Tetrahedron xxx (2014) 1–9

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Highly functionalised cyclohexa-1,3-dienes by sulfonyl Nazarov reagents

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ARTICLE INFO

Article history:
Received 13 March 2014
Received in revised form 21 April 2014
Accepted 23 April 2014
Available online xxx

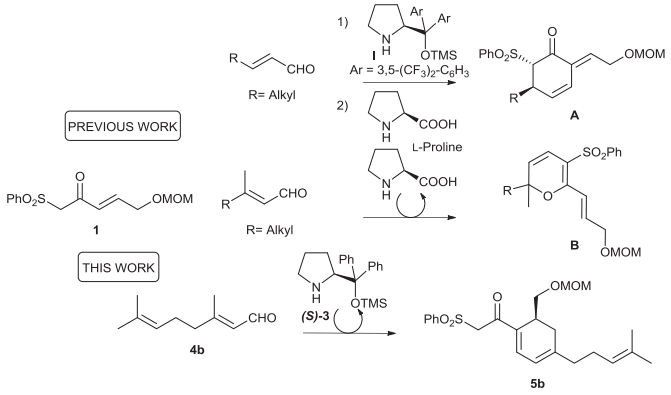
Keywords:
Sulfones
Asymmetric Diels–Alder
Nazarov reagents
Cyclohexa-1,3-dienes
Hayashi–Jørgensen organocatalyst

ABSTRACT

The Hayashi–Jørgensen organocatalyst has made possible a sulfonyl Nazarov analogue reagent to give a Diels–Alder reaction at the double bond, without involving the activated methylene affording chiral highly functionalised cyclohexa-1,3-dienes.

1. Introduction

The chemistry of Nazarov reagents has increased in the last years due to their versatility and possibility to be excellent starting materials for the synthesis of biologically active compounds.[1] The sulfone group, both as a powerful electron withdrawing group and as an easily removable substituent,[2] is ideal for the substitution of the carboethoxymethyl group in the Nazarov reagent. Sulfone and sulfoxide analogues of Nazarov reagents have been used as dienophiles in asymmetric Diels–Alder reactions with dienes and employing a chiral metallic Lewis acid as catalyst or in anionic polycyclisations.[3] In our group, the reactivity of Nazarov reagent **1** has been developed in a divergent manner for diversity oriented syntheses (Scheme 1).[4,5] The interest of a compound like **1** is, besides the fact that it can act as a Nazarov reagent, the extra functionality provided by the hydroxyl group, which can be further employed for the synthesis of diversity oriented compounds or as a linker in solid support chemistry.[6] It was observed that employing organocatalyst **I** and L-Proline in a tandem reaction different cyclohexenones **A** were obtained diastereoselectively.[4] On the other hand, using L-Proline or derivatives, MacMillan catalysts, thioureas or even chiral phosphoric acids in the reaction of **1** with



Scheme 1. Reactivity of Nazarov reagent **1** with unsaturated aldehydes and prenal derivatives.

β,β-disubstituted aldehydes, racemic pyrans **B** were obtained instead of the cyclohexenone ring (Scheme 1).[5]

Monosubstituted unsaturated aldehydes have been widely used in organocatalysis for the synthesis of very interesting compounds.[7] However, β-methyl-β-disubstituted unsaturated aldehydes have been much less used in organocatalysis. Prof. Serebryakov et al. have developed the asymmetric synthesis of cyclohexa-1,3-dienes from prenal and unsaturated esters or derivatives,[8] Watanabe et al., using Proline as organocatalyst, made citral to dimerise through a Diels–Alder reaction[9] and Christmann

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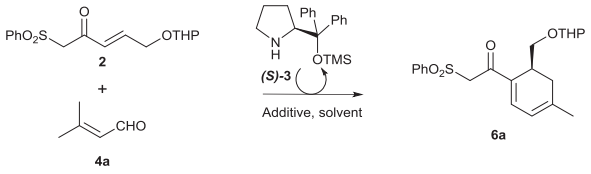
0040-4020/$ – see front matter © 2014 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2014.04.076

et al. reported an intramolecular Rauhut–Curier-type reaction via dienamine activation.[10] We realised that neither us, nor Prof. Serebryakov had employed the Hayashi–Jørgensen organocatalyst.[11] Thus, we decided to test the reactivity of sulfone **1** with citral **4b** using organocatalyst (*S*)-**3**. To our delight the reaction worked and surprisingly led to a new structure, namely cyclohexa-1,3-dienes, instead of cyclohexenones or pyran rings, constituting the first time that a Nazarov reagent acts as dienophile using organocatalysis (Scheme 1). This fact gives an idea that organocatalysis is still an undeveloped area and that a reaction can be diversely directed just by tuning the organocatalyst used.

2. Results and discussion

Cyclohexa-1,3-dienes and their derivatives are structurally important since they are versatile intermediates for the synthesis of natural products and biologically active compounds.[12] We started our study (Table 1) using commercially available 3-methyl-butenal **4a** and sulfone **2** since, as we previously demonstrated,[4,5] it behaves exactly the same as **1** but the tetrahydropyranyl (THP) protecting group is much more easily removable.

Table 1
Reaction of Nazarov reagent **2** with **4a**[a]



Entry	**2**/**4a** Ratio	Additive (20 mol %)	Solvent	Time[b]	Yield[c] (%)
1	2/1	—	2-Propanol	47 h	42
2	1/2	—	2-Propanol	44 h	49
3	2/1	B.A.	2-Propanol	47 h	50
4	2/1	BinapOH	2-Propanol	46 h	27
5	2/1	*p*-TsOH	2-Propanol	40 h	13
6	2/1	Na_2CO_3	2-Propanol	7 days	17
7	2/1	K_2CO_3	2-Propanol	6 days	31
8	2/1	$CsCO_3$	2-Propanol	2 days	60
9	2/1	LiOAc· H_2O	2-Propanol	3 days	65
10	2/1	NaOAc	2-Propanol	6 days	63
11	2/1	$FeCl_3·6H_2O$	2-Propanol	42 h	S.M.
12	2/1	$ZnCl_2$	2-Propanol	47 h	S.M.
13	2/1	—	Hexane	80 h	23
14	2/1	—	Toluene	79 h	66
15	2/1	—	CH_2Cl_2	74 h	67
16	2/1	—	$CHCl_3$	71 h	73
17	2/1	—	Et_2O	30 h	26
18	2/1	—	THF	46 h	32
19	2/1	—	MeOH	56 h	DEC
20	2/1	—	EtOH	49 h	75[d]
21	1/2	—	EtOH	24 h	40
22	1/1	—	EtOH	45 h	7
23	**2/1**	**B.A.**	**EtOH**	**48 h**	**79**[e]

Bold value signifies the best conditions with the best results found.
[a] All the reactions were carried out at rt, in the corresponding solvent at 0.18 M and 50 mol % (*S*)-**3**.
[b] Time in which highest yield was observed with no decomposition (the consumption of starting materials was monitored by TLC).
[c] Isolated yield after chromatography on silica gel.
[d] 89% ee determined by HPLC.
[e] 92% ee determined by HPLC. B.A.=benzoic acid. BinapOH=(*S*)-(+)-1,19-binaphthyl-2,29-diyl hydrogen phosphate. S.M.=Starting Material. DEC=decomposition.

A screening of different sulfone/aldehyde ratios, solvents and additives was carried out in order to test the importance of the β-substituent.

As shown in Table 1, the sulfone/aldehyde ratio did not change the reaction yield substantially, (entries 1 and 2). Use of acid additives (entries 3–5) decreased yields comparing to initial conditions except for benzoic acid (entry 3). Brønsted bases had similar effect, and although lithium or sodium acetate made a good improvement, the reaction time increased (entries 6–10). Lewis acids did not produce any reaction (entries 11 and 12). Solvent screening (entries 13–20) proved EtOH to be the best solvent. After testing the sulfone/aldehyde ratio (entries 21 and 22) and the use of benzoic acid (entry 23) we found the best conditions were a sulfone/aldehyde ratio of 2/1 and 20% of benzoic acid in EtOH. The ee was measured for the best conditions (entries 20 and 23) observing that the use of benzoic acid slightly increased the yield and the enantiomeric excess (ee) as before. Finally we carried out a study of catalyst loading (Table 2), finding that a 50 mol % catalyst was the optimum amount needed for the best yield and ee. The absolute stereochemistry was determined by X-ray analysis of an analogue as shown later on.

Table 2
Catalyst load screening[a]

Entry	Catalyst (*S*)-**3** (mol %)	Yield[b] (%)	ee[c] (%)
1	5	S.M.	—
2	10	S.M.	—
3	20	39	89
4	**50**	**79**	**92**
5	100	75	90

Bold value signifies the best conditions with the best results found.
[a] All the reactions were carried out at rt, in EtOH at 0.18 M in 48 h, with a 2/1 ratio of **2**/**4a** and 20 mol % benzoic acid.
[b] Isolated yield of **6a** after chromatography on silica gel.
[c] ee determined by HPLC analysis, carried out on a CHIRALCEL IC column; *n*-hexane/2-propanol [60/40 (v/v)]; flow rate: 1.0 mL/min.

