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Tandem addition–cyclization mediated by sulfanyl radicals: a versatile strategy for iridoids synthesis

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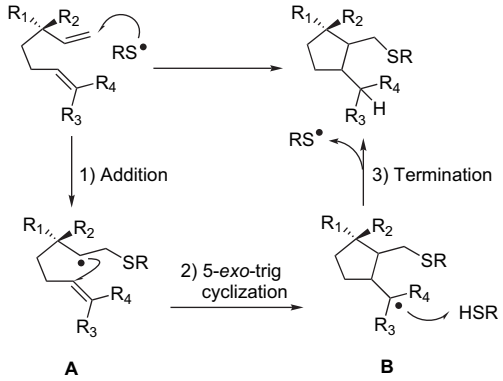
ABSTRACT

Sulfanyl radicals trigger a tandem addition–cyclization protocol in linalool or citronelene derivatives for the efficient construction of the iridane monoterpene skeleton. Best results in yields and diastereoselectivity were obtained when phenylethylsulfanyl was used as radical initiator. We have proved the utility of this protocol with the enantiospecific synthesis of natural iridane dehydroiridomyrmecin starting from a (−)-linalyl acetate ester derivative in five steps with a 28% overall yield.

1. Introduction

Iridanes are an interesting group of natural monoterpenes, due mainly to their structural variety—over 100 naturally occurring compounds belonging to this family have been reported—and wide range of biological properties including antibiotic, anti-tumour, antioxidant, antibacterial and antiviral activities.[1] The interest of these molecules is shown in the number of imaginative routes delineated for their synthesis,[2] although the first example of radical-induced cyclization leading to this skeleton was reported very recently.[3] Of the different types of sulfur-centered radicals used in organic synthesis,[4] the sulfanyl radical (RS$^{\bullet}$) is one of the most attractive[5] and its ability to add to a multiple bond intramolecularly deserving special attraction.[6] This strategy has been successfully employed in the synthesis of alkaloids and other bioactive heterocycles.[7–13]

Considering all the above and the different selectivity of the addition of sulfanyl radicals to double bonds reported elsewhere, we surmised that tandem processes of sulfanyl radical addition–cyclization of dienes possessing the basic structure of 3,7-dimethylocta-1,6-diene could be a suitable approach to the synthesis of natural iridoids. According to this proposal, the key addition step should be both chemoselective towards the monosubstituted double bond and also regioselective to the less substituted extreme of the olefin. The thus-generated radical centered at C-2 (**A**) should originate the cyclopentane ring present in the iridane backbone via a 5-*exo*-*trig* process. The capture by the cyclic radical **B** of a hydrogen radical from a thiol molecule would lead to completion of the process (Scheme 1).



Scheme 1. Tandem addition–cyclization reaction triggered by sulfanyl radicals: formation of the iridane ring.

In this paper, we describe the results obtained in the construction of five-membered rings possessing the carbon framework of the iridane skeleton via radical cyclization promoted by the regioselective addition of sulfanyl radicals to suitable polyprenes related to linalool. We previously published a short summary of this

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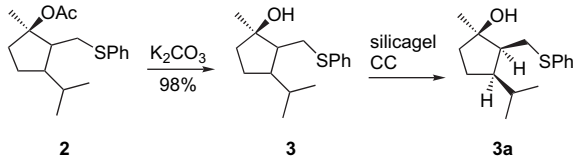
methodology.[14] Herein the enantiospecific synthesis of the natural iridoid dehydroiridomyrmecin and other achievements will be described in detail.

2. Results and discussion

We started our study by making commercial linalyl acetate react with the radical generated by treating PhSH (1 equiv) with AIBN (1 equiv) in refluxing benzene. Under these conditions the products obtained resulting from the expected addition–cyclization, **2**, represented only 29%, while 40% of starting material was recovered (Table 1, entry 1). From the mixture of diastereomers **2**, the major component **3a** could be isolated as the corresponding alcohol (Scheme 2). Different experimental conditions failed to substantially improve the yield of **2**, and only a 35% of the desired cyclized adduct was obtained when the equivalents of thiophenol were doubled relative to those of the starting material (Table 1, entry 2). Gratifyingly, when 2 equiv of 2-phenylethylthiol and 4-nitrophenylthiol were also made to react with linalyl acetate, the hoped-for conversion took place with 87 and 16% yields, respectively (Table 1, entries 3 and 4). To account for this result, it is postulated that the higher instability of the alkylsulfanyl radical would favourably shift the equilibrium in the initial addition step,[15] making the process more efficient and, therefore, more attractive from a synthetic perspective. Due to the nucleophilic nature of the initially originated carbon-centered radical, the conjugation of the radical-accepting olefin with an ester enabled us to improve the efficiency of the process (Table 1, entries 5–7), except when the reaction was triggered with 4-nitrophenylsulfanyl radical.

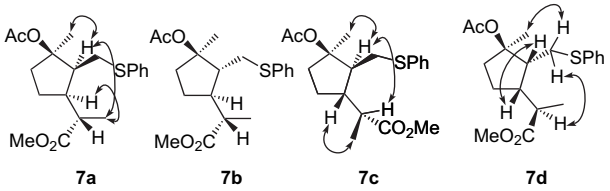
Our efforts then focused on analyzing the diastereoselectivity of the process. Thus, the addition–cyclization reaction of sulfanyl radical with the unsaturated ester **6** could be studied with detail, as three (**7a**, **7c** and **7d**) out of the four diastereomers originated (**7a**–**d**) could be isolated via semi preparative HPLC—the ratio of the four stereoisomers obtained was 47:25:22:6.[16] The relative configurations of these molecules were assigned after analysis of the corresponding NOEDIFF experiences and coupling constant values (Fig. 1).

The stereoselectivity observed could be interpreted in terms of the conformational preferences of the intermediate carbon-centered radical according to the Beckwith–Houk model, suggesting that the stereochemistry of 5-hexenyl ring closures is consistent with the involvement of both cyclohexane chair-like and boat-like transition structures.[17] Thus, the major isomer, **7a**, is formed via a chair-like transition state (**A**) where the most sterically



2 **3** **3a**

Scheme 2. Synthesis of **3**.



