *S. dugesii*,[208] and *S. leucantha*.[209] *trans*-1,2-Dihydrosalvifaricin (**514**) was the other example in this subgroup that was isolated from *S. fulgens* in 2006.[22]

*2.2.2.11. 1,16-Cyclocleroda*nes. Compounds **515**–**519** were C-1,16-cyclocleroda*nes*, which are usually called languidulanes.[210] Compound **517** also was isolated previously from *S. sousae*[203] and *S. urolepis*.[211] The main feature of these compounds is the presence of a seven-membered ring, with an α,β-unsaturated ketone function, due to the linkage of C-l with C-16 of a clerodane skeleton.[13,187,203,212,213] Four new diterpenoids, salvilanguidulines A–D (**520**–**523**), with a rearranged clerodane skeleton were isolated from *S. languidula*. All of them contain an epoxy spiro γ-lactone function and a C1–C13 bond. Their structures were established by spectroscopic methods, and X-ray crystallographic analysis was carried out for the structure confirmation of **520**.[214]

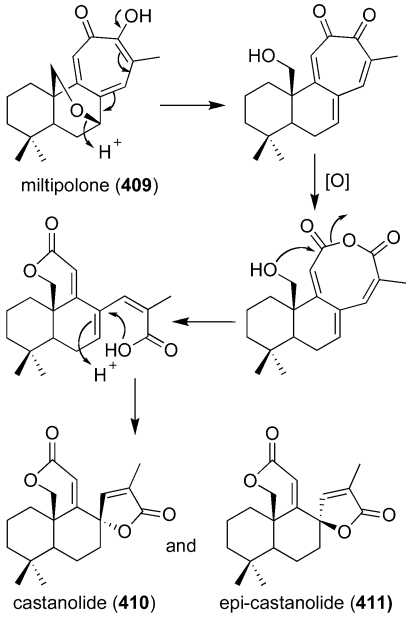
2.2.2.12. 5,6-Seco-clerodanes. **524**–**531** were eight 5,6-seco-clerodanes isolated from genus *Salvia*. In 2005, salvixalapadiene (**525**) and isosalvixalapadiene (**526**), with an unprecedented carbocyclic skeleton, have been obtained from the leaves of *S. xalapensis*.[213] Following that, the similar compound salvifulgenolide (**524**) was isolated from the aerial parts of *S. fulgens* Cav. The structure was established by spectroscopic methods and confirmed by X-ray analysis.[22] Salvianduline C (**527**) and salvireptanolide (**528**) were two examples in this subgroup that were isolated from *S. lavanduloides*[215] and *S. reptans*,[202] respectively. Rhyacophiline (**529**) and 7,8-didehydrorhyacophiline (**531**) were two other 5,6-seco-clerodanes, with a 7,12:12,20:15,16-triepoxy structural

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Scheme 10. Biogenetic Pathway Proposed for 389

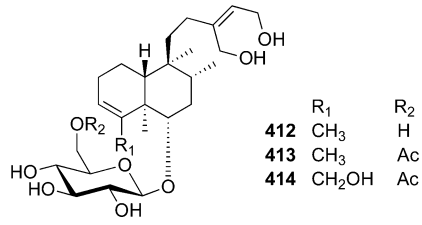


Scheme 11. Biogenetic Pathway Proposed for 388



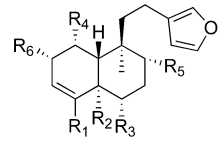
moiety, that were isolated from *S. rhyacophila* and *S. reflexa*, respectively.[199,216]

2.2.2.13. 5,10-Seco- and 9,10-Seco-clerodanes. Cardiophyllidin (**532**) and polystachyne F (**533**) were two examples of 5,10-seco-clerodanes that were isolated from the aerial parts of *S. cardiophylla* and *S. polystachya*, respectively. The structures

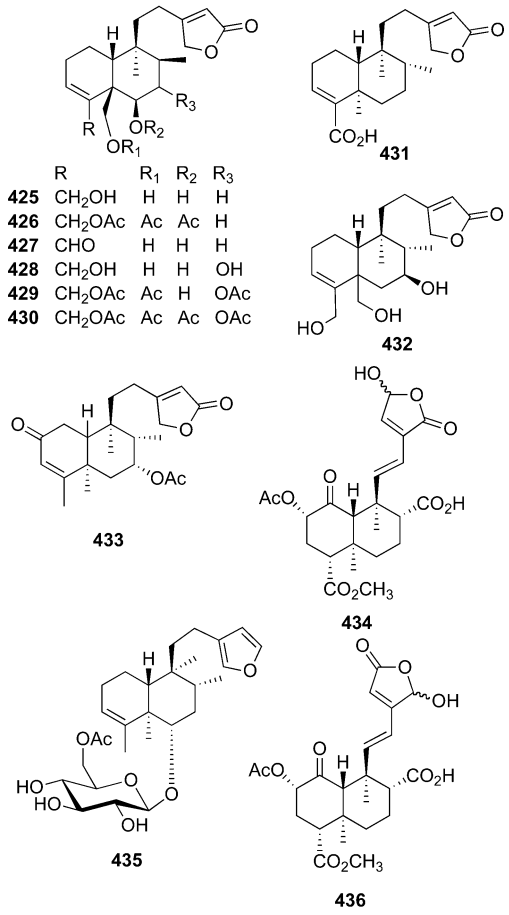


	R_1	R_2
412	CH_3	H
413	CH_3	Ac
414	CH_2OH	Ac

Figure 26. Clerodane-15,16-diols.



	R_1	R_2	R_3	R_4	R_5	R_6
415	CH_2OH	CH_2OAc	OH	H	CH_3	H
416	CHO	CH_2OAc	OH	H	CH_3	H
417	CO_2H	CH_3	H	H	CH_3	H
418	CO_2H	CH_3	H	OH	CH_3	H
419	CO_2CH_3	CH_3	H	OH	CH_2OH	H
420	CO_2H	CH_3	H	H	CH_2OAc	H
421	CO_2CH_3	CH_3	H	OH	CH_2OH	OH
422	CO_2CH_3	CH_3	H	OH	CH_2OAc	H
423	CO_2CH_3	CH_3	H	OH	CHO	H
424	CH_3	CO_2H	OH	H	CH_3	H



	R	R_1	R_2	R_3
425	CH_2OH	H	H	H
426	CH_2OAc	Ac	Ac	H
427	CHO	H	H	H
428	CH_2OH	H	H	OH
429	CH_2OAc	Ac	H	OAc
430	CH_2OAc	Ac	Ac	OAc

Figure 27. 15,16-Epoxyclerodanes.

were established by spectroscopic methods and further verified by X-ray method.[86,217,218] Almanza and co-workers published two papers on *S. lavanduloides* and *S. haenkei* and reported the isolation and identification of two 9,10-seco-clerodanes: salviandulines A (**534**) and B (**535**). **536** was an acetyl

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

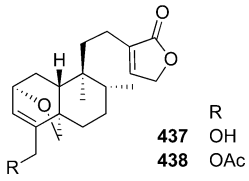


Figure 28. 2,19-Epoxyclerodane-16,15-olides.

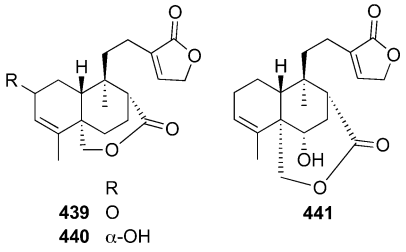


Figure 29. Clerodane-17,19:16,15-diolides.

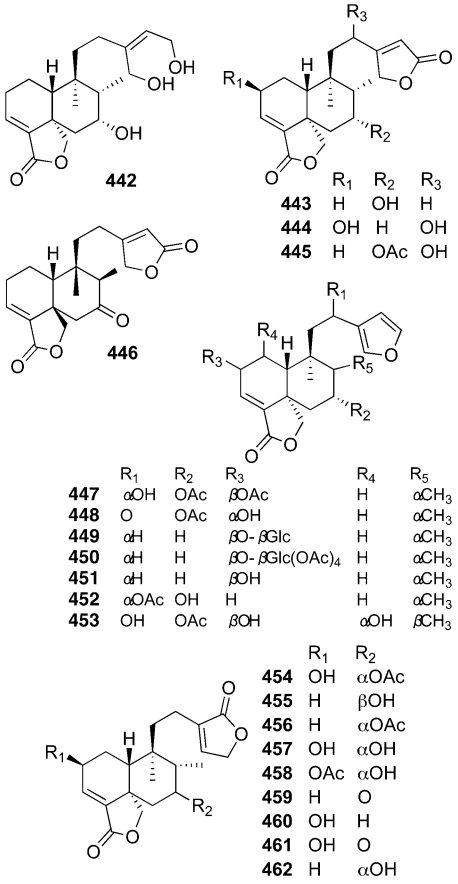


Figure 30. Clerodan-18,19-olides.

derivative of **535**. Their structures were established by high-resolution NMR and X-ray diffraction analysis.[190,219]

2.2.2.14. Diterpene Dimers. From the surface exudate of the aerial parts of *S. wagneriana*, two bisditerpenoids, **537** and **538**, were obtained. They could be derived biogenetically from a Diels–Alder-type cycloaddition between the furan ring of one clerodane diterpene and the C-3/C-4 double bond of the other one.[220]

2.2.2.15. Other Clerodanes. Blepharolide A (**539**), a 5,6-unsaturated octahydro-1*H*-cyclopropa[*a*]naphthalene derivative, has been isolated from *S. blepharophylla* Brandegee ex

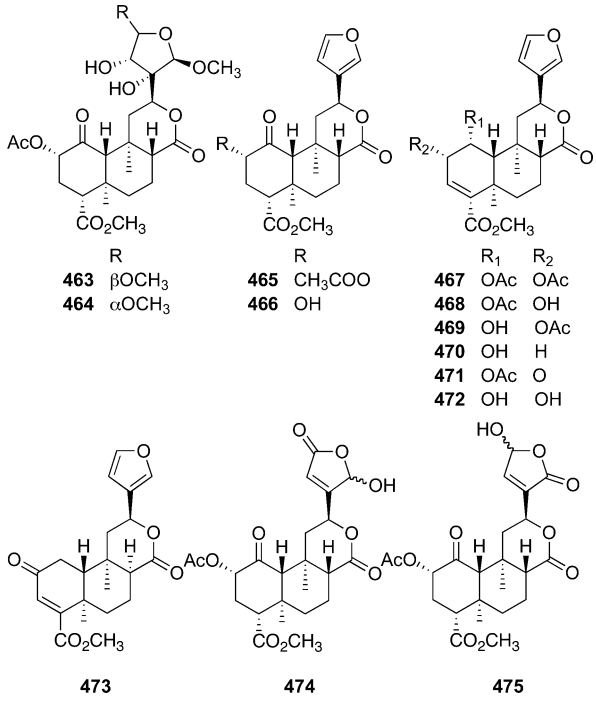


Figure 31. Clerodan-17,12-olides.

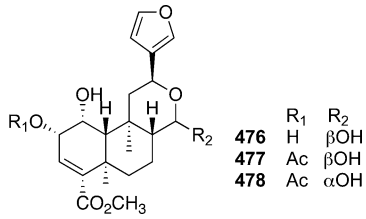


Figure 32. 12,17-Epoxyclerodanes.

Epling. The relative stereochemistry for **539** was determined by X-ray diffraction.[221] Investigation of the roots of *S. lavanduloides* gave a new neoclerodane diterpene, salvianduline D (**540**), containing a 2,6-dioxabicyclo[2.2.1]heptane structural moiety.[222] Spiroleucantholide (**541**), isolated from the aerial parts of *S. leucantha* CAV, was the first report of spiro-6/6 A/B ring diterpenoid derived from a neoclerodane skeleton. The structure was established by spectroscopic methods, including X-ray analysis.[209] Salvileucalin B (**542**), having an unprecedented rearranged neoclerodane skeleton, was isolated from the aerial parts of *S. leucantha* Cav. The absolute structure was elucidated by spectroscopic analysis, X-ray crystallographic analysis, and vibrational circular dichroism. **542** represents a novel neoclerodane, characterized by a tricyclo[3.2.1.0^{2,7}]octane substructure. This molecule exerted cytotoxic activity against A549 and HT-29 cells with IC_{50} values of 5.23 and 1.88 μg/mL, respectively.[223] **543**–**549** were seven rearranged neoclerodanes, isolated from genus *Salvia*, with a seven-membered ring A or a seven-membered ring B. Salviandulin E (**548**) was isolated from *S. leucantha* twice.[209,224] Dugesin A (**549**) was one example in this subgroup that was isolated from *S. dugesii*.[208] A possible biosynthetic pathway of these compounds was also proposed (Scheme 12).[183,208,209,213,221,224]

2.2.3. Pimaranes. Pimarane diterpenes belong to the tricyclic hydrophenanthrene nucleus diterpenoids group; biosyntheticaly it is closely related with labdane and is found in many different plant families.[225] Pimarane diterpenes

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

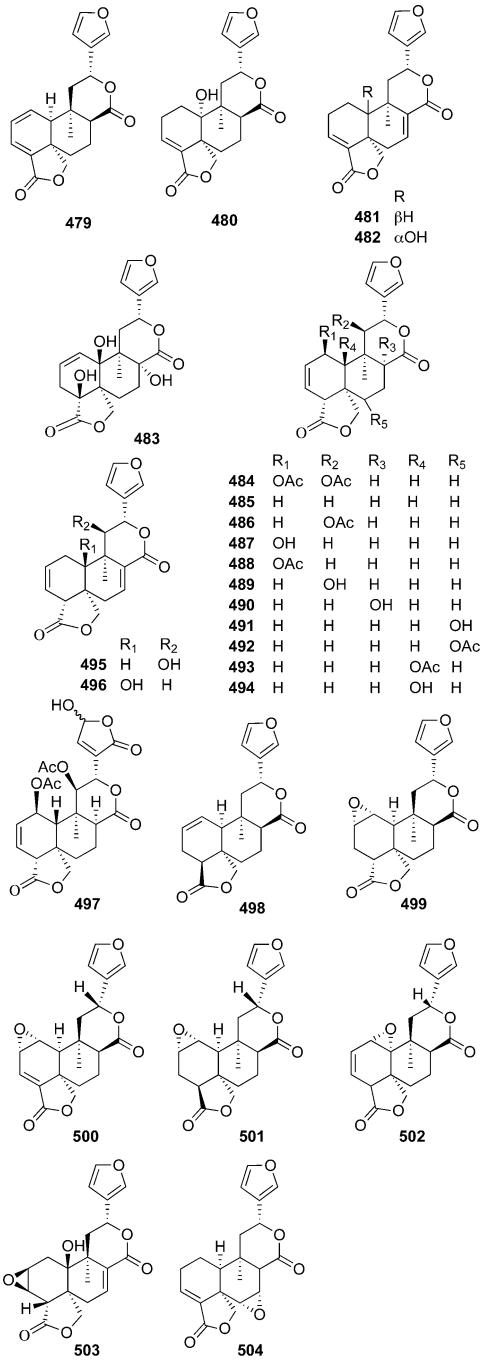


Figure 33. Clerodane-17,12:18,19-diolides.

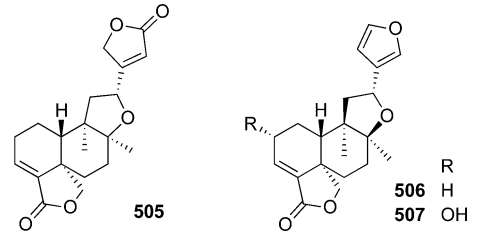


Figure 34. 8,12-Epoxyclerodan-18,19-olides.

comprised a smaller group of components of *Salvia* plants. Among the members of the genus *Salvia*, *S. parryi* is considered to be abundant in pimarane diterpenes.

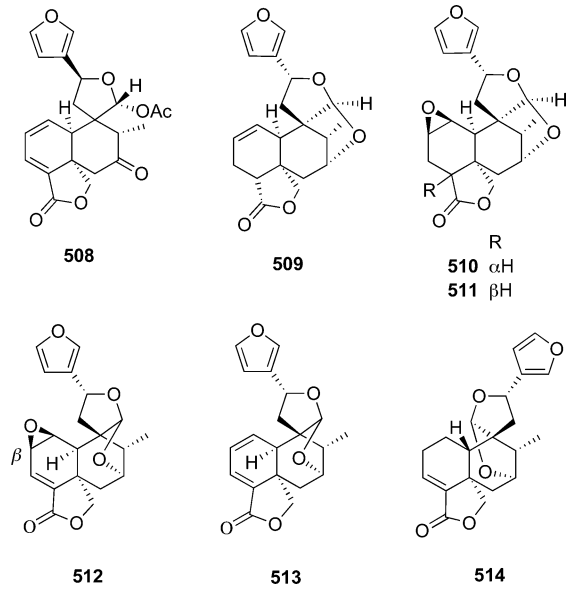


Figure 35. C-9 Spiroclerodanes.

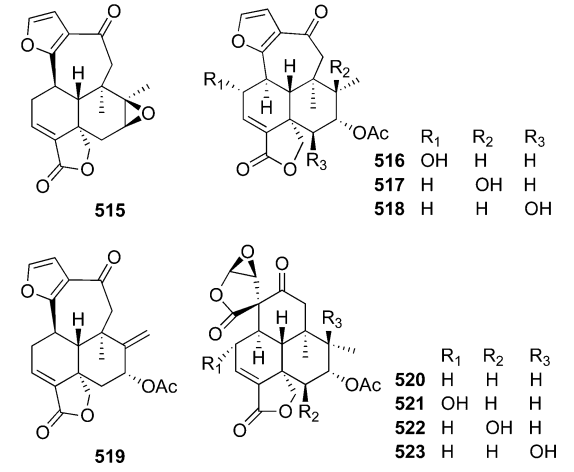
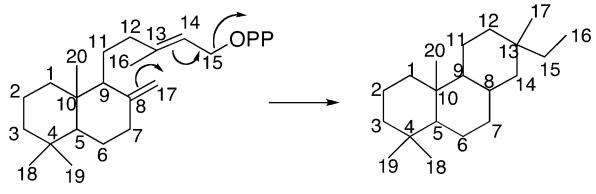


Figure 36. 1,16-Cycloclerodanes.



Twenty pimarane diterpenes (**550**−**569**) have been obtained from *Salvia* species. Six pimarane-type diterpenes (**550**−**552**, **562**, **567**, and **568**) were isolated from the acetone extract of roots of *S. parryi*. Parryin (**569**) represents the first example of a biogenetically new type of tricyclic 6/7/5-membered ring diterpene, isolated from the same species. Biogenetically, **569** might be generated by rearrangement of **550** (Scheme 13).[5] Sandaracopimaric acid (**553**) was a pimarane diterpene that was obtained from *S. fulgens*.[183] Investigation of *S. microphylla* gave four pimarane diterpenes, **554**−**557**.[183] **560**, **561**, **563**, and **564** were four examples in this subgroup that were isolated from *S. greggii*.[186,226] Of them, **560** was also obtained from *S. wiedemannii* by Topçu and Ulubelen in 1990.[65] The next year, the other pimarane-type diterpene 14-oxo-pimaric acid (**565**) was isolated by them from the same plant.[109]

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

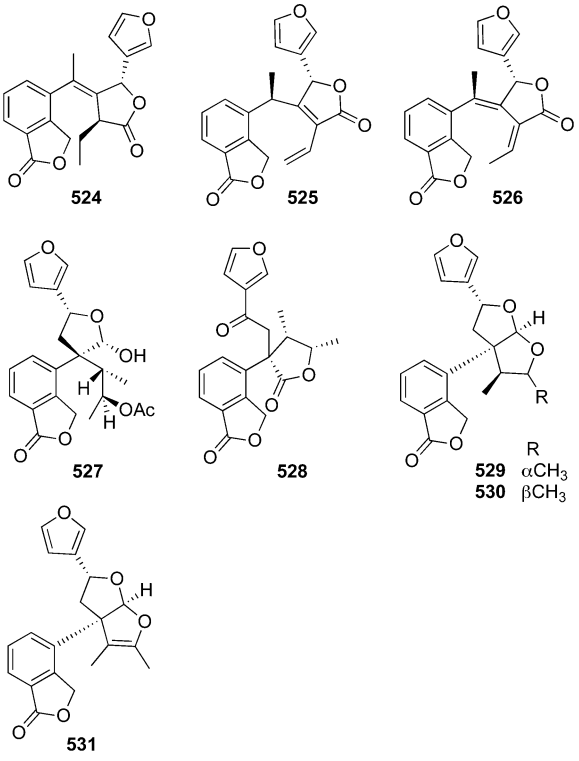


Figure 37. 5,6-Seco-clerodanes.

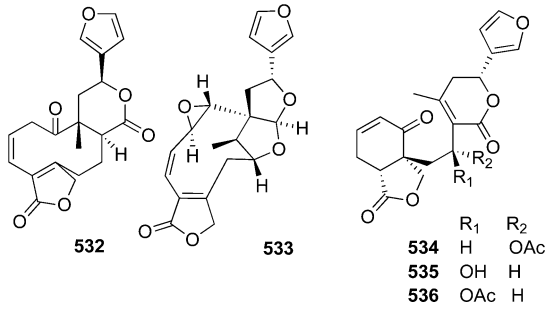


Figure 38. 5,10-Seco- and 9,10-seco-clerodanes.

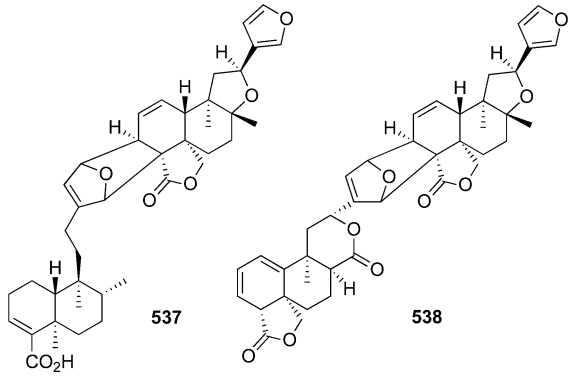


Figure 39. Diterpene dimers.

2.2.4. Labdanes. Labdane, belonging to the bicyclic diterpenoids group, comprises a decalin system and a C-6 ring, which may be open or closed with an oxygen atom, as in manoyl oxide and its derivatives. Labdane-type diterpenes have a widespread occurrence in nature and exhibit a broad spectrum of significant biological activities. In this subgroup, 18 labdane diterpenoids have been isolated from *Salvia* species.

570−579 were 10 labdane-type diterpenes, isolated from *S. eupatorium*, *S. sclarea*, and *S. officinalis*. Investigation of *S.*

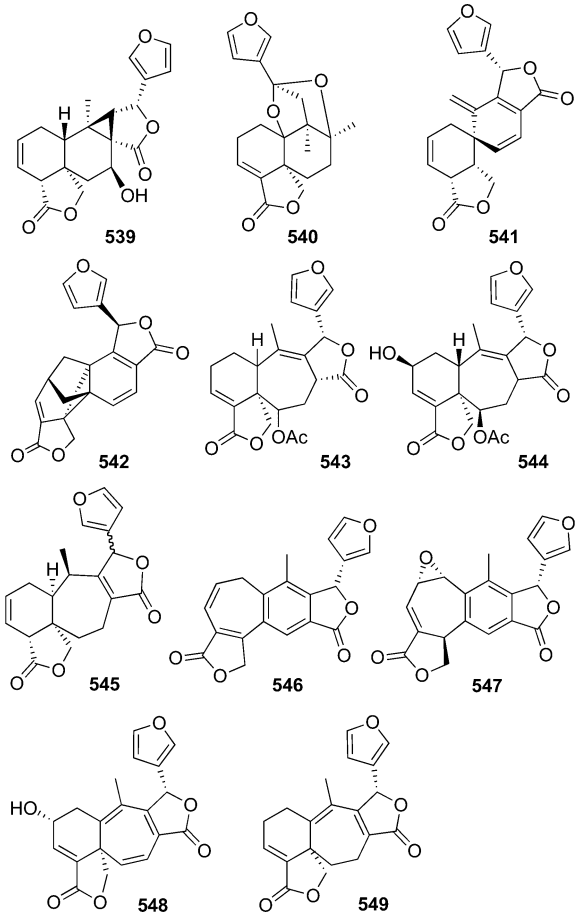
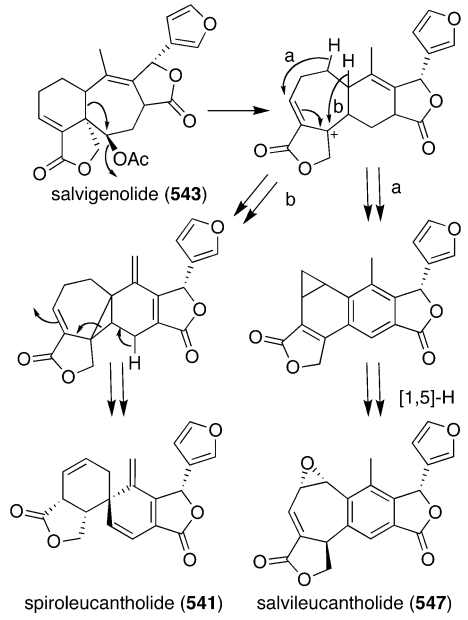


Figure 40. Other clerodane diterpenoids.