Once the best conditions were established for this reaction, several β,β-alkylsubstituted aldehydes **4a**–**f**, were tested with differently protected sulfones **1** and **2** (Table 3).

When sulfone **1** was used, yields were from moderate to good except for compounds **5c** and **5e** (entries 3 and 5) due to a possible oxo-Michael reaction.[13] The enantiomeric excess in all cases vary from good to excellent. Similar behaviour was observed when using sulfone **2**. In this case and in order to corroborate the obtained results, enantiomeric catalyst (*R*)-**3** was used (entries 7, 9 and 13) obtaining the corresponding enantiomers with similar ee, adding more versatility to this procedure.

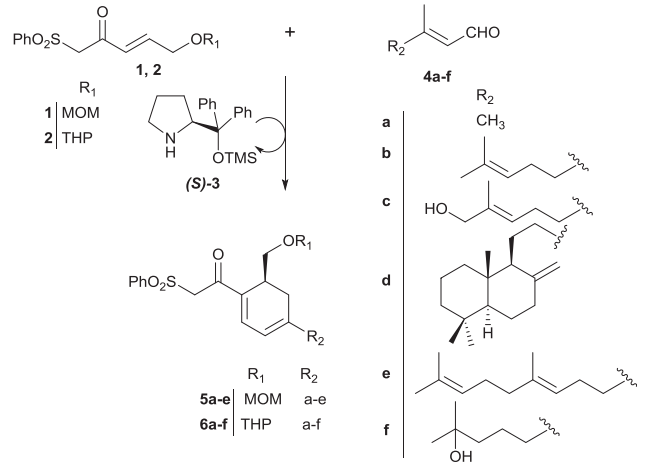
It can be concluded that when both β-substituents are alkyl groups, cyclohexa-1,3-diene derivatives **5**/**6** are obtained from low to good yields (16–79%) and in good to excellent ee (75–92%).

Compounds **5**/**6** obtention can be understood through a Diels–Alder mechanism between dienamine **II** formed between the catalyst and the α,β-unsaturated aldehyde,[14] and the Nazarov reagent acting as dienophile similarly as in the cases of Prof. Serebryakov et al.[8] It is noteworthy that in this reaction the diene is established with the methyl group and not with the methylene group as in the case of the Rauhut–Curier-type reaction of Christmann et al. (Fig. 1).[10a] Intermediate **III** is demonstrated by NMR and HRMS experiments and observed its slowly transformation into the final products.

With these results in hand we decided to test the behaviour when one of the alkyl groups is changed to an aromatic ring. Using Nazarov reagent **2** with different aromatic aldehydes under the same conditions, cyclohexa-1,3-dienes **7** were formed instead of cyclohexa-1,3-dienes **6** (Table 4). The stereochemistry at the new chiral centre in **7** is proposed to come from a 1,5-*H* sigmatropic rearrangement, since the formation of the same intermediate **III** is observed with both aliphatic and aromatic substituents. As shown in Table 4, yields and enantiomeric excesses are good in all cases.

In order to see the value of this reaction, different compounds in a diversity oriented strategy were obtained. Compound **5a** was submitted to oxygen atmosphere and direct sunlight using Rose

Table 3
Reaction of Nazarov reagents **1**,**2** with prenals **4a**–**f**[a]



Entry	Sulfone	Aldehyde	Product	Yield[b] (%)	ee[c] (%)
1	**1**	**4a**	**5a**	62	79
2	**1**	**4b**	**5b**	69	82
3	**1**	**4c**	**5c**	20	80
4	**1**	**4d**	**5d**	58	75
5	**1**	**4e**	**5e**	24	39
6	**2**	**4a**	**6a**	**79**	**92**
7[d]	**2**	**4a**	*ent*-**6a**	75	−92
8	**2**	**4b**	**6b**	62	90
9[d]	**2**	**4b**	*ent*-**6b**	65	−91
10	**2**	**4c**	**6c**	49	80
11	**2**	**4d**	**6d**	16	88
12	**2**	**4d**	**6e**	33	89
13[d]	**2**	**4e**	*ent*-**6e**	36	−89
14	**2**	**4f**	**6f**	32	91

Bold value signifies the best conditions with the best results found.
[a] All the reactions were carried out at rt, in EtOH at 0.18 M in 48 h, with a 2/1 ratio of sulfone/aldehyde, 50 mol % (*S*)-**3** and 20 mol % benzoic acid.
[b] Isolated yield after chromatography on silica gel.
[c] ee determined by HPLC analysis, carried out on a CHIRALCEL IC column; *n*-hexane/2-propanol [60/40 (v/v)]; flow rate: 1.0 mL/min.
[d] Using catalyst (*R*)-**3**.

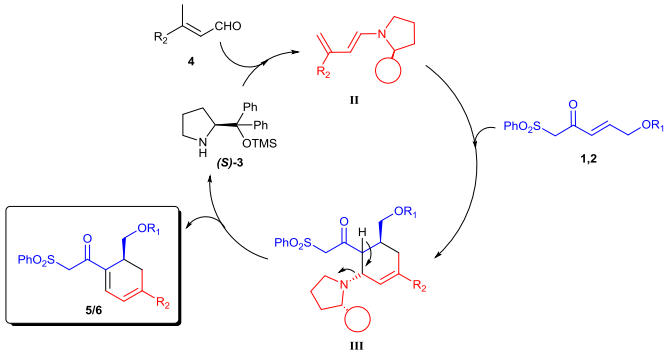
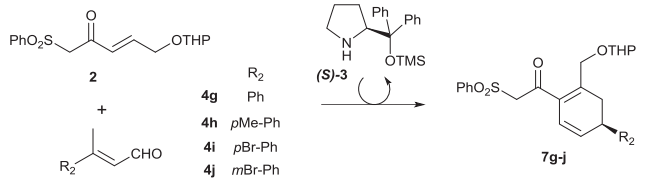


Fig. 1. Proposed Diels–Alder mechanism for the synthesis of **5**/**6**.

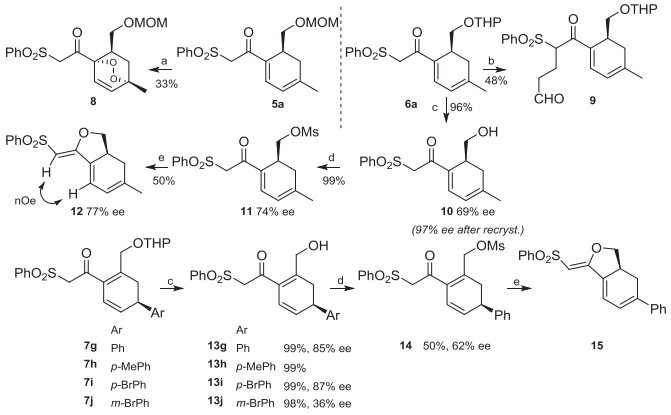
Bengal as catalyst to provide **8** in moderate yield (Scheme 2). Diene **6a** was made to react with acrolein affording **9** in good yield. Unfortunately compound **9** was much less reactive than expected and did not react when submitted to intramolecular hetero-Diels–Alder conditions, and when compound **6a** was submitted to a variety of dienophiles (dihydropyran, maleimide and *N*-phenylmaleimide, maleic anhydride, 2-pentenal or diphenylmethanimine) only starting materials or degradation products were obtained. Thus compound **6a** was deprotected affording **10**, although with some racemisation, but we were able to crystallise it and allowing us to establish the absolute configuration of

Table 4
Reaction of Nazarov reagent **2** with aromatic-β-substituted unsaturated aldehydes[a]



Entry	Aldehyde	Product	Yield[b] (%)	ee[c] (%)
1	**4g**	**7g**	59	91
2	**4h**	**7h**	69	90
3	**4i**	**7i**	59	91
4	**4j**	**7j**	**81**	**93**

Bold value signifies the best conditions with the best results found.
[a] All the reactions were carried out at rt, in EtOH at 0.18 M in 48 h, with a 2/1 ratio of **2**/**4g**–**j**, 50 mol % (*S*)-**3** and 20 mol % benzoic acid.
[b] Isolated yield after chromatography on silica gel.
[c] ee determined by HPLC analysis, carried out on a CHIRALCEL AD-H column; *n*-hexane/isopropyl alcohol [80/20–70/30 (v/v)]; flow rate: 1.0 mL/min.