7a **7b** **7c** **7d**

Figure 1. Selected NOEs observed for compounds **7a**, **7c** and **7d**.

demanding substituent at C-1 (CH_3 group)[18] adopts a pseudo-equatorial position. This transition state leads to a cyclopentane ring closure where the acetoxy, phenylthiomethyl and isopropyl groups are disposed cis (Fig. 2). A second chair-like transition structure (**B**) with the methyl group at C-1 being pseudo-axially disposed may well account for the stereochemistry of diastereomer **7d**. In this case, the phenylthiomethyl group is disposed *anti* to the acetoxy and *syn* to the chain at C-3. Finally, the formation of diastereomers **7c** and **7b** can be rationalized by considering the involvement of boat-like transition structures **C** and **D**. It is interesting to note the complete diastereoselectivity in the formation of the stereocenter at C-8, regardless of the relative configuration at C-3. To account for this result, the carbon-centered radicals originated after the cyclization step are proposed to adopt the conformations shown in Figure 3, where the methoxy carbonyl and phenylthiomethyl groups are disposed *anti*, thus minimizing stereoelectronic repulsions. In these preferred conformations, the approaching of phenylthiol to transfer the hydrogen radical occurs in the less hindered face to afford compounds **7a**–**d**. This selectivity in the proton abstraction has been previously observed by other authors.[19]

Once proved the success in the construction of the five-membered ring, it was then analyzed the influence of both, the substituent at C-3 and the electronic density in the double bond acceptor of the carbon-centered radical upon the process to gain a deeper understanding of this transformation. Thus, when methyl (2*E*,6*R*)-2,6-dimethyl-6-pivaloyloxy-2,7-octadienoate (**11**) and

Table 1
Addition–cyclization reaction mediated by sulfanyl radicals

Entry	Compound	R_1	R_2	R_3	R_4	R′	Product	Yield (%)	Diastereomeric ratio (a/b/c/d)
1	**1**	OAc	CH_3	CH_3	CH_3	Ph	**2**	29[a]	Not determined
2	**1**	OAc	CH_3	CH_3	CH_3	Ph	**2**	35	40:23:20:17
3	**1**	OAc	CH_3	CH_3	CH_3	$PhCH_2CH_2$	**4**	87	46:26:17:11
4	**1**	OAc	CH_3	CH_3	CH_3	4-$NO_2C_6H_4$	**5**	16	Not determined
5	**6**	OAc	CH_3	CH_3	CO_2Me	Ph	**7**	90	47:25:22:6
6	**6**	OAc	CH_3	CH_3	CO_2Me	$PhCH_2CH_2$	**8**	93	50:25:16:9
7	**6**	OAc	CH_3	CH_3	CO_2Me	4-$NO_2C_6H_4$	**9**	16	Not determined
8	**6**	OAc	CH_3	CH_3	CO_2Me	*t*-Bu[b]	**10**	95	48:23:20:19
9	**11**	$OCOC(CH_3)_3$	CH_3	CH_3	CO_2Me	Ph	**12**	87	46:20:17:17
10	**13**	CH_3	H	CH_3	CO_2Me	Ph	**14**	85	54:20:19:7
11	**15**	OAc	CH_3	CO_2Et	CO_2Et	Ph	**16**	80	36:28:18:18
12	**17**	CH_3	H	CO_2Et	CO_2Et	Ph	**18**	96	58:21:14:7

[a] A 40% of **1** was recovered.
[b] Four equivalents of *t*-BuSH were required.

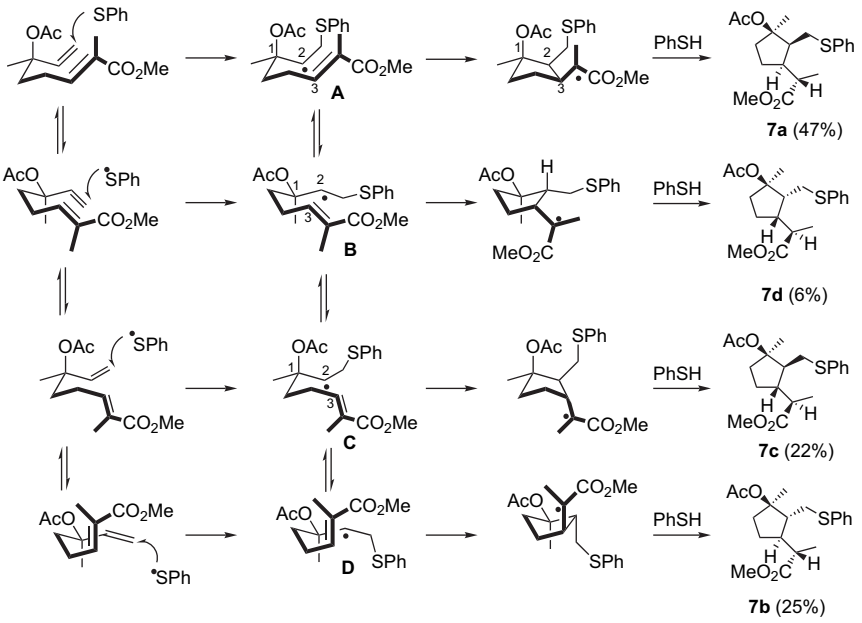


Figure 2. Mechanistic proposal for the cyclization of **6**.

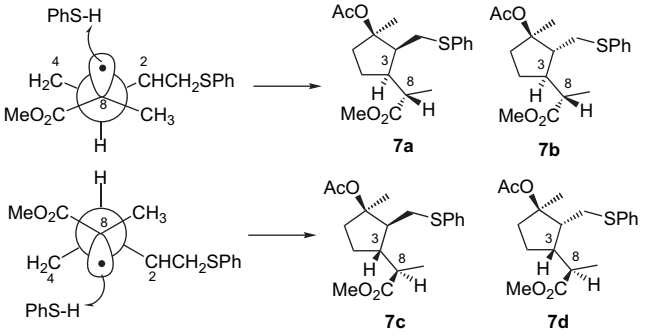
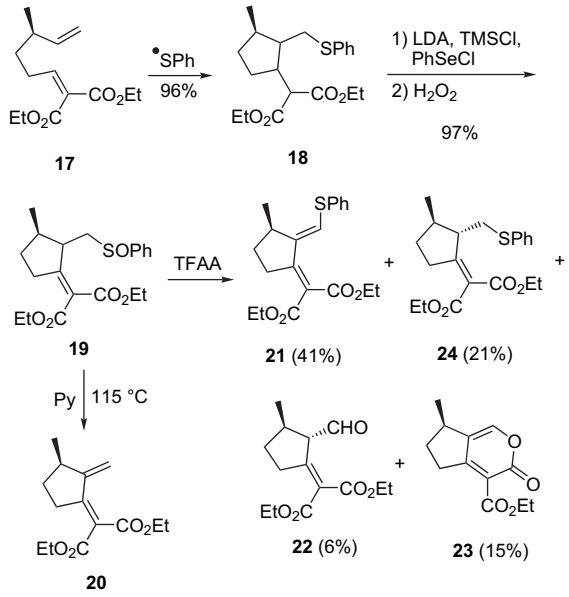


Figure 3.



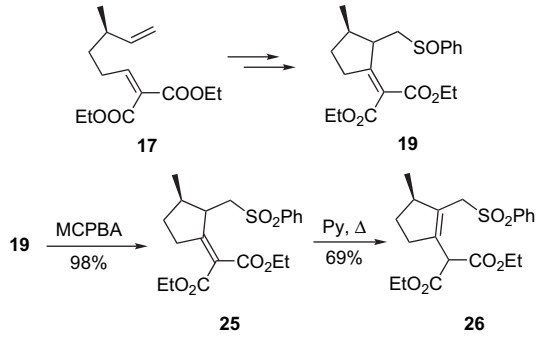
Scheme 3. Synthesis of compounds **19**–**24**.

methyl (2*E*,6*R*)-2,6-dimethylocta-2,7-dienoate (**13**) were made to react with phenylsulfanyl radical, good yields of **12** and **14**, respectively, were obtained (entries 9 and 10). On the other hand, it was noted that an increase in the electronic deficiency of the olefin acceptor of the carbon-centered radical not only speeded up the process (entries 11 and 12) but also, in the case of diester **17**, led to an increase in the diastereoselectivity of the addition–cyclization, producing a 58:21:14:7 ratio of **18** (entry 12).