Scheme 12. Biogenetic Pathway Proposed from 543 to 541 and 547



dx.doi.org/10.1021/cr200058f | Chem. Rev. 2012, 112, 5967−6026

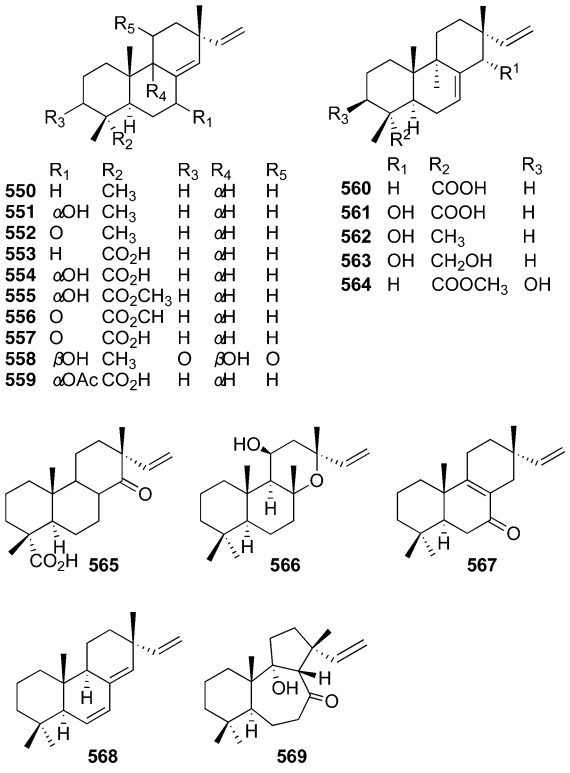
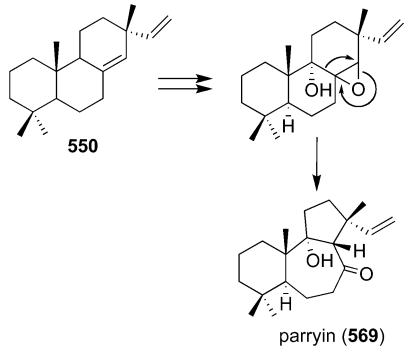
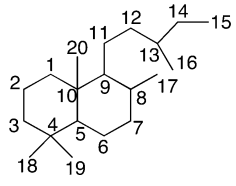


Figure 41. Pimaranes.

Scheme 13. Biogenetic Pathway Proposed Parryin (569)





eupatorium gave three labdane-type diterpenes, **570**−**572**. Sclareol (**573**) (from *S. sclarea*)[51] and manool (**574**) (from *S. officinalis*[172]and *S. sclarea*[51]) were found to be active against *Staphylococcus aureus*. Recently, four others (**576**−**579**) were obtained from the aerial parts of *S. palaestina* Bentham. Their structural elucidation was accomplished by extensive spectroscopic methods including 1D and 2D NMR experiments as well as ESIMS analysis and chemical analysis.[227] **580** was a trinorlabdane-type diterpene, isolated from the aerial parts of *S. palaestina* Bentham.[227] Compounds **581**−**584** were four tetranorlabdane-type diterpenes, obtained from aerial parts of *S. aethiopis*. Among them, **583** and **584** had a five-membered lactone ring.[228,229] 6α-Hydroxyambreinolide (**585**) was one

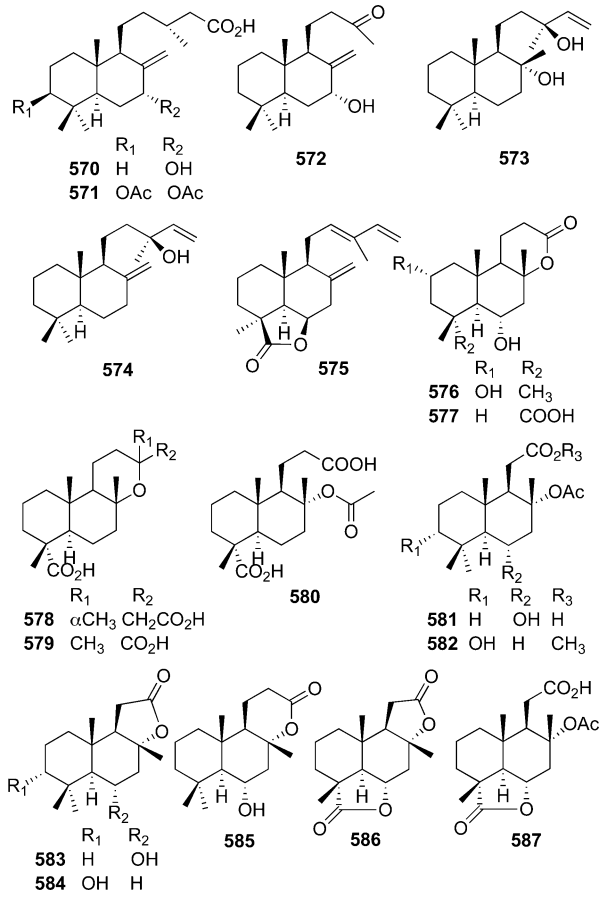


Figure 42. Labdanes.

example in this subgroup that was isolated from *S. yosgadensis*.[228]

2.2.5. Other Diterpenoids. 2,6-Dimethyl-10-(*p*-tolyl)-undeca-2,6-diene (**588**) was a diterpene isolated from the steam-distilled oil of *S. dorisiana*.[230] Salviolone (**589**) was

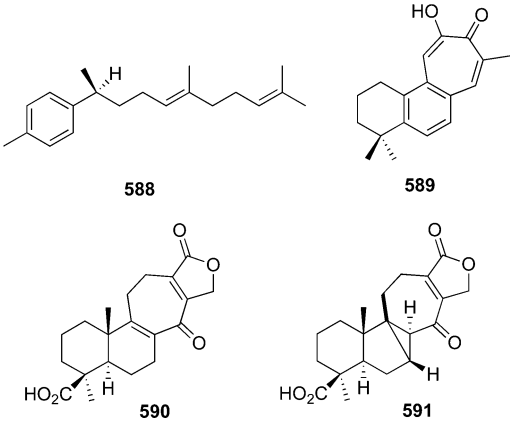


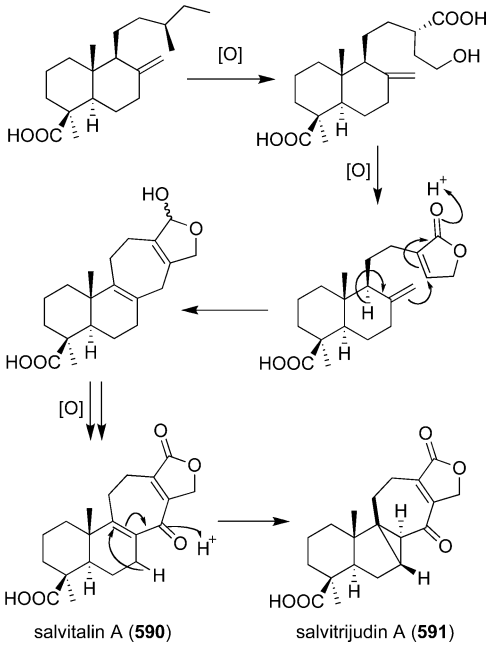
Figure 43. Other diterpenoids.

isolated from *S. miltiorrhiza* with a 6/6/7-membered ring systerm.[13,231] In 2010, salviatalin A (**590**) and salvitrijudin A (**591**), two diterpenes with novel skeletons derived biosynthetically from labdane skeleton, were isolated from the roots of *S. digitaloides*. Their structures were determined using 1D NMR, 2D NMR, and HRESI-MS spectroscopic analyses. **590** isolated by a bioassay-guided fractionation showed a potent inhibitory

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

effect on superoxide anion production in GMLP/CB-activated human neutrophils as well as other anti-inflammatory effects.[232] Salviatalin A (**590**) and salvitrijudin A (**591**) were also evaluated for cytotoxicity against KB, A549, HCT-8, and DU145 cell lines. Neither of them showed a significant cytotoxicity. As two novel rearranged labdane-type diterpenes with unique 6/6/7 and 6/5/3/7-membered ring carbon skeletons, the biosynthetic pathway to both compounds is of great interest. A plausible biosynthetic pathway is illustrated in Scheme 14.

Scheme 14. Biogenetic Pathway Proposed for Salviatalin A (590) and Salvitrijudin A (591)



2.3. Sesterterpenoids

2.3.1. C-23 Terpenoids. For this subgroup of C-23 terpenoids with a new basic skeleton was proposed the name of apianane; seven C23 terpenes with unprecedented novel skeletons have been discovered from genus *Salvia*. The structures have a 6/6/7-, a 6/6/8-, or a 6/6/5/5-ring skeleton,

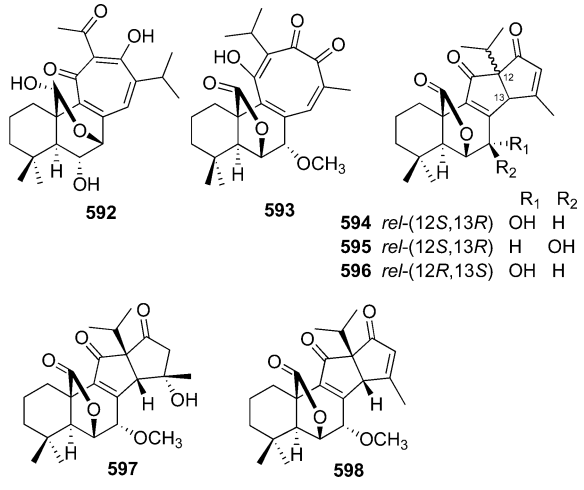
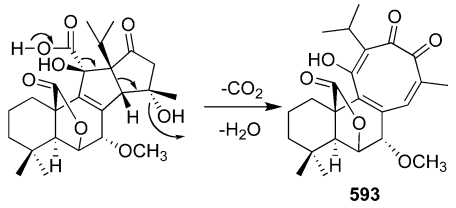


Figure 44. C-23 terpenoids.

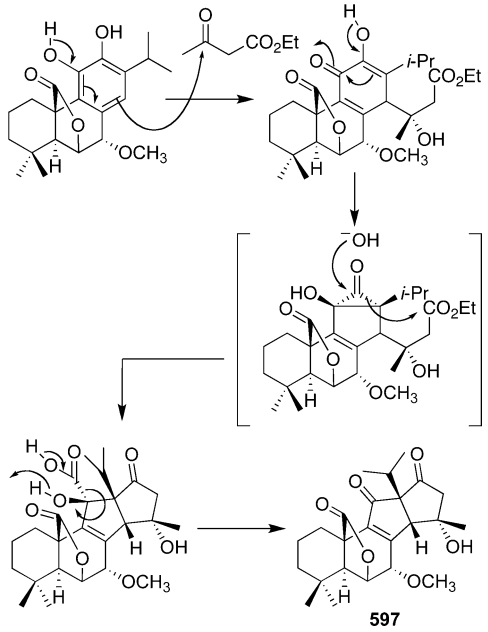
with a lactone between C-6 and C-22 (except **592**). Among them, three apianane terpenoids, rel-(5*S*,6*S*,7*S*,10*R*,12*S*,13*R*)-7-hydroxy-11,16-dioxoapiana-8,14-dien-22,6-olide (**594**), rel-(5*S*,6*S*,7*R*,10*R*,12*S*,13*R*)-7-hydroxy-11,16-dioxoapiana-8,14-dien-22,6-olide (**595**), and rel-(5*S*,6*S*,7*S*,10*R*,12*R*,13*S*)-7-hydroxy-11,16-dioxoapiana-8,14-dien-22,6-olide (**596**), were isolated from the leaves of *S. officinalis*.[233] Przewalskin A (**592**), a novel C-23 terpenoid with a 6/6/7-carbon ring skeleton, was isolated from *S. przewalskii*. Its structure was determined by comprehensive 1D NMR, 2D NMR, and MS spectroscopic analysis. **592** showed modest anti-HIV-1 activity with EC_{50} = 41 μg/mL.[234] A new C-23 terpenoid, 13,14-dioxo-11-hydroxy-7-methoxyhassane-8,11,15-trien-22,6-olide (**593**), was isolated from the aerial parts of *S. apiana* Jeps. A possible common biosynthetic origin of **593** is reported (Scheme 15).[235] Two

Scheme 15. Biogenetic Pathway Proposed for 593



new C-23 terpenoids, 14-hydroxy-7-methoxy-11,16-dioxoapian-8-en-22,6-olide (**597**) and 7-methoxy-11,16-dixooapian-8,14-dien-22,6-olide (**598**), were isolated from the same plant. The structure of **598** was confirmed by X-ray analysis. **597** could be biogenetically derived from an abietanic diterpene as indicated in Scheme 16.[236]

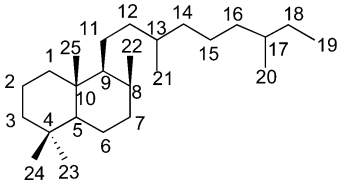
Scheme 16. Biogenetic Pathway Proposed for 597



2.3.2. C-25 Terpenoids. Sesterterpenes usually come from the aerial parts of *S.* spp. Salvileucolide methyl ester (**610**), which was isolated as the major constituent from aerial parts of *S. hypoleuca*[237] and *S. sahendica*,[238] both species that are endemic to Iran. The absolute configuration of the sesterterpenoid **610** was established by X-ray single diffraction

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

analysis, and the configuration at C-16 was determined to be *R*.[239] **605**−**607** were salvileucolide methyl ester derivatives that were isolated from the same plant with a hydroperoxide group.[240]



Investigation of *S. yosgadensis* gave five 19,20-dinorsesterterpenes, yosgadensonol (**599**), 13-*epi*-yosgadensonol (**600**), yosgadensolide A (**603**), **604**, and yosgadensolide B (**615**), consisting of a partial structure of manoyl oxide and differing in the functionality at C-13.[228,241] 6-Dehydroxyyosgadensonol (**601**) and 6-dehydroxy-13-*epi*-yosgadensonol (**602**) are epimeric dinorsesterterpenes that were isolated from *S. limbata*.[149]

Salvimirzacolide (**608**), salvisyriacolide (**609**), and **614** were three examples in this subgroup that were isolated from *S. mirzayanii*,[242] *S. syriaca*,[243] and *S. hypoleuca*,[240] respectively. The phytochemical study of *S. palaestina* aerial parts led to the isolation of three new sesterterpenes (**611**−**613**).[227] Another two 19,20-dinorsesterterpenes isolated were 3-*epi*-salviaethiopisolide (**616**) and salviaethiopisolide (**617**), which occur in *S. aethiopis* collected from Salamanca of Spain.[229] The aerial parts fractions of *S. hypoleuca* afforded six sesterterpene lactones, **618**−**623**, with a lactone ring between C-4 and C-6.[237,240]

2.4. Triterpenoids and Steroids

A total of 74 triterpenoids and steroids have been found in *Salvia* species since 1976. (Table 3) According to their structure, this group is further classified into six subgroups: ursane-type triterpenoids, oleanane-type triterpenoids, lupane-type triterpenoids, dammarane triterpenoids, steroids, and other triterpenoids.

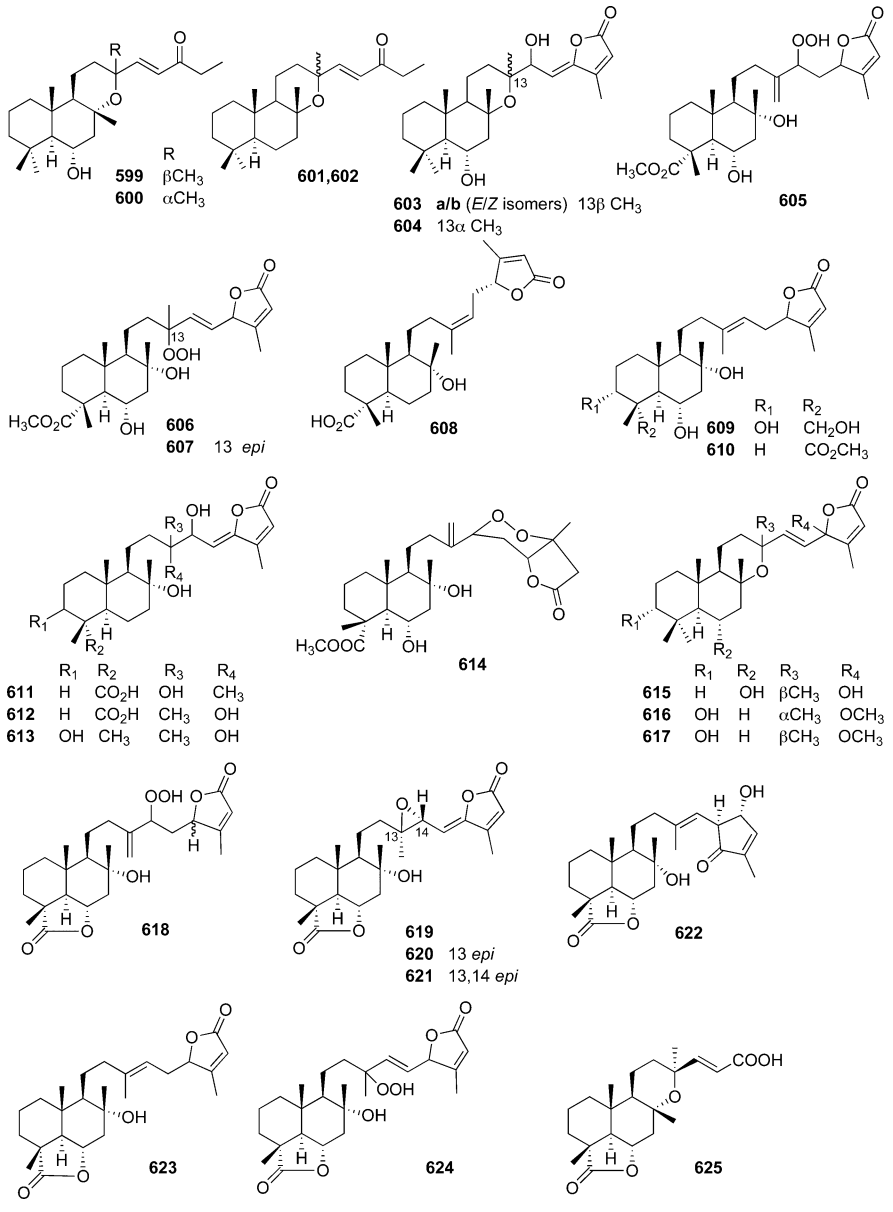


Figure 45. C-25 terpenoids.

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Table 3. Sesterterpenes 592−625

no.	name	plant	ref
592	przewalskin A	*S. przewalskii*	234
593	13,14-dioxo-11-hydroxy-7-methoxy-hassane-8,11,15-trien-22,6-olide	*S. apiana*	235
594	rel-(5*S*,6*S*,7*S*,10*R*,12*S*,13*R*)-7-hydroxy-11,16-dioxoapiana-8,14-dien-22,6-olide	*S. officinalis*	233
595	rel-(5*S*,6*S*,7*R*,10*R*,12*S*,13*R*)-7-hydroxy-11,16-dioxoapiana-8,14-dien-22,6-olide	*S. officinalis*	233
596	rel-(5*S*,6*S*,7*S*,10*R*,12*R*,13*S*)-7-hydroxy-11,16-dioxoapiana-8,14-dien-22,6-olide	*S. officinalis*	233
597	14-hydroxy-7-methoxy-11,16-dioxoapian-8-en-22,6-olide	*S. apiana*	236
598	7-methoxy-11,16-dioxoapian-8,14-dien-22,6-olide	*S. apiana*	236
599	yosgadensonol	*S. yosgadensis*	228
600	13-*epi*-yosgadensonol	*S. yosgadensis*	228
601	6-dehydroxyyosgadensonol	*S. limbata*	149
602	6-dehydroxy-13-*epi*-yosgadensonol	*S. limbata*	149
603	6*α*,14-dihydroxymanoyloxide-15,17-dien-16,19-olide (=yosgadensolide A)	*S. yosgadensis*	241
604	6*α*,14-dihydroxy-13-*epi*-manoyloxide-15,17-dien-16,19-olide	*S. yosgadensis*	241
605	salvileucolide methyl ester derivative	*S. hypoleuca*	240
606	salvileucolide methyl ester derivative	*S. hypoleuca*	240
607	salvileucolide methyl ester derivative	*S. hypoleuca*	240
608	salvimirzacolide	*S. mirzayanii*	242
609	salvisyriacolide	*S. syriaca*	243
610	salvileucolide methyl ester	*S. hypoleuca*	237
		S. sahendica	238, 239
611	8*α*,13,14-threo-trihydroxylabd-15,17-dien-16,19-olide-23-oic acid	*S. palaestina*	227
612	8*α*,13,14-erythro-trihydroxylabd-15,17-dien-16,19-olide-23-oic acid	*S. palaestina*	227
613	3*α*,8*α*,13,14-erythro-tetrahydroxylabd-15,17-dien-16,19-olide	*S. palaestina*	227
614	cyclic peroxide	*S. hypoleuca*	240
615	6*α*,16-dihydroxymanoyloxide-14,17-dien-16,19-olide (= yosgadensolide B)	*S. yosgadensis*	241
616	3-*epi*-salviaethiopisolide	*S. aethiopis*	229
617	salviaethiopisolide	*S. aethiopis*	229
618	14-hydroperoxy-13(21)-dehydro-13,14-dihydrosalvileucolide-6,23-lactone	*S. hypoleuca*	240
619	15,16-dehydrosalvileucolide-6,23-lactone-*trans*-epoxide	*S. hypoleuca*	240
620	15,16-dehydrosalvileucolide-6,23-lactone-*cis*-epoxide	*S. hypoleuca*	240
621	13,14-bis-*epi*-*trans*-epoxide	*S. hypoleuca*	240
622	salvileucolidone	*S. hypoleuca*	240
623	salvileucolide-6,23-lactone	*S. hypoleuca*	237
624	8-hydroxy-13-hydroperoxylabd-14,17-dien-19,16:23,6*α*-diolide	*S. sahendica*	429
625	17,18,19,20-tetranor-13-*epi*-manoyloxide-14-en-16-oic acid-23,6*α*-olide	*S. sahendica*	429

2.4.1. Ursanes. Oleanolic acid (**627**) and salvistamineol (**628**) were isolated from *S. officinalis* and *S. staminea*, respectively.[244,245] Six new ursane-type triterpenoids (**629**−**633** and **646**) were isolated from the roots of *S. kronenburgii*.[246,247] From the aerial parts of *S. argentea*, four new ursene triterpenoids (**634**−**637**) were obtained.[248] 3-Oxours-12-ene-1*β*,11*α*-diol (**638**) (from *S. haenkei*),[190] 3-*epi*-ursolic acid (**639**) (from *S. lanata*),[249] santolinoic acid (**640**) (from *S. santolinifolia*),[250] and salvin A (**641**) (from *S. santolinifolia*)[163] were four examples in this subgroup. In 2009, a new ursane-type triterpenoid (**649**) was isolated from the aerial parts of *S. chinensis*.[251] **648** and **650** were two triterpenoids isolated from *S. hierosolymitana*. Of them, **650** had a *p*-coumaroyl group at C-23.[252]

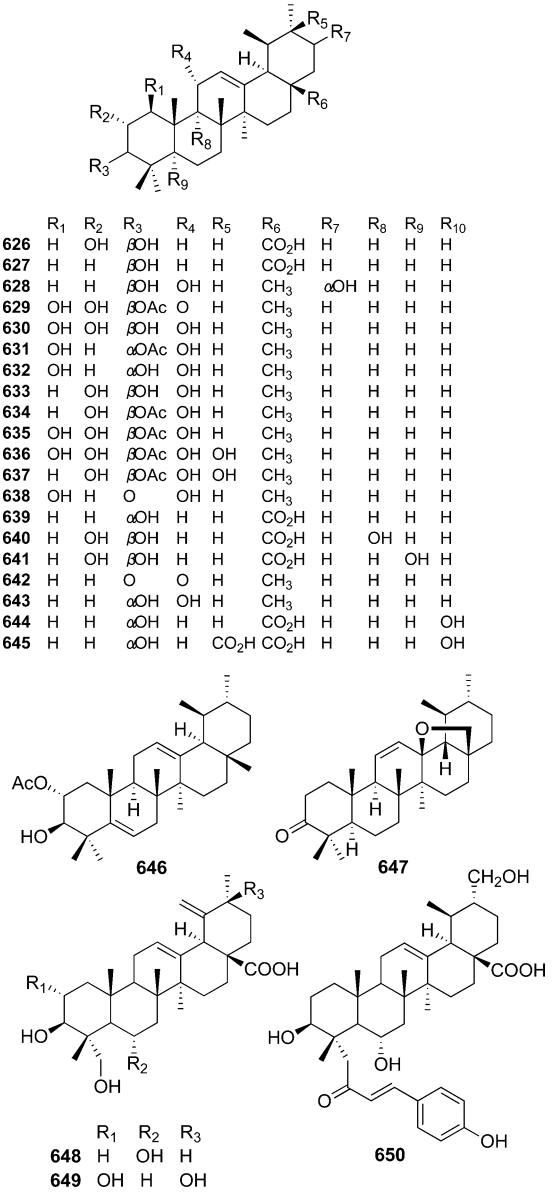


Figure 46. Ursanes.