Scheme 2. (a) O_2 atmosphere, Rose Bengal (25 mol %), sunlight, MeOH, rt, 4 h; (b) acrolein (2 equiv), K_2CO_3 (8 equiv), THF, rt, 4 h; (c) *p*-TsOH·H_2O (50 mol %), THF/H_2O (1/1), rt; (d) MsCl, Et_3N, DMAP, DCM, rt; (e) DBU, DCM, rt.

cyclohexadienes **6** and **7** formed in the organocatalytic reaction (Fig. 2).[15] Mesylation of **10** afforded **11**, which by treatment in basic conditions led to triene **12**. The double bond stereochemistry of this enolether was established by NOE's experiments (Scheme 2). Aromatic derivatives **7g**–**j** were submitted to the same conditions, i.e., deprotection and mesylation, but the resulting compounds were more unstable than aliphatics and only mesylated phenyl derivative **14** obtained from **13g** could be isolated. Aromatic triene **15** was observed by NMR, after basic treatment of **14**, but was not stable enough to be fully characterised. Compounds as **13g** are precursors of carbonyliron complexes and further studies will be conducted in this way.[16]

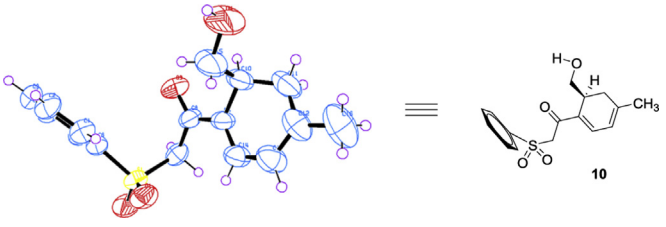
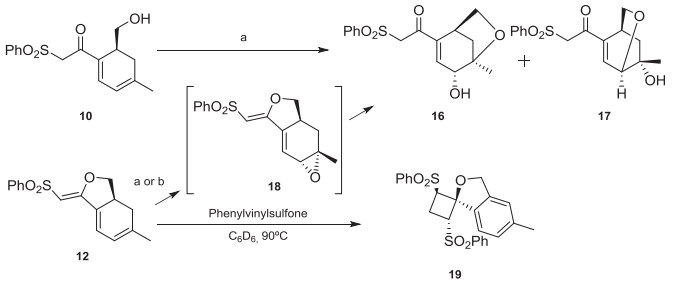


Fig. 2. ORTEP diagram for compound **10**.

More diversity oriented structures were obtained from reactivity studies of diene **10** and triene **12** (Scheme 3, Table 5). When **10** was treated with *m*-CPBA a 1/1 mixture of tetrahydrofuran and tetrahydropyran **16**/**17** was obtained in moderate yield. However, if



Scheme 3. (a) *m*-CPBA, $CDCl_3$, 0 °C − rt; (b) $CHCl_3$, heat (37 °C).

Table 5
Reactivity of compounds **9** and **10**[a]

Entry	S.M.	Conditions	Time (h)	Product	Yield[b] (%)
1	**10**	*m*-CPBA	15	**16**+**17 (1/1)**	38
2	**12**	*m*-CPBA	6	**16**	62
3	**12**	Heat[c] (37 °C)	72	**16**	53
4	**12**	PVS,[d] 90 °C	2.5	**19**	42

[a] For more details see ESI.
[b] Isolated yield after chromatography on silica gel.
[c] Under air atmosphere.
[d] Phenylvinylsulfone.

compound **12** was submitted to the same conditions, or just heating, only **16** was obtained in better yields in a chemo, regio- and stereocontrolled way. This substructure is present in quinocycline and isoquinocycline compounds with antibiotic and cytotoxic activities.[17] In this case it was possible to isolate intermediate epoxide **18**, corroborating the mechanism of the reaction. Analogues of these compounds have been used for the synthesis of natural products.[18] This kind of compounds is related to Bruceantin, an antitumour agent isolated from *Bruceas* species.[19] When compound **12** was heated in benzene in the presence of phenylvinylsulfone (PVS) cyclobutane **19** was obtained by a [2+2] cycloaddition in moderate yield, adding even more versatility to these compounds.

3. Conclusions

In conclusion, it has been made a sulfone Nazarov reagent to react in organocatalytic conditions in a Diels–Alder manner for the first time. This reaction has made possible to obtain diverse chiral highly functionalised cyclohexa-1,3-dienes, depending on whether the aldehyde substitution is an alkyl or aryl group. These kinds of cyclohexadienes have been used in Diels–Alder bioconjugation of diene modified oligonucleotides.[20] Herein, we report their application for the synthesis of different bicyclic or tricyclic compounds in a diversity oriented synthesis, opening the way for the use of these compounds in bioconjugation chemistry.

4. Experimental section

4.1. General experimental methods

Unless otherwise stated, all chemicals were purchased as the highest purity commercially available and were used without further purification, except for **1**,[4] **2**,[5] 10-hydroxycitral **4c**,[21] **4d**, farnesal **4e**[22] and **4f**,[23] which were synthesised according to the literature procedures. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were measured on 200, 400 and 600 MHz spectrometers and performed in $CDCl_3$ or C_6D_6, and referenced to the residual peak of $CHCl_3$ at δ 7.26 ppm and δ 77.0 ppm or to the residual peak of C_6H_6 at δ 7.15 ppm and δ 128.6 ppm, for ^1H and ^{13}C, respectively. Chemical shifts are reported in δ parts per million and coupling constants (J) are given in hertz. High-resolution mass spectra were recorded on an ESI-Q-TOF mass spectrometer, using chemical ionisation (ammonia as gas) or Fast Atom Bombardment (FAB) technique. For some of the samples, electrospray ionisation (ESI) was employed. Optical rotations were determined in 1 dm cell. HPLC analysis were carried out on a chiral column [amylose tris(3,5-dimethylphenycarbamate)] or [cellulose tris(3,5-dichlorophenycarbamate)] on silica gel using *n*-hexane/2-propanol. Column chromatography was performed using silica gel 60 (230–400 mesh), with solvent systems indicated in the relevant experimental procedures. Dichloromethane was distilled from calcium hydride. Tetrahydrofuran and diethyl ether were distilled from sodium/benzophenone ketyl under argon atmosphere prior to use. Hexane was distilled prior to use.

4.2. General procedure for the synthesis of cyclohexadienes, 5a–e, 6a–f and 7g–j

β-Ketosulfone (**1**,**2**) (0.18 mmol) and the corresponding aldehyde (0.08 mmol) were dissolved in 1 ml of EtOH. Next, catalyst (*S*)-**3** (50 mol %), and benzoic acid (20 mol %) were added successively and left stirring at room temperature for 48 h. All products were purified by flash chromatography on silica gel using different mixtures of *n*-hexane/ethyl acetate.

*4.2.1. (S)-1-(6-((Methoxymethoxy)methyl)-4-(methyl)-cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**5a**).* Yellow oil (17.4 mg, 62%): ν_{max} (liquid film) 2929, 1718, 1629, 1570, 1448, 1383, 1309, 1290, 1151; δ_H (200 MHz; $CDCl_3$) 7.89 (2H, d, J=6.9 Hz), 7.81–7.24 (3H, m), 7.03 (1H, d, J=5.9 Hz), 6.02–5.78 (1H, m), 4.54 (2H, s), 4.45 (2H, d, J=8.1 Hz), 3.31 (3H, s), 3.21–3.16 (3H, m), 2.55–2.28 (1H, m), 1.92 (3H, s), 1.65–1.58 (1H, m); δ_C (50 MHz; $CDCl_3$) 186.6, 148.4, 140.7, 139.0, 134.3, 133.1, 129.4 (2CH), 128.8 (2CH), 119.2, 96.6, 66.0, 62.8, 55.4, 31.1, 30.8, 24.4; EIHRMS: calcd for $C_{18}H_{22}O_5S$ (M+Na): 373.1086; found: 373.1080 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=325 nm; t_R (minor)= 37.5 min; t_R (major)=41.6 min; $[\alpha]_D^{25}$ −9.57 (*c* 1.42, $CHCl_3$).

*4.2.2. (S)-1-(6-((Methoxymethoxy)methyl)-4-(4-methylpent-3-en-1-yl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**5b**).* Yellow oil (23.1 mg, 69%): ν_{max} (liquid film) 2956, 2929, 2873, 1715, 1651, 1566, 1446, 1323, 1288, 1153; δ_H (400 MHz; $CDCl_3$) 7.89 (2H, d, J=7.0 Hz), 7.72–7.47 (3H, m), 7.06 (1H, d, J=6.0 Hz), 6.02–5.80 (1H, m), 5.12–4.76 (1H, m), 4.54 (2H, s), 4.54–4.51 (1H, m), 4.49–4.41 (1H, m), 3.31 (3H, s), 3.19–3.14 (3H, m), 2.53 (1H, d, J=17.8 Hz), 2.23–2.11 (4H, m), 1.69 (3H, s), 1.61 (3H, s), 1.40–1.35 (1H, m); δ_C (100 MHz; $CDCl_3$) 186.6, 152.0, 140.7, 139.0, 134.3, 133.4, 132.7, 129.4 (2CH), 128.8 (2CH), 123.3, 118.6, 96.6, 65.9, 62.8, 55.4, 38.2, 30.7, 29.7, 26.0, 25.9, 17.9; EIHRMS: calcd for $C_{23}H_{30}O_5S$ (M+Na): 441.1712; found: 441.1706 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=325 nm; t_R (minor)=31.6 min; t_R (major)=34.5 min; $[\alpha]_D^{25}$ −4.56 (*c* 0.57, $CHCl_3$).