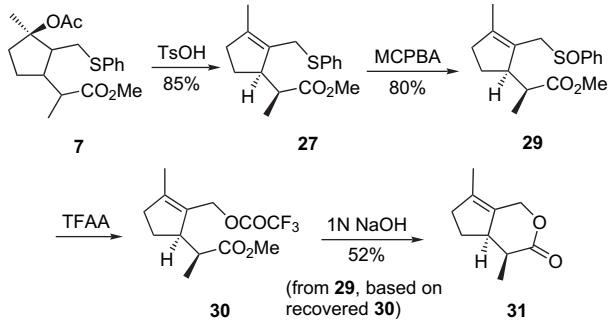
Given the high efficiency found in the preparation of **18**, different chemical transformations of this diastereomeric mixture were studied with the aim of not only fitting the functionality of these intermediates to those of natural iridoids but also of making the mixture of diastereomers to converge into a single isomer, thus producing a valuable synthetic intermediate in the preparation of these compounds. In this context, the α-selenylation of **18** followed by treatment with H_2O_2 led to sulfoxide **19** where the disappearance of the stereocenters at C-3 and C-8 involved a first simplification (Scheme 3).

Heating of **19** in refluxing pyridine led to the elimination of the corresponding sulfinic acid affording mixtures of conjugated dienes with ratios varying with reaction times. Diene **20** was obtained as major reaction product (50% yield) when reflux was maintained for 9 h. When diester **19** was treated with Tf_2O, vinylsulfide **21** was obtained in a 41% yield, together with only 6% of the expected aldehyde, 15% of lactone **23** and 21% of **24** as a result of the reduction of the sulfoxide moiety. Thus, although sulfoxide **19** did not progress efficiently towards the Pummerer rearranged derivative, once aldehyde **22** is formed, it evolves to γ-lactone **23** via its enolic form. Vinylsulfide **21** did not evolve to the expected aldehyde when allowed to react with concentrated HCl.[20] This transformation was achieved upon treatment with $HgCl_2$,[20] leading to 28% of aldehyde **22** together with 26% of **23** (yields based on recovered starting material).

Continuing with the reactivity studies of these sulfur derivatives, sulfoxide **19** was chemoselectively oxidized with MCPBA at 0 °C to the corresponding sulfone **25** almost quantitatively. The presence of the sulfone then enabled deconjugation of the double bond on **25** when this compound was heated in refluxing pyridine. Allylic sulfone **26** was thus obtained as a single enantiomer in four steps starting from readily available acyclic ester **17** with a 69% yield (Scheme 4).

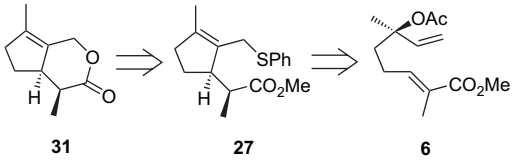


Scheme 4. Synthesis of enantiopure **26** from **17**.



Scheme 6. Enantioselective synthesis of (−)-dehydroiridomyrmecin **31**.

With these results in mind we felt that this protocol could be used to efficiently synthesize natural iridoids. To test the feasibility of this methodology natural dehydroiridomyrmecin **31**, isolated from *Actinidia polygama* Miq, was selected.[21] The enantioselective synthesis of this natural product **31** was designed to start with commercially available (−)-linalool. The key step of this strategy rests on the phenylsulfanyl radical-mediated 5-*exo*-*trig* cyclization of **6** to obtain, after regioselective deacetylation, the key intermediate **27**, which already possesses the stereochemistry and carbon framework of the natural product (Scheme 5).



Scheme 5. Retrosynthesis of (−)-dehydroiridomyrmecin.

As we mentioned earlier (Table 1, entry 5), exposure of ester **6** to phenylsulfanyl radical afforded cyclopentane **7** in high yield. When compound **7** was allowed to react with 2,4,6-collidine at reflux for 40 h, only a 30% of the hoped-for elimination product was obtained together with a 51% of unaltered starting material. Gratifyingly, it was found that **7** could be deacetylated to efficiently lead to olefin **27** after being treated with TsOH in refluxing benzene (Scheme 6). According to the results shown in Table 1, **27** was constituted by a couple of enantiomers in an approximate ratio of 3:1 (see Fig. 2), the major enantiomer being as shown in Scheme 6. Moving forward with the synthetic planning, phenylsulfide **27** was chemoselectively oxidized with MCPBA at a low temperature[22] to produce phenylsulfoxide **29**. When this compound was exposed to Pummerer experimental conditions,[23] trifluoroacetate **30** was obtained as result of the nucleophilic displacement of $PhSOCOCF_3$.[24] Chemoselective saponification of the trifluoroacetate ester in **30** with 1 N NaOH at rt afforded natural dehydroiridomyrmecin (**31**) with a 46% yield together with a 11% of starting trifluoroacetate **30** (Scheme 6). Since no enantiomeric separation was performed, (−)-dehydroiridomyrmecin was synthesized in a 50% ee. In this sense, the sign of the optical rotation $[\alpha]_D$ of synthetic (−)-dehydroiridomyrmecin (−46.2 (*c* 1.0, $CHCl_3$)) matched that of the natural compound (−106.5 (*c* 0.9, $CHCl_3$)). Finally, the spectroscopic data of **31** fully agree with those reported for natural dehydroiridomyrmecin. The enantioselective synthesis of (−)-dehydroiridomyrmecin starting from the (−)-linalyl acetate ester derivative **6** was thus completed in five steps with a 28% overall yield. Furthermore, the stereocontrolled synthesis of lactone **31** from (−)-linalool proved the absolute configuration of dehydroiridomyrmecin, as originally suggested by Sakai and co-workers.[21]

3. Conclusion

In conclusion, we describe a tandem addition–cyclization protocol triggered either by phenyl- or phenylethylsulfanyl radical, for the construction of the iridane skeleton, when applied to acyclic derivatives of linalool or citronellene. The reactivity of the cyclization products was studied and it was found that the sulfide moiety could be transformed into other functional groups suitable for the synthesis of natural products. Although the utility of this route has been already proved with the enantioselective synthesis of the natural iridoid dehydroiridomyrmecin, we believe that the versatility and modulability of this protocol is promising enough to warrant new achievements in the preparation of other natural iridoids.

4. Experimental section

4.1. General procedure for radical cyclization

A solution of the corresponding thiol (11.4 mmol, 2.0 equiv) and AIBN (939 mg, 5.72 mmol, 1.0 equiv) in benzene (114 mL) was added dropwise (8 mL/h) under an argon atmosphere to a boiling solution of the corresponding acyclic diene (5.72 mmol, 1.0 equiv) in benzene (57 mL) (TLC monitoring). The solvent was evaporated under reduced pressure. Purification of the residue by column chromatography afforded the corresponding cyclic compounds.