2.4.2. Oleananes. **651** was an oleanane-type triterpenoid isolated from *S. hierosolymitana*.[252] **652**−**656** were five oleanane-type triterpenoids, all with a double bond between C-12 and C-13, isolated from four *Salvia* species: *S. kronenburgii*, *S. argentea*, *S. virgata*, and *S. santolinifolia*.[163,247,248,253] **658**−**660** were three oleanane-type triterpenoids, with two double bonds between C-12 and C-13, C-4 and C-23, isolated from three *Salvia* species: *S. hierosolymitana*, *S. carduacea*, and *S. palaestina*.[227,252,254] Przewanoic acids A and B (**662** and **661**), isolated from *S. przewalskii*, have a 12,13-cyclo group.[255] Investigation of *S. lanigera* gave an oleanane-type triterpene (**667**), with a lactone between C-28 and C-13.[77]

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Table 4. Triterpenoids 626−699

no.	name	plant	ref	no.	name	plant	ref
626	maslinic acid (= 2α-hydroxyoleanolic acid)	*S. canariensis*	430	**662**	przewanoic acid A	*S. przewalskii*	255
627	oleanolic acid	*S. officinalis*	244	**663**	1β,11α-dihydroxyolean-18-en-3-one	*S. deserta*	258
		S. amplexicaulis	431	**664**	23-hydroxygermanicone	*S. pomifera*	70
		S. ballotaeflora	432	**665**	olean-13(18)-ene-2α,3β,11α-triol	*S. pinnata*	371
		S. longystyla	433	**666**	olean-(13)18-ene-2β,3β-diol	*S. horminum*	378
628	3β,11α,21α-trihydroxyurs-12-ene (= salvistamineol)	*S. staminea*	245	**667**	3β-hydroxyoleanan-13β→28 lactone	*S. lanigera*	77
629	1β,2α-dihydroxy-3β-acetoxy-11-oxours-12-ene	*S. kronenburgii*	246	**668**	2α,20β-dihydroxy-3β-acetoxyurs-9(11),12-diene	*S. kronenburgii*	246
630	1β,2α,3β,11α-tetrahydroxyurs-12-ene	*S. kronenburgii*	247	**669**	1β,2α-dihydroxy-3β-acetoxyurs-9(11),12-diene	*S. kronenburgii*	246
631	3α-acetoxyurs-12-ene-1β,11α-diol	*S. kronenburgii*	247	**670**	deacetyloxysessein-7α-(3β-hydroxyolean-12-en-28-oate) (= reglin)	*S. regla*	125
632	1β,3α,11α-trihydroxyurs-12-ene	*S. kronenburgii*	247	**671**	lupeol	*S. palaestina*	140
633	2α,3β,11α-trihydroxyurs-12-ene	*S. kronenburgii*	247	**672**	lup-20(29)-ene-2α,3β-diol	*S. palaestina*	140
634	3β-acetoxy-urs-12-ene-2α,11α-dial	*S. argentea*	248	**673**	lup-20(29)-ene-3β,23-diol	*S. palaestina*	140
635	3β-acetoxy-urs-12-ene-1β,2α,11α-triol	*S. argentea*	248	**674**	2α-methoxylup-20(29)-en-3β-ol	*S. palaestina*	140
636	3β-acetoxy-urs-12-ene-1β,2α,11α,20β-tetraol	*S. argentea*	248	**675**	palestinol	*S. triloba*	344
637	3β-acetoxy-urs-12-ene-2α,11α,20β-triol	*S. argentea*	248	**676**	7β-hydroxylup-20(29)-en-3-one	*S. pratensis*	363
638	3-oxours-12-ene-1β,11α-diol	*S. haenkei*	190	**677**	1β,11α-dihydroxylup-20(29)-en-3-one	*S. deserta*	258
639	3-*epi*-ursolic acid	*S. lanata*	249	**678**	(1β,3β)-lup-20(29)-ene-1,3,30-triol	*S. sclareoides*	373
640	santolinoic acid	*S. santolinifolia*	250	**679**	3α-*O*-acetyl-20(29)-lupen-2α-ol	*S. trijuga*	45
641	2α,3β,5α-trihydroxyurs-12-en-28-oic acid (= salvin A)	*S. santolinifolia*	163	**680**	1β,11α,20-trihydroxylupan-3-one	*S. deserta*	258
642	3,11-dioxoursun-12-ene	*S. mellifera*	434	**681**	lupane-3β,11α,20-triol	*S. phlomoides*	257
643	urs-12-ene-3α,11α-diol	*S. willeana*	435	**682**	3β-acetoxylupane-11α,20-diol	*S. phlomoides*	257
644	3α,24-dihydroxyolean-12-en-28-oic acid	*S. nicolsoniana*	436	**683**	3-oxolupane-11α,20-diol	*S. phlomoides*	257
645	3α,24-dihydroxyolean-12-en-28,30-dioic acid	*S. nicolsoniana*		**684**	monogynol A	*S. macrochlamys*	256
646	2α-acetoxyurs-5,12-diene-3β,11α-diol	*S. kronenburgii*	247	**685**	3α-hydroxy-20-oxo-30-norlupane	*S. nubicola*	276
647	3-oxo-13(28)-epoxyursan-11-ene	*S. mellifera*	434	**686**	3β-*O*-*trans*-*p*-coumaroylmonogynol A	*S. montbretii*	355
648	3β,6α,23-trihydroxyurs-12,19(29)-dien-28-oic acid	*S. hierosolymitana*	252	**687**	3β-*O*-*cis*-*p*-coumaroylmonogynol A	*S. montbretii*	355
649	2α,3β,20β,23-tetrahydroxyurs-12,19 (29)-dien-28-oic acid	*S. chinensis*	251	**688**	santolin B	*S. santolinifolia*	259
650	23-(trans-*p*-coumaroyloxy)-3β,6α,30-trihydroxyurs-12-en-28-oic acid	*S. hierosolymitana*	252	**689**	santolin A	*S. santolinifolia*	259
651	2α,3β-dihydroxyolean-28-oic acid	*S. hierosolymitana*	252	**690**	santolin C	*S. santolinifolia*	259
652	1β,2α,3β,11α-tetrahydroxyolean-12-ene	*S. kronenburgii*	247	**691**	20*S*,24*R*-epoxydammar-12β,25-diol-3-one	*S. bicolor*	369
653	3β-acetoxyolean-l2-ene-2α,11α-dial	*S. argentea*	248	**692**	7β,25-dihydroxy-(20*S*,24*R*)-epoxydammaran-3-one (= salvilymitone)	*S. hierosolymitana*	260
654	3β-acetoxyolean-12-ene-lβ,2α,11α-triol	*S. argentea*	248	**693**	(20*S*,24*R*)-epoxydammarane-3β,7α,25-triol (= salvilymitol)	*S. hierosolymitana*	260
655	3β-hydroxy-l-oxoolean-12-en-28-oic acid (= virgatic acid)	*S. virgata*	253	**694**	salvadiol	*S. bucharica*	261
656	3α,6α,24-trihydroxyolean-12-en-28-oic acid (= salvin B)	*S. santolinifolia*	163	**695**	salvadione A	*S. bucharica*	262
657	salvinemorol	*S. nemorosa*	402	**696**	salvadione B	*S. bucharica*	262
658	24-nor-2α,3β-dihydroxyolean-4(23),12-ene	*S. hierosolymitana*	252	**697**	brassicasterone	*S. multicaulis*	80
659	2*R*,3*R*-dihydroxy-24-nor-4(23),12-oleanadien-28-oic acid	*S. carduacea*	254	**698**	1-oxo-7α-hydroxysitosterol	*S. glutinosa*	264
660	2α,3α,16α-trihydroxy-24-nor-4(23),12-oleandien-28-oic acid	*S. palaestina*	227	**699**	stigmast-4-en-3-one	*S. amplexicaulis*	263
661	przewanoic acid B	*S. przewalskii*	255				

Reglin (**670**) was an ester consisting of a abietane quinone diterpene and triterpenoid acyl moiety.[125]

2.4.3. Lupanes. From an acetone extract of the roots of *S. palaestina*, four lupane-type triterpenes (**671**−**674**) were obtained, with a double bond between C-20 and C-29.[140] **680**−**684**, **686**, and **687** were other seven lupane-type triterpenes from four *Salvia* species: *S. deserta*, *S. phlomoides*, *S. macrochlamys*, and *S. montbretii*, with a hydroxy group at C-20.[256−258]

2.4.4. Dammaranes. Three new 20,24-epoxydammarane triterpenes, santolins A (**689**), B (**688**), and C (**690**), were isolated from the AcOEt-soluble fraction of the MeOH extract of *S. santolinifolia*.[259] Salvilymitone (**692**) and salvilymitol (**693**), two new triterpenoids, were obtained from *S. hierosolymitana*.[260]

2.4.5. Other Triterpenoids. Ahmad and co-workers published two papers on *S. bucharica* in 1999, reporting the isolation and identification of salvadiol (**694**) and salvadiones A

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

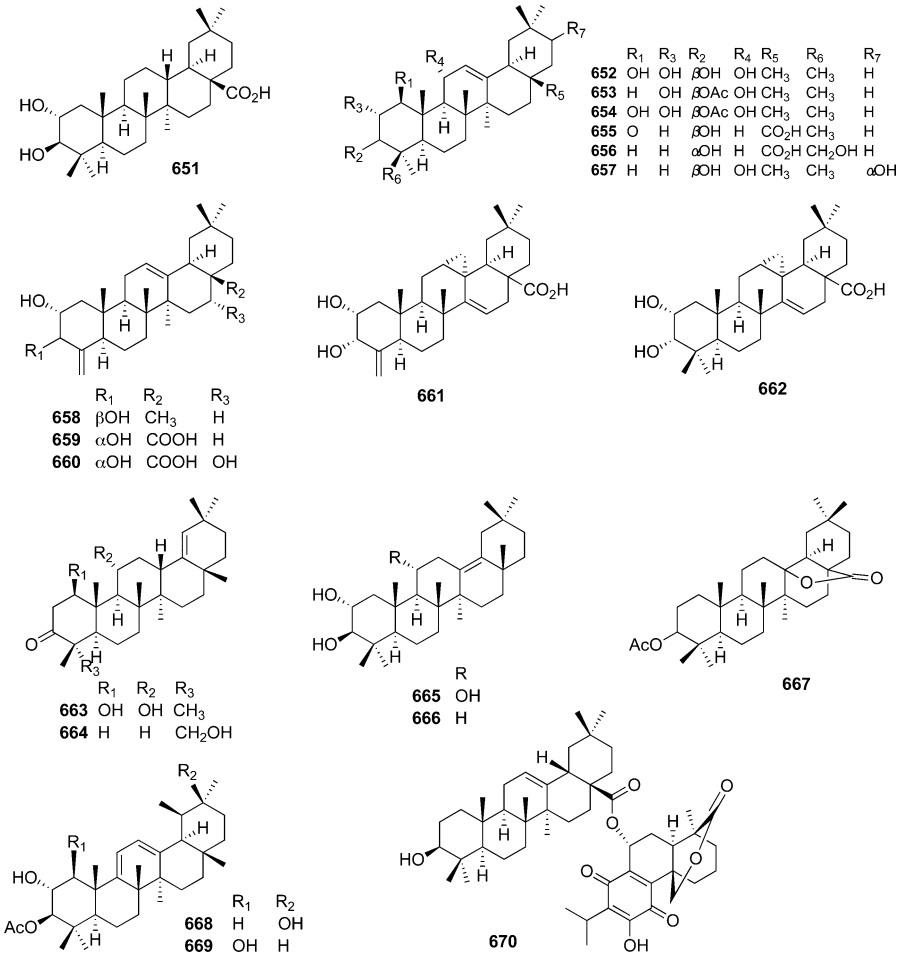


Figure 47. Oleans.

(**695**) and B (**696**). **694** has a novel carbon skeleton that is supposed to be derived from icetexone precursor through the addition of epoxy triene, which could be formed by autoxidation of myrcene. The coupling of both units can be rationalized in terms of a Diels−Alder-type reaction as shown in Scheme 17.[261,262]

2.4.6. Steroids. Brassicasterone (**697**), 1-oxo-7α-hydroxysitosterol (**698**), and stigmast-4-en-3-one (**699**) were three steroids isolated from *S. multicaulis*, *S. glutinosa*, and *S. amplexicaulis*, respectively.[80,263,264]

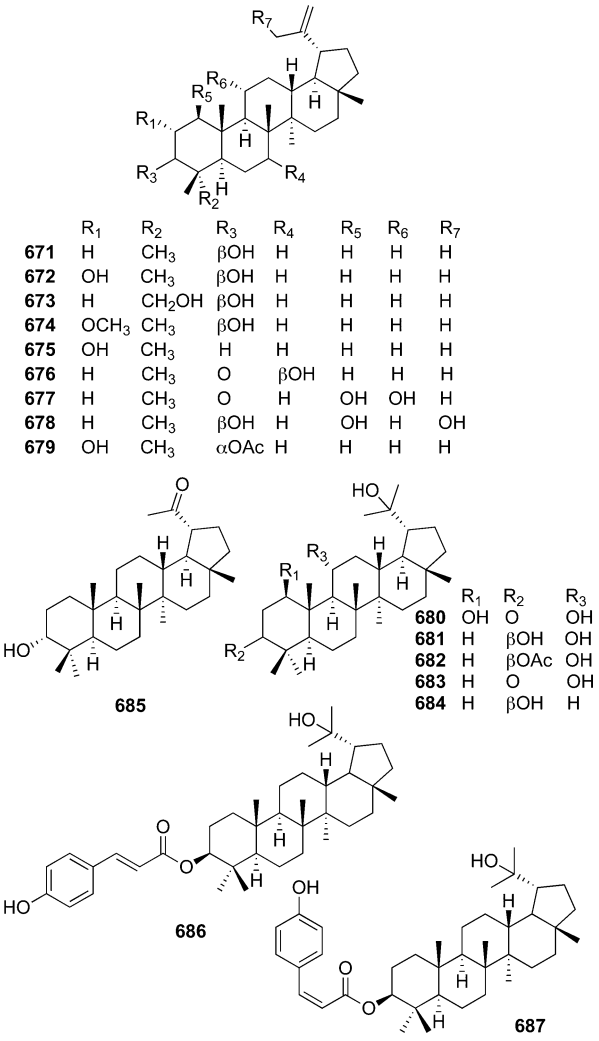
2.5. Polyphenols

There are two major groups of active constituents in *Salvia* spp: besides the previously mentioned lipophilic component terpenoids, another group of metabolites are water-soluble polyphenolics mainly including salvianolic acid B, danshensu, protocatechualdehyde, and so on. According to structures of the polyphenols, this group is further classified into two subgroups: phenolic acids and flavonoids (Table 5).

2.5.1. Phenolic Acids. Since the 1980s, Chinese and Japanese scientists have studied the water-soluble constituents from Danshen and isolated more than 20 phenolic acids from this plant. These phenolic acids include caffeic acid monomers and oligomers, and the latter are also called depsides or salvianolic acids. The structures of these phenolic acids are summarized in Figure 52. Phenolic acids play an important role in the prevention of human diseases. The most prominent effects of the phenolic acids in Tanshen are antioxidant, antiblood coagulation, and cell protection.[37]

Przewalskinone B (**700**) was a new anthraquinone that was isolated from *S. przewalskii*.[265] The polar phenolic acids constitute the major part of the water-soluble components of the *Salvia* species. **702** and **707** were benzene derivatives, which were isolated from *S. moorcroftiana*.[25,266,267] **703** and **704** were two phenolic esters from the acetone extract of *S. microphylla*.[55] From the rhizome of *S. miltiorrhiza*, a new cyclic phenyllactamide (**701**) was isolated.[268] The other compound **705** was isolated from the same plant.[61] Three new phenolic glycosides **708**, **709**, and **714** were isolated from *S. officinalis*.[269,270] Eugenylglucoside (**706**) was a glycosidic bound flavor precursor that was isolated from the same plant.[271] Further investigation of the same plant gave another six compounds: **710**−**713**,[269,272] **719**, and **720**.[273] In 2009, phytochemical investigations of the EtOAc-soluble fraction of the whole plants of *S. plebeia* led to the isolation of a new phenylbutanone glucoside, salviaplebeiaside (**726**).[274] Further investigation of this plant, salvianolic acid L (**727**), a rosmarinic acid dimer, was isolated. **727** was a significantly better antioxidant activity than trolox, caffeic acid, and rosmarinic acid, with the latter being the major phenolic antioxidant in this plant.[275] The identity of **727** was corroborated by acid hydrolysis (Scheme 18), which yielded two products, **774** and its 3-monoester (**775**), together with the known **776**. The structures of compounds **774** and **775** were fully elucidated and assigned using 2D NMR techniques.

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026



	R_1	R_2	R_3	R_4	R_5	R_6	R_7
671	H	CH_3	βOH	H	H	H	H
672	OH	CH_3	βOH	H	H	H	H
673	H	CH_2OH	βOH	H	H	H	H
674	OCH_3	CH_3	βOH	H	H	H	H
675	OH	CH_3	H	H	H	H	H
676	H	CH_3	O	βOH	H	H	H
677	H	CH_3	O	H	OH	OH	H
678	H	CH_3	βOH	H	OH	H	OH
679	OH	CH_3	αOAc	H	H	H	H

	R_1	R_2	R_3
680	OH	O	OH
681	H	βOH	OH
682	H	βOAc	OH
683	H	O	OH
684	H	βOH	H

Figure 48. Lupanes.

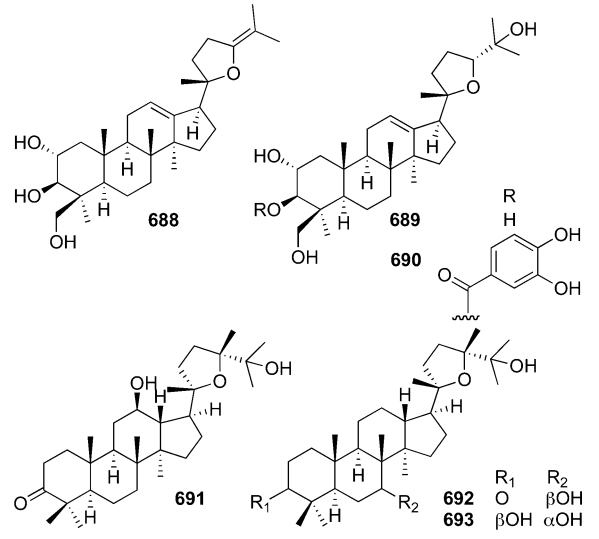


Figure 49. Dammaranes.

2.5.2. Flavonoids. A new flavanone, nubatin (**737**), has been isolated from *S. nubicola* collected from Quetta, Pakistan.[276] **738**−**745** were six flavonoids that were isolated and identified from *S. officinalis*.[140,269,277] **746** and **747**, two

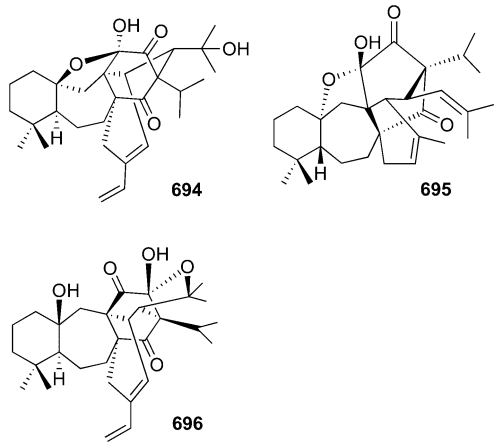
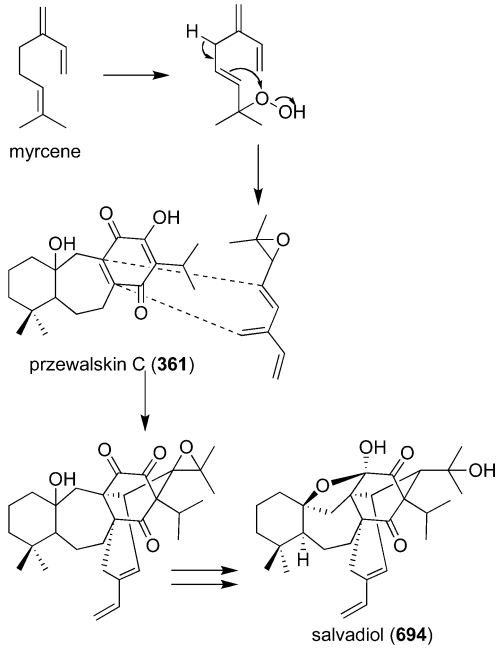


Figure 50. Other triterpenoids.

Scheme 17. Biogenetic Pathway Proposed for Salvadiol (646)



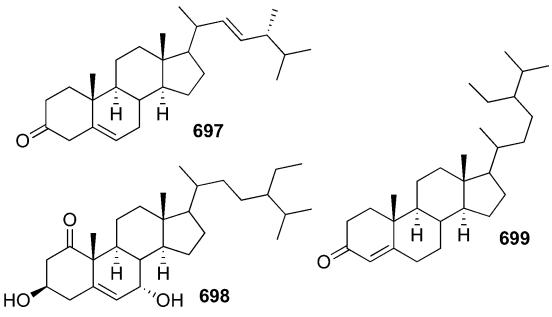


Figure 51. Steroids.

new flavone glycosides with an unusual interglycosidic linkage, have been isolated from the petals of *S. uliginosa*.[9] **748** was a new anthocyanin from the same plant that constituted the anthocyanin component of the pigment responsible for blue flower color in the same plant.[278] Zahid and co-workers published three papers on *S. moorcroftiana* during 2001−2003,

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Table 5. Polyphenols and Others 700−791

no.	name	plant	ref
700	przewalskinone B	*S. przewalskii*	265
701	2,10,11-trihydroxy-8-methoxy-1,6,7,8-tetrahydro-2H-benzo[*e*]azecine-3,5-dione	*S. miltiorrhiza*	268
702	nonyl 4-hydroxybenzoate	*S. moorcroftiana*	25
703	eicosaheptanoic acid 2-(*p*-hydroxyphenyl)ethyl ester	*S. microphylla*	55
704	hexacosylferulate	*S. microphylla*	55
705	4-(1-hydroxy-5-methylnaphthalen-2-yl)-2-methyl-4-oxobutyl acetate (= salvianonol)	*S. miltiorrhiza*	61
706	eugenylglucoside	*S. officinalis*	271
707	4-hydroxy-2-isopropyl-5-methylphenyl *O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranoside	*S. moorcroftiana*	25
708	*trans*-*p*-coumaric acid 4-*O*-(2′-*O*-β-D-apiofuranosyl)-β-D-glucopyranoside	*S. officinalis*	269
709	*cis*-*p*-coumaric acid 4-*O*-(2′-*O*-β-D-apiofuranosyl)-β-D-glucopyranoside	*S. officinalis*	269
710	4-hydroxyacetophenone 4-*O*-(6′-*O*-β-D-apiofuranosyl)-β-D-glucopyranoside	*S. officinalis*	269
711	6-*O*-caffeoyl-β-D-fructofuranosyl-(2→1)-α-D-glucopyranoside	*S. officinalis*	272
712	1-*O*-caffeoyl-β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside	*S. officinalis*	272
713	1-*O*-*p*-hydroxybenzoyl-β-D-apiofuranosyl-(1→6)-β-D-glucopyranoside	*S. officinalis*	272
714	1-*O*-(2,3,4-trihydroxy-3-methyl)butyl-6-*O*-feruloyl-β-D-glucopyranoside	*S. officinalis*	270
715	octanol ester of *cis*-*O*-methyl caffeic acid dimer	*S. forskahlei*	79
716	octanol ester of *trans*-*O*-methyl caffeic acid dimer	*S. forskahlei*	79
717	4,4′-bisbenzoic acid heptyl ester	*S. multicaulis*	80
718	di(4,4′-hexyloxycarbonylphenyl) ether	*S. heldrichiana*	341
719	melitric acid A	*S. officinalis*	273
	salvianolic acid I	*S. cavaleriei*	437
720	methyl melitrate A	*S. officinalis*	273
721	salvianolic acid D	*S.miltiorrhiza*	438
722	salvianolic acid E	*S.miltiorrhiza*	438
723	prionitiside A	*S. prionitis*	376
724	prionitiside B	*S. prionitis*	376
725	salvianolic acid J	*S. flava*	377
726	4-{4-*O*-[6-(4-hydroxybenzoyl)-*O*-β-D-glucopyranosyl]-3-hydroxyphenyl}butan-2-one (= salviaplebeiaside)	*S. plebeia*	274
727	7,8-dihydroxy-2-(3,4-dihydroxyphenyl)-1,2-dihydronaphthalene-1,3-dicarboxylic acid di(1-carboxy-2-(3,4-dihydroxyphenyl))ethyl ester (= salvianolic acid L)	*S. officinalis*	275
728	lithospermate B	*S. miltiorrhiza*	346
729	salvianolic acid B	*S. miltiorrhiza*	351
730	dimethyl heptamethylsalvianolate B	*S. miltiorrhiza*	351
731	salvianolic acid C	*S. miltiorrhiza*	351
732	yunnaneic acid A	*S. yunnanensis*	353
733	yunnaneic acid B	*S. yunnanensis*	353
734	yunnaneic acid D	*S. yunnanensis*	353
735	yunnaneic acid C	*S. yunnanensis*	353
736	sagerinic acid	*S. officinalis*	439
737	nubatin	*S. nubicola*	276
738	6,8-di-*C*-glucosylapigenin (= vicenin-2)	*S. officinalis*	269, 277
739	luteolin 7-*O*-β-D-glucoside	*S. officinalis*	269, 277
		S. triloba	440
740	luteolin 7-*O*-glucuronide	*S. officinalis*	269, 277
741	luteolin 3′-*O*-glucuronide	*S. officinalis*	269, 277
742	6-hydroxyluteolin 7-*O*-glucoside	*S. officinalis*	269, 277
743	6-methoxyluteolin 7-*O*-glucoside	*S. tomentosa*	441
744	6-hydroxyluteolin 5-*O*-glucoside	*S. verticillata*	442
		S. tomentosa	443
745	6-hydroxyluteolin 7-*O*-glucuronide	*S. officinalis*	269
746	apigenin 7-*O*-β-D-glucopyranosyl-(1‴→4″)-β-D-glucopyranoside(apiyenin 7-*O*-cellobioside)	*S. uliginosa*	9
747	apigenin 7,4′-*O*,*O*-di-β-D-glucopyranoside (apigenin 7,4′-*O*,*O*-diglucoside)	*S. uliginosa*	9
748	delphinidin 3-*O*-[6-*O*-(*p*-coumaroyl)-β-D-glucopyranoside]-5-*O*-[4-*O*-acetyl-6-*O*-malonyl-β-D-glucopyranoside]	*S. uliginosa*	278
749	genkwanin 4′-*O*-α-L-arabinopyranosyl-(1→6)-β-D-galactopyranoside	*S. moorcroftiana*	267
750	genkwanin 4′-*O*-{α-L-rhamnopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→ 6)]-β-D-galactopyranoside}	*S. moorcroftiana*	267
751	genkwanin 4′-[*O*-α-L-rhamnopyranosyl-(1→2)-β-D-galactopyranoside]	*S. moorcroftiana*	25
752	genkwanin 4′-[*O*-α-L-arabinopyranosyl-(1→3)-α-L-rhamnopyranoside]	*S. moorcroftiana*	25
753	8-methoxygenistein 7-*O*-α-L-rhamnoside 4′-*O*-β-D-glucoside	*S. triloba*	279
754	salvionoside A	*S. nemorosa*	280
755	salvionoside B	*S. nemorosa*	280
756	salvionoside C	*S. nemorosa*	280