*4.2.3. (S,E)-1-(6-((Methoxymethoxy)methyl)-4-(4-methyl-5-hydroxy-pent-3-en-1-yl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl) ethan-1-one (**5c**).* Yellow oil (6.9 mg, 20%): ν_{max} (liquid film) 3452, 2935, 2885, 1716, 1637, 1564, 1446, 1379, 1309, 1292, 1151; δ_H (200 MHz; $CDCl_3$) 7.89 (2H, d, J=7.0 Hz), 7.75–7.48 (3H, m), 7.06 (1H, d, J=5.8 Hz), 5.94 (1H, d, J=4.9 Hz), 5.43–5.32 (1H, m), 4.54 (2H, s), 4.54–4.35 (2H, d, J=9.1 Hz), 4.00 (2H, s), 3.31 (3H, s), 3.22–3.19 (3H, m), 2.53 (1H, d, J=18.2 Hz), 2.35–2.19 (4H, m), 1.69 (3H, s), 1.33–1.08 (1H, m); δ_C (50 MHz; $CDCl_3$) 186.6, 151.5, 140.5, 139.0, 136.1, 134.3, 133.5, 129.4 (2CH), 128.7 (2CH), 124.4, 118.9, 96.6, 68.8, 65.9, 62.8, 55.5, 37.6, 30.6, 29.7, 25.6, 13.9; EIHRMS: calcd for $C_{23}H_{30}O_6S$ (M+Na): 457.1661; found: 457.1655 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl

alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=325 nm; t_R (minor)=58.8 min; t_R (major)=67.9 min; $[\alpha]_D^{25}$ −1.02 (*c* 1.08, $CHCl_3$).

*4.2.4. 1-((6S)-(6-((Methoxymethoxy)methyl)-4-(2-((1S,4aS,8aS)-5,5,8a-trimethyl-2-methylenedecahydronaphthalen-1-yl)ethyl)-2-(phenylsulfonyl))ethan-1-one (**5d**).* Yellow oil (25.7 mg, 58%): ν_{max} (liquid film) 2937, 2848, 1718, 1649, 1566, 1446, 1321, 1309, 1151; δ_H (200 MHz; $CDCl_3$) 7.89 (2H, d, *J*=7.9), 7.71–7.40 (3H, m), 7.06 (1H, d, *J*=5.7 Hz), 5.97–5.79 (1H, m), 4.84 (1H, s), 4.54 (2H, s), 4.54–4.42 (4H, m), 4.27 (1H, s), 3.31 (3H, s), 3.21–3.16 (3H, m), 2.59–2.40 (1H, m), 2.44–0.74 (24H, m); δ_C (50 MHz; $CDCl_3$) 186.6, 153.2, 148.6, 140.9, 138.9, 134.3, 133.7, 129.4 (2CH), 128.8 (2CH), 118.2, 106.6, 96.6, 65.9, 62.8, 56.7, 55.7, 55.4, 42.3, 40.0, 39.9, 39.3, 38.5, 33.8, 33.5, 30.7, 28.6, 24.7, 21.9, 19.6, 19.2, 14.7; EIHRMS: calcd for $C_{33}H_{46}O_5S$ (M+Na): 577.2964; found: 577.2958 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=325 nm; t_R (minor)=31.4 min; t_R (major)=33.3 min; $[\alpha]_D^{25}$ +13.98 (*c* 2.21, $CHCl_3$).

*4.2.5. (S,E)-1-(6-((Methoxymethoxy)methyl)-4-(4,8-dimethylnon-3,7-dien-1-yl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**5e**).* Yellow oil (9.3 mg, 24%): ν_{max} (liquid film) 2926, 2856, 1716, 1651, 1566, 1448, 1379, 1309, 1288, 1153; δ_H (200 MHz; $CDCl_3$) 7.89 (2H, d, *J*=8.2 Hz), 7.68–7.42 (3H, m), 7.06 (1H, d, *J*=5.8 Hz), 6.02–5.83 (1H, m), 5.28–4.93 (2H, m), 4.54 (2H, s), 4.50–4.40 (2H, m), 3.31 (3H, s), 3.22–3.11 (3H, m), 2.54 (1H, d, *J*=18.2 Hz), 2.31–2.14 (8H, m), 1.68 (3H, s), 1.61 (6H, s), 1.35–1.10 (1H, m); δ_C (50 MHz; $CDCl_3$) 186.9, 152.1, 140.8, 136.3, 134.3, 133.4, 133.3, 130.4, 129.4 (2CH), 128.8 (2CH), 124.4, 123.3, 118.6, 96.6, 66.0, 62.8, 55.4, 39.9, 38.3, 30.7, 29.7, 26.9, 25.9 ($2CH_2$), 17.9, 16.3; EIHRMS: calcd for $C_{28}H_{38}O_5S$ (M+Na): 509.2338; found: 509.2332 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=325 nm; t_R (major)= 29.1 min; t_R (minor)=34.8 min; $[\alpha]_D^{25}$ −12.07 (*c* 1.42, $CHCl_3$).

*4.2.6. (S)-1-(6-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-4-(methyl) cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**6a**). Note*: The presence of THP protecting group makes many of NMR signals, both ^1H and ^{13}C, to appear twice. Hence, for compounds with THP group only NMR shift values for one isomer are given here.

Yellow oil (24.6 mg, 79%): ν_{max} (liquid film) 2941, 2868, 1718, 1637, 1570, 1446, 1383, 1323, 1309, 1288, 1153; δ_H (200 MHz; $CDCl_3$) 7.89 (2H, d, *J*=8.3 Hz), 7.71–7.50 (3H, m), 7.02 (1H, d, *J*=5.9 Hz), 6.02–5.73 (1H, m), 4.57–4.33 (3H, m), 3.83–3.69 (1H, m), 3.50–3.35 (2H, m), 3.21–3.10 (1H, m), 3.09–2.98 (1H, m), 2.67–2.48 (1H, m), 1.92 (3H, s), 1.84–1.39 (7H, m); δ_C (50 MHz; $CDCl_3$) 186.6, 148.6, 140.7, 139.0, 134.3, 133.1, 129.4 (2CH), 128.8 (2CH), 119.2, 99.2, 65.5, 62.8, 62.4, 31.4, 31.1, 30.8, 25.6, 24.4, 19.7; EIHRMS: calcd for $C_{21}H_{26}O_5S$ (M+Na): 413.1399; found: 413.1393 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=325 nm; t_R (minor)=41.5 min; t_R (major)=49.9, 66.5 min; $[\alpha]_D^{25}$ −15.0 (*c* 0.16, $CHCl_3$).

*4.2.7. (R)-1-(6-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-4-(methyl) cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**ent-6a**).* Yellow oil (23.4 mg, 75%); $[\alpha]_D^{25}$ +8.9 (*c* 0.9, $CHCl_3$).

*4.2.8. (S)-1-(6-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-4-(4-methylpent-3-en-1-yl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl) ethan-1-one (**6b**).* Yellow oil (22.7 mg, 62%): ν_{max} (liquid film) 2941, 2870, 1716, 1651, 1566, 1446, 1381, 1321, 1309, 1288, 1153; δ_H (200 MHz; $CDCl_3$) 7.89 (2H, d, *J*=8.1 Hz), 7.68–7.40 (3H, m), 7.04 (1H, d, *J*=5.9 Hz), 5.98–5.83 (1H, m), 5.11–5.01 (1H, m), 4.62–4.33 (3H, m), 3.88–3.60 (1H, m), 3.59–3.27 (2H, m), 3.26–2.92 (2H, m), 2.57–2.39 (1H, m), 2.25–2.13 (4H, m), 1.72–1.39 (13H, m); δ_C (50 MHz; $CDCl_3$) 186.7, 152.1, 140.6, 139.1, 134.3, 133.4, 132.6, 129.3 (2CH), 128.8 (2CH), 123.3, 118.7, 99.1, 65.5, 62.9, 62.4, 38.2, 30.8, 30.7, 29.8, 25.9, 25.8, 25.7, 19.5, 17.9; EIHRMS: calcd for $C_{26}H_{34}O_5S$ (M+Na): 481.2025; found: 481.2019 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=325 nm; t_R (minor)=36.6 min; t_R (major)=43.4 min, 56.8 min; $[\alpha]_D^{25}$ −15.1 (*c* 2.63, $CHCl_3$).