*4.1.1. 1-Acetoxy-7-phenylthioiridane (**2**)*

According to the general procedure described above, the resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 25:1) on silica gel to afford 35% of **2** as a diastereomeric mixture.

*4.1.2. (1R,2S,3R)-1-Hydroxy-7-phenylthioiridane (**3a**)*

To a solution of **2** (100 mg, 0.32 mmol) in MeOH (5 mL), K_2CO_3 (133 mg, 0.96 mmol) was added at rt and stirred for 48 h (TLC monitoring). The solvent was removed under reduced pressure and the residue obtained was dissolved in H_2O and extracted with *t*-BuOMe. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 20:1) to afford 40 mg of **3a**. IR (film) ν_{max} 3443, 3058, 2957, 1731, 1584, 1479, 1374, 1151, 1025, 737, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.80 (3H, d, *J*=5.6 Hz), 0.90 (3H, d, *J*=5.6 Hz), 1.40 (3H, br s), 1.42–1.50 (1H, m), 1.51–1.75 (4H, m), 1.80–1.92 (1H, m), 1.93–2.10 (1H, m), 2.48 (1H, s), 2.90–3.10 (2H, m), 7.15–7.22 (1H, m), 7.28 (2H, br t, *J*=7.4 Hz), 7.37 (2H, br d, *J*=7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 22.1, 27.1, 29.0, 31.2, 32.1, 39.8, 49.7, 51.1, 80.8, 126.5, 129.0, 130.1 136.6; HRFABMS calcd for $C_{16}H_{24}OSNa$ $[M+Na]^+$ 287.1445, found 287.1442.

*4.1.3. Methyl 1-acetoxy-7-phenylthioiridan-9-oate (**7**)*

According to the general procedure, the resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 20:1) on

silica gel to afford 90% of **7** as a diastereomeric mixture at a 47:25:22:6 ratio. The mixture was subjected to HPLC (mobile phase: 0–5 min, hexane/*t*-BuOMe, 97:3; 5–15 min, hexane/*t*-BuOMe, 96:4; 15–50 min, hexane/*t*-BuOMe, 9:1) to give pure **7a**, **7c** and **7d**.

*4.1.3.1. Methyl (1R,2S,3R,8S)-1-acetoxy-7-phenylthioiridan-9-oate (**7a**).* t_R=34.5 min; $[\alpha]_D$ +17.0 (*c* 0.7, CH_2Cl_2); IR (film) ν_{max} 2949, 1736, 1437, 1368, 1248, 1169, 1135, 1086, 740, 692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.10 (3H, d, *J*=6.7 Hz), 1.40–1.68 (2H, m), 1.50 (3H, s), 1.90–2.30 (4H, m), 1.94 (3H, s), 2.54 (1H, dq, *J*=6.7, 9.9 Hz), 2.76 (1H, dd, *J*=5.6, 13.0 Hz), 3.05 (1H, dd, *J*=5.6, 13.0 Hz), 3.60 (3H, s), 7.09–7.16 (1H, m), 7.19–7.33 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.6, 22.3, 25.7, 25.9, 30.3, 35.7, 41.1, 43.9, 50.8, 51.6, 88.4, 126.2, 129.0, 129.6, 137.5, 170.2, 176.6; HRFABMS calcd for $C_{19}H_{26}O_4SNa$ $[M+Na]^+$ 373.1449, found 373.1447.

*4.1.3.2. Methyl (1R,2S,3S,8R)-1-acetoxy-7-phenylthioiridan-9-oate (**7c**).* t_R=28.3 min; $[\alpha]_D$ −52.9 (*c* 1.0, CH_2Cl_2); IR (film) ν_{max} 3057, 2972, 2948, 2878, 1733, 1582, 1480, 1438, 1368, 1254, 1168, 1088, 1022, 940, 741, 691 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.20 (3H, d, *J*=7.1 Hz), 1.50–1.60 (1H, m), 1.62 (3H, s), 1.70–1.86 (2H, m), 1.96 (1H, dt, *J*=6.3, 9.1 Hz), 2.03 (3H, s), 2.12–2.23 (1H, m), 2.38–2.48 (1H, m), 2.80 (1H, dq, *J*=7.1, 5.1 Hz), 3.05 (1H, dd, *J*=6.3, 13.1 Hz), 3.30 (1H, dd, *J*=6.3, 13.1 Hz), 3.61 (3H, s), 7.20 (1H, t, *J*=7.2 Hz), 7.28–7.41 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.3, 22.3, 23.6, 25.1, 33.8, 36.3, 42.0, 47.1, 51.4, 52.2, 90.3, 126.0, 129.0, 129.2, 137.2, 170.2, 175.7; HRFABMS calcd for $C_{19}H_{26}O_4SNa$ $[M+Na]^+$ 373.14495, found 373.1449.

*4.1.3.3. Methyl (1R,2R,3S,8R)-1-acetoxy-7-phenylthioiridan-9-oate (**7d**).* t_R=37.2 min; $[\alpha]_D$ −0.8 (*c* 0.75, CH_2Cl_2); IR (film) ν_{max} 2938, 1731, 1436, 1368, 1255, 1195, 1167, 1053 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.08 (3H, d, *J*=6.7 Hz), 1.37–1.50 (1H, m), 1.67 (3H, s), 1.68–1.87 (2H, m), 1.98 (3H, s), 2.23 (1H, ddd, *J*=9.2, 6.3, 15.4 Hz), 2.36–2.46 (1H, m), 2.54 (1H, dq, *J*=6.7, 10.9 Hz), 2.67–2.77 (2H, m), 2.85 (1H, dd, *J*=3.7, 12.2 Hz), 3.65 (3H, s), 7.15–7.22 (1H, m), 7.25–7.32 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.2, 20.8, 22.8, 26.5, 30.9, 36.2, 41.0, 45.2, 48.0, 51.7, 92.7, 126.5, 129.1, 129.9, 137.0, 170.7, 176.8; HRFABMS calcd for $C_{19}H_{26}O_4SNa$ $[M+Na]^+$ 373.1449, found 373.1451.

*4.1.4. Methyl 7-phenylthio-1-pivaloyloxiiridan-9-oate (**12**)*

According to the general procedure described for radical cyclization, the resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 25:1) on silica gel to afford 87% of **12** as a diastereomeric mixture at a 46:20:17:17 ratio. The mixture was subjected to HPLC (mobile phase: 0–5 min, hexane/*t*-BuOMe, 97:3; 5–15 min, hexane/*t*-BuOMe, 96:4; 15–50 min, hexane/*t*-BuOMe, 9:1) to give pure **12a**.