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Table 5. continued

no.	name	plant	ref
757	(6*R*,9R)-3-oxo-α-ionol β-D-glucopyranoside	*S. officinalis*	271
758	(6*R*,9S)-3-oxo-α-ionol β-D-glucopyranoside	*S. officinalis*	271
759	(*E*)-4-[5-(hydroxymethyl)furan-2-yl]but-3-en-2-one	*S. miltiorrhiza*	61
760	5-(methoxymethyl)-1*H*-pyrrole-2-carbaldehyde	*S. miltiorrhiza*	136
761	salvianolic acid N	*S. yunnanensis*	16
		S. chinensis	358
		S. prionitis	376
762	5-(3-hydroxypropyl)-7-methoxy-2-(3′-methoxy-4′-hydroxyphenyl)-3-benzo[*b*]furancarbaldehyde	*S. miltiorrhiza*	282
763	salvianolic acid A	*S. yunnanensis*	283
		S. flava	377
		S. prionitis	376
		S.miltiorrhiza	444
764	methyl salvianolate A	*S. yunnanensis*	283
765	ethyl salvianolate A	*S. yunnanensis*	283
766	lithospermic acid	*S. yunnanensis*	283
767	*cis*-lithospermic acid	*S. yunnanensis*	283
768	lignan secoisolariciresinol diester	*S. plebeia*	284, 285
769	secoisolariciresinol branched fatty diester	*S. plebeia*	285
770	sagecoumarin	*S. miltiorrhiza*	281
		S. officinalis	273
771	(1*S*,2*R*,4*R*)-1,8-epoxy-*p*-menthan-2-yl-*O*-β-D-glucopyranoside	*S. officinalis*	271
772	ethyl *O*-β-D-glucopyranosyl tuberonate	*S. officinalis*	270
773	loliolide	*S. divinorum*	445

reporting the isolation and identification of four new flavonoid glycosides **749**−**752**.[25,266,267] **753** was isolated from *S. triloba*.[279]

2.6. Others

From the aerial parts of *S. nemorosa*, three new megastigmane glycosides, salvionosides A−C (**754**−**756**), were isolated.[280] Investigation of *S. miltiorrhiza* gave two compounds: a 2,5-disubstituted furan (**759**) and a N-containing compound (**760**).[61,136] From the ethanol extract of Dalmatian sage (*S. officinalis*), three glycosidic bound flavor precursors (**771**, **757**, and **758**) were isolated. Of them, **771** had an epoxy ring between C-1 and C-8, and **757** and **758** were C-13 norisoprenoids.[271] Further investigation of the same plant gave another three compounds: sagecoumarin (**770**),[278] **772**,[270] and **774**.[275] Of them, **770** was also isolated from *S. miltiorrhiza*.[281] **762** was another example that was isolated from the same plant.[282] Zhang and co-workers published two papers on *S. yunnanensis* in 2008, reporting the isolation and identification of salvianolic acid N (**761**), salvianolic acid A (**763**), methyl salvianolate A (**764**), ethyl salvianolate A (**765**), lithospermic acid (**766**), and *cis*-lithospermic acid (**767**). Among them, **761** both inhibited HIV-1 IN in vitro and also reduced HIV-1 p24 antigen in MT-4 cell lines.[16,283] **768** and **769** were two lignan diesters from the seeds of *S. plebeia*.[284,285]

3. BIOLOGICAL ACTIVITIES

Salvia is a large and widespread genus with a diversity of ethnobotanical uses. Many plants from *Salvia* genus have been used for centuries, especially by the Chinese to promote longevity, especially Danshen (*Salvia miltiorrhiza*). Tanshinones are a group of natural products isolated from *S. miltiorrhiza* and other *S.* spp as early as in 1934. The major components of tanshinones are tanshinone IIA (**255**), 3-hydroxytanshinone, tanshinone IIB, and cryptotanshinone (**266**). These compounds have been observed to possess various pharmacological activities including antibacterial, antidermatophytic, antioxidant, anti-inflammatory, antineoplastic, and antiplatelet aggregation activities. In the past few decades, *Salvia* constituents have attracted considerable attention from medicinal chemists and clinicians as antimicrobial, antioxidant, antitumor, and antifeeding agents. Many natural *Salvia* constituents from different species, as well as hemisynthetic derivatives, have been tested by many research groups. A few have shown very potent activity against bacteria and tumor cell lines. Pharmacological effects of genus *Salvia* and active compounds are shown in Table 6.

3.1. Antimicrobial Activity

The antimicrobial activities of forskalinone (**53**) and the dimeric cinnamic acid ester (**715**), isolated from *S. forskahler*, were tested against standard bacterial strains and a yeast. The results showed that **53** was moderately active against *Staphylococcus epidermidis* (670 μg/mL) and slightly active against *Enterococcus faecalis* (168 μg/mL). Compound **715** showed a slight activity against *Candida albicans* (156 μg/mL).[79]Compounds **101** (from *S. africana-lutea*) exhibited MICs of 28 μM against *Mycobacterium tuberculosis*.[286] Potent antibacterial activity was exhibited by horminone (**162**) and 7-acetylhorminone (**163**) against *Staphylococcus aureus* ATCC 6538 P (6.5 and 10 μg/mL), *Staphylococcus epidermidis* ATCC 12226 (1.5 and 6 μg/mL), and *Bacillus subtilis* ATCC 6633 (1.5 and 3 μg/mL). Horminone was also found to be active against *Enterococcus faecalis* ATCC 29212 (14 μg/mL). *O*-Methylpisiferic acid (**49**) was active only against *Bacillus subtilis* ATCC 6633.[73] **210**, **235**, **358**, **255**, and **360**, respectively, were active against *S. aureus* (30−25, >45, 25, 3−2, and 25−20 μg/mL), *S. albus* (25, 35−30, >45, >60, and 20−15 μg/mL), and *B. subtilis* (6−4, >45, 10−8, 6−4, and 6−4 μg/mL).[287] 1-Oxoferruginol (**58**) showed activity against *B. subtilis* (15.6 μg/mL), *S. aureus* (15.6 μg/mL), and *S. epidermidis* (15.6 μg/mL) and a modest activity against *P. mirabilis* (>250 μg/mL); microstegiol had a little activity against *B. subtilis* (>250 μg/mL).[84] Sclareol showed high activity against *Staphylococcus aureus* (15.6 μg/

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

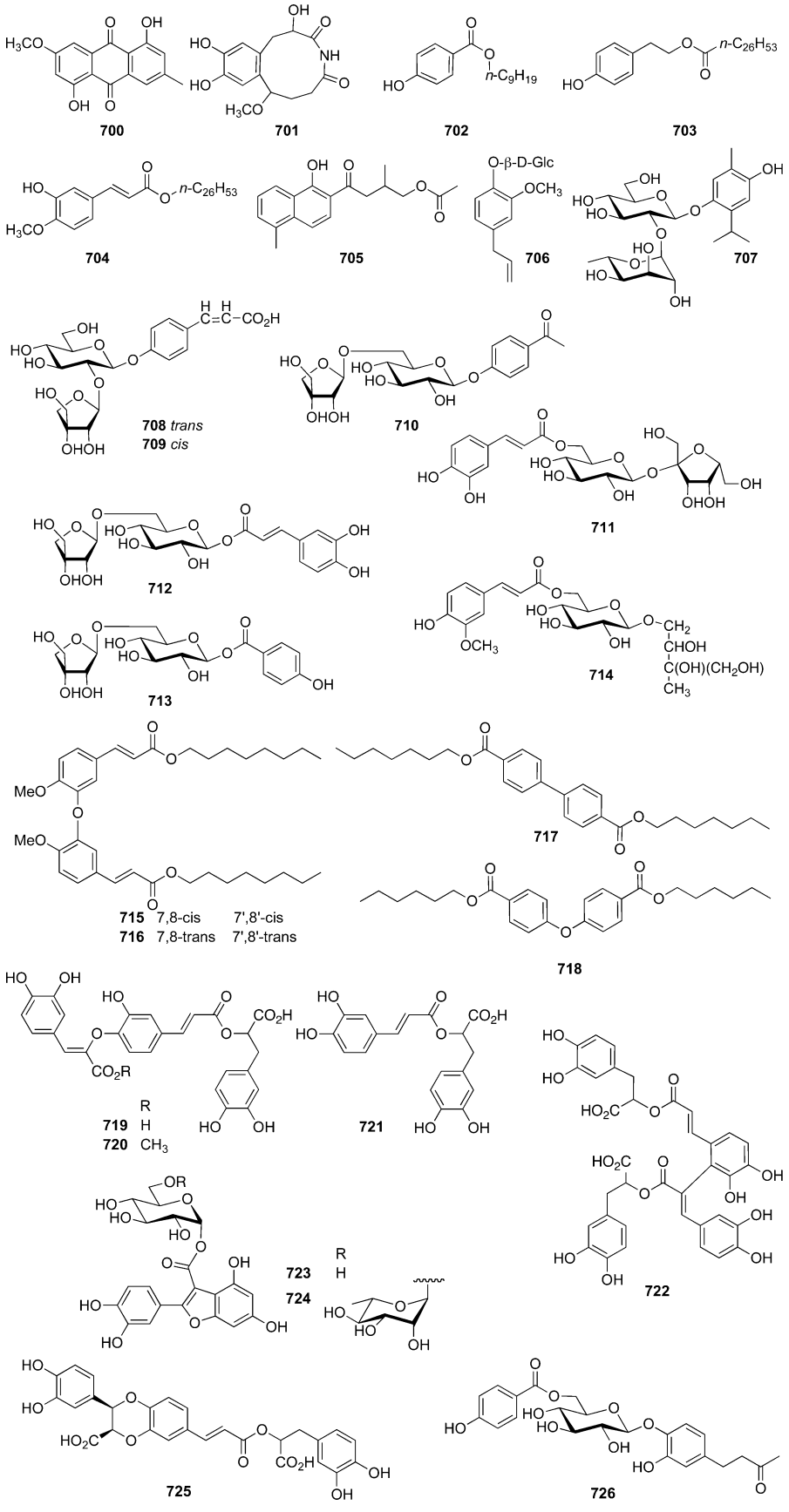


Figure 52. continued

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

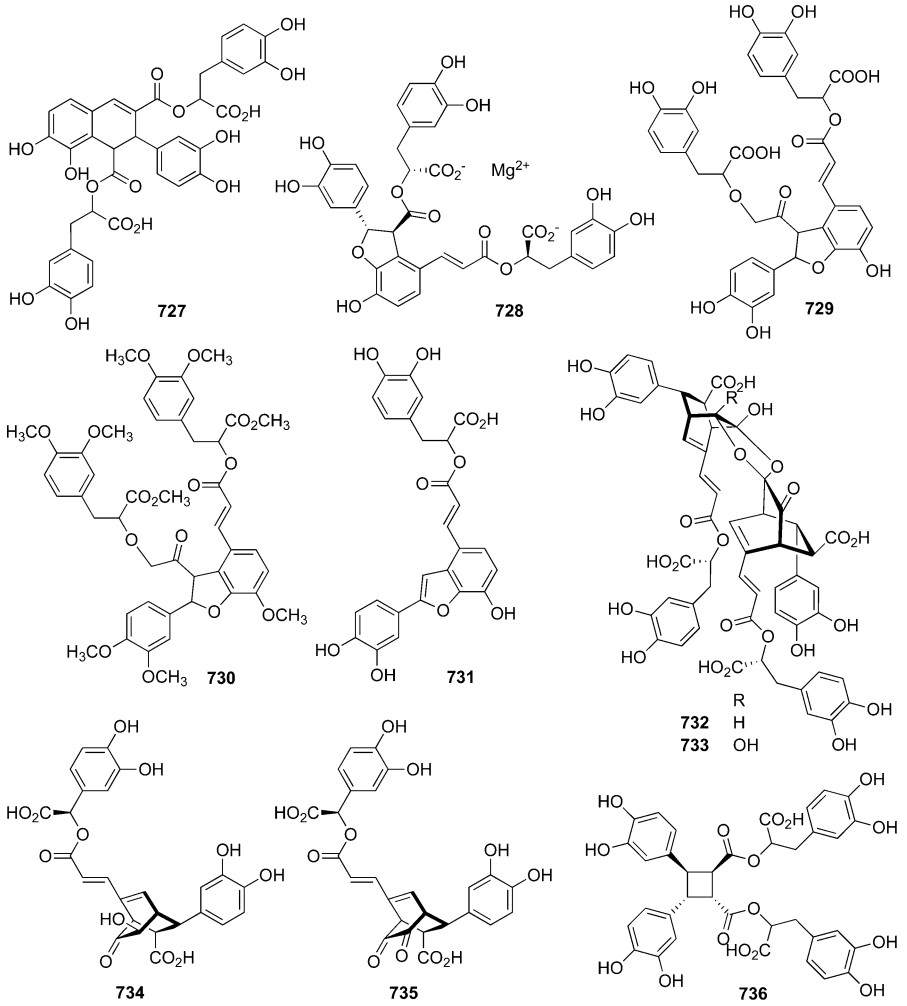
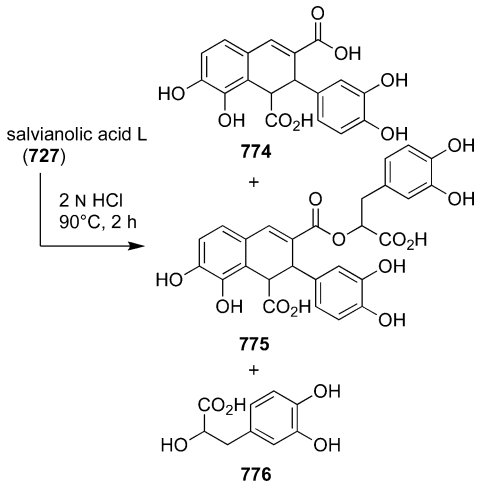


Figure 52. Phenolic acids.

Scheme 18. Degradation Study of Salvianolic Acid L (727)



mL), *S. epidermis* (15.6 μg/mL), *Escherichia coli* (62.5 μg/mL), *Proteus vulgaris* (62.5 μg/mL), and *Pseudomonas aeruginosa* (31.3 μg/mL).[288] Compound **575** was found to possess antibacterial activity against *Staphylococcus aureus*.[289] Salvipisone and aethiopinone showed antibacterial activity against *S. aureus* (MIC range, 18.75−37.5 μg/mL) and *S. epidermidis* (9.37−75.0 μg/mL).[290] Compound **350** showed antimicrobial activities against two Gram-positive organisms, *Staphylococcus aureus* and *Micrococcus luteus*, with MIC values of 20.0 and 15.0 μM, respectively.[146] The minimum inhibitory concentrations (MICs) of oleanolic acid (**627**) and ursolic acid were 8 and 4 μg/mL, respectively. These two compounds also showed antimicrobial activity against *Streptococcus pneumoniae* and methicillin-resistant *Staphylococcus aureus* (MRSA).[244]

3.2. Antioxidant Activity

Because of limitations in recent years in using synthetic antioxidant compounds in the food products because of their side effects, natural sources have became more important to find proper and safe food antioxidants. *Salvia* species can be one of the natural sources for this purpose with good culinary qualities, and their extracts are commonly used to increase the shelf life of foods.[291] The antioxidant effects of phenolic acids include antilipid-peroxidation and radical scavenging. The antioxidant activities of the methanol extracts of six *Salvia* species (*S. caespitosa*, *S. hypargeia*, *S. euphratica*, *S. sclarea*, *S. candidissima*, and *S. aethiopis*) from Turkey were examined. In the DPPH free radical-scavenging test system, the most active plant was *S. euphratica*, with an IC_{50} value of 20.7 ± 1.22 μg/mL, followed by *S. sclarea* (IC_{50} = 23.4 ± 0.97 μg/mL) among the polar subfractions. In the β-carotene/linoleic acid test system, the polar extract of *S. hypargeia* was superior to the polar extracts of other *Salvia* species studied (69.2% ± 1.90%). This activity was followed by *S. sclarea* with 63.5% ± 4.24%

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

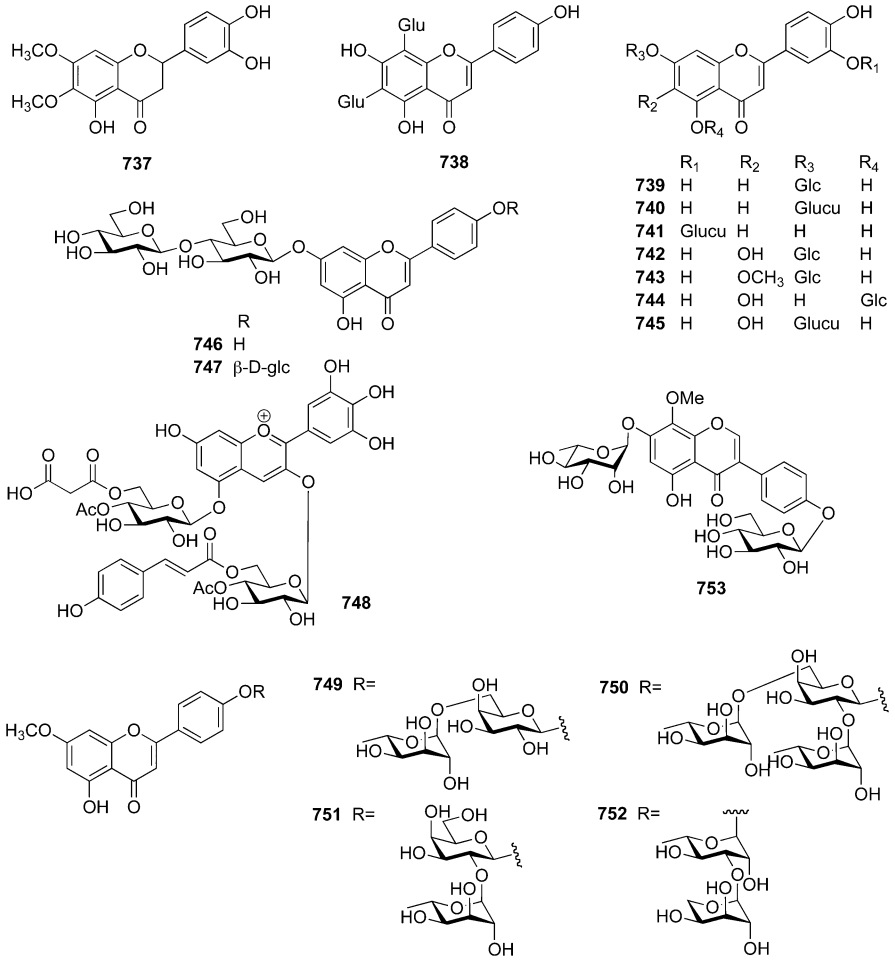


Figure 53. Flavonoids.

inhibition rate. The inhibition rate of the synthetic antioxidant, butylated hydroxytoluene (BHT), was also determined to be 96%. Because the polar extracts of *Salvia* species dealt with here exhibited excellent antioxidant activities when compared to BHT, it seems possible to keep perishable fat-containing food longer by direct addition of an extract of sage.[292] Candesalvoquinone (**304**), candelabroquinone (**171**), 12-*O*-methylcandesalvone (**305**), candesalvone B methyl ester (**307**), and candelabrone (**51**) were evaluated for antioxidant activity in enzyme-dependent (IC_{50} values 3.49−10.42 μg) and enzyme-independent (IC_{50} values 1.40−13.40 μg) systems of lipid peroxidation.[141] The antioxidant activities of the sage polyphenols, consisting of flavone glycosides and a range of rosmarinic acid derivatives, were evaluated for their capacity to scavenge DPPH and superoxide anion radicals. The antioxidant activity of the flavonoids was variable, and those with a catechol B-ring (luteolin glycosides) were more active than those without (apigenin glycosides).[277] Rosmariquinone, dehydrorosmariquinone, miltirone I, tanshinone IIA, cryptotanshinone, and dihydrotanshinone were extracted from *S. miltiorrhiza*. The antioxidant activity of these quinones in lard at 100 °C was determined with a Rancimat. The following structural features are associated with increased activity: (1) additional conjugated double bonds in the A ring; (2) a dihydrofuran ring rather than a furan ring; (3) an isopropyl substituent ortho to a quinone carbonyl rather than a dihydrofuran ring.[293] Antioxidant activity of the compounds isolated from *S. officinalis* was evaluated by the oil stability index method. Among them: carnosol, rosmanol, *epi*-rosmanol, isorosmanol, galdosol, and carnosic acid exhibited remarkably strong activity, which was comparable to that of α-tocopherol.[107] Rosmarinic acid and carnosol were the main compounds in all the antioxidant phenolic extracts isolated from *S. officinalis*.[294] Among abietane diterpenes, inuroyleanol (**103**) showed the highest DPPH (1,1-diphenyl-2-picrylhydrazyl)-scavenging activity as well as the highest inhibition on lipid peroxidation in β-carotene−linoleic acid system. In contrast, inuroyleanol (**103**) revealed the lowest superoxide anion scavenging activity while abietane 7-oxoroyleanone-12-methyl ether (**183**) showed the highest activity with an equal antioxidant potent to the well-known antioxidant L-ascorbic acid, even more active than BHT and α-tocopherol. Royleanone (**166**) showed higher antioxidant activity in the two systems than both horminone (**162**) and 7-acetylhorminone (**163**). Considering these results in both DPPH and β-carotene−linoleic acid systems, we can conclude that quinonoids or fully substituted C ring phenolic abietane diterpenoids having no substituent other than a keto group at C-7 would have decreased activity. In DPPH free radical-scavenging test method, 7-acetoxyroyleanone-12-methyl ether, which is a methyl derivative of 7-acetylhorminone (**163**) at C-12, showed higher activity as much as 4−5 times of **163**; this effect can be attributable to the higher scavenging power of the methoxy group at C-12. In fact, in the literature, the higher activity of carnosic acid, which possessed *ortho*-dihydroxy groups on aromatic ring C with comparison of royleanonic acid having hydroxy-*p*-benzoquinone moiety, has been previously

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

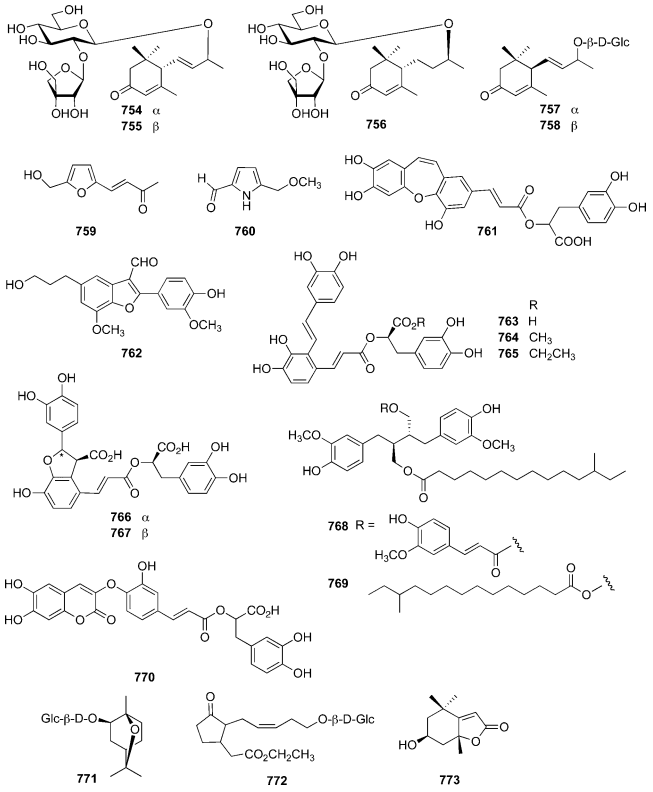


Figure 54. Others.

explained by inhibition of the oxidation through donating H atoms to scavenge free radicals[107,111,295] in the two systems (DPPH and β-carotene−linoleic acid). Therefore, *ortho*-dihydroxy phenols, or one being a hydroxy and the other a methoxy, can form more stable radicals by donating H atoms as observed for inuroyleanol (**103**); thus, these types of abietanes are expected to be more active antioxidants than abietanes that contain the monohydroxy phenol or *p*-quinoid C ring abietanes. Formation of reactive oxygen species (ROS) has been proposed to be an important step leading to neuronal death related to a variety of neurodegenerative diseases, such as stroke, Alzheimer's disease (AD), and Parkinson's disease (PD). These diseases primarily affect the elderly populations and are considered to be responsible for ca. 60 of all dementia in people aged 65 or older. Plants of *Salvia* genus have been used since antiquity in the treatment of various neuro-degenerative diseases. Caffeic acid, danshensu, rosmarinic acid, prolithospermic acid, salvianolic acid A (**763**), and salvianolic acid B showed inhibitory activity against the lipid peroxidation induced by iron cysteine and the erythrocyte hemolysis induced by hydrogen peroxide. In these studies, salvianolic acid A (**763**) was the most potent compound. Caffeic acid and its polymers show free radical scavenging activity. The tetrameric lithospermic acid B and its Mg^{2+} salt show the strongest activity; the trimeric lithospermic acid (**766**) and dimeric rosmarinic acid show lower but similar efficacy, whereas the monomeric caffeic acid shows the lowest activity. Rosmarinic acid, salvianolic acid A (**763**), and salvianolic acid B (**729**) exhibit strong antilipoperoxidant activity, acting by scavenging superoxide anion radical (O_2^-). Structure−activity relationships (SARs) indicated that the *o*-hydroxy groups and a saturated connection between the aromatic rings are important for free radical scavenging.[37]