*4.2.9. (R)-1-(6-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-4-(4-methylpent-3-en-1-yl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl) ethan-1-one (ent-**6b**).* Yellow oil (23.8 mg, 65%): $[\alpha]_D^{25}$ +7.81 (*c* 0.71, $CHCl_3$).

*4.2.10. (S)-1-(6-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-4-(4-methyl-5-hydroxy-pent-3-en-1-yl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**6c**).* Yellow oil (18.6 mg, 49%): ν_{max} (liquid film) 3449, 2943, 2870, 1718, 1651, 1564, 1446, 1383, 1321, 1309, 1290, 1153; δ_H (200 MHz; $CDCl_3$) 7.89 (2H, d, *J*=7.6 Hz), 7.68–7.49 (3H, m), 7.04 (1H, d, *J*=5.7 Hz), 6.01–5.85 (1H, m), 5.49–5.31 (1H, m), 4.66–4.40 (3H, m), 3.99 (2H, s), 3.84–3.64 (1H, m), 3.57–3.31 (2H, m), 3.26–3.00 (2H, m), 2.71–2.50 (1H, m), 2.37–2.20 (4H, m), 1.67 (3H, s), 1.59–1.35 (7H, m); δ_C (50 MHz; $CDCl_3$) 186.7, 151.3, 140.5, 139.1, 136.1, 134.3, 133.4, 129.4 (2CH), 128.8 (2CH), 124.4, 118.9, 99.0, 68.7, 65.6, 62.8, 62.1, 37.6, 30.8, 30.6, 29.7, 25.6, 25.0, 19.5, 13.9; EIHRMS: calcd for $C_{26}H_{34}O_6S$ (M+Na): 497.1974; found: 497.1947 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=360 nm; t_R (minor)=60.4, 64.0 min; t_R (major)=89.7, 124.6 min; $[\alpha]_D^{25}$ −5.78 (*c* 2.49, $CHCl_3$).

*4.2.11. 1-((6S)-6-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-4-(2-((1S,4aS,8aS)-5,5,8a-trimethyl-2-methylenedecahydronaphthalen-1-yl)ethyl)-2-(phenylsulfonyl)ethan-1-one (**6d**).* Yellow oil (7.6 mg, 16%): ν_{max} (liquid film) 2941, 2868, 1718, 1649, 1564, 1448, 1321, 1309, 1155; δ_H (200 MHz; $CDCl_3$) 7.97–7.83 (2H, m), 7.73–7.40 (3H, m), 7.05 (1H, d, *J*=5.8 Hz), 6.03–5.84 (1H, m), 4.85 (1H, s), 4.61–4.31 (4H, m), 3.93–3.68 (1H, m), 3.57–3.28 (2H, m), 3.22–2.94 (2H, m), 2.63–2.43 (1H, m), 2.40–0.69 (32H, m); δ_C (50 MHz; $CDCl_3$) 186.7, 153.4, 148.6, 140.8, 139.0, 134.3, 133.6, 129.3 (2CH), 128.8 (2CH), 118.3, 106.6, 98.7, 65.4, 62.9, 62.1, 57.9, 55.8, 42.4, 40.0, 39.9, 39.3, 38.6, 37.1, 33.8, 33.5, 30.6, 29.9, 25.6, 24.7, 21.9, 19.6 ($2CH_2$), 19.2, 14.7; EIHRMS: calcd for $C_{36}H_{50}O_5S$ (M+Na): 617.3277; found: 617.3271 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=360 nm; t_R (minor)=35.4 min; t_R (major)=40.0, 49.0 min; $[\alpha]_D^{25}$ +22.90 (*c* 1.43, $CHCl_3$).

*4.2.12. (S,E)-1-(6-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-4-(4,8-dimethylnon-3,7-dien-1-yl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**6e**).* Yellow oil (14.1 mg, 33%): ν_{max} (liquid film) 2937, 2868, 1716, 1651, 1566, 1448, 1381, 1321, 1309, 1288, 1155; δ_H (200 MHz; $CDCl_3$) 7.95–7.82 (2H, m), 7.73–7.40 (3H, m), 7.04 (1H, d, *J*=6.0 Hz), 5.98–5.82 (1H, m), 5.21–4.98 (2H, m), 4.60–4.32 (3H, m), 3.87–3.66 (1H, m), 3.57–3.28 (2H, m), 3.25–2.98 (2H, m), 2.66–2.42 (1H, m), 2.35–2.12 (4H, m), 2.11–1.83 (4H, m), 1.78–1.45 (16H, m); δ_C (50 MHz; $CDCl_3$) 186.7, 152.0, 140.6, 139.1, 134.3, 133.8, 133.5, 130.3, 129.3 (2CH), 128.8 (2CH), 124.4, 123.3, 118.5, 98.7, 66.1, 62.9, 62.4, 39.9, 38.3, 30.8, 30.7, 29.8, 26.9, 25.9, 25.7, 25.6, 23.6, 19.5, 17.9; EIHRMS: calcd for $C_{31}H_{42}O_5S$ (M+Na): 549.2641; found: 549.2645 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=360 nm; t_R (minor)=29.3 min; t_R (major)=33.6, 40.8 min; $[\alpha]_D^{25}$ −3.87 (*c* 1.60, $CHCl_3$).

4.2.13. (R)-1-(6-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-4-(4,8-dimethylnon-3,7-dien-1-yl)cyclohexa-1,3-dien-1-yl)-2-

Please cite this article in press as: Peña, J.; et al., Tetrahedron (2014), http://dx.doi.org/10.1016/j.tet.2014.04.076

*(phenylsulfonyl)ethan-1-one (ent-**6e**).* Yellow oil (15.1 mg, 36%): $[\alpha]_D^{25}$ +18.57 (*c* 0.56, $CHCl_3$).

*4.2.14. (S)-1-(6-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-4-(4-methyl-4-hydroxy-pentan-1-yl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**6f**).* Yellow oil (12.2 mg, 32%): ν_{max} (liquid film) 3460, 2943, 2870, 1716, 16,457, 1566, 1448, 1379, 1323, 1309, 1290, 1153; δ_H (200 MHz; $CDCl_3$) 7.89 (2H, d, *J*=8.5 Hz), 7.75–7.46 (3H, m), 7.02 (1H, d, *J*=5.8 Hz), 5.97–5.79 (1H, m), 4.57–4.29 (3H, m), 3.93–3.63 (1H, m), 3.51–3.24 (2H, m), 3.21–2.92 (2H, m), 2.74–2.41 (1H, m), 2.30–2.01 (4H, m), 1.76–1.33 (9H, m), 1.32–1.14 (6H, m); δ_C (50 MHz; $CDCl_3$) 186.6, 152.4, 140.7, 139.1, 134.3, 133.3, 129.4 (2CH), 128.8 (2CH), 119.1, 99.3, 70.6, 65.6, 62.8, 62.3, 43.5, 38.3, 38.0, 31.1, 30.8, 29.7, 29.6, 28.9, 25.6, 19.6; EIHRMS: calcd for $C_{26}H_{36}O_6S$ (M+Na): 499.2130; found: 499.2125 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=350 nm; t_R (minor)=44.6; t_R (major)=51.4, 61.9 min; $[\alpha]_D^{25}$ +13.91 (*c* 1.86, $CHCl_3$).

*4.2.15. (R)-2-(1-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-5-(phenyl) cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**7g**).* Yellow oil (21.3 mg, 59%): ν_{max} (liquid film) 2941, 2870, 1718, 1647, 1545, 1447, 1323, 1309, 1292, 1153; δ_H (400 MHz; $CDCl_3$) 7.91 (2H, d, *J*=7.3 Hz), 7.73–7.48 (3H, m), 7.47–7.34 (5H, m), 7.22 (1H, d, *J*=6.3 Hz), 6.53 (1H, dd, *J*=6.1, 2.6 Hz), 4.65–4.38 (3H, m), 3.89–3.69 (1H, m), 3.49–3.35 (2H, m), 3.35–3.27 (1H, m), 3.15–3.00 (2H, m), 2.84–2.53 (1H, m), 1.89–1.30 (6H, m); δ_C (100 MHz; $CDCl_3$) 186.5, 146.2, 140.0, 138.7, 134.6, 134.5, 134.1, 129.3, 129.1 (2CH), 128.6 (4CH), 126.0 (2CH), 119.2, 98.9, 64.9, 62.8, 61.9, 30.5, 30.9, 30.3, 25.3, 19.3; EIHRMS: calcd for $C_{26}H_{28}O_5S$ (M+Na): 475.1555; found: 475.1549 (M+Na). ee: determined by HPLC: CHIRALPAK AD-H column; *n*-hexane/isopropyl alcohol [70/30 (v/v)]; flow rate: 1.0 mL/min; λ=340 nm; t_R (major)=25.4, 27.0 min; t_R (minor)=36.1 min; $[\alpha]_D^{25}$ +18.42 (*c* 1.33, $CHCl_3$).