*4.1.4.1. Methyl (1R,2S,3R,8S)-7-phenylthio-1-pivaloyloxiiridan-9-oate (**12a**).* t_R=27.8 min; $[\alpha]_D$ +6.0 (*c* 0.97, CH_2Cl_2); IR (film) ν_{max} 2972, 1726, 1480, 1288, 1164, 1132, 739 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.10 (9H, s), 1.15 (3H, d, *J*=6.7 Hz), 1.37–1.66 (2H, m), 1.49 (3H, s), 2.00 (2H, t, *J*=8.0 Hz), 2.10–2.24 (1H, m), 2.27 (1H, q, *J*=5.8 Hz), 2.55 (1H, dq, *J*=6.7, 10.5 Hz), 2.76 (1H, dd, *J*=6.0, 12.9 Hz), 3.07 (1H, dd, *J*=5.1, 12.9 Hz), 3.60 (3H, s), 7.08–7.15 (1H, m), 7.18–7.32 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.7, 26.0, 26.3, 27.2 (3çC), 29.8, 32.5, 36.0, 41.2, 44.1, 51.0, 51.6, 87.9, 126.1, 129.0 (2C), 129.4 (2C), 138.8, 176.7; HRFABMS calcd for $C_{22}H_{32}O_4SNa$ $[M+Na]^+$ 415.1914, found 415.1915.

*4.1.5. Methyl 7-phenylthioiridan-9-oate (**14**)*

According to the general procedure for radical cyclization, the resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 20:1) on silica gel to afford 85% of **14** as a diastereomeric mixture at a 54:20:19:7 ratio. The mixture was subjected to HPLC (mobile phase: 0–5 min, hexane/*t*-BuOMe, 97:3; 5–15 min, hexane/*t*-BuOMe, 96:4; 15–50 min, hexane/*t*-BuOMe, 9:1) to give pure **14a** and **14c**.

*4.1.5.1. Methyl (1R,2S,3S,8R)-7-phenylthioiridan-9-oate (**14a**).* t_R= 17.3 min; $[\alpha]_D$ +4.9 (*c* 0.8, CH_2Cl_2); IR (film) ν_{max} 2950, 2869, 1735, 1583, 1480, 1437, 1167, 739, 691 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.04 (3H, d, *J*=7.0 Hz), 1.07–1.26 (1H, m), 1.15 (3H, d, *J*=6.8 Hz), 1.33–1.50 (1H, m), 1.55–1.74 (1H, m), 1.75–1.85 (1H, m), 1.90–2.05 (1H, m), 2.10–2.30 (2H, m), 2.48 (1H, dq, *J*=6.8, 10.6 Hz), 2.60 (1H, t, *J*=11.9 Hz), 3.02 (1H, dd, *J*=4.1, 11.9 Hz), 3.70 (3H, s), 7.17–7.25 (1H, m), 7.27–7.40 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.8, 22.8, 28.6, 31.8, 34.9, 37.7, 40.4, 45.8, 46.4, 51.6, 126.1, 129.0 (2C), 129.6 (2C), 137.0, 177.1; HRFABMS calcd for $C_{17}H_{24}O_2SNa$ $[M+Na]^+$ 315.1395, found 315.1397.

*4.1.5.2. Methyl (1R,2S,3R,8S)-7-phenylthioiridan-9-oate (**14c**).* t_R= 16.5 min; IR (film) ν_{max} 2949, 2869, 1734, 1583, 1480, 1438, 1259, 1162, 739, 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (3H, d, *J*=6.7 Hz), 1.05 (3H, d, *J*=7.0 Hz), 1.05–1.22 (1H, m), 1.35–1.55 (2H, m), 1.57–1.72 (2H, m), 1.80 (1H, q, *J*=6.8 Hz), 1.92 (1H, t, *J*=7.5 Hz), 2.46 (1H, t, *J*=6.9 Hz), 2.93 (1H, dd, *J*=6.0, 12.5 Hz), 3.00 (1H, dd, *J*=6.0, 12.5 Hz), 3.56 (3H, s), 7.05–7.12 (1H, m), 7.15–7.30 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0, 20.4, 28.2, 33.2, 38.6, 39.8, 43.1, 48.2, 49.2, 51.4, 125.8, 128.9 (2C), 129.1 (2C), 137.5, 176.3; HRFABMS calcd for $C_{17}H_{24}O_2SNa$ $[M+Na]^+$ 315.1395, found 315.1396.

*4.1.6. Diethyl 1-acetoxy-7-phenylthioiridan-9,10-dioate (**16**)*

According to the general procedure described for radical cyclization, the resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 8:1) on silica gel to afford 80% of **16** as a diastereomeric mixture at a 36:28:18:18 ratio. The mixture was subjected to HPLC (mobile phase: 0–5 min, hexane/*t*-BuOMe, 97:3; 5–15 min, hexane/*t*-BuOMe, 96:4; 15–50 min, hexane/*t*-BuOMe, 9:1) to give pure **16a** and **16d**.

*4.1.6.1. Diethyl (1R,2S,3R)-1-acetoxy-7-phenylthioiridan-9,10-dioate (**16a**).* t_R=51.3 min; IR (film) ν_{max} 2958, 2924, 2853, 1736, 1729, 1583, 1481, 1463, 1443, 1367, 1248, 1188, 1155, 1082, 1026, 967, 859, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.23 (3H, t, *J*=7.1 Hz), 1.26 (3H, t, *J*=7.1 Hz), 1.60 (3H, s), 1.70–1.80 (1H, m), 1.92–2.00 (2H, m), 2.00 (3H, s), 2.23 (1H, ddd, *J*=4.8, 10.2, 14.8 Hz), 2.37 (1H, q, *J*=7.1 Hz), 2.81 (1H, dd, *J*=7.2, 13.1 Hz), 2.90–2.98 (1H, m), 3.17 (1H, dd, *J*=5.5, 13.1 Hz), 3.60 (1H, d, *J*=11.0 Hz), 4.16 (2H, q, *J*=7.1 Hz), 4.18 (2H, q, *J*=7.1 Hz), 7.16–7.20 (1H, m), 7.25–7.34 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 14.3, 22.4, 25.4, 26.0, 30.2, 35.9, 39.7, 51.2, 53.9, 61.7, 61.8, 88.8, 126.3, 129.1 (2C), 129.4 (2C), 138.9, 168.8, 169.1, 170.2; HRFABMS calcd for $C_{22}H_{30}O_6SNa$ $[M+Na]^+$ 445.1660, found 445.1661.

*4.1.6.2. Diethyl (1R,2R,3S)-1-acetoxy-7-phenylthioiridan-9,10-dioate (**16d**).* t_R=63.7 min; IR (film) ν_{max} 3058, 2978, 2935, 2874, 1729, 1584, 1480, 1439, 1368, 1258, 1231, 1176, 1152, 1066, 1025, 937, 861, 803 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.13 (3H, t, *J*=7.2 Hz), 1.20 (3H, t, *J*=7.1 Hz), 1.40–1.58 (2H, m), 1.59 (3H, s), 1.73–1.86 (2H, m), 1.93 (3H, s), 2.16–2.30 (1H, m), 2.74–2.90 (2H, m), 2.95–3.06 (1H, m), 3.56 (1H, d, *J*=11.6 Hz), 4.08 (2H, q, *J*=7.2 Hz), 4.13 (2H, q, *J*=7.2 Hz), 7.10–7.16 (1H, m), 7.18–7.29 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.3, 20.8, 22.8, 26.3, 31.4, 36.2, 40.6, 48.6, 53.9, 61.7 (2C), 92.4, 126.5, 129.2 (2C), 129.6 (2C), 136.9, 168.7, 169.3, 170.7; HRFABMS calcd for $C_{22}H_{30}O_6SNa$ $[M+Na]^+$ 445.1660, found 445.1661.