3.3. Cytotoxicity Activity

It is reported that cancer causes 7 million deaths each year and results in 12.5% of deaths worldwide (World Heath Organization (WHO). Cancer. www.who.int/cancer/ (accessed January 29, 2006)). Plants have played an important role as a source of effective anticancer agents, and it is significant that over 60% of currently used anticancer agents are derived in one way or another from natural sources including plants, marine organisms, and micro-organisms[111,296,297] In 2000, Liu's study demonstrated that the aqueous extract of *S. miltiorrhiza* had profound effects on HepG2 hepatoma cells in vitro. It reduced the proliferation of these cells, caused changes in their morphology, and induced cell death by apoptosis.[298] The hypoxia-inducible factor-1 (HIF-1) has become an important target in the development of anticancer drugs. Sibiriquinone A, sibiriquinone B, cryptotanshinone (**266**), and dihydrotanshinone I (**263**), isolated from *S. miltiorrhiza*, potently inhibited hypoxia-induced luciferase expression with IC_{50} values of 0.34, 3.36, 1.58, and 2.05 μM on AGS cells, a human gastric cancer cell line, and 0.28, 3.18, 1.36, and 2.29 μM on Hep3B cells, a human hepatocarcinoma cell line, respectively.[299] Danshenol A (**271**) showed inhibited growth of K562 (IC_{50} = 0.53 μg/mL), T-24 (IC_{50} = 7.94 μg/mL), QGY (IC_{50} = 4.65 μg/mL), and Me180 (IC_{50} = 6.89 μg/mL) cell lines. Yunnannin A (**226**) showed moderate inhibitory activity on QGY (IC_{50} = 16.75 μg/mL) and Me180 (IC_{50} = 5.84 μg/mL) cells.[132] The cytotoxic activity of carnosol (**210**), 20-deoxocarnosol, and 16-hydroxycarnosol (**212**) were evaluated in vitro against A2780 ovarian cancer, SW1573 nonsmall-cell lung cancer, WiDr colon cancer, T-47D breast cancer, and HBL-100 breast cancer cells. All of them showed GI_{50} values in the range 3.6−35 μM for the five cell lines, with the A2780 and HBL-100 cell lines being the most sensitive, with GI_{50} values in the range 3.6−5.4 μM.[117] Taxodione, isolated from *S. staminea*, showed significant cytotoxicity in a panel of cell lines: BC1, LU1, COL2, KB, KB-VI, LNCaP, P388, and A2780, with IC_{50} values of 1.2, 5.1, 0.7, 3.4, 4.1, 0.7, 0.3, and 9.0 μg/mL, respectively.[245] Salvileucalin B (**542**) exerted cytotoxic activity against A549 and HT-29 cells with IC_{50} values of 5.23 and 1.88 μg/mL, respectively.[223]

3.4. Anti-HIV Activity

In the 30 years since the "acquired immune deficiency syndrome" (AIDS) was first recognized, over 40 million people have become infected by the human immunodeficiency virus (HIV). Many secondary metabolites from plants as a source of potential natural compounds with in vitro anti-HIV activity have been screened. A new polyphenol, salvianolic acid N (**761**), isolated from the aqueous extracts of the roots of *S. yunnanensis*, is inhibited on HIV-1 RT and IN, and the IC_{50} values were 67.10−193.39 μg/mL and 1.78−18.5 μg/mL, respectively. The nontoxic concentration of salvianolic acid N is also inhibitory on HIV-1 p24 antigen expression in MT-4 cell lines; the TC_{50} value of cellular toxicity is 3.7−24.10 μg/mL, the IC_{50} of inhibition on P24 in MT-4 cell cultures was 0.649−4.28 μg/mL, and the selective index (SI) was 5.63−5.70.[16] Przewalskin A (**592**) and B(**397**) exhibited modest anti-HIV-1 activity with EC_{50} values of 41 and 30 μg/mL.[23417] The anti-HIV-1 activities of salvianolic acid A (**763**), methyl salvianolate A (**764**), ethyl salvianolate A (**765**), lithospermic acid (**766**), and *cis*-lithospermic acid (**767**) were tested for the inhibition of P24 antigen in HIV-1 infected MT-4 cell cultures, with EC_{50} values of 2.07, 1.62, 1.44, 3.99, and 6.11 μg/mL, respectively.[283]

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Table 6. Summary of Pharmacological Effects of Genus *Salvia* and Active Compounds

plant	active compound(s) or extract	pharmacologic effect(s)	ref
Salvia	carnosol (**210**)	antibacterial activity	287
Salvia	7α-methoxyrosmanol (**235**)	antibacterial activity	287
Salvia	salvicanol (**358**)	antibacterial activity	287
Salvia	tanshinone IIA (**255**)	antibacterial activity	287
Salvia	demethylsalvicanol (**360**)	antibacterial activity	287
S. aegyptiaca	crude acetone and methanol extracts	central nervous system depressant properties	24
		anti-inflammatory	24
		antipyretic actions	24
S. aethiopis	methanol extracts	antioxidant activity	292
S. africana-lutea	methyl 12-*O*-methylcarnosoate (**101**)	against *Mycobacterium tuberculosis*	286
		cytotoxic activity	286
S. anastomosans	cariocal (**348**)	cytotoxic activity	74
S. blepharochlaena	*O*-methylpisiferic acid (**49**)	antibacterial	73
	horminone (**162**)	antibacterial	73
	7-acetylhorminone (**163**)	antibacterial	73
S. broussonetii	brussonol (**370**)	antifeedant	58
	11-hydroxy-12-methoxyabietatriene (**485**)	antifeedant	58
	Demethylcryptojaponol (**105**)	antifeedant	58
	6*R*-hydroxydemethylcryptojaponol (**766**)	antifeedant	58
	14-deoxycoleon U (**136**)	antifeedant	58
S. caespitosa	methanol extracts	antioxidant activity	292
S. candelabrum	candesalvoquinone (**304**)	antioxidant activities	141
	candelabroquinone (**171**)	antioxidant activities	141
	12-*O*-methylcandesalvone (**305**)	antioxidant activities	141
	candesalvone B methyl ester (**307**)	antioxidant activities	141
	candelabrone (**51**)	antioxidant activities	141
S. candidissima	methanol extracts	antioxidant activity	292
S. cilicica	7-hydroxy-12-methoxy-20-norabieta-1,5(10),7,9,12-pentaene-6,14-dione (**161**)	antileishmanial activity	57
	abieta-8,12-dien-11,14-dione (**165**)	antileishmanial activity	57
	oleanolic acid (**627**)	antileishmanial activity	57
	ursolic acid	antileishmanial activity	57
	ferruginol (**50**)	antileishmanial activity	57
	inuroyoleanol	antileishmanial activity	57
	cryptanol (**122**)	antileishmanial activity	57
S. cinnabarina	3,4-secoisopimara-4(18),7,15-triene-3-oic acid (**303**)	antispasmodic activity	142
		inhibits mouse intestinal motility in vivo	144
		inhibits rat urinary bladder contractility in vitro	143
S. divinorum	salvinorin A (**465**)	κ-opioid receptor	19, 176
	1β,2α,3β,11α-tetrahydroxyurs-12-ene	cytotoxic activity	246
S. dolomitica	crude extract	antibacterial activity	396
S. eriophora	crude extract	cardiovascular activities	3
	4,14-dihydroxysaprorthoquinone (**313**)	cardiovascular activities	3
	aethiopinone	cardiovascular activities	3
	ferruginol (**50**)	cardiovascular activities	3
	4,12-dihydroxysapriparaquinone	cardiovascular activities	3
	6,7-dehydroroyleanone	cardiovascular activities	3
S. euphratica	methanol extracts	antioxidant activity	292
S. forskahlei	forskalinone (**53**)	antimicrobial activity	79
	octanol ester of *cis*-*O*-methyl caffeic acid dimer (**715**)	antimicrobial activity	79
S. gilliessi	5-*epi*-icetexone (**366**)	epimastigotes of *Trypanosoma cruzi* (Tulahuen)	161
S. greggii	salvigreside D (**435**)	antibacterial activity	174
S. hypargeia	crude extract	cytotoxic activity	399, 292
	6α-hydroxysalvinolone (**136**)	cytotoxic activity	399
	taxodione	cytotoxic activity	399
S. jaminiana	acetone extract	antibacterial activity	394
S. leriaefolia	8(17),12*E*,14-labdatrien-6,19-olide (**575**)	antibacterial activity	289
S. leucantha	salvileucalin B (**542**)	cytotoxic activity	223
S. macrochlamys	monogynol A (**684**)	antioxidant activity	256
S. mellifera	royleanone	cytotoxic activity	347
	ferruginol (**50**)	cytotoxic activity	347
	taxodione	cytotoxic activity	347

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Table 6. continued

plant	active compound(s) or extract	pharmacologic effect(s)	ref
	7α-hydroxyroyleanone	cytotoxic activity	347
	demethylsalvican-11−12-dione	cytotoxic activity	347
	isotanshinone III	cytotoxic activity	347
S. menthaefolia	methanol crude extract	cytotoxic activity	388
S. miltiorrhiza	dihydrotanshinone	acetylcholinesterase inhibitors	300
	cryptotanshinone (**266**)	acetylcholinesterase inhibitors	300
	tanshinone I (**264**)	acetylcholinesterase inhibitors	300
	tanshinone IIA (**255**)	acetylcholinesterase inhibitors	300
	5-(3-hydroxypropyl)-7-methoxy-2-(3′-methoxy-4′-hydroxyphenyl)-3-benzo[*b*] furancarbaldehyde (**762**)	potency in bovine adenosine A1 radioligand binding	282
S. miltiorrhiza	aqueous ethanol extract	enhancing effects on cell growth and differentiation	385
	aqueous extract	reduce hepatic fibrosis	281
	aqueous extract	antitumor	298
	salvianolic acid B (**729**)	enhancing effects on cell growth and differentiation	385
	galdosol (**237**)	benzodiazepine receptor	384
	tanshinone IIB (**261**)	neuroprotective activity	383
	sibiriquinone A	antitumor	299
	sibiriquinone B	antitumor	299
	cryptotanshinone (**266**)	antitumor	299
	dihydrotanshinone I (**263**)	antitumor	299
	tanshinone I (**264**)	antitumor	299
	tanshinone IIA (**255**)	antitumor	299
	12-deoxytanshinquinone B (**190**)	antitumor	299
	salvianen (**291**)	antitumor	136
	neotanshinlactone (**274**)	antitumor	133
	dihydroranshinone	antioxidant activity	293
	tanshinone I (**264**)	antioxidant activity	293, 389
	methylenetanshinone	antioxidant activity	293
	cryptomshinone	antioxidant activity	293
	tanshinone IIB (**261**)	antioxidant activity	293
	danshenxinkun B	antioxidant activity	293
	tanshinone IIA (**255**)	antioxidant activity	293
	dehydrorosmariquinone	antioxidant activity	293
	milurone I	antioxidant activity	293
S. miltiorrhiza	rosmariquinone	antioxidant activity	293
	tanshinone IIA (**255**)	antitumor	379
S. moorcraftiana	acetone extract	phytotoxic activity antifungal activity	400
	5-hydroxy-7,4′-dimethoxyflavone	enzyme inhibition activity (α-glucosidase)	400
	oleanolic acid (**627**)	enzyme inhibition activity (α-glucosidase)	400
S. multicaulis	multicaulin (**138**)	antituberculous activity	95
	12-demethylmulticauline (**139**)	antituberculous activity	95
	multiorthoquinone (**207**)	antituberculous activity	95
	12-demethylmultiorthoquinone (**208**)	antituberculous activity	95
	12-methyl-5-dehydroacetyl-horminone (**187**)	antituberculous activity	95
	salvipimarone (**558**)	antituberculous activity	95
S. nipponica	salvianolic acid B (**729**)	inhibitory effect on superoxide anion generation	380
	ursolic acid	inhibitory effect on superoxide anion generation	380
	3-*epi*-corosolic acid	inhibitory effect on superoxide anion generation	380
	2α,3α-23-trihydroxyurs-12-en-28-oic acid	inhibitory effect on superoxide anion generation	380
	oleanolic acid 3-*O*-ferulate	inhibitory effect on superoxide anion generation	380
	friedelin	inhibitory effect on superoxide anion generation	380
	caffeic acid methyl ester	inhibitory effect on superoxide anion generation	380
	vanillic acid	inhibitory effect on superoxide anion generation	380
S. nubicola	nubiol (**33**)	active against *Pseudomonas aeruginosa*	23

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

Table 6. continued

plant	active compound(s) or extract	pharmacologic effect(s)	ref
S. officinalis	*n*-hexane and the chloroform extracts	anti-inflammatory	334
	crude extracts	antioxidative activity	294, 386, 390
	oleanolic acid (**627**)	antimicrobial Activity	244
	ursolic acid	antimicrobial Activity	244
	7,8-dihydroxy-2-(3,4-dihydroxyphenyl)-1,2-dihydronaphthalene-1,3-dicarboxylic acid 3-(1-carboxy-2-(3,4-dihydroxyphenyl))ethyl ester (**775**)	antioxidative activity	275
	7α-methoxyrosmanol (**235**)	benzodiazepine receptor	384
	rosmarinic acid	antioxidative activity	277
	salvianolic acid K	antioxidative activity	277
	salvianolic acid I	antioxidative activity	277
	sagecoumarin (**770**)	antioxidative activity	277
	sagerinic acid	antioxidative activity	277
	luteolin 7-glucoside	antioxidative activity	277
	luteolin 7-glucuronide	antioxidative activity	277
	luteolin 30-glucuronide	antioxidative activity	277
	6-hydroxyluteolin 7-glucoside	antioxidative activity	277
	apigenin 6,8-di-C-glucoside	antioxidative activity	277
	safficinolide (**112**)	antiviral activity	63
	sageone (**143**)	antiviral activity	63
	carnosic acid (**104**)	lipid absorption inhibitor	393
S. pachyphylla	pachyphyllone (**249**)	cytotoxic activity	117
	carnosol (**210**)	cytotoxic activity	117
	20-deoxocarnosol	cytotoxic activity	117
	isorosmanol	cytotoxic activity	117
	8β-hydroxy-9(11),13-abietadien-12-one	cytotoxic activity	117
S. palaestina	cirsimaritin	antibacterial activity	446, 447
	sclareol	antibacterial activity	288
S. plebeia	ethyl acetate extracts	antioxidant activities	337
	6-methoxyluteolin-7-glucoside	antioxidant activities	336
	β-sitosterol	antioxidant activities	336
	2′-hydroxy-5′-methoxybiochanin A	antioxidant activities	336
S. prionitis	7,8-seco-*para*-ferruginone (**350**)	antimicrobial activities	146
	4-hydroxysaprorthoquinone (**316**)	inhibition against topoisomerase I	146
	prionoid D (**315**)	cytotoxic activity	150
	prionoid E (**317**)	cytotoxic activity	150
	3-oxo-4-hydroxysaprorthoquinone	cytotoxic activity	146
S. przewalskii	przewalskin A (**592**)	anti-HIV-1 activity	234
	przewalskin B (**399**)	anti-HIV activity	17
S. radula	crude extract	antibacterial activity	396
S. sahendica	1,4-dihydro-6-methyl-2-(1-methylethyl)-5-(4-methylpent-4-enyl)naphthalene-1,4-dione (**332**)	antifungal activity	106
	sahandinone (**325**)	antifungal activity	106
	horminone (**162**)	antifungal activity	106
S. santolinifolia	santolinoic acid (**640**)	inhibitory activity against enzymes acetylcholinesterase and butyrylcholinesterase	250
S. sclarea	methanol extracts	antioxidant activity	292
	salvipisone	antibiotic resistance and antibiofilm activity	290
	aethiopinone	antibiotic resistance and antibiofilm activity	290
S. sclareoides	acetone extract	anticholinesterase activity	373
S. semiatrata	tilifolidione (**376**)	cytotoxic activity	74
	semiatrin (**444**)	antifeedant activity	387
S. staminea	taxodione	cytotoxic activity	245
S. syriaca	ferruginol	antihypertensive activiy	345
	3β-hydroxystigmast-5-en-7-one	antihypertensive activiy	345
S. trijuga	trijugins I	cytotoxicity	45
	hyptadienic acid	cytotoxicity	45
S. verbenaca	crude extract	antibacterial activity	396
S. viridis	1-oxoferruginol	antibacterial activity	84
S. yunnanensis	salvianolic acid N (**761**)	anti-HIV	16
	salvianolic acid A (**763**)	anti-HIV-1	283

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967–6026

Table 6. continued

plant	active compound(s) or extract	pharmacologic effect(s)	ref
	methyl salvianolate A (**764**)	anti-HIV-1	283
	ethyl salvianolate A (**765**)	anti-HIV-1	283
	lithospermic acid (**766**)	anti-HIV-1	283
	cis-lithospermic acid (**767**)	anti-HIV-1	283
	yunnannin A (**226**)	antitumor	132
	danshenol A (**271**)	antitumor	132

3.5. Others

Acetylcholinesterase (AChE) inhibitors are the only registered drugs used to treat Alzheimer's disease (AD). Dihydrotanshinone, cryptotanshinone, tanshinone, and tanshinone A were active AChE inhibitory, with *c* log *P* values of 2.4, 3.4, 4.8, and 5.8, respectively, which indicate that these compounds have the potential to penetrate the blood−brain barrier.[300] The crude extract of *S. eriophora* and five isolated compounds (4,14-dihydroxysaprorthoquinone, aethiopinone, ferruginol, 4,12-dihydroxysapriparaquinone, and 6,7-dehydroroyleanone) were tested for their cardiovascular activities using Wistar Albino rats and showed activity. A significant reduction in the direct blood pressure was observed together with a slight increase in the heart rate, which did not reach a significant level.[3] The comparative cytotoxic effects of demethylsalvicanol, 14-deoxycoleon U (**136**), and demethylcryptojaponol (**105**) were tested on insect Sf9 and mammalian CHO cells. Demethylsalvicanol was a moderate antifeedant to *L. decemlineata*, and 14-deoxycoleon U (**136**) was the strongest antifeedant, whereas demethylcryptojaponol (**105**) was toxic to this insect.[58] The clerodane diterpenoid salvinorin A (**465**), the main active component of the psychotropic herb *S. divinorum*, was a potent agonist at the κ-opioid receptor.[19,176] Safficinolide (**112**) showed a yield reduction of VSV (vesicular stomatitis virus), whereas sageone (**143**) showed virus inactivation activity against VSV and HSV (herpes simplex virus type 1).[63]

4. CONCLUSION

Beside the above-mentioned components, *Salvia* species also contain volatile components comprised mainly of monoterpenoids such as (*S*)-(−)-α-pinene, (*R*)-(+)-α-pinene, camphene, β-pinene, 3-carene, terpinolene, myrcene, β-phellandrene, limonene, 1,8-cineole, camphor, borneol, spathulenol, β-caryophyllene, cadinadiene, β-caryophyllene oxide, bourbonene, and iso-β-caryophyllene monoterpenoids almost embodied the aerial parts, especially in the flower of the plants.[230,301−314]

To date, over 730 secondary metabolites have been reported from *Salvia* species. The main secondary metabolite constituents of *Salvia* species are terpenoids and flavonoids. Of these, more than 80% are terpenoids, especially abietane and clerodane diterpenoids; relatively, sequiterpenoids and triterpenoids are rare in the *Salvia* species, which is in agreement with the biosynthesis of terpenoids. In the high plant, the biosynthesis of terpenoids proceeds via two different pathways located in different cellular cytoplasms. The mevalonate (MVA) pathway in the cytoplasm is responsible for the biosynthesis of sesquiterpenoids and triterpenoids, whereas plastides contain the 1-deoxy-D-xylulose-5-phosphate (DOXP) pathway for the biosynthesis of monoterpenoids (the main constitution of essential oil) and diterpenoid.[315,316] Terpenoids and flavonoids dominate the medicinal chemistry of the *Salvia* plant; many studies have demonstrated that aerial parts of these plants contain flavonoids, triterpenoids, and monoterpenes, particularly in the flowers and leaves, while diterpenoids are found mostly in the roots. However, a literature survey indicates that some American *Salvia* species also contain diterpenoids in the aerial parts, and in a few *Salvia* species, triterpenoids and flavones are present in the roots.[317,318]

Even though Danshen is officially listed in the Chinese Pharmacopoeia and is used widely and successfully in clinics in China, the exact mechanism for its therapeutic basis is poorly understood. In contrast, over the last 50 years, the chemical constituents and biological activities of Tanshen have been well studied. According to their structural characteristics and physical/chemical properties, the constituents of Danshen have been divided into two groups. The first group contains phenolic acids such as salvianolic acid and lithospermic acid B, which are water-soluble. The second group contains abietane type-diterpene quinone pigments such as tanshinone I, tanshinone IIA, tanshinone IIB, and cryptotanshinone, which are more lipophilic. Both of the groups contribute to the biological activities of Danshen.

The phytochemical studies of the aerial parts and roots of European and Asiatic *Salvia* spp. led to the isolation of a number of diterpenoids with an abietane skeleton in almost 100% of the species studied.[162] The same chemical profile has been found for some Californian salvias (subgenus Audibertia).[64,75,166,319] On the other hand, the phytochemical study of the aerial parts of several species of American salvias (subgenus Calosphace) led to the isolation of several diterpenes, mainly of the neoclerodane-type, in the major part of the sections studied, although some abietane- and icetexane-type diterpenoids have been isolated from few spp., belonging to sections Erythrostachys, Conzatianna, and Tomentellae.[162] The occurrence of abietane and clerodane are well-established as chemosystematic markers in the *Salvia* genus.[320]

Pharmacological and phytochemical research carried out during the past four decades confirms many traditional uses for plants of the genus *Salvia* in various diseases. There is, however, a need for further studies to evaluate other folk uses of these plants and to test other less well-known and widespread species such as *S. leriifolia*. Despite showing good pharmacological or therapeutic effects, there is still a need for more precise studies to determine and separate the active compounds and elucidate their mechanisms of action where possible.[28] A further action mechanism study of active components of *Salvia* plant will shed light on understanding the role of a physiological system, such as a detailed investigation of salvinorin A's mode of action, and will likely help to illuminate the role of the kappergic system in human brain function. A recent study also reveals that tanshinone IIA is a new activator of human cardiac KCNQ1/KCNE1 (IKs) potassium channels.[321] As for pharmacological or therapeutic effects, the water-soluble component was less studied; much more attention should be paid directed to the biologically active, water-soluble components. On the other

dx.doi.org/10.1021/cr200058f | *Chem. Rev.* 2012, 112, 5967−6026

hand, many related *Salvia* species are also sold well in China because of their same therapeutic effects as *S. miltiorrhiza*. Simultaneously, wild *S. miltiorrhiza* decreases gradually. Therefore, investigation of the active components in the related *Salvia* species is very important for the rational utilization of *Salvia* species and protection of wild *S. miltiorrhiza*.

As a total of 730 constituents were isolated from 134 *Salvia* species of the over 1000 species suggested, there are still many diterpenoids waiting isolation,[322,323] limited work has been carried out on the aerial parts of *Salvia* species, and further extensive phytochemical investigation on *Salvia* species is necessary. A comprehensive spectrum of diterpenoid from different *Salvia* species will provide some clues to understand the taxonomic relationship of *Salvia* species. On the other hand, to fully gain command of the profile of diterpenoids, a detailed understanding of the steps of different diterpene biosynthesis and the identification of the associated genes is essential. And the research input is likely to continue in search of new natural products for application in the pharmaceutical, food, and cosmetics industries. It is important to note that most of the research done on *Salvia* employs in vitro-based studies, and in vivo tests should be encouraged. This review did not cover the chemical synthesis of the active components[324−333] isolated from genus *Salvia*, which is beyond the scope of the review.

AUTHOR INFORMATION

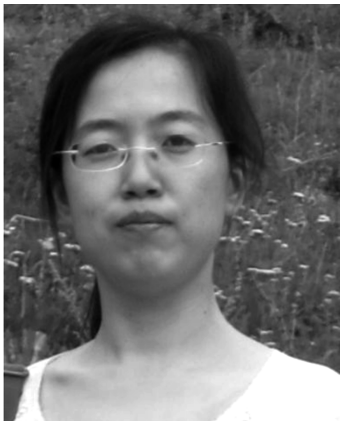
Corresponding Author

*E-mail: Q.-W.S.: shiqingwen@hebmu.edu.cn; H.K.: kiyota@biochem.tohoku.ac.jp; B.C.: hbydcongbin@hebmu.edu.cn. Tel.: 86-311 86265634 or 81-22-717-8785 or 86-311 86266406.

Notes

The authors declare no competing financial interest.

Biographies



Yi-Bing Wu (born in 1981 in Xingtai, Hebei Province) received her Bachelor and Master degrees from School of Pharmaceutical Sciences, Hebei Medical University, in 2003 and 2006, respectively. Her master thesis is studies on the antitumor components of *Inula britannica* L. Now she works in the Division of Medicinal Chemistry of Hebei Medical University as a lecturer. She is currently carrying out doctoral research with Professor Qing-Wen Shi at Hebei Medical University, studying the isolation, chemical modification, and structure−activity relationship of bioactive natural products.

Zhi-Yu Ni (born in 1975 in Shijiazhaung, Hebei Province) is associate professor of Department of Forensic Medicine, Hebei Medical University. She obtained her Bachelor Degree from Hebei Medical University in 1998 and Master Degree from Hebei Medical University in 2001, and earned her Ph.D. from Hebei Medical University in 2005. Her study area is forensic toxicology, and her research interests are focused on the phytotoxin constituents of medicinal plants and their antitumor activities.