*4.2.16. (R)-2-(1-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-5-(4-methylphenyl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**7h**).* Yellow oil (25.7 mg, 69%): ν_{max} (liquid film) 2941, 2870, 1720, 1645, 1539, 1448, 1383, 1323, 1309, 1292, 1155; δ_H (400 MHz; $CDCl_3$) 7.96–7.83 (2H, m), 7.74–7.37 (3H, m), 7.22–7.16 (5H, m), 6.50 (1H, ddd, *J*=6.1, 2.7, 1.3 Hz), 4.60–4.49 (3H, m), 3.81–3.70 (1H, m), 3.49–3.35 (2H, m), 3.35–3.27 (1H, m), 3.15–3.00 (2H, m), 2.72–2.57 (1H, m), 2.37 (3H, s), 1.80–1.26 (6H, m); δ_C (100 MHz; $CDCl_3$) 186.4, 146.5, 140.2, 139.5, 139.0, 138.7, 136.7, 134.6, 128.8 (2CH), 128.6 (2CH), 129.6 (2CH), 126.2 (2CH), 118.4, 98.8, 64.9, 62.7, 61.8, 30.9, 30.8, 27.8, 25.3, 21.2, 19.3; EIHRMS: calcd for $C_{27}H_{30}O_5S$ (M+Na): 489.1712; found: 489.1706 (M+Na). ee: determined by HPLC: CHIRALPAK AD-H column; *n*-hexane/isopropyl alcohol [70/30 (v/v)]; flow rate: 1.0 mL/min; λ=420 nm; t_R (minor) 13.6, 15.6 min; t_R (major)=18.7, 20.8 min; $[\alpha]_D^{25}$ +44.70 (*c* 0.97, $CHCl_3$).

*4.2.17. (R)-2-(6-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-5-(4-bromophenyl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**7i**).* Yellow oil (25.0 mg, 59%): ν_{max} (liquid film) 2947, 2870, 1718, 1647, 1544, 1448, 1383, 1323, 1309, 1290, 1155; δ_H (200 MHz; $CDCl_3$) 7.98–7.85 (2H, m), 7.75–7.33 (3H, m), 7.27–7.16 (5H, m), 6.60–6.42 (1H, m), 4.67–4.34 (3H, m), 3.86–3.67 (1H, m), 3.57–3.38 (2H, m), 3.35–3.23 (1H, m), 3.19–3.03 (2H, m), 2.78–2.58 (1H, m), 1.84–1.29 (6H, m); δ_C (50 MHz; $CDCl_3$) 186.7, 144.7, 139.9, 139.5, 139.0, 135.0, 134.4, 129.4 (2CH), 128.7 (2CH), 127.8 (2CH), 127.6 (2CH), 123.4, 119.9, 98.6, 65.2, 63.1, 62.2, 27.9, 31.1, 30.6, 25.6, 19.7; EIHRMS: calcd for $C_{26}H_{27}BrO_5S$ (M+Na): 553.0660; found: 553.0655 (M+Na). ee: determined by HPLC: CHIRALPAK AD-H column; *n*-hexane/isopropyl alcohol [80/20 (v/v)]; flow rate: 1.0 mL/min; λ=350 nm; t_R (major) 30.3, 31.8 min; t_R (minor)=34.6 min; $[\alpha]_D^{25}$ +46.80 (*c* 1.02, $CHCl_3$).

*4.2.18. (R)-2-(6-((Tetrahydro-2H-pyran-2-yl)oxy)methyl)-5-(3-bromophenyl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**7j**).* Yellow oil (34.3 mg, 81%): ν_{max} (liquid film) 2943, 2870, 1717, 1651, 1547, 1448, 1408, 1323, 1309, 1290, 1155; δ_H (200 MHz; $CDCl_3$) 7.91 (2H, d, *J*=7.8 Hz), 7.74–7.39 (3H, m), 7.33–7.13 (5H, m), 6.50 (1H, dd, *J*=6.0, 2.6 Hz), 4.64–4.39 (3H, m), 3.83–3.65 (1H, m), 3.63–3.26 (3H, m), 3.23–2.94 (2H, m), 2.78–2.55 (1H, m), 1.88–1.34 (6H, m); δ_C (50 MHz; $CDCl_3$) 186.8, 144.7, 141.9, 141.7, 139.7, 138.9, 134.4 (2CH), 132.0, 130.4, 129.4 (2CH), 128.7 (2CH), 124.7, 123.1, 120.6, 98.7, 65.1, 63.0, 62.2, 31.2, 30.8, 28.2, 25.6, 19.7; EIHRMS: calcd for $C_{26}H_{27}BrO_5S$ (M+Na): 553.0660; found: 553.0655 (M+Na). ee: determined by HPLC: CHIRALPAK AD-H column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=350 nm; t_R (major)=23.6 min; t_R (minor)=26.9 min; $[\alpha]_D^{25}$ +30.09 (*c* 1.29, $CHCl_3$).

4.3. Synthesis of 1-((1*S*,4*S*,7*R*)-7-((methoxymethoxy)methyl)-4-methyl-2,3-dioxabicyclo[2.2.2]oct-5-en-1-yl)-2-(phenylsulfonyl)ethan-1-one (8)

Compound **5a** (22 mg, 0.06 mmol) and Rose Bengal (15 mg, 0.015 mmol) were dissolved in 1 ml of MeOH and left to stir under O_2 atmosphere and solar light for 4 h. After the solvent was evaporated in vacuo, flash chromatography (*n*-hexane/EtOAc, 6:4) afforded **8** as a yellow oil (7 mg, 33%). ν_{max} (liquid film) 2957, 2929, 2873, 1728, 1448, 1323, 1311, 1290, 1149; δ_H (200 MHz; $CDCl_3$) 8.01 (2H, d, *J*=8.2 Hz), 7.75–7.52 (3H, m), 6.80 (1H, d, *J*=8.5 Hz), 6.46 (1H, d, *J*=8.5 Hz), 4.74–4.36 (2H, m), 4.22 (2H, s), 3.45–3.26 (2H, m), 3.19 (3H, s), 3.18–3.06 (1H, m), 2.41–2.15 (2H, m), 1.48 (3H, s); δ_C (50 MHz; $CDCl_3$) 191.3, 139.9, 137.4, 134.2, 129.3 (2CH), 129.0 (2CH), 128.0, 96.5, 83.6, 76.3, 68.9, 62.4, 55.8, 39.0, 33.1, 21.1; EIHRMS: calcd for $C_{18}H_{22}O_7S$ (M+Na): 405.0984; found: 405.0978 (M+Na). $[\alpha]_D^{25}$ +8.15 (*c* 0.92, $CHCl_3$).

4.4. Synthesis of 5-((6*S*)-4-methyl-6-(((tetrahydro-2*H*-pyran-2-yl)oxy)methyl)cyclohexa-1,3-dien-1-yl)-5-oxo-4-(phenylsulfonyl)pentanal (9)

A mixture of compound **6a** (26 mg, 0.067 mmol) and potassium carbonate (74 mg, 0.536 mmol) was suspended in THF (0.7 ml) under an Argon atmosphere. The suspension was stirred at room temperature for 10 min, and acrolein (9 μL, 0.133 mmol) was then added. The reaction mixture was stirred for 17 h and then filtered through Celite®, which was washed with ethyl acetate. The combined organic layers were washed with water, dried over Na_2SO_4, filtered and all the volatiles evaporated. Flash chromatography (*n*-hexane/EtOAc, 7:3) afforded **9** as a yellow oil (15 mg, 48%). ν_{max} (liquid film) 2941, 2870, 1722, 1651, 1637, 1566, 1446, 1386, 1321, 1309, 1288, 1149; δ_H (200 MHz; $CDCl_3$) 9.68 (1H, s), 7.91–7.29 (5H, m), 6.97 (1H, dd, *J*=11.7, 5.8 Hz), 5.99–5.79 (1H, m), 4.93 (1H, dd, *J*=9.3Hz, 4.8 Hz), 4.61–4.40 (1H, m), 3.97–3.62 (1H, m), 3.62–3.24 (2H, m), 3.24–2.89 (2H, m), 2.75–2.10 (3H, m), 1.92 (3H, s), 1.77–1.39 (9H, m); δ_C (50 MHz; $CDCl_3$) 200.5, 190.3, 148.8, 140.0, 136.9, 133.9, 133.8, 129.9 (2CH), 129.1 (2CH), 119.2, 98.7, 67.0, 62.6, 62.4, 40.6, 31.1, 30.9, 30.7, 25.7 ($2CH_2$), 24.4, 19.7; EIHRMS: calcd for $C_{24}H_{30}O_6S$ (M+Na+MeOH): 501.1923; found: 501.1917 (M+Na+MeOH). $[\alpha]_D^{25}$ −2.34 (*c* 1.45, $CHCl_3$).