4.2. Synthesis of cyclopentane derivative 26 from acyclic diene 17

*4.2.1. Diethyl 7-phenylsulfinyl-3(8)-iriden-9,10-dioate (**20**)*

To a solution of diisopropylamine (4.9 mL, 35.0 mmol, 10.0 equiv) and *n*-BuLi (2 M in pentane, 8.7 mL, 17.5 mmol, 5.0 equiv) in anhydrous THF (24 mL) under an argon atmosphere and cooled at −78 °C,

diethyl 7-phenylthioiridan-9,10-dioate (**18**) (1273 mg, 3.50 mmol, 1.0 equiv) in 10 mL of THF was added and stirred for 15 min. Then TMSCl (2.70 mL, 23.0 mmol, 6.6 equiv) was added and the reaction mixture was stirred for 15 min more. Finally PhSeCl (4420 mg, 23.0 mmol, 6.6 equiv) in 10 mL of THF was added and the reaction mixture was stirred for 5 min (TLC monitoring), diluted with *t*-BuOMe and quenched with NH_4Cl solution. The aqueous phase was extracted with *t*-BuOMe. The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was dissolved in 100 mL of CH_2Cl_2 and oxidized with H_2O_2 (30%) (1.1 mL, 11.0 equiv) at rt. The reaction mixture was stirred for 1 h 45 min (TLC monitoring), washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 1:1) to afford 1200 mg (97%) of the corresponding sulfoxide **19** as colourless oil. A solution of sulfoxide **19** (118 mg, 0.31 mmol) in pyridine (1.0 mL) under an argon atmosphere was heated at 115 °C for 9 h (TLC monitoring). The reaction mixture was diluted with *t*-BuOMe and washed with 1 N HCl and $NaHCO_3$ solution. The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 8:1) to afford 58 mg (74%) of a mixture of dienes, from which **20** was the major component. The mixture was subjected to HPLC (mobile phase: 0–5 min, hexane/*t*-BuOMe, 97:3; 5–15 min, hexane/*t*-BuOMe, 96:4; 15–50 min, hexane/*t*-BuOMe, 9:1) to give **20**: t_R=13.1 min; IR (film) ν_{max} 2961, 2932, 2871, 1721, 1632, 1610, 1462, 1447, 1413, 1367, 1289, 1263, 1238, 1218, 1172, 1127, 1096, 1037, 907, 865, 803 cm^{-1}; ^1H NMR (500 MHz, $(CD_3)_2CO$) δ 0.98 (3H, d, *J*=6.6 Hz), 1.08–1.16 (7H, m,), 1.84–1.93(1H, m,), 2.37–2.45 (1H, m), 2.62 (1H, dt, *J*=8.8, 19.5 Hz), 2.94 (1H, ddd, *J*=3.2, 8.5, 19.5 Hz), 4.03–4.11 (4H, m), 5.10 (1H, d, *J*=2.3 Hz), 5.37 (1H, d, *J*=2.5 Hz); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) δ 18.6, 18.9, 22.8, 36.9, 37.0, 44.9, 65.8, 66.2, 117.6 (2C), 158.1, 161.9, 169.2, 171.8; HRFABMS calcd for $C_{14}H_{20}O_4Na$ $[M+Na]^+$ 275.1660, found 275.1661.

*4.2.2. Treatment of sulfoxide **19** with trifluoroacetic anhydride*

Trifluoroacetic anhydride (0.27 mL, 1.98 mmol, 4.0 equiv) was added to a stirred solution of sulfoxide **19** (187 mg, 0.49 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (20 mL) at 0 °C. The reaction mixture was stirred for 2 h 30 min (TLC monitoring) and washed with NH_4Cl solution and brine. The aqueous phase was extracted with CH_2Cl_2 three times. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 15:1–1:1) to afford 37 mg of sulfide **24** (21%), 73 mg of thioenolether **21** (41%), together with 8 mg (6%) of aldehyde **22** and 16 mg (15%) of **23** as a white solid. A 4% yield of starting material **19** was recovered.

*4.2.3. Diethyl (1R)-7-phenylthio-2(7)E,3(8)-iridadien-9,10-dioate (**21**)*

IR (film) ν_{max} 3059, 2959, 2935, 2904, 2869, 1714, 1610, 1555, 1479, 1442, 1366, 1264, 1229, 1187, 1103, 1036, 843, 806, 744, 691 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.05 (3H, d, *J*=7.1 Hz), 1.11 (3H, t, *J*=7.2 Hz), 1.20 (3H, t, *J*=7.1 Hz), 1.50–1.56 (1H, m), 1.82–1.92 (1H, m), 2.84–3.00 (2H, m), 3.05 (1H, ddd, *J*=2.6, 9.2, 19.1 Hz), 4.02–4.10 (2H, m), 4.13 (2H, q, *J*=7.1 Hz), 6.91 (1H, br s), 7.18–7.32 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 14.4, 18.5, 30.9, 32.4, 38.7, 60.9, 61.5, 117.9, 127.7, 129.1, 129.5 (2C), 130.0 (2C), 135.2, 143.0, 156.9, 164.7, 167.9; HRFABMS calcd for $C_{20}H_{24}O_4SNa$ $[M+Na]^+$ 383.1293, found 383.1291.

*4.2.4. Diethyl (1R,2S)-7-oxo-3(8)-iriden-9,10-dioate (**22**)*

IR (film) ν_{max} 3056, 2958, 2926, 2854, 1736, 1669, 1628, 1448, 1369, 1302, 1234, 1149, 1095, 1032, 741 cm^{-1}; ^1H NMR (500 MHz, $CO(CD_3)_2$) δ 1.08 (3H, d, *J*=6.9 Hz), 1.21–1.29 (1H, m), 1.24 (3H, t, *J*=7.1 Hz), 1.25 (3H, t, *J*=7.1 Hz), 1.50 (1H, octuplet, *J*=4.2 Hz), 2.06–2.13 (1H, m), 2.66 (1H, ddd, *J*=4.5, 8.3, 18.7 Hz), 2.78–2.87 (1H, m), 3.02–3.12 (1H, m), 4.20 (2H, q, *J*=7.1 Hz), 4.21 (2H, q, *J*=7.1 Hz), 10.05 (1H, s); ^{13}C NMR (125 MHz, $CO(CD_3)_2$) δ 13.6 (2C), 18.8, 30.5, 34.2, 38.6, 51.2, 61.7, 61.8, 146.0, 152.1, 166.6, 166.7, 188.3; HRFABMS calcd for $C_{14}H_{20}O_5Na$ $[M+Na]^+$ 291.1209, found 29.1212.