Qing-Wen Shi (born in 1964 in Cangzhou, Hebei Province) is Professor and Director of Division of Natural Medicine, deputy dean of School of Pharmaceutical Sciences, Hebei Medical University. He got his Bachelor degree from the School of Pharmaceutical Sciences, Hebei Medical University, in 1985. In the same year he assumed the position of Assistant Professor in Natural Medicine Laboratory of Hebei Medical University. He received his Master degree from Shandong Medical University in 1990 and obtained his Ph.D. from Tohoku University, Japan, in 2000. As a postdoctoral and associate researcher, he worked in Institut National de la Recherche Scientifique, Institut Armand-Frapier, Quebec University, Canada, for 4 years. In 2004 he came back to China and was promoted to a full professor. He visited Tohoku University and McGill University as a visiting researcher for 3−6 months from 2006 to 2011. His research interests are focused on the chemical constituents of medicinal plants and their biological activities.

Mei Dong (born in 1963 in Shijiazhaung, Hebei Province) is Professor of Department of Forensic Medicine, Hebei Medical University. She got her Bachelor degree from the College of Forestry of Hebei in 1984 and Master degree from Hebei Normal University in 1996, and obtained her Ph.D. from Shinshu University, Japan, in 2000. She visited Department of Environmental Biochemistry, Graduate School of Medicine, Chiba University, as a visiting researcher in 2005−2010. Her research interests are focused on the phytotoxins constituents of medicinal plants and their antitumor activities.

Hiromasa Kiyota (born in 1966 in Sendai, Japan) is Associate Professor of Biooganic Chemistry at Tohoku University, Japan. He received his B.S. degree (1989, soil science, Prof. Hidenori Wada) and M.S. degree (1991, organic chemistry, Prof. Kenji Mori and Associate Prof. Takeshi Kitahara) from the University of Tokyo. In 1991 he assumed the position of Assistant Professor at Prof. K. Mori's Laboratory, moved to Prof. Takayuki Oritani's Laboratory in 1994, and was promoted to Associate Professor (Prof. Shigefumi Kuwahara) in 2002. In 1995 he received his Ph.D. from the University of Tokyo (Prof. Kenji Mori) about the synthesis of optically active insect pheromones. He joined the research group of Prof. Steven V. Ley at Cambridge University, U.K., as Visiting Academic (2001−2002). In 2003 he received The Japan Bioscience, Biotechnology and Agrochemistry Society Award for the Encouragement of Young Scientists. His research interests extend over a wide range of natural product chemistry, especially on the synthesis of biologically active compounds such as antibiotics, phytotoxins, plant hormones, insect pheromones, marine products, perfumery, etc.

Yu-Cheng Gu graduated with first honours degree in Pharmacy in 1984 at the Hebei Medical University and obtained his M.Sc. on natural products at the Institute of Materia Medica, China Academy of Traditional Chinese Medicine, in 1989. He worked for five years as an assistant professor in the China Japan Friendship Institute of Clinical Medical Sciences in Beijing. In 1998, he received his Ph.D. in natural products at the Edinburgh Napier University followed by two years of postdoctoral work at Huddersfield University. He joined Syngenta at its Jealott's Hill International Research Centre as a natural products chemist in 2002 and is now principal scientist. His research interests are natural products from terrestrial and marine organisms, bioactive compound application in agrichemical and pharmaceutical areas, and polysaccharide chemistry. From 2004, he received honorary professorships from the Hebei Medical University and Wuhan Polytechnic University and visiting professorships from the Peking Union Medical College, Chinese Academy of Medical Sciences, Central China Normal University, Hubei Academy of Agricultural Sciences, Shanghai Southern Pesticide Research Centre, and Jilin University of China.

Bin Cong (born in 1957, Qiqihar, Heilongjiang Province) is Professor of Department of Forensic Medicine, Hebei Medical University. He got his Bachelor degree from Hebei Medical University in 1983 and Master degree from Xi'an Medical University in 1989, and in 1998 he obtained his Ph.D. from Hebei Medical University. He was in Shinshu University (Japan) as a visiting scholar in 1994. His research field is concentrated on the phytotoxic constituents of medicinal plants and their antitumor activities.

ACKNOWLEDGMENTS

We are grateful for the financially supports from National Natural Science Foundation of China (81072551), Key Projects of Science & Technology of Hebei Province (11276103D-89), Scientific Research Foundation for the Returned Overseas Chinese Scholars of Hebei Province (2006-02), and Scientific

Research Foundation of Hebei Province (08B032 and C2010000489). We also wish to extend our sincere thanks for the financial support of Syngenta Ltd. (2011-Hebei Medical University-Syngenta-03) and Japan Society for the Promotion of Science (Nos. 19580120 and 22580112). We would like to thank Dr. John Clough at Syngenta Jealott's Hill International Research Centre for his contributions to the preparation and proofreading of the manuscript.

REFERENCES

(1) Fernandez-Alonso, J. L.; Vega, N.; Filgueira, J. J.; Perez, G. *Biochem. Syst. Ecol.* **2003**, *31*, 617.
(2) García Vallejo, M. C.; Moujir, L.; Burillo, J.; León Guerra, L.; González, M.; Díaz Peñate, R.; San Andrés, L.; Gutiérrez Luis, J.; López Blanco, F.; Ruiz de Galarreta, C. M. *Flavour Frag. J.* **2006**, *21*, 72.
(3) Ulubelen, A.; Birman, H.; Öksüz, S.; Topçu, G.; Kolak, U.; Barla, A.; Voelter, W. *Planta Med.* **2002**, *68*, 818.
(4) Mohammadhosseini, M.; Pazoki, A.; Akhlaghi, H. *Chem. Nat. Compd.* **2008**, *44*, 127.
(5) Guajardo Touche, E. M.; Loprz, E. G.; Reyes, A. P.; Sánchez, H.; Honecker, F.; Achenbach, H. *Phytochemistry* **1997**, *45*, 387.
(6) Ulubelen, A.; Öksüz, S.; Kolak, U.; Tan, N.; Bozok-Johansson, C.; Celik, C.; Kohlbau, H. J.; Voelter, W. *Phytochemistry* **1999**, *52*, 1455.
(7) Salehi, P.; Sonboli, A.; Dayeni, M.; Eftekhar, F.; Yousefzadi, M. *Chem. Nat. Compd.* **2008**, *44*, 102.
(8) Kamatou, G. P. P.; Makunga, N. P.; Ramogola, W. P. N.; Viljoen, A. M. *J. Ethnopharmacol.* **2008**, *119*, 664.
(9) Veitch, N. C.; Grayer, R. J.; Irwin, J. L.; Takeda, K. *Phytochemistry* **1998**, *48*, 389.
(10) Watzke, A.; O'Malley, S. J.; Bergman, R. G.; Ellman, J. *J. Nat. Prod.* **2006**, *69*, 1231.
(11) Wang, B.-Q. *J. Med. Plant. Res.* **2010**, *4*, 2813.
(12) Wei, Y. J.; Li, S. L.; Li, P. *Biomed. Chromatogr.* **2007**, *21*, 1.
(13) Chang, H. M.; Cheng, K. P.; Choang, T. F.; Chow, H. F.; Chui, K. Y.; Hon, P. M.; Tan, F. W. L.; Yang, Y.; Zhong, Z. P. *J. Org. Chem.* **1990**, *55*, 3537.
(14) Ren, Z. H.; Tong, Y. H.; Xu, W.; Ma, J.; Chen, Y. *Phytomedicine* **2010**, *17*, 212.
(15) Fronza, M.; Murillo, R.; Ślusarczyk, S.; Adams, M.; Hamburger, M.; Heinzmann, B.; Laufer, S.; Merfort, I. *Bioorg. Med. Chem.* **2011**, *19*, 4876.
(16) Zhang, Z. F.; Chen, H. S.; Peng, Z. G.; Li, Z. R.; Jiang, J. D. *J. Asian Nat. Prod. Res.* **2008**, *10*, 252.
(17) Xu, G.; Hou, A. J.; Zheng, Y. T.; Zhao, Y.; Li, X. L.; Peng, L. Y.; Zhao, Q. S. *Org. Lett.* **2007**, *9*, 291.
(18) Esmaeili, A.; Rustaiyan, A.; Nadimi, M.; Larijani, K.; Nadjafi, F.; Tabrizi, L.; Chalabian, F.; Amiri, H. *Nat. Prod. Res.* **2008**, *22*, 516.
(19) Li, Y. Q.; Husbands, S. M.; Mahon, M. F.; Traynor, J. R.; Rowan, M. G. *Chem. Biodiversity* **2007**, *4*, 1586.
(20) Shirota, O.; Nagamatsu, K.; Sekita, S. *J. Nat. Prod.* **2006**, *69*, 1782.
(21) Bücheler, R.; Gleiter, C. H.; Schwoerer, P.; Gaertner, I. *Pharmacopsychiatry* **2005**, *38*, 1.
(22) Narukawa, Y.; Fukui, M.; Hatano, K.; Takeda, T. *J. Nat. Med.* **2006**, *60*, 58.
(23) Ali, M. S.; Ibrahim, S. A.; Ahmed, S.; Lobkovsky, E. *Chem. Biodiversity* **2007**, *4*, 98.
(24) Al-Yousuf, M. H.; Bashir, A. K.; Ali, B. H.; Tanira, M. O. M.; Blunden, G. *J. Ethnopharmacol.* **2002**, *81*, 121.
(25) Zahid, M.; Saeed, M.; Asim, M.; Ishrud, O.; Wu, S.; Ahmad, V. U.; Pan, Y. *Helv. Chim. Acta* **2003**, *86*, 2021.
(26) Amaro-Luis, J. M.; Herrera, J. R.; Luis, J. G. *Phytochemistry* **1998**, *47*, 895.
(27) Vortherms, T. A.; Roth, B. L. *Mol. Interventions* **2006**, *6*, 257.
(28) Imanshahidi, M.; Hosseinzadeh, H. *Phytother. Res.* **2006**, *20*, 427.
(29) Abdel-Moneim, F. M.; Elgamal, M. H. A.; Fayez, M. B. E.; Salam, L. A. R. *Phytochemistry* **1967**, *6*, 1035.
(30) Passannanti, S.; Paternostro, M.; Piozzi, F. *Phytochemistry* **1983**, *22*, 1044.
(31) Perry, N. S. L.; Bollen, C.; Perry, E. K.; Ballard, C. *Pharmacol., Biochem. Behav.* **2003**, *75*, 651.
(32) Cantrell, C. L.; Franzblau, S. G.; Fischer, N. H. *Planta Med.* **2001**, *67*, 685.
(33) Jiang, R. W.; Lau, K. M.; Hon, P. M.; Mak, T. C. W.; Woo, K. S.; Fung, K. P. *Curr. Med. Chem.* **2005**, *12*, 237.
(34) Ulubelen, A. *Phytochemistry* **2003**, *64*, 395.
(35) Gali-Muhtasib, H.; Hilan, C.; Khater, C. *J. Ethnopharmacol.* **2000**, *71*, 513.
(36) Prisinzano, T. E. *Life Sci.* **2005**, *78*, 527.
(37) Wang, X.; Morris-Natschke, S. L.; Lee, K. H. *Med. Res. Rev.* **2007**, *27*, 133.
(38) Kabouche, A.; Kabouche, Z. *Stud. Nat. Prod. Chem.* **2008**, *35*, 753.
(39) Topçu, G. *J. Nat. Prod.* **2006**, *69*, 482.
(40) Lu, Y.; Yeap Foo, L. *Phytochemistry* **2002**, *59*, 117.
(41) Ulubelen, A.; Topçu, G.; Tuzlaci, E. *J. Nat. Prod.* **1992**, *55*, 1518.
(42) Wang, Y.; Li, Z.; Zhang, H.; Sha, Y.; Pei, Y.; Hua, H. *Chem. Pharm. Bull.* **2008**, *56*, 843.
(43) Li, Y.; Wu, Y. Q.; Du, X.; Shi, Y. P. *Planta Med.—Nat. Prod., Med. Plant Res.* **2003**, *69*, 782.
(44) Xu, G.; Peng, L. Y.; Li, X. L.; Zhao, Y.; Tu, L.; Zhao, Q. S.; Sun, H. D.; Lu, Y.; Mao, L.; Zheng, Q. T. *Helv. Chim. Acta* **2005**, *88*, 2370.
(45) Pan, Z. H.; Wang, Y. Y.; Li, M. M.; Xu, G.; Peng, L. Y.; He, J.; Zhao, Y.; Li, Y.; Zhao, Q. S. *J. Nat. Prod.* **2010**, *73*, 1146.
(46) Xu, G.; Peng, L. Y.; Hou, A. J.; Yang, J.; Han, Q. B.; Xu, H. X.; Zhao, Q. S. *Tetrahedron* **2008**, *64*, 9490.
(47) González, A. G.; Grillo, T. A.; Ravelo, A. G.; Luis, J. G.; Calle, J.; Rivera, A. *J. Nat. Prod.* **1989**, *52*, 1307.
(48) Liu, Y.; Li, C.; Shi, J. G.; Shi, Y. P. *Helv. Chim. Acta* **2009**, *92*, 335.
(49) Maurer, B.; Hauser, A. *Helv. Chim. Acta* **1983**, *66*, 2223.
(50) González, A. G.; Luis, J. G.; Grillo, T. A.; Vázquez, J. T.; Calle, J.; Rivera, A. *J. Nat. Prod.* **1991**, *54*, 579.
(51) Ulubelen, A.; Topçu, G. *Phytochemistry* **1994**, *36*, 971.
(52) Ali, M. S.; Ahmed, W.; Armstrong, A. F.; Ibrahim, S. A.; Ahmed, S.; Parvez, M. *Chem. Pharm. Bull.* **2006**, *54*, 1235.
(53) González, A. G.; Grillo, T. A.; Aguiar, Z. E. *Phytochemistry* **1991**, *30*, 3462.
(54) González, A. G.; Grillo, T. A.; Luis, J. G.; Vázquez, J. T.; Rodriguez, M. L.; Ravelo, J. L.; Calle, J.; Rivera, A. *Phytochemistry* **1990**, *29*, 3581.
(55) Aydoğmuş, Z.; Yeşİlyurt, V.; Topçu, G. *Nat. Prod. Res.* **2006**, *20*, 775.
(56) Ulubelen, A.; Miski, M.; Mabry, T. J. *J. Nat. Prod.* **1981**, *44*, 119.
(57) Tan, N.; Kaloga, M.; Radtke, O. A.; Kiderlen, A. F.; Öksüz, S.; Ulubelen, A.; Kolodziej, H. *Phytochemistry* **2002**, *61*, 881.
(58) Fraga, B. M.; Diaz, C. E.; Guadano, A.; Gonzalez-Coloma, A. *J. Agric. Food Chem.* **2005**, *53*, 5200.
(59) Ulubelen, A.; Topçu, G. *J. Nat. Prod.* **1992**, *55*, 441.
(60) Xu, G.; Peng, L. Y.; Zhao, Y.; Li, X. L.; Tu, L.; Zhao, Q. S.; Sun, H. D. *Chem. Pharm. Bull.* **2005**, *53*, 1575.
(61) Don, M.; Shen, C.; Syu, W.; Ding, Y.; Sun, C. *Phytochemistry* **2006**, *67*, 497.
(62) Luis, J. G.; Qui ones, W.; Echeverri, F. *Phytochemistry* **1994**, *36*, 115.
(63) Tada, M.; Okuno, K.; Chiba, K.; Ohnishi, E.; Yoshii, T. *Phytochemistry* **1994**, *35*, 539.
(64) González, A. G.; Aguiar, Z. E.; Grillo, T. A.; Luis, J. G. *Phytochemistry* **1992**, *31*, 1691.
(65) Topçu, G.; Ulubelen, A. *Phytochemistry* **1990**, *29*, 2346.
(66) Michavila, A.; De La Torre, M. C.; Rodríguez, B. *Phytochemistry* **1986**, *25*, 1935.
(67) Kawazoe, K.; Yamamoto, M.; Takaishi, Y.; Honda, G.; Fujita, T.; Sezik, E.; Yesilada, E. *Phytochemistry* **1999**, *50*, 493.

(68) Ulubelen, A.; Tuzlaci, E. *J. Nat. Prod.* **1990**, *53*, 1597.
(69) Fraga, B. M.; González, A. G.; Herrera, J. R.; Luis, J. G.; Ravelo, A. G. *Phytochemistry* **1985**, *25*, 269.
(70) Topçu, G.; Ulubelen, A.; Eris, C. *Phytochemistry* **1994**, *36*, 743.
(71) Ulubelen, A.; Topçu, G. *Phytochemistry* **1992**, *31*, 3949.
(72) Ulubelen, A.; Evren, N.; Tuzlaci, E.; Johansson, C. *J. Nat. Prod.* **1988**, *51*, 1178.
(73) Ulubelen, A.; Öksüz, S.; Topçu, G.; Gören, A. C.; Voelter, W. *J. Nat. Prod.* **2001**, *64*, 549.
(74) Esquivel, B.; Sánchez, A. A.; Vergara, F.; Matus, W.; Hernandez-Ortega, S.; Ramírez-Apan, M. T. *Chem. Biodiversity* **2005**, *2*, 738.
(75) Luis, J. G.; San Andres, L. *Phytochemistry* **1993**, *33*, 635.
(76) Ulubelen, A.; Topçu, G. *Phytochemistry* **1991**, *30*, 2085.
(77) Al-Hazimi, H. M. G.; Miana, G. A.; Deep, M. S. H. *Phytochemistry* **1987**, *26*, 1091.
(78) Al-Hazimi, H. M. G. *Phytochemistry* **1986**, *25*, 1238.
(79) Ulubelen, A.; Sönmez, U.; Topçu, G.; Johansson, C. B. *Phytochemistry* **1996**, *42*, 145.
(80) Ulubelen, A.; Tan, N.; Sönmez, U.; Topçu, G. *Phytochemistry* **1998**, *47*, 899.
(81) Ulubelen, A.; Tan, N.; Topçu, G. *Phytochemistry* **1997**, *45*, 1221.
(82) Ulubelen, A.; Topçu, G.; Tan, N. *Phytochemistry* **1992**, *31*, 3637.
(83) Ulubelen, A.; Topçu, G.; Sönmez, U.; Choudhary, M. I.; Rahman, A. U. *Phytochemistry* **1995**, *40*, 861.
(84) Ulubelen, A.; Öksüz, S.; Kolak, U.; Bozok-Johansson, C.; Celik, C.; Voelter, W. *Planta Med.* **2000**, *66*, 458.
(85) Ulubelen, A. *J. Nat. Prod.* **1989**, *52*, 1313.
(86) González, A. G.; Herrera, J. R.; Luis, J. G.; Ravelo, A. G.; Ferro, E. A. *Phytochemistry* **1988**, *27*, 1540.
(87) González, A. G.; Rodríguez, C. M.; Luis, J. G. *Phytochemistry* **1987**, *26*, 1471.
(88) Ahmed, A. A.; Mohamed, A. E. H.; Karchesy, J.; Asakawa, Y. *Phytochemistry* **2006**, *67*, 424.
(89) Tan, N.; Topçu, G.; Ulubelen, A. *Phytochemistry* **1998**, *49*, 175.
(90) Ulubelen, A.; Topçu, G.; Terem, B. *Phytochemistry* **1987**, *26*, 1534.
(91) Lin, H. C.; Chang, W. L. *Phytochemistry* **2000**, *53*, 951.
(92) Topçu, G.; Kartal, M.; Ulubelen, A. *Phytochemistry* **1997**, *44*, 1393.
(93) Topçu, G.; Ulubelen, A. *J. Nat. Prod.* **1996**, *59*, 734.
(94) Hueso-Rodríguez, J. A.; Jimeno, M. L.; Rodríguez, B.; Savona, G.; Bruno, M. *Phytochemistry* **1983**, *22*, 2005.
(95) Ulubelen, A.; Topçu, G.; Johansson, C. B. *J. Nat. Prod.* **1997**, *60*, 1275.
(96) Sairafianpour, M.; Bahreininejad, B.; Witt, M.; Ziegler, H. L.; Jaroszewski, J. W.; Staerk, D. *Planta Med.* **2003**, *69*, 846.
(97) Luis, J. G.; Andrés, L. S.; Perales, A. *Tetrahedron* **1993**, *49*, 4993.
(98) González, A. G.; Aguiar, Z. E.; Luis, J. G.; Ravelo, A. G.; Domínguez, X. *Phytochemistry* **1988**, *27*, 1777.
(99) González, A.; Aguiar, Z.; Luis, J.; Ravelo, A.; Domínguez, X. *J. Nat. Prod.* **1989**, *52*, 1231.
(100) Simoes, F.; Michavila, A.; Rodriguez, B.; Garcia-Alvarez, M. C.; Hasan, M. *Phytochemistry* **1986**, *25*, 755.
(101) González, A. G.; Aguiar, Z. E.; Luis, J. G.; Ravelo, A. G. *Tetrahedron* **1989**, *45*, 5203.
(102) Rodríguez-Hahn, L.; García, A.; Esquivel, B.; Cárdenas, J. *Can. J. Chem.* **1987**, *65*, 2687.
(103) Nakao, M.; Fukushima, T. *J. Pharm. Soc. Jpn.* **1934**, *54*, 154.
(104) Hohmann, J. *Biochem. Syst. Ecol.* **2003**, *31*, 427.
(105) Nagy, G.; Günther, G.; Máthé, I.; Blunden, G.; Yang, M.; Crabb, T. A. *Phytochemistry* **1999**, *52*, 1105.
(106) Jassbi, A. R.; Mehrdad, M.; Eghtesadi, F.; Ebrahimi, S. N.; Baldwin, I. T. *Chem. Biodivers.* **2006**, *3*, 916.
(107) Miura, K.; Kikuzaki, H.; Nakatani, N. *J. Agric. Food Chem.* **2002**, *50*, 1845.
(108) Nagy, G.; Günther, G.; Máthé, I.; Blunden, G.; Yang, M.; Crabb, T. A. *Phytochemistry* **1999**, *51*, 809.
(109) Topçu, G.; Ulubelen, A. *Phytochemistry* **1991**, *30*, 2412.
(110) Rodríguez-Hahn, L.; Esquivel, B.; Sánchez, C.; Cárdenas, J.; Estebanes, L.; Soriano-García, M.; Toscano, R.; Ramamoorthy, T. P. *Tetrahedron Lett.* **1986**, *27*, 5459.
(111) Kabouche, A.; Kabouche, Z.; Öztürk, M.; Kolak, U.; Topçu, G. *Food Chem.* **2007**, *102*, 1281.
(112) Sabri, N. N.; Abou-Donia, A. A.; Ghazy, N. M.; Assad, A. M.; El-Lakany, A. M.; Sanson, D. R.; Gracz, H.; Barnes, C. L.; Schlemper, E. O.; Tempesta, M. S. *J. Org. Chem.* **1989**, *54*, 4097.
(113) Al-Hazimi, H. M. G.; Deep, M. S.; Miana, G. A. *Phytochemistry* **1984**, *23*, 919.
(114) Marrero, J. G.; Andrés, L. S.; Luis, J. G. *Chem. Pharm. Bull.* **2005**, *53*, 1524.
(115) Luis, J. G.; Grillo, T. A.; Qui ones, W.; Kishi, M. P. *Phytochemistry* **1994**, *36*, 251.
(116) Amaro-Luis, J. M. *Pharm. Acta Helv.* **1997**, *72*, 233.
(117) Guerrero, I. C.; Andres, L. S.; León, L. G.; Machín, R. P.; Padrón, J. M.; Luis, J. G.; Delgadillo, J. *J. Nat. Prod.* **2006**, *69*, 1803.
(118) Fraga, B. M.; González, A. G.; Herrera, J. R.; Luis, J. G.; Perales, A.; Ravelo, A. G. *Phytochemistry* **1985**, *24*, 1853.
(119) Luis, J. G.; Grillo, T. A. *Phytochemistry* **1993**, *34*, 863.
(120) Tada, M.; Hara, T.; Hara, C.; Chiba, K. *Phytochemistry* **1997**, *45*, 1475.
(121) Dominguez, X. A.; Gonzalez, F. H.; Aragon, R.; Gutierrez, M.; Marroquin, J. S.; Watson, W. *Planta Med.* **1976**, *30*, 237.
(122) Cárdenas, J.; Rodríguez-Hahn, L. *Phytochemistry* **1995**, *38*, 199.
(123) Watson, W. H.; Taira, Z.; Dominguez, X. A.; Gonzales, H.; Guiterrez, M.; Aragon, R. *Tetrahedron Lett.* **1976**, *29*, 2501.
(124) Nieto, M.; García, E. E.; Giordano, O. S.; Tonn, C. E. *Phytochemistry* **2000**, *53*, 911.
(125) Ortega, A.; Cárdenas, J.; Gage, D. A.; Maldonado, E. *Phytochemistry* **1995**, *39*, 931.
(126) Jimenez E, M.; Portugal M, E.; Lira-Rocha, A.; Soriano-Garcia, M.; Toscano, R. A. *J. Nat. Prod.* **1988**, *51*, 243.
(127) Ulubelen, A.; Topçu, G.; Chen, S.; Cai, P.; Snyder, J. K. *J. Org. Chem.* **1991**, *56*, 7354.
(128) Kolak, U. *Turk. J. Chem.* **2007**, *31*, 363.
(129) Escudero, J.; Perez, L.; Rabanal, R. M.; Valverde, S. *Phytochemistry* **1983**, *22*, 585.
(130) Luo, H. W.; Wu, B. J.; Wu, M. Y.; Yong, Z. G.; Niwa, M.; Hirata, Y. *Phytochemistry* **1985**, *24*, 815.
(131) Esquivel, B.; Calderón, J. S.; Flores, E.; Sánchez, A. A.; Rosas Rivera, R. *Phytochemistry* **1997**, *46*, 531.
(132) Xu, G.; Peng, L.; Lu, L.; Weng, Z.; Zhao, Y.; Li, X.; Zhao, Q.; Sun, H. *Planta Med.* **2006**, *72*, 84.
(133) Wang, X.; Bastow, K. F.; Sun, C. M.; Lin, Y. L.; Yu, H. J.; Don, M. J.; Wu, T. S.; Nakamura, S.; Lee, K. H. *J. Med. Chem.* **2004**, *47*, 5816.
(134) Dong, Y.; Morris-Natschke, S. L.; Lee, K. H. *Nat. Prod. Rep.* **2011**, *28*, 529.
(135) Luo, H. W.; Ji, J.; Wu, M. Y.; Yong, Z. G. *Chem. Pharm. Bull.* **1986**, *34*, 3166.
(136) Don, M. J.; Shen, C. C.; Lin, Y. L.; Syu, W. J.; Ding, Y. H.; Sun, C. M. *J. Nat. Prod.* **2005**, *68*, 1066.
(137) Lin, F. W.; Damu, A. G.; Wu, T. S. *J. Nat. Prod.* **2006**, *69*, 93.
(138) Lin, F. W.; Damu, A. G.; Wu, T. S. *Heterocycles* **2006**, *68*, 159.
(139) Lee, I. S.; Kaneda, N.; Suttisri, R.; El-Lakany, A. M.; Sabri, N. N.; Kinghorn, A. D. *Planta Med.* **1998**, *64*, 632.
(140) Hussein, A. A.; de la Torre, M. C.; Rodríguez, B.; Hammouda, F. M.; Hussiney, H. A. *Phytochemistry* **1997**, *45*, 1663.
(141) Janicsák, G.; Hohmann, J.; Zupkó, I.; Forgo, P.; Rédei, D.; Falkay, G.; Máthé, I. *Planta Med.* **2003**, *69*, 1156.
(142) Romussi, G.; Ciarallo, G.; Bisio, A.; Fontana, N.; De Simone, F.; De Tommasi, N.; Mascolo, N.; Pinto, L. *Planta Med.* **2001**, *67*, 153.
(143) Capasso, R.; Izzo, A. A.; Romussi, G.; Capasso, F.; De Tommasi, N.; Bisio, A.; Mascolo, N. *Planta Med.* **2004**, *70*, 185.
(144) Capasso, R.; Izzo, A. A.; Capasso, F.; Romussi, G.; Bisio, A.; Mascolo, N. *Planta Med.* **2004**, *70*, 375.
(145) Hohmann, J.; Janicsak, G.; Forgo, P.; Redei, D.; Mathe, I.; Bartok, T. *Planta Med.* **2003**, *69*, 254.