4.5. General procedure for the deprotection with pTsOH: synthesis of compounds 10, 13g–j

Tetrahydropyranyl derivative (1 mmol) and *p*-toluenesulfonic acid monohydrate (0.5 mmol) were dissolved in 10 ml of a 1:1

mixture of THF/H_2O, and the whole mixture was stirred until no starting material was observed (typically 3–7 days). The reaction was quenched with H_2O, extracted with EtOAc and the combined organics were washed with $NaHCO_3$ (5%), H_2O and brine, dried (Na_2SO_4), filtered and concentrated in vacuo to afford the desired product.

*4.5.1. (S)-1-(6-(Hydroxymethyl)-4-(4-methyl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**10**).* Pale yellow solid (293.8 mg, 96%): mp 116–118 °C; ν_{max} (liquid film) 3446, 2932, 2872, 1718, 1635, 1566, 1446, 1321, 1309, 1288, 1152; δ_H (200 MHz; $CDCl_3$) 7.95–7.82 (2H, m), 7.76–7.49 (3H, m), 7.05 (1H, d, *J*=5.8 Hz), 6.01–5.81 (1H, m), 4.55 (1H, d, *J*=13.5 Hz), 4.38 (1H, d, *J*=13.5 Hz), 3.51–3.27 (2H, m), 3.15–2.90 (1H, m), 2.46–2.37 (2H, m), 1.93 (3H, s); δ_C (50 MHz; $CDCl_3$) 187.6, 149.0, 141.0, 139.0, 134.4, 133.4, 129.4 (2CH), 128.7 (2CH), 119.1, 62.7, 62.6, 33.5, 31.2, 24.3; EIHRMS: calcd for $C_{16}H_{18}O_4S$ (M+Na): 329.0823; found: 329.0818 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=325 nm; t_R (minor)=28.5 min; t_R (major)=53.6 min; $[\alpha]_D^{25}$ −27.40 (*c* 0.16, $CHCl_3$).

*4.5.2. (R)-2-(6-(Hydroxymethyl)-5-(phenyl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**13g**).* Yellow oil (364.3 mg, 99%): ν_{max} (liquid film) 3487, 3061, 2931, 2872, 1718, 1645, 1544, 1446, 1314, 1309, 1153; δ_H (200 MHz; $CDCl_3$) 7.92 (2H, d, *J*=7.0 Hz), 7.74–7.48 (3H, m), 7.47–7.32 (5H, m), 7.24 (1H, d, *J*=6.2 Hz), 6.53 (1H, dd, *J*=6.2, 2.7), 4.52 (1H, d, *J*=13.5 Hz), 4.28–4.10 (1H, m), 3.61–3.32 (2H, m), 3.29–3.09 (1H, m), 3.04 (1H, d, *J*=1.6 Hz), 2.76 (1H, dd, *J*=17.9, 8.6 Hz); δ_C (50 MHz; $CDCl_3$) 187.5, 146.4, 140.3, 139.2, 134.8 (2C), 134.2, 129.2 (2CH), 128.7 (2CH), 128.5, 125.9 (4CH), 119.2, 62.5, 62.7, 33.6, 28.1; EIHRMS: calcd for $C_{21}H_{20}O_4S$ (M+H): 369.1161; found: 369.1155 (M+H). ee: determined by HPLC: CHIRALPAK AD-H column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=430 nm; t_R (minor)=35.9 min; t_R (major)=39.3 min; $[\alpha]_D^{25}$ +13.62 (*c* 0.94, $CHCl_3$).

*4.5.3. (R)-2-(6-(Hydroxymethyl)-5-(4-methylphenyl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**13h**).* Yellow oil (378.2 mg, 99%): ν_{max} (liquid film) 3442, 2923, 2873, 1714, 1643, 1514, 1446, 1354, 1309, 1153; δ_H (200 MHz; $CDCl_3$) 7.96–7.81 (2H, m), 7.73–7.41 (3H, m), 7.28–7.13 (5H, m), 6.50 (1H, dd, *J*=6.2, 2.6), 4.60 (1H, d, *J*=13.5 Hz), 4.43 (1H, d, *J*=13.5 Hz), 3.57–3.30 (2H, m), 3.26–3.08 (1H, m), 3.02 (1H, d, *J*=4.7 Hz), 2.73 (1H, dd, *J*=20.5, 8.6 Hz), 2.37 (3H, s); δ_C (50 MHz; $CDCl_3$) 187.6, 146.7, 140.8, 139.8, 138.9 (2C), 136.4, 134.4, 130.0 (2CH), 128.9 (2CH), 128.8 (2CH), 126.1 (2CH), 118.5, 62.9, 62.8, 33.8, 28.3, 21.5; EIHRMS: calcd for $C_{22}H_{22}O_4S$ (M+Na): 405.1136; found: 405.1141 (M+Na).

*4.5.4. (R)-2-(6-(Hydroxymethyl)-5-(4-bromophenyl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**13i**).* Yellow oil (441.5 mg, 99%): ν_{max} (liquid film) 3477, 2941, 2872, 1718, 1643, 1543, 1489, 1446, 1312, 1309, 1153; δ_H (200 MHz; $CDCl_3$) 7.91 (2H, d, *J*=8.3 Hz), 7.73–7.48 (3H, m), 7.47–7.36 (4H, m), 7.23 (1H, d, *J*=6.1 Hz), 6.52 (1H, dd, *J*=6.2, 2.7 Hz), 4.60 (1H, d, *J*=13.4 Hz), 4.43 (1H, d, *J*=13.5 Hz), 3.62–3.26 (1H, m), 3.26–3.05 (2H, m), 3.00 (1H, d, *J*=1.7 Hz), 2.87–2.64 (1H, m); δ_C (50 MHz; $CDCl_3$) 187.4, 144.9, 139.9, 138.7, 138.0, 135.1, 134.3, 129.3 (2CH), 128.5 (2CH), 127.5 (2CH), 127.4 (2CH), 123.4, 119.5, 62.7, 62.3, 33.5, 27.8; EIHRMS: calcd for $C_{21}H_{19}O_4SBr$ (M+Na): 469.0085; found: 469.0079 (M+Na). ee: determined by HPLC: CHIRALPAK AD-H column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=350 nm; t_R (major)=30.6 min; t_R (minor)=38.8 min; $[\alpha]_D^{25}$ +5.88 (*c* 1.75, $CHCl_3$).

*4.5.5. (R)-2-(6-(Hydroxymethyl)-5-(4-bromophenyl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**13j**).* Yellow oil (437.1 mg, 98%): ν_{max} (liquid film) 3502, 3062, 2929, 2872, 1718, 1645, 1545, 1473, 1446, 1312, 1309, 1153; δ_H (200 MHz; $CDCl_3$) 8.00–7.82 (2H, m), 7.77–7.41 (6H, m), 7.30 (1H, s), 7.25–7.19 (1H, m), 6.52 (1H, dd, *J*=6.2, 2.7 Hz), 4.61 (1H, d, *J*=13.5 Hz), 4.43 (1H, d, *J*=13.5 Hz), 3.42 (1H, d, *J*=12.3 Hz), 3.29–3.11 (2H, m), 2.99 (1H, d, *J*=1.7 Hz), 2.86–2.60 (1H, m); δ_C (50 MHz; $CDCl_3$) 187.5, 144.5, 141.3, 139.6, 138.7, 138.7, 134.3, 132.1, 131.9, 130.2, 129.3 (2CH), 128.9 (2CH), 124.5, 122.9, 120.1, 62.7, 62.3, 33.5, 27.9; EIHRMS: calcd for $C_{21}H_{19}O_4SBr$ (M+Na): 469.0085; found: 469.0079 (M+Na). ee: determined by HPLC: CHIRALPAK AD-H column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=360 nm; t_R (minor)=31.2 min; t_R (major)=35.1 min; $[\alpha]_D^{25}$ +23.29 (*c* 0.97, $CHCl_3$).

4.6. General procedure for mesylation reaction: synthesis of compounds 11 and 14

Hydroxyl derivative (1 mmol), 4-(dimethylamino)pyridine (0.2 mmol) and triethylamine (1.3 mmol) were dissolved in 10 ml of DCM, and then methanesulfonyl chloride (1.2 mmol) was added. The mixture was stirred at room temperature for 40 min. The reaction was quenched with H_2O and extracted with ethyl acetate after 10 min. The organic layers were washed with HCl (2 M), $NaHCO_3$ (5%), H_2O and brine, dried (Na_2SO_4), filtered and concentrated in vacuo to afford the desired product.