*4.2.5. Ethyl (7R)-3,5,6,7-tetrahydro-7-methyl-3-oxocyclopenta[c]pyran-4-carboxylate (**23**)*

Mp (hexane) 105–108 °C; $[\alpha]_D$ +37.0 (*c* 1.0, CH_2Cl_2); IR (film) ν_{max} 3075, 2985, 2924, 2877, 1740, 1686, 1549, 1465, 1391, 1314, 1279, 1224, 1200, 1146, 1042, 901, 854 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.24 (3H, d, *J*=6.7 Hz), 1.37 (3H, t, *J*=7.1 Hz), 1.55–1.64 (1H, m), 2.22–2.32 (1H, m), 2.87–2.96 (1H, m), 3.02 (1H, br sextuplet, *J*=7.0 Hz), 3.15 (1H, ddd, *J*=3.7, 8.2, 18.8 Hz), 4.35 (2H, q, *J*=7.1 Hz), 7.33 (1H, br s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 19.2, 32.8, 34.6, 35.0, 61.6, 113.2, 129.2, 146.8, 159.0, 164.3, 169.5; HRFABMS calcd for $C_{12}H_{14}O_4Na$ $[M+Na]^+$ 245.0789, found 245.0791.

*4.2.6. Diethyl (1R,2S)-7-phenylthio-3(8)-iriden-9,10-dioate (**24**)*

IR (film) ν_{max} 3058, 2957, 2929, 2870, 1721, 1638, 1582, 1479, 1439, 1367, 1239, 1176, 1092, 1057, 1033, 741 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.93 (3H, d, *J*=7.1 Hz), 1.22 (3H, t, *J*=7.1 Hz), 1.28 (3H, t, *J*=7.1 Hz), 1.36–1.44 (1H, m), 1.92–2.02 (1H, m), 2.38–2.48 (1H, m), 2.64–2.88 (3H, m), 2.92–2.98 (1H, m), 3.25 (1H, dd, *J*=3.7, 12.7 Hz), 4.14 (2H, q, *J*=7.1 Hz), 4.18–4.26 (2H, dq, *J*=2.5, 7.1 Hz), 7.17 (1H, tt, *J*=1.2, 7.2 Hz), 7.25–7.30 (2H, m), 7.35–7.39 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 14.3, 20.4, 30.4, 31.7, 37.1, 37.2, 51.7, 61.1, 61.2, 123.0, 126.4, 129.0 (2C), 130.0 (2C), 136.1, 165.3, 165.4, 168.6; HRFABMS calcd for $C_{20}H_{26}O_4SNa$ $[M+Na]^+$ 385.1441, found 385.1443.

*4.2.7. Treatment of thioenolether **21** with $HgCl_2/CdCO_3$*

To a mixture of **21** and **24** at a 2.5:1 ratio (130 mg, 0.36 mmol) dissolved in acetone (18 mL), $CdCO_3$ (213 mg, 1.22 mmol) and $HgCl_2$ (1.5 g, 5.56 mmol) were added at rt. The mixture was refluxed for 48 h (TLC monitoring), the inorganic salts were filtered off and the residue obtained was diluted with water, extracted with *t*-BuOMe, washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 15:1–1:1) to afford 10 mg (14%) of **22** and 15 mg (26%) of **23** as white solids. A 68% yield of **21** was recovered.

*4.2.8. Diethyl (1R)-7-phenylsulfonyl-3(8)-iriden-9,10-dioate (**25**)*

To a solution of 7-phenylsulfinyl-3(8)-iriden-9,10-dioate (**19**) (450 mg, 1.19 mmol, 1.0 equiv) in 20 mL of CH_2Cl_2, MCPBA (316 mg, 1.28 mmol, 1.08 equiv) was added at 0 °C. The reaction mixture was stirred for 10 min at 0 °C and for 50 min at rt (TLC monitoring), washed sequentially with aqueous $NaHCO_3$, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 1:1) to afford 460 mg (98%) of the corresponding sulfone **25** as a mixture of epimers at C-2 in a 3:1 ratio. Data for compound **25**: IR (film) ν_{max} 2963, 1720, 1638, 1561, 1499, 1447, 1367, 1304, 1230, 1179, 1150, 1058, 1030, 740, 690 cm^{-1}. Isomer 2*S*: ^1H NMR (500 MHz, $CDCl_3$) δ 0.93 (3H, d, *J*=7.0 Hz), 1.26 (6H, q, *J*=7.0 Hz), 1.52 (1H, m), 1.98 (1H, m), 2.64 (1H, br dd, *J*=9.0, 19.8 Hz), 2.69–2.83 (2H, m), 3.06 (1H, dd, *J*=11.5, 13.8 Hz), 3.20 (1H, br d, *J*=11.5 Hz), 3.40 (1H, dd, *J*=2.2, 13.8 Hz), 4.11–4.23 (4H, m), 7.56 (2H, t, *J*=7.6 Hz), 7.64 (1H, t, *J*=7.6 Hz), 7.93 (2H, d, *J*=7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 14.3, 19.9, 29.8, 30.7, 36.6, 47.3, 58.2, 61.2, 61.5, 123.9, 128.3 (2C), 129.4 (2C), 133.8, 140.2, 164.8, 165.1, 166.8. Isomer 2*R*: (only distinctive signals) ^1H NMR (500 MHz, $CDCl_3$) δ 1.11 (3H, d, *J*=7.0 Hz), 1.30 (6H, m), 1.45 (1H, m), 1.82 (1H, m), 2.61–2.79 (2H, m),

3.17 (1H, dd, J=3.0, 14.4 Hz), 3.27 (1H, dd, J=8.6, 14.4 Hz), 3.75 (1H, br t, J=8.0 Hz), 4.11–4.31 (4H, m); (only distinctive signals) ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 15.6, 31.2, 31.9, 36.9, 42.9, 55.7, 61.2, 61.7, 123.2, 128.2 (2C), 129.4 (2C), 133.7, 140.9, 164.9, 165.5, 167.3.

*4.2.9. Diethyl (1R)-7-phenylsulfonyl-2-iriden-9,10-dioate (**26**)*

Sulfone **25** (70 mg, 0.17 mmol) was dissolved in 0.9 mL of pyridine under an argon atmosphere and heated at 113 °C for 9 h 30 min. The reaction mixture was diluted with *t*-BuOMe (50 mL), washed with 1 N HCl, brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 10:1) to afford 48 mg of **26** (69%). Data for compound **26**: IR (film) ν_{max} 2950, 1740, 1654, 1445, 1367, 1306, 1150, 1028, 787 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (3H, t, J=7.2 Hz), 1.26 (6H, m), 1.32 (1H, m), 2.32 (1H, m), 2.41 (1H, m), 2.60 (1H, m), 3.81 (1H, d, J=13.6 Hz), 3.99 (1H, d, J=13.6 Hz), 4.18 (4H, br q, J=7.2 Hz), 4.38 (1H, s), 7.54 (1H, br t, J=7.6 Hz), 7.63 (1H, br t, J=7.6 Hz), 7.88 (1H, br d, J=7.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.2, 14.3, 18.5, 31.4, 32.6, 42.0, 52.3, 54.4, 61.7, 61.9, 128.8 (2C), 129.4 (2C), 133.9, 140.0, 138.4, 139.2, 167.1, 167.6.