(146) Chen, X.; Ding, J.; Ye, Y. M.; Zhang, J. S. *J. Nat. Prod.* **2002**, *65*, 1016.
(147) Li, M.; Zhang, J. S.; Ye, Y. M.; Fang, J. N. *J. Nat. Prod.* **2000**, *63*, 139.
(148) Ulubelen, A.; Sönmez, U.; Topçu, G. *Phytochemistry* **1997**, *44*, 1297.
(149) Ulubelen, A.; Topçu, G.; Sönmez, U.; Eriş, C.; Özgen, U. *Phytochemistry* **1996**, *43*, 431.
(150) Chang, J.; Xu, J.; Li, M.; Zhao, M.; Ding, J.; Zhang, J. *Planta Med.* **2005**, *71*, 861.
(151) Boya, M. T.; Valverde, S. *Phytochemistry* **1981**, *20*, 1367.
(152) Topçu, G.; Eriş, C.; Ulubelen, A. *Phytochemistry* **1996**, *41*, 1143.
(153) Rodríguez, B.; Fernández-Gadea, F.; Savona, G. *Phytochemistry* **1984**, *23*, 1805.
(154) Gökdil, G.; Topçu, G.; Sönmez, U.; Ulubelen, A. *Phytochemistry* **1997**, *46*, 799.
(155) Ulubelen, A.; Topçu, G.; Tan, N. *Tetrahedron Lett.* **1992**, *33*, 7241.
(156) Ulubelen, A.; Topçu, G.; Tan, N.; Lin, L. J.; Cordell, G. A. *Phytochemistry* **1992**, *31*, 2419.
(157) Yang, B. J.; Huang, X. L.; Huang, Y.; Wang, X. M.; Lin, L. L.; But, P. H.; Zhuang, G. F. *Acta Bot. Sin.* **1988**, *30*, 524.
(158) Li, M.; Zhang, J. S.; Chen, M. Q. *J. Nat. Prod.* **2001**, *64*, 971.
(159) Xu, J.; Chang, J.; Zhao, M.; Zhang, J. *Phytochemistry* **2006**, *67*, 795.
(160) Watson, W.; Taira, Z.; Dominguez, X.; Gonzalez, H.; Gutierrez, M.; Aragon, R. *Tetrahedron Lett.* **1976**, *29*, 2501.
(161) Sanchez, A.; Jimenezortiz, V.; Sartor, T.; Tonn, C.; Garcia, E.; Nieto, M.; Burgos, M.; Sosa, M. *Acta Trop.* **2006**, *98*, 118.
(162) Esquivel, B.; Flores, M.; Hernández-Ortega, S.; Toscano, R. A.; Ramamoorthy, T. P. *Phytochemistry* **1995**, *39*, 139.
(163) Mehmood, S.; Riaz, N.; Nawaz, S. A.; Afza, N.; Malik, A.; Choudhary, M. I. *Arch. Pharm. Res.* **2006**, *29*, 195.
(164) Pan, Z. H.; He, J.; Li, Y.; Zhao, Y.; Wu, X. D.; Wang, K.; Peng, L. Y.; Xu, G.; Zhao, Q.-S. *Tetrahedron Lett.* **2010**, *51*, 5083.
(165) Gonzalez, A. G.; Herrera, J. R.; Luis, J. G.; Ravelo, A. G.; Perales, A. *J. Nat. Prod.* **1987**, *50*, 341.
(166) Luis, J. G.; Grillo, T. A. *Tetrahedron* **1993**, *49*, 6277.
(167) Kong, D. Y.; Liu, X. J.; Teng, M. K.; Rao, Z. H. *Acta Pharm. Sin.* **1985**, *20*, 747.
(168) Al Yousuf, M. H.; Bashir, A. K.; Blunden, G.; Crabb, T. A.; Patel, A. V. *Phytochemistry* **2002**, *61*, 361.
(169) Sun, X. R.; Luo, H. W.; Sakai, T.; Niwa, M. *Tetrahedron Lett.* **1991**, *32*, 5797.
(170) Luo, H. W.; Chen, S. X.; Lee, J.; Snyder, J. K. *Phytochemistry* **1988**, *27*, 290.
(171) Asari, F.; Kusumi, T.; Zheng, G. Z.; Cen, Y. Z.; Kakisawa, H. *Chem. Lett.* **1990**, *19*, 1885.
(172) Djarmati, Z.; Jankov, R. M.; Djordjevic, A.; Ribar, B.; Lazar, D.; Engel, P. *Phytochemistry* **1992**, *31*, 1307.
(173) Sim, G. A.; Hamor, T. A.; Paul, I. C.; Robertson, J. M. *Proc. Chem. Soc.* **1961**, *2*, 75.
(174) Kawahara, N.; Tamura, T.; Inoue, M.; Hosoe, T.; Kawai, K.-i.; Sekita, S.; Satake, M.; Goda, Y. *Phytochemistry* **2004**, *65*, 2577.
(175) Bigham, A. K.; Munro, T. A.; Rizzacasa, M. A.; Robins-Browne, R. M. *J. Nat. Prod.* **2003**, *66*, 1242.
(176) Lee, D. Y. W.; Ma, Z. Z.; Liu-Chen, L.-Y.; Wang, Y. L.; Chen, Y.; Carlezon, W. A., Jr; Cohen, B. *Bioorg. Med. Chem.* **2005**, *13*, 5635.
(177) Maldonado, E.; Ortega, A. *Phytochemistry* **1997**, *46*, 1249.
(178) Esquivel, B.; Hernández, L. M.; Cárdenas, J.; Ramamoorthy, T. P.; Rodríguez-Hahn, L. *Phytochemistry* **1989**, *28*, 561.
(179) Sánchez, A. A.; Esquivel, B.; Pera, A.; Cárdenas, J.; Soriano-García, M.; Toscano, A.; Rodriguez-Hahn, L. *Phytochemistry* **1987**, *26*, 479.
(180) Cuevas, G.; Collera, O.; García, F.; Cárdenas, J.; Maldonado, E.; Ortega, A. *Phytochemistry* **1987**, *26*, 2019.
(181) Rodriguez-Hahn, L.; Alvarado, G.; Cardenas, J.; Esquivel, B.; Gavino, R. *Phytochemistry* **1994**, *35*, 447.
(182) Esquivel, B.; Vallejo, A.; Gavino, R.; Cárdenas, J.; Sánchez, A. A.; Ramamoorthy, T. P.; Rodriguez-Hahn, L. *Phytochemistry* **1988**, *27*, 2903.
(183) Esquivel, B.; Cardenas, J.; Rodriguez-Hahn, L.; Ramamoorthy, T. P. *J. Nat. Prod.* **1987**, *50*, 738.
(184) Esquivel, B.; Hernandez, M.; Ramamoorthy, T. P.; Cardenas, J.; Rodriguez-Hahn, L. *Phytochemistry* **1986**, *25*, 1484.
(185) Esquivel, B.; Mendez, A.; Ortega, A.; Soriano-Garcia, M.; Toscano, A.; Rodriguez-Hahn, L. *Phytochemistry* **1985**, *24*, 1769.
(186) Kawahara, N.; Inoue, M.; Kawai, K. I.; Sekita, S.; Satake, M.; Goda, Y. *Phytochemistry* **2003**, *63*, 859.
(187) Esquivel, B.; Calderón, J.; Sánchez, A.; Zárate, M.; Sánchez, L. *Phytochemistry* **1997**, *45*, 781.
(188) Maldonado, E.; Cárdenas, J.; Bojórquez, H.; Escamilla, E. M.; Ortega, A. *Phytochemistry* **1996**, *42*, 1105.
(189) Fontana, G.; Savona, G.; Rodríguez, B. *J. Nat. Prod.* **2006**, *69*, 1734.
(190) Almanza, G.; Balderrama Cecilia, L. *Tetrahedron* **1997**, *53*, 14719.
(191) Valdes, L. J., III; Butler, W. M.; Hatfield, G. M.; Paul, A. G.; Koreeda, M. *J. Org. Chem.* **1984**, *49*, 4716.
(192) Munro, T. A.; Rizzacasa, M. A. *J. Nat. Prod.* **2003**, *66*, 703.
(193) Valdes, L. J., III; Chang, H. M.; Visger, D. C.; Koreeda, M. *Org. Lett.* **2001**, *3*, 3935.
(194) Ortega, A.; Blount, J. F.; Manchand, P. S. *J. Chem. Soc., Perkin Trans. 1* **1982**, *17*, 2505.
(195) Harding, W. W.; Tidgewell, K.; Schmidt, M.; Shah, K.; Dersch, C. M.; Snyder, J.; Parrish, D.; Deschamps, J. R.; Rothman, R. B.; Prisinzano, T. E. *Org. Lett.* **2005**, *7*, 3017.
(196) Ma, Z.; Deng, G.; Dai, R.; Xu, W.; Liu-Chen, L.; Lee, D. Y. W. *Tetrahedron Lett.* **2010**, *51*, 5480.
(197) Kutrzeba, L. M.; Ferreira, D.; Zjawiony, J. K. *J. Nat. Prod.* **2009**, *72*, 1361.
(198) Savona, G.; Paternostro, M. P.; Piozzi, F.; Hanson, J. R. *J. Chem. Soc., Perkin Trans. 1* **1979**, *6*, 533.
(199) del Carmen Fernández, M.; Esquivel, B.; Cárdenas, J.; Sánchez, A. A.; Toscano, R. A.; Rodríguez-Hahn, L. *Tetrahedron* **1991**, *47*, 7199.
(200) Hu, D. P.; Kawazoe, K.; Takaishi, Y. *Phytochemistry* **1997**, *46*, 781.
(201) Maldonado, E.; Ortega, A. *Phytochemistry* **2000**, *53*, 103.
(202) Esquivel, B.; Esquivel, O.; Cárdenas, J.; Adela Sánchez, A.; Ramamoorthy, T. P.; Alfredo Toscano, R.; Rodríguez-Hahn, L. *Phytochemistry* **1991**, *30*, 2335.
(203) Esquivel, B.; Ochoa, J. *Phytochemistry* **1988**, *27*, 483.
(204) Esquivel, B.; Cardenas, J.; Ramamoorthy, T. P.; Rodriguez-Hahn, L. *Phytochemistry* **1986**, *25*, 2381.
(205) García-Alvarez, M. C.; Hasan, M.; Michavila, A.; Fernández-Gadea, F.; Rodríguez, B. *Phytochemistry* **1985**, *25*, 272.
(206) Eguren, L.; Fayos, J.; Perales, A.; Savona, G.; Rodriguez, B. *Phytochemistry* **1984**, *23*, 466.
(207) Savona, G.; Raffa, D.; Bruno, M.; Rodríguez, B. *Phytochemistry* **1983**, *22*, 784.
(208) Xu, G.; Peng, L.; Niu, X.; Zhao, Q.; Li, R.; Sun, H. *Helv. Chim. Acta* **2004**, *87*, 949.
(209) Narukawa, Y.; Hatano, K.; Takeda, T. *J. Nat. Med.* **2006**, *60*, 206.
(210) Rodríguez-Hahn, L.; Esquivel, B.; Cárdenas, J. *Prog. Chem. Org. Nat. Prod.* **1994**, *63*, 107.
(211) Sanchez, A. A.; Esquivel, B.; Ramamoorthy, T. P.; Rodriguez-Hahn, L. *Phytochemistry* **1995**, *38*, 171.
(212) Maldonado, E.; Ortega, A. *Phytochemistry* **1997**, *45*, 1461.
(213) Esquivel, B.; Tello, R.; Sánchez, A. A. *J. Nat. Prod.* **2005**, *68*, 787.
(214) Cárdenas, J.; Pavón, T.; Esquivel, B.; Toscano, A.; Rodríguez-Hahn, L. *Tetrahedron Lett.* **1992**, *33*, 581.
(215) Maldonado, E. *Phytochemistry* **1992**, *31*, 217.
(216) Nieto, M.; Oscar Gallardo, V.; Rossomando, P. C.; Tonn, C. E. *J. Nat. Prod.* **1996**, *59*, 880.

(217) González, A. G.; Herrera, J. R.; Luis, J. G.; Ravelo, A. G.; Rodriguez, M. L.; Ferro, E. *Tetrahedron Lett.* **1988**, *29*, 363.
(218) Ortega, A.; Bautista, E.; Maldonado, E. *Chem. Pharm. Bull.* **2006**, *54*, 1338.
(219) Ortega, A.; Cárdenas, J.; Toscano, A.; Maldonado, E.; Aumelas, A.; Calsteren, M. R. V.; Jankowski, C. *Phytochemistry* **1991**, *30*, 3357.
(220) Bisio, A.; De Tommasi, N.; Romussi, G. *Planta Med.* **2004**, *70*, 452.
(221) Bisio, A.; Fontana, N.; Romussi, G.; Ciarallo, G.; De Tommasi, N.; Pizza, C.; Mugnoli, A. *Phytochemistry* **1999**, *52*, 1535.
(222) Maldonado, E.; de los Angeles Flores, M.; Salazar, B.; Ortega, A. *Phytochemistry* **1994**, *37*, 1480.
(223) Aoyagi, Y.; Yamazaki, A.; Nakatsugawa, C.; Fukaya, H.; Takeya, K.; Kawauchi, S.; Izumi, H. *Org. Lett.* **2008**, *10*, 4429.
(224) Esquivel, B.; Dominguez, R. M.; Hernández-Ortega, S.; Toscano, R. A.; Rodríguez-Hahn, L. *Tetrahedron* **1994**, *50*, 11593.
(225) van Tamelen, E. E.; Marson, S. A. *Bioorg. Chem.* **1982**, *11*, 219.
(226) Bruno, M.; Savona, G.; Fernández-Gadea, F.; Benjamin, R. *Phytochemistry* **1986**, *25*, 475.
(227) Cioffi, G.; Bader, A.; Malafronte, A.; Dal Piaz, F.; De Tommasi, N. *Phytochemistry* **2008**, *69*, 1005.
(228) Topçu, G.; Ulubelen, A.; Tam, T. C. M.; Che, C. T. *J. Nat. Prod.* **1996**, *59*, 113.
(229) Gonzalez, M. S.; San Segundo, J. M.; Grande, M. C.; Medarde, M.; Bellido, I. S. *Tetrahedron* **1989**, *45*, 3575.
(230) Halim, A. F.; Collins, R. P. *J. Agric. Food Chem.* **1975**, *23*, 506.
(231) Haro, G.; Takenori, K.; Midori, O. I.; Hiroshi, K.; Zhao, W.; Chen, J.; Guo, Y. T. *Tetrahedron Lett.* **1988**, *29*, 4603.
(232) Wu, S. J.; Chan, H. H.; Hwang, T. L.; Qian, K.; Morris-Natschke, S.; Lee, K. H.; Wu, T. S. *Tetrahedron Lett.* **2010**, *51*, 4287.
(233) Miura, K.; Kikuzaki, H.; Nakatani, N. *Phytochemistry* **2001**, *58*, 1171.
(234) Xu, G.; Hou, A. J.; Wang, R. R.; Liang, G. Y.; Zheng, Y. T.; Liu, Z. Y.; Li, X. L.; Zhao, Y.; Huang, S. X.; Peng, L. Y. *Org. Lett.* **2006**, *8*, 4453.
(235) Luis, J. G.; Lahlou, E. H.; Andres, L. S. *Tetrahedron* **1996**, *52*, 12309.
(236) Luis, J. G.; Lahlou, E. H.; Andrés, L. S.; Sood, G. H. N.; Ripoll, M. M. *Tetrahedron Lett.* **1996**, *37*, 4213.
(237) Rustaiyan, A.; Niknejad, A.; Nazarians, L.; Jakupovic, J.; Bohlmann, F. *Phytochemistry* **1982**, *21*, 1812.
(238) Moghaddam, F. M.; Zaynizadeh, B.; Rüedi, P. *Phytochemistry* **1995**, *39*, 715.
(239) Linden, A.; Juch, M.; Matloubi Moghaddam, F.; Zaynizadeh, B.; Rüedi, P. *Phytochemistry* **1996**, *41*, 589.
(240) Rustaiyan, A.; Koussari, S. *Phytochemistry* **1988**, *27*, 1767.
(241) Topçu, G.; Ulubelen, A.; Tam, T. C. M. *Phytochemistry* **1996**, *42*, 1089.
(242) Moghaddam, F. M.; Amiri, R.; Alam, M.; Hossain, M. B.; van der Helms, D. *J. Nat. Prod.* **1998**, *61*, 279.
(243) Rustaiyan, A.; Sadjadi, A. *Phytochemistry* **1987**, *26*, 3078.
(244) Horiuchi, K.; Shiota, S.; Hatano, T.; Yoshida, T.; Kuroda, T.; Tsuchiya, T. *Biol. Pharm. Bull.* **2007**, *30*, 1147.
(245) Topçu, G.; Altiner, E. N.; Gozcu, S.; Halfon, B.; Aydogmus, Z.; Pezzuto, J. M.; Zhou, B. N.; Kingston, D. G. I. *Planta Med.* **2003**, *69*, 464.
(246) Topçu, G.; Türkmen, Z.; Ulubelen, A.; Schilling, J. K.; Kingston, D. G. I. *J. Nat. Prod.* **2004**, *67*, 118.
(247) Topçu, G.; Ulubelen, A. *J. Nat. Prod.* **1999**, *62*, 1605.
(248) Bruno, M.; Savona, G.; Hueso-Rodríguez, J. A.; Pascual, C.; Rodríguez, B. *Phytochemistry* **1987**, *26*, 497.
(249) Mukherjee, K. S.; Bhattacharya, M. K.; Ghosh, P. K. *Phytochemistry* **1982**, *21*, 2416.
(250) Ahmad, Z.; Mehmood, S.; Ifzal, R.; Malik, A.; Afza, N.; Ashraf, M.; Jahan, E. *Turk. J. Chem.* **2007**, *31*, 495.
(251) Wang, Y. L.; Song, D. D.; Li, Z. L.; Yuan, T.; Zhang, H. L.; Pei, Y. H.; Jing, Y. K.; Hua, H. M. *Phytochemistry Lett.* **2009**, *2*, 81.
(252) De Felice, A.; Bader, A.; Leone, A.; Sosa, S.; Loggia, R. D.; Tubaro, A.; De Tommasi, N. *Planta Med.* **2006**, *72*, 643.
(253) Ulubelen, A.; Ayanolu, E. *Phytochemistry* **1976**, *15*, 309.
(254) Ballesta-Acosta, M. C.; Pascual-Villalobos, M. J.; Rodríguez, B. *J. Nat. Prod.* **2002**, *65*, 1513.
(255) Wang, N.; Niwa, M.; Luo, H. W. *Phytochemistry* **1988**, *27*, 299.
(256) Topçu, G.; Ertas, A.; Kolak, U.; Ozturk, M.; Ulubelen, A. *Arkivoc* **2007**, *7*, 195.
(257) García-Alvarez, M. C.; Savonat, G.; Rodríguez, B. *Phytochemistry* **1981**, *20*, 481.
(258) Savona, G.; Bruno, M.; Rodríguez, B. *Phytochemistry* **1987**, *26*, 3305.
(259) Ahmad, Z.; Fatima, I.; Mehmood, S.; Ifzal, R.; Malik, A.; Afza, N. *Helv. Chim. Acta* **2008**, *91*, 73.
(260) Pedreros, S.; Rodríguez, B.; De La Torre, M. C.; Bruno, M.; Savona, G.; Perales, A.; Torres, M. R. *Phytochemistry* **1990**, *29*, 919.
(261) Ahmad, V. U.; Zahid, M.; Ali, M. S.; Choudhary, M. I.; Akhtar, F.; Ali, Z.; Iqbal, M. Z. *Tetrahedron Lett.* **1999**, *40*, 7561.
(262) Ahmad, V. U.; Zahid, M.; Ali, M. S.; Ali, Z.; Jassbi, A. R.; Abbas, M.; Clardy, J.; Lobkovsky, E.; Tareen, R. B.; Iqbal, M. Z. *J. Org. Chem.* **1999**, *64*, 8465.
(263) Kolak, U.; Ari, S.; Birman, H.; Hasancebi, S.; Ulubelen, A. *Planta Med.* **2001**, *67*, 761.
(264) Topçu, G.; Tan, N.; Kökdil, G.; Ulubelen, A. *Phytochemistry* **1997**, *45*, 1293.
(265) Lu, X. Z.; Xu, W. H.; Naoki, H. *Phytochemistry* **1992**, *31*, 708.
(266) Ishurd, O.; Zahid, M.; Khan, T.; Pan, Y. *Fitoterapia* **2001**, *72*, 720.
(267) Zahid, M.; Ishrud, O.; Pan, Y.; Asim, M.; Riaz, M.; Uddin Ahmad, V. *Carbohydr. Res.* **2002**, *337*, 403.
(268) Choi, J. S.; Kang, H. S.; Jung, H. A.; Jung, J. H.; Kang, S. S. *Fitoterapia* **2001**, *72*, 30.
(269) Lu, Y.; Yeap Foo, L. *Phytochemistry* **2000**, *55*, 263.
(270) Wang, M.; Kikuzaki, H.; Zhu, N.; Sang, S.; Nakatani, N.; Ho, C. T. *J. Agric. Food Chem.* **2000**, *48*, 235.
(271) Wang, M.; Shao, Y.; Huang, T. C.; Wei, G. J.; Ho, C. T. *J. Agric. Food Chem.* **1998**, *46*, 2509.
(272) Wang, M.; Shao, Y.; Li, J.; Zhu, N.; Rangarajan, M.; LaVoie, E. J.; Ho, C. T. *J. Nat. Prod.* **1999**, *62*, 454.
(273) Lu, Y.; Foo, L. Y.; Wong, H. *Phytochemistry* **1999**, *52*, 1149.
(274) Jin, Q. *Nat. Prod. Sci.* **2009**, *15*, 106.
(275) Lu, Y.; Foo, L. Y. *Tetrahedron Lett.* **2001**, *42*, 8223.
(276) Ali, M. S.; Ahmed, S.; Ibrahim, S. A.; Tareen, R. B. *Chem. Biodiversity* **2005**, *2*, 910.
(277) Lu, Y.; Yeap Foo, L. *Food Chem.* **2001**, *75*, 197.
(278) Ishikawa, T.; Kondo, T.; Kinoshita, T.; Haruyama, H.; Inaba, S.; Takeda, K.; Grayer, R. J.; Veitch, N. C. *Phytochemistry* **1999**, *52*, 517.
(279) El-Sayed, N. H.; Khalifa, T. I.; Ibrahim, M. T.; Mabry, T. J. *Fitoterapia* **2001**, *72*, 850.
(280) Takeda, Y.; Zhang, H.; Matsumoto, T.; Otsuka, H.; Oosio, Y.; Honda, G.; Tabata, M.; Fujita, T.; Sun, H.; Sezik, E. *Phytochemistry* **1997**, *44*, 117.
(281) Huang, Y. T.; Lee, T. Y.; Lin, H. C.; Chou, T. Y.; Yang, Y. Y.; Hong, C. Y. *Can. J. Physiol. Pharmacol.* **2001**, *79*, 566.
(282) Yang, Z.; Hon, P. M.; Chui, K. Y.; Xu, Z. L.; Chang Chi Ming, H. M. *Tetrahedron Lett.* **1991**, *32*, 2061.
(283) Zhang, Z. F.; Peng, Z. G.; Gao, L.; Dong, B.; Li, J. R.; Li, Z. Y.; Chen, H. S. *J. Asian Nat. Prod. Res.* **2008**, *10*, 391.
(284) Powell, R. G.; Platiner, R. D. *Phytochemistry* **1976**, *15*, 1963.
(285) Plattner, R. D.; Powell, R. G. *Phytochemistry* **1978**, *17*, 149.
(286) Hussein, A. A.; Meyer, J. J. M.; Jimeno, M. L.; Rodríguez, B. *J. Nat. Prod.* **2007**, *70*, 293.
(287) Moujir, L.; Gutierrez-Navarro, A. M.; San Andres, L.; Luis, J. G. *Phytochemistry* **1993**, *34*, 1493.
(288) Ulubelen, A.; Miski, M.; Johansson, C.; Lee, E.; Mabry, T. J.; Matlin, S. A. *Phytochemistry* **1985**, *24*, 1386.
(289) Habibi, Z.; Eftekhar, F.; Samiee, K.; Rustaiyan, A. *J. Nat. Prod.* **2000**, *63*, 270.
(290) Walencka, E.; Rozalska, S.; Wysokinska, H.; Razalski, M.; Kuzma, L.; Rozalska, B. *Planta Med.* **2007**, *73*, 545.