*4.6.1. (S)-1-(6-(Methanesulfonyl)oxymethyl)-4-(4-methyl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**11**).* Yellow oil (380.2 mg, 99%): ν_{max} (liquid film) 2939, 1718, 1651, 1637, 1568, 1446, 1323, 1309, 1292, 1153; δ_H (200 MHz; $CDCl_3$) 7.95–7.84 (2H, m), 7.72–7.50 (3H, m), 7.10 (1H, d, *J*=5.9 Hz), 5.94 (1H, d, *J*=5.9 Hz), 4.51 (1H, d, *J*=13.5 Hz), 4.38 (1H, d, *J*=13.5 Hz), 3.91 (1H, dd, *J*=10.7, 8.3 Hz), 3.79 (1H, dd, *J*=10.7, 5.0 Hz), 3.31–3.16 (1H, m), 2.95 (3H, s), 2.50–2.35 (2H, m), 1.94 (3H, s); δ_C (50 MHz; $CDCl_3$) 186.6, 148.9, 142.2, 139.0, 134.5, 130.7, 129.5 (2CH), 128.6 (2CH), 119.4, 67.8, 62.7, 37.5, 30.8, 30.4, 24.3; EIHRMS: calcd for $C_{17}H_{20}O_6S_2$ (M+Na): 407.0599; found: 407.0593 (M+Na). ee: determined by HPLC: CHIRALPAK IC column; *n*-hexane/isopropyl alcohol [60/40 (v/v)]; flow rate: 1.0 mL/min; λ=350 nm; t_R (minor)=69.0 min; t_R (major)=79.0 min; $[\alpha]_D^{25}$ −9.00 (*c* 1.1, $CHCl_3$).

*4.6.2. (R)-1-(6-(Methanesulfonyl)oxymethyl)-4-(4-phenyl)cyclohexa-1,3-dien-1-yl)-2-(phenylsulfonyl)ethan-1-one (**14**).* Yellow oil (223.0 mg, 50%): ν_{max} (liquid film) 2963, 2932, 1718, 1650, 1541, 1446, 1354, 1323, 1309, 1292, 1174, 1153; δ_H (200 MHz; $CDCl_3$) 7.92 (2H, d, *J*=7.9 Hz), 7.76–7.49 (3H, m), 7.49–7.37 (5H, m), 7.34 (1H, d, *J*=6.2 Hz), 6.58 (1H, dd, *J*=6.3, 2.7 Hz), 4.58 (1H, d, *J*=13.4 Hz), 4.44 (1H, d, *J*=13.4 Hz), 4.22 (1H, d, *J*=5.7 Hz), 3.96 (1H, t, *J*=6.7 Hz), 3.49–3.38 (1H, m), 2.93 (3H, s), 2.78 (2H, ddd, *J*=11.3, 9.0, 2.8 Hz); δ_C (50 MHz; $CDCl_3$) 186.3, 146.4, 141.5, 138.6, 134.4, 132.1, 130.9, 129.6, 129.4 (2CH), 128.5 (4CH), 126.1 (2CH), 119.2, 67.6, 62.7, 37.2, 30.4, 27.8; EIHRMS: calcd for $C_{22}H_{22}O_6S_2$ (M+Na): 469.0755; found: 469.0750 (M+Na). ee: determined by HPLC: CHIRALPAK AD-H column; *n*-hexane/isopropyl alcohol [70/30 (v/v)]; flow rate: 1.0 mL/min; λ=325 nm; t_R (minor)=17.9 min; t_R (major)=23.2 min; $[\alpha]_D^{25}$ +7.22 (*c* 0.36, $CHCl_3$).

4.7. Synthesis of (*Z*)-5-methyl-1-((phenylsulfonyl)methylene)-1,3,3a,4-tetrahydroisobenzofuran (12)

Compound **11** (162 mg, 0.38 mmol) was dissolved in 4 ml of DCM, and then 1,8-diazabicyclo[5.4.0]undec-7-ene (85 μl, 0.57 mmol) was added. The mixture was stirred at room temperature for 35 min. The reaction was quenched with H_2O and extracted with ethyl acetate after 10 min. The organic layers were washed with H_2O, dried (Na_2SO_4), filtered and concentrated in vacuo. Flash chromatography

(*n*-hexane/EtOAc, 6:4) afforded **12** as a yellow oil (56.1 mg, 50%). ν_{max} (liquid film) 3066, 2929, 2900, 1610, 1579, 1446, 1304, 1140; δ_H (200 MHz; benzene-d_6) 8.32–8.21 (2H, m), 7.14–6.97 (3H, m), 5.92 (1H, s), 5.84–5.73 (1H, m), 5.43–5.35 (1H, m), 4.01 (1H, t, J=8.6 Hz), 3.19–3.02 (1H, m), 2.26–2.01 (1H, m), 1.37 (3H, s), 1.32–1.08 (2H, m); δ_C (50 MHz; benzene-d_6) 162.1, 145.4, 140.2, 131.9, 130.4, 128.6 (2CH), 127.9 (2CH), 122.8, 120.2, 97.0, 77.9, 35.3, 31.2, 22.9; EIHRMS: calcd for $C_{16}H_{16}O_3S$ (M+H): 289.0898; found: 289.0893 (M+H). ee: determined by HPLC: CHIRALPAK AD-H column; *n*-hexane/isopropyl alcohol [70/30 (v/v)]; flow rate: 1.0 mL/min; λ=350 nm; t_R (minor)= 16.9 min; t_R (major)=19.4 min; $[\alpha]_D^{25}$ −86.50 (*c* 1.57, MeOH).

4.8. Synthesis of compounds 16, 17 (and 18)

Procedure a: To a solution of 1 mmol of starting material (**10**, 45.9 mg, 0.15 mmol or **12**, 46.1 mg, 0.16 mmol) in $CDCl_3$ (10 ml) was added *m*-CPBA (70% pure, 1 equiv) and the reaction was left to stir for the specified time (15 h for compound **10** and 6 h for compound **12**). Flash chromatography (EtOAc/MeOH, 95:5) afforded the corresponding product (1/1 mixture of **16**/**17**, 18.4 mg, 38% starting from **10**; only **16**, 31.9 mg, 62% starting from **12**).

Procedure b: A solution of **12** (38.4 mg, 0.13 mmol) in $CHCl_3$ (1 ml) was heated at 37 °C under normal air atmosphere for 72 h. Flash chromatography (EtOAc/MeOH, 95:5) afforded **16** (22.1 mg, 53%).

*4.8.1. 1-((1S,4R,5R)-4-Hydroxy-5-methyl-6-oxabicyclo[3.2.1]oct-2-en-2-yl)-2-(phenylsulfonyl)ethan-1-one (**16**).* Yellow oil: ν_{max} (liquid film) 3471, 2970, 2932, 2873, 1712, 1666, 1625, 1448, 1379, 1321, 1309, 1259, 1150; δ_H (600 MHz; $CDCl_3$) 7.95–7.80 (2H, m), 7.75–7.47 (3H, m), 6.72 (1H, d, J=3.9 Hz), 4.49 (2H, s), 3.91–3.85 (1H, m), 3.85–3.79 (1H, m), 3.48–3.38 (1H, m), 3.34 (1H, d, J=7.5 Hz), 1.63 (1H, d, J=8.0 Hz), 1.56 (1H, dd, J=8.0 Hz, 4.0 Hz), 1.45 (3H, s); δ_C (150 MHz; $CDCl_3$) 187.3, 144.2, 141.9, 138.7, 134.4, 129.4 (2CH), 128.5 (2CH), 81.4, 73.7, 72.4, 62.4, 35.7, 35.3, 21.8; EIHRMS: calcd for $C_{16}H_{18}O_5S$ (M+Na): 345.0773; found: 345.0767 (M+Na). $[\alpha]_D^{25}$ −13.05 (*c* 0.95, $CHCl_3$).

*4.8.2. 1-((4S,7S)-7-Hydroxy-7-methyl-2-oxabicyclo[2.2.2]oct-5-en-5-yl)-2-(phenylsulfonyl)ethan-1-one (**17**).* Yellow oil: ν_{max} (liquid film) 3464, 2929, 1710, 1664, 1626, 1448, 1321, 1309, 1153; δ_H (600 MHz; $CDCl_3$) 7.98–7.80 (2H, m), 7.74–7.50 (3H, m), 7.32 (1H, d, J=4.6 Hz), 4.59 (1H, d, J=13.6 Hz), 4.38 (1H, d, J=13.6 Hz), 3.59–3.30 (3H, m), 2.21 (1H, d, J=15.4 Hz), 2.09–1.83 (2H, m), 1