4.3. Synthesis of (−)-dehydroiridomyrmecin (31)

*4.3.1. Methyl 7-phenylthio-1-iriden-9-oate (**27**)*

p-TsOH (5 mg) was added to a stirred solution of **7** (91 mg, 0.26 mmol) in benzene (4 mL) and heated at reflux for 10 min (TLC monitoring). The reaction mixture was diluted with *t*-BuOMe and washed with aqueous $NaHCO_3$ solution. The organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 6:1) to afford 64 mg of **27**. IR (film) ν_{max} 2946, 2844, 1731, 1583, 1479, 1437, 1378, 1197, 1170, 1088, 1024, 741, 691 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (3H, d, J=7.1 Hz), 1.50 (3H, br s), 1.69–1.81 (1H, m), 1.90–2.04 (1H, m), 2.13–2.25 (2H, m), 2.82 (1H, dq, J=4.0, 7.0 Hz), 3.15–3.23 (1H, m), 3.51 (1H, br d, J=12.9 Hz), 3.62 (3H, s), 3.89 (1H, br d, J=12.9 Hz), 7.18–7.40 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 15.0, 24.4, 31.8, 36.9, 41.0, 50.0, 51.6, 126.5, 128.3 (2C), 130.9 (3C), 136.7, 138.9, 175.9; HRFABMS calcd for $C_{17}H_{22}O_2SNa$ $[M+Na]^+$ 313.1238, found 313.1239.

*4.3.2. Methyl 7-phenylsulfinyl-1-iriden-9-oate (**29**)*

To a stirred solution of **27** (220 mg, 0.75 mmol) in CH_2Cl_2 (8 mL) under an argon atmosphere, MCPBA (186 mg, 0.75 mmol) in CH_2Cl_2 (6 mL) at −78 °C was added. The reaction mixture was stirred at this temperature for 5 min (TLC monitoring), diluted with CH_2Cl_2 (25 mL), washed with $NaHCO_3$ and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude was purified by column chromatography (hexane/*t*-BuOMe, 1:1) to afford 25 mg of methyl 7-phenylsulfonyl-1-iriden-9-oate **28** (5%), together with 184 mg of methyl 7-phenylsulfinyl-1-iriden-9-oate **29** (80%) as a diastereomeric mixture at a 1:1 ratio. Data for compound **28**: IR (film) ν_{max} 2925, 1730, 1447, 1306, 1150, 1085, 747, 689 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (3H, d, J=7.0 Hz), 1.18 (3H, s), 1.60–1.70 (1H, m), 1.90–2.03 (1H, m), 2.11 (2H, m), 2.85 (1H, dq, J=3.8, 7.0 Hz), 3.10–3.20 (1H, m), 3.55 (3H, s), 3.92 (1H, d, J=14.4 Hz), 4.05 (1H, d, J=14.4 Hz), 7.47–7.53 (2H, m), 7.58–7.63 (1H, m), 7.79–7.84 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 14.6, 24.4, 36.7, 40.5, 50.8, 51.5, 54.8, 123.7, 128.3 (2C), 129.1 (2C), 133.7, 138.9, 145.3, 175.6; HRFABMS calcd for $C_{17}H_{22}O_4SNa$ $[M+Na]^+$ 345.1136, found 345.1134. Data for compound **29**: IR (film) ν_{max} 2935, 1727, 1443, 1378, 1259, 1198, 1086, 1043, 751, 692 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (3H, d, J=7.0 Hz), 1.10 (3H, d, J=7.0 Hz), 1.16 (3H, s), 1.50 (3H, s), 1.55–1.75 (2H, m), 1.80–1.95 (2H, m), 2.05–2.19 (2H, m), 2.17 (2H, t, J=7.3 Hz), 2.65 (1H, dq, J=3.9, 7.0 Hz), 2.76 (2H, dq, J=3.7, 6.7 Hz), 2.91 (1H, m), 3.45–3.65 (2H, m), 3.55 (3H, s), 3.56 (3H, s), 3.67–3.80 (2H, m), 7.40–7.65 (10H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 14.0, 14.5, 14.6, 24.6, 25.1, 36.7, 36.9, 40.9, 41.2, 51.0 (2C), 51.5, 51.6, 56.5, 57.0, 124.1 (2C), 124.3 (2C), 125.0, 125.3, 125.5, 128.9 (2C), 129.1 (2C), 131.0, 131.1, 143.8, 143.9, 144.2, 175.5, 175.8; HRFABMS calcd for $C_{17}H_{22}O_3S$ $[M+H]^+$ 307.1367, found 307.1365.

*4.3.3. (−)-Dehydroiridomyrmecin (**31**)*

Trifluoroacetic anhydride (1.02 mL, 7.32 mmol) was added to a stirred solution of sulfoxide **29** (560 mg, 1.83 mmol) in CH_2Cl_2 (73 mL) at 0 °C. The mixture was stirred for 30 min at 0 °C and then 1 N aq NaOH (18.3 mL) and THF (60 mL) were added and stirring was continued for 4 h at rt (TLC monitoring). The reaction mixture was extracted with diethyl ether and the combined organic layer was washed with aqueous NH_4Cl and brine. Evaporation of the solvent followed by column chromatography (petroleum ether 30–40 °C/diethyl ether, 5:1) furnished 60 mg of trifluoroacetate **30** and 140 mg of dehydroiridomyrmecin **31** (46%). Data for compound **30**: IR (film) ν_{max} 2952, 1783, 1734, 1457, 1348, 1220, 1164 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (3H, d, J=7.0 Hz), 1.74 (3H, s), 1.74–1.82 (1H, m), 1.97–2.05 (1H, m), 2.15–2.35 (2H, m), 2.75 (1H, dq, J=3.9, 7.0 Hz), 3.03 (1H, br s), 3.56 (3H, s), 4.88 (1H, d, J=12.2 Hz), 4.97 (1H, d, J=12.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 14.4, 24.6, 37.3, 41.2, 50.1, 51.5, 63.4, 124.6, 128.4, 144.9, 175.6. (−)-Dehydroiridomyrmecin (**31**): $[\alpha]_D$ −46 (c 1.0, $CHCl_3$); IR (film) ν_{max} 2948, 1733, 1437, 1376, 1206, 1156 cm^{-1}; ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 1.01 (3H, d, J=7.2 Hz), 1.40–1.51 (1H, m), 1.70 (3H, s), 1.85–1.97 (1H, m), 2.20–2.30 (1H, m), 2.35–2.45 (1H, m), 2.90 (1H, quint, J=7.2 Hz), 3.15–3.25 (1H, m), 4.77 (1H, d, J=13.1 Hz), 4.87 (1H, d, J=13.1, Hz); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 11.6, 13.6, 27.1, 38.3, 40.3, 46.9, 65.8, 130.0, 137.0, 174.9; HRCIMS calcd for $C_{10}H_{15}O_2$ $[M+H]^+$ 167.1072, found 167.1070.

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Supplementary data

Detailed description of the preparation of the acyclic precursors **6**, **11**, **13**, **15** and **17** as well as their spectral data is included. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.03.058.

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