(291) Gu, L. W.; Weng, X. C. *Chin. Oils Fats* **1997**, *22*, 37.
(292) Tepe, B.; Sokmen, M.; Akpulat, H. A.; Sokmen, A. *Food Chem.* **2006**, *95*, 200.
(293) Weng, X. C.; Gordon, M. H. *J. Agric. Food Chem.* **1992**, *40*, 1331.
(294) Santos-Gomes, P. C.; Seabra, R. M.; Andrade, P. B.; Fernandes-Ferreira, M. *Plant Sci.* **2002**, *162*, 981.
(295) Wei, G. J.; Ho, C. T. *Food Chem.* **2006**, *96*, 471.
(296) Cragg, G. M.; Newman, D. J.; Snader, K. M. *J. Nat. Prod.* **1997**, *60*, 52.
(297) Valeriote, F.; Grieshaber, C. K. *J. Exp. Ther. Oncol.* **2002**, *2*, 228.
(298) Liu, J.; Shen, H. M.; Ong, C. N. *Cancer Lett.* **2000**, *153*, 85.
(299) Dat, N. T.; Jin, X.; Lee, J. H.; Lee, D.; Hong, Y. S.; Lee, K.; Kim, Y. H.; Lee, J. J. *J. Nat. Prod.* **2007**, *70*, 1093.
(300) Ren, Y.; Houghton, P. J.; Hider, R. C.; Howes, M. J. R. *Planta Med.* **2004**, *70*, 201.
(301) Kelen, M.; Tepe, B. *Bioresour. Technol.* **2008**, *99*, 4096.
(302) Liang, Q.; Liang, Z. S.; Wang, J. R.; Xu, W. H. *Food Chem.* **2009**, *113*, 592.
(303) Karousou, R.; Vokou, D.; Kokkini, S. *Biochem. Syst. Ecol.* **1998**, *26*, 889.
(304) van de Waal, M.; Niclass, Y.; Snowden, R. L.; Bernardinelli, G.; Escher, S. *Helv. Chim. Acta* **2002**, *85*, 1246.
(305) Et-Keltawi, N. E.; Croteau, R. *Phytochemistry* **1986**, *25*, 1603.
(306) Bayrak, A.; Akgul, A. *Phytochemistry* **1987**, *26*, 846.
(307) Haznedaroglu, M. Z.; Karabay, N. U.; Zeybek, U. *Fitoterapia* **2001**, *72*, 829.
(308) Sonboli, A.; Fakhari, A. R.; Sefidkon, F. *Chem. Nat. Compd.* **2005**, *41*, 168.
(309) Tzakou, O.; Pitarokili, D.; Chinou, I. B.; Harvala, C. *Planta Med.* **2001**, *67*, 81.
(310) Bisio, A.; Ciarallo, G.; Romussi, G.; Fontana, N.; Mascolo, N.; Capasso, R.; Biscardi, D. *Phytother. Res.* **1998**, *12*, S117.
(311) Ravid, U.; Putievsky, E.; Bassat, M.; Ikan, R.; Weinstein, V. *Flavour Frag. J.* **1986**, *1*, 121.
(312) Länger, R.; Mechtler, C.; Jurenitsch, J. *Phytochem. Anal.* **1996**, *7*, 289.
(313) Tabanca, N.; Demirci, B.; Baser, K. H. C.; Aytac, Z.; Ekici, M.; Khan, S. I.; Jacob, M. R.; Wedge, D. E. *J. Agric. Food Chem.* **2006**, *54*, 6593.
(314) Sivropoulou, A.; Nikolaou, C.; Papanikolaou, E.; Kokkini, S.; Lanaras, T.; Arsenakis, M. *J. Agric. Food Chem.* **1997**, *45*, 3197.
(315) Lichtenthaler, H. K. *Annu. Rev. Plant Biology* **1999**, *50*, 47.
(316) Chinou, I. *Curr. Med. Chem.* **2005**, *12*, 1295.
(317) Bozan, B.; Ozturk, N.; Kosar, M.; Tunalier, Z.; Baser, K. H. C. *Chem. Nat. Compd.* **2002**, *38*, 198.
(318) Rodriguez-Hahn, L.; Esquivel, B.; Cardenas, J.; Ramamoorthy, T. P. In *Advances in Labiate Science*; Harley, R. M., Reynolds, T., Eds.; Royal Botanic Gardens: Kew, United Kingdom, 1992; p 335.
(319) Luis, J. G.; Qui ones, W.; Grillo, T. A.; Kishi, M. P. *Phytochemistry* **1994**, *35*, 1373.
(320) Patudin, A. V.; Romanova, A.; Sokolov, W. S.; Pribylova, G. *Planta Med.* **1974**, *26*, 201.
(321) Sun, D. D.; Wang, H. C.; Wang, X. B.; Luo, Y.; Jin, Z. X.; Li, Z. C.; Li, G. R.; Dong, M. Q. *Eur. J. Pharmacol.* **2008**, *590*, 317.
(322) Ohsaki, A.; Kawamata, S.; Ozawa, M.; Kishida, A.; Gong, X.; Kuroda, C. *Tetrahedron Lett.* **2011**, *52*, 1375.
(323) Bisio, A.; Damonte, G.; Fraternale, D.; Giacomelli, E.; Salis, A.; Romussi, G.; Cafaggi, S.; Ricci, D.; De Tommasi, N. *Phytochemistry* **2011**, *72*, 265.
(324) Moghaddam, F. M.; Farimani, M. M. *Tetrahedron Lett.* **2010**, *51*, 540.
(325) Hagiwara, H.; Suka, Y.; Nojima, T.; Hoshi, T.; Suzuki, T. *Tetrahedron* **2009**, *65*, 4820.
(326) Ma, Z.; Deng, G.; Lee, D. Y. W. *Tetrahedron Lett.* **2010**, *51*, 5207.
(327) Fichna, J.; Lewellyn, K.; Yan, F.; Roth, B. L.; Zjawiony, J. K. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 160.
(328) Lee, D. Y. W.; Yang, L.; Xu, W.; Deng, G.; Guo, L.; Liu-Chen, L. Y. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 5749.
(329) Bikbulatov, R. V.; Stewart, J.; Jin, W.; Yan, F.; Roth, B. L.; Ferreira, D.; Zjawiony, J. K. *Tetrahedron Lett.* **2008**, *49*, 937.
(330) Lee, D. Y.; Karnati, V. V.; He, M.; Liu-Chen, L. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3744.
(331) Huang, W. G.; Li, J. Y.; Luo, Y.; Li, J.; Lu, W. *Chin. Chem. Lett.* **2009**, *20*, 1461.
(332) Jiang, Y. Y.; Li, Q.; Lu, W.; Cai, J. C. *Tetrahedron Lett.* **2003**, *44*, 2073.
(333) Bi, Y. F.; Xu, H. W.; Liu, X. Q.; Zhang, X. J. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 4892.
(334) Baricevic, D.; Sosa, S.; Della Loggia, R.; Tubaro, A.; Simonovska, B.; Krasna, A.; Zupancic, A. *J. Ethnopharmacol.* **2001**, *75*, 125.
(335) Nagy, G.; Gunther, G.; Mathe, I.; Blunden, G.; Yang, M. H.; Crabb, T. A. *Biochem. Syst. Ecol.* **1998**, *26*, 797.
(336) Weng, X. C.; Wang, W. *Food Chem.* **2000**, *71*, 489.
(337) Gu, L.; Weng, X. *Food Chem.* **2001**, *73*, 299.
(338) Li, H. B.; Chen, F. *J. Chromatogr., A* **2001**, *932*, 91.
(339) Ali, M. S.; Yousuf Dardass, A. K.; Ahmad, S.; Saleem, M.; Firdous, S.; Uddin Ahmad, V. *Fitoterapia* **2000**, *71*, 347.
(340) Topçu, G.; Tan, N.; Ulubelen, A.; Sun, D.; Watson, W. H. *Phytochemistry* **1995**, *40*, 501.
(341) Ulubelen, A.; Topçu, G. *Phytochemistry* **1995**, *40*, 1473.
(342) Lin, L. Z.; Cordell, G. A.; Lin, P. *Phytochemistry* **1995**, *40*, 1469.
(343) Ahmad, V. U.; Zahid, M.; Ali, M. S.; Jassbi, A. R.; Abbas, M.; Ali, Z.; Iqbal, M. Z. *Phytochemistry* **1999**, *52*, 1319.
(344) Firdous, S.; Dardass, A. K. Y.; Khan, K. M.; Usmani, S. B.; Ahmad, V. U. *Fitoterapia* **1999**, *70*, 326.
(345) Ulubelen, A.; Öksüz, S.; Kolak, U.; Birman, H.; Voelter, W. *Planta Med.* **2000**, *66*, 627.
(346) Zhang, Y.; Akao, T.; Nakamura, N.; Duan, C. L.; Hattori, M.; Yang, X. W.; Liu, J. X. *Planta Med.* **2004**, *70*, 138.
(347) Moujir, L.; Gutiérrez-Navarro, A. M.; San Andrés, L.; Luis, J. G. *Phytother. Res.* **1996**, *10*, 172.
(348) Ortega, A.; Maldonado, E.; Jankowski, C. K.; Van Calsteren, M. R.; Díz, E. *Phytochem. Anal.* **1994**, *5*, 302.
(349) Rodriguez-Hahn, L.; O'Reilly, R.; Esquivel, B.; Maldonado, E.; Ortega, A.; Cardenas, J.; Toscano, R. A.; Chan, T. M. *J. Org. Chem.* **1990**, *55*, 3522.
(350) Lin, H. C.; Ding, H. Y.; Chang, W. L. *J. Nat. Prod.* **2001**, *64*, 648.
(351) Ai, C. B.; Li, L. N. *J. Nat. Prod.* **1988**, *51*, 145.
(352) Khetwal, K. S.; Pathak, R. P.; Vashisht, A.; Pant, N. *J. Nat. Prod.* **1992**, *55*, 947.
(353) Tanaka, T.; Nishimura, A.; Kouno, I.; Nonaka, G.; Young, T. J. *J. Nat. Prod.* **1996**, *59*, 843.
(354) Ulubelen, A.; Topçu, G. *J. Nat. Prod.* **2000**, *63*, 879.
(355) Ulubelen, A.; Topçu, G.; Lotter, H.; Wagner, H.; Eri, C. *Phytochemistry* **1994**, *36*, 413.
(356) Luis, J. G.; González, A. G.; Andrés, L. S.; Mederos, S. *Phytochemistry* **1992**, *31*, 3272.
(357) González, A. G.; Andrés, L. S.; Aguiar, Z. E.; Luis, J. G. *Phytochemistry* **1992**, *31*, 1297.
(358) Qian, T. X.; Li, L. N. *Phytochemistry* **1992**, *31*, 1068.
(359) Li, B.; Niu, F. D.; Lin, Z. W.; Zhang, H. J.; Wang, D. Z.; Sun, H. D. *Phytochemistry* **1991**, *30*, 3815.
(360) Ikeshiro, Y.; Hashimoto, I.; Iwamoto, Y.; Mase, I.; Tomita, Y. *Phytochemistry* **1991**, *30*, 2791.
(361) González, A. G.; Barrera, J. B.; Díaz, J. G.; Pérez, E. M. R.; Yanes, A. C.; Rauter, P.; Pozo, J. *Phytochemistry* **1990**, *29*, 321.
(362) Dentali, S. J.; Hoffmann, J. J. *Phytochemistry* **1990**, *29*, 993.
(363) Anaya, J.; Caballero, M. C.; Grande, M.; Navarro, J. J.; Tapia, I.; Almeida, J. F. *Phytochemistry* **1989**, *28*, 2206.
(364) Lin, L. Z.; Cordell, G. A. *Phytochemistry* **1989**, *28*, 2846.
(365) Canigueral, S.; Iglesias, J.; Sánchez-Ferrando, F.; Virgili, A. *Phytochemistry* **1988**, *27*, 221.

(366) Hernández, M.; Esquivel, B.; Cárdenas, J.; Rodríguez-Hahn, L.; Ramamoorthy, T. P. *Phytochemistry* **1987**, *26*, 3297.
(367) Pereda-Miranda, R.; Delgado, G.; De Vivar, A. R. *Phytochemistry* **1986**, *25*, 1931.
(368) Michavila, A.; Fernández-Gadea, F.; Rodríguez, B. *Phytochemistry* **1985**, *25*, 266.
(369) Valverde, S.; Escudero, J.; Cristóbal López, J.; Ma Rabanal, R. *Phytochemistry* **1985**, *24*, 111.
(370) Kusumi, T.; Ooi, T.; Hayashi, T.; Kakisawa, H. *Phytochemistry* **1985**, *24*, 2118.
(371) Ulubelen, A.; Topçu, G. *Phytochemistry* **1984**, *23*, 133.
(372) Frontana, B.; Cárdenas, J.; Rodríguez-Hahn, L. *Phytochemistry* **1994**, *36*, 739.
(373) Rauter, A.; Branco, I.; Lopes, R.; Justino, J.; Silva, F.; Noronha, J.; Cabrita, E.; Brouard, I.; Bermejo, J. *Fitoterapia* **2007**, *78*, 474.
(374) Mukherjee, K. S.; Ghosh, P. K.; Mukherjee, R. K. *Phytochemistry* **1983**, *22*, 1296.
(375) Savona, G.; Bruno, M.; Paternostro, M.; Marco, J. L.; Rodríguez, B. *Phytochemistry* **1982**, *21*, 2563.
(376) Zhao, L. M.; Liang, X. T.; Li, L. N. *Phytochemistry* **1996**, *42*, 899.
(377) Ai, C. B.; Deng, Q. H.; Song, W. Z.; Li, L. N. *Phytochemistry* **1994**, *37*, 907.
(378) Ulubelen, A.; Brieskorn, C. H.; Zdemir, N. *Phytochemistry* **1977**, *16*, 790.
(379) Zhou, L.; Chan, W. K.; Xu, N.; Xiao, K.; Luo, H.; Luo, K. Q.; Chang, D. C. *Life Sci.* **2008**, *83*, 394.
(380) Chan, H. H.; Hwang, T. L.; Su, C. R.; Reddy, M. V. B.; Wu, T. S. *Phytomedicine* **2011**, *18*, 148.
(381) Xu, G.; Peng, L. Y.; Tu, L.; Li, X. L.; Zhao, Y.; Zhang, P. T.; Zhao, Q. S. *Helv. Chim. Acta* **2009**, *92*, 409.
(382) Lin, L. Z.; Wang, X. M.; Huang, X. L.; Huang, Y. *Acta Pharm. Sin.* **1990**, *25*, 154.
(383) Yu, X. Y.; Lin, S. G.; Zhou, Z. W.; Chen, X.; Liang, J.; Duan, W.; Yu, X. Q.; Wen, J. Y.; Chowbay, B.; Li, C. G. *Neurosci. Lett.* **2007**, *417*, 261.
(384) Kavvadias, D.; Monschein, V.; Sand, P.; Riederer, P.; Schreier, P. *Planta Med.* **2003**, *69*, 113.
(385) Lay, I. S.; Chiu, J. H.; Shiao, M. S.; Lui, W. Y.; Wu, C. W. *Planta Med.* **2003**, *69*, 26.
(386) Karpiska, M.; Borowski, J.; Danowska-Oziewicz, M. *Food Chem.* **2001**, *72*, 5.
(387) Simmonds, M. S. J.; Blaney, W. M.; Esquivel, B.; Rodriguez-Hahn, L. *Pestic. Sci.* **1996**, *47*, 17.
(388) Fiore, G.; Nencini, C.; Cavallo, F.; Capasso, A.; Bader, A.; Giorgi, G.; Micheli, L. *Phytother. Res.* **2006**, *20*, 701.
(389) Zhang, K. Q.; Bao, Y.; Wu, P.; Rosen, R. T.; Ho, C. T. *J. Agric. Food Chem.* **1990**, *38*, 1194.
(390) Cuvelier, M. E.; Berset, C.; Richard, H. *J. Agric. Food Chem.* **1994**, *42*, 665.
(391) Mukherjee, K. S.; Ghosh, P. K.; Badruddoza, S. *Phytochemistry* **1981**, *20*, 1441.
(392) Esquivel, B.; Cardenas, J.; Toscano, A.; Soriano-Garcia, M.; Rodriguez-Hahn, L. *Tetrahedron* **1985**, *41*, 3213.
(393) Ninomiya, K.; Matsuda, H.; Shimoda, H.; Nishida, N.; Kasajima, N.; Yoshino, T.; Morikawa, T.; Yoshikawa, M. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1943.
(394) Kabouche, A.; Boutaghane, N.; Kabouche, Z.; Seguin, E.; Tillequin, F.; Benlabed, K. *Fitoterapia* **2005**, *76*, 450.
(395) Pettit, G. R.; Klinger, H.; Jorgensen, N. O. N.; Occolowitz, J. *Phytochemistry* **1966**, *5*, 301.
(396) Kamatou, G. P. P.; Van Vuuren, S. F.; Van Heerden, F. R.; Seaman, T.; Viljoen, A. M. *S. Afr. J. Bot.* **2007**, *73*, 552.
(397) Ahmed, B.; Al-Howiriny, T. A.; Al-Rehaily, A. J.; Mossa, J. S. *Z. Naturforsch., C* **2004**, *59*, 9.
(398) Fontana, G.; Savona, G.; Rodríguez, B. *Magn. Reson. Chem.* **2006**, *44*, 962.
(399) Ulubelen, A.; Topçu, G.; Chai, H. B.; Pezzuto, J. M. *Pharm. Biol.* **1999**, *37*, 148.
(400) Khan, T.; Zahid, M.; Asim, M. *Phytomedicine* **2002**, *9*, 749.
(401) Ulubelen, A.; Tuzlaci, E. *Planta Med.* **1987**, *53*.
(402) Ulubelen, A.; Topçu, G.; Sönmez, U.; Eris, C. *Phytochemistry* **1994**, *35*, 1065.
(403) González, A. G.; Andrés, L. S.; Luis, J. G.; Brito, I.; Rodríguez, M. L. *Phytochemistry* **1991**, *30*, 4067.
(404) Galicia, M. A.; Esquivel, B.; Sánchez, A. A.; Cárdenas, J.; Ramamoorthy, T.; Rodríguez-Hahn, L. *Phytochemistry* **1988**, *27*, 217.
(405) Pereda-Miranda, R.; Hernández, L.; López, R. *Planta Med.* **1992**, *58*, 223.
(406) Ulubelen, A. *Planta Med.* **1990**, *56*, 82.
(407) Mendes, E.; Marco, J. L.; Rodriguez, B.; Jimeno, M. L.; Lobo, A. M.; Prabhakar, S. *Phytochemistry* **1989**, *28*, 1685.
(408) Lin, L. Z.; Blasko, G.; Cordell, G. A. *Phytochemistry* **1989**, *28*, 177.
(409) Rodriguez, B. *Z. Naturforsch., B* **2003**, *58*, 324.
(410) Yong, Z. J. H. *Nat. Prod. Res. Dev.* **1995**, *4*, 1.
(411) Rodríguez-Hahn, L.; Esquivel, B.; Sánchez, C.; Estebanes, L.; Cárdenas, J.; Soriano-García, M.; Toscano, R.; Ramamoorthy, T. *Phytochemistry* **1989**, *28*, 567.
(412) Sabri, N. N.; Abou-Donia, A. A.; Assad, A. M.; Ghazy, N. M.; El-Lakany, A. M.; Tempesta, M. S.; Sanson, D. R. *Planta Med.* **1989**, *55*, 582.
(413) Nagy, G.; Dobos, Á.; Günther, G.; Yang, M. H.; Blunden, G.; Crabb, T. A.; Máthé, I. *Planta Med.* **1998**, *64*, 288.
(414) Janicsák, G.; Hohmann, J.; Nikolova, M.; Genova, E.; Zupkó, I.; Forgo, P.; Máthé, I. *Planta Med* **2007**, 73.
(415) Ulubelen, A. *Planta Med.* **1989**, *55*, 397.
(416) Ikeshiro, Y.; Mase, I.; Tomita, Y. *Phytochemistry* **1989**, *28*, 3139.
(417) Bakshi, B.; Hassarajani, S.; Mulchandani, N.; Shankar, J. *Planta Med.* **1984**, *50*, 355.
(418) Wang, N.; Luo, H.; Niwa, M.; Ji, J. *Planta Med.* **1989**, *55*, 390.
(419) Xuezhao, L.; Houwei, L.; Masatake, N. *Planta Med.* **1990**, *56*, 87.
(420) Ikeshiro, Y.; Mase, I.; Tomita, Y. *Planta Med.* **1991**, *57*, 588.
(421) Lin, L. Z.; Wang, X. M.; Huang, X. L.; Huang, Y.; Yang, B. J. *Planta Med* **1988**, *54*, 443.
(422) Long-ze, L.; Xiao-Ming, W.; Xiu-Lan, H.; Yong, H.; Cordell, G. A. *Phytochemistry* **1989**, *28*, 3542.
(423) Sanchez, C.; Cardenas, J.; Rodriguez-Hahn, L.; Ramamoorthy, T. *Phytochemistry* **1989**, *28*, 1681.
(424) Esquivel, B.; Sanchez, A. A. *Nat. Prod. Res.* **2005**, *19*, 413.
(425) Savona, G.; Paternostro, M. P.; Piozzi, F.; Hanson, J. R.; Hitchcock, P. B.; Thomas, S. A. *J. Chem. Soc., Perkin Trans. 1* **1978**, *6*, 643.
(426) Rodriguez, B.; Pascual, C.; Savona, G. *Phytochemistry* **1984**, *23*, 1193.
(427) Ortega, A.; Maldonado, E. *Phytochemistry* **1994**, *35*, 1063.
(428) Esquivel, B.; Martinez, N.; Cárdenas, J.; Ramamoorthy, T.; Rodríguez-Hahn, L. *Planta Med.* **1989**, *55*, 62.
(429) Moghaddam, F. M.; Farimani, M. M.; Seirafi, M.; Taheri, S.; Khavasi, H. R.; Sendker, J.; Proksch, P.; Wray, V.; Edrada, R. A. *J. Nat. Prod.* **2010**, *73*, 1601.
(430) Savona, G.; Bruno, M. *J. Nat. Prod.* **1983**, *46*, 593.
(431) Ulubelen, A.; Brieskorn, C. H. *Planta Med.* **1977**, *31*, 80.
(432) Domínguez, X. A.; Gonzalez, H. F. *Phytochemistry* **1972**, *11*, 2641.
(433) Delgardo, G.; Ríos, M. *Planta Med.* **1990**, *56*, 243.
(434) Gonzalez, A. G.; Andres, L. S.; Ravelo, A. G.; Luis, J. G.; Bazzocchi, I. L.; West, J. *Phytochemistry* **1990**, *29*, 1691.
(435) De la Torre, M. C.; Bruno, M.; Piozzi, F.; Savona, G.; Rodriguez, B.; Arnold, N. A. *Phytochemistry* **1990**, *29*, 668.
(436) Pereda-Miranda, R.; Delgado, G.; de Vivar, A. R. *J. Nat. Prod.* **1986**, *49*, 225.
(437) Zhang, H. J.; Li, L. N. *Planta Med.* **1994**, *60*, 70.
(438) Ai, C.; Li, L. *Planta Med.* **1992**, *58*, 197.
(439) Lu, Y.; Foo, L. Y. *Phytochemistry* **1999**, *51*, 91.

(440) Abdalla, M. F.; Saleh, N. A. M.; Gabr, S.; Abu-Eyta, A. M.; El-Said, H. *Phytochemistry* **1983**, *22*, 2057.
(441) Ulubelen, A.; Miski, M.; Neuman, P.; Mabry, T. J. *J. Nat. Prod.* **1979**, *42*, 261.
(442) Ulubelen, A.; Topçu, G. *J. Nat. Prod.* **1984**, *47*, 1068.
(443) Ulubelen, A.; Miski, M.; Mabry, T. J. *J. Nat. Prod.* **1981**, *44*, 586.
(444) Li, L. N.; Tan, R.; Chen, W. M. *Planta Med.* **1984**, *50*, 227.
(445) Valdes, L. J., III *J. Nat. Prod.* **1986**, *49*, 171.
(446) Miski, M.; Ulubelen, A.; Johansson, C.; Mabry, T. J. *J. Nat. Prod.* **1983**, *46*, 874.
(447) Pereda-Miranda, R.; Delgado, G. *J. Nat. Prod.* **1986**, *49*, 1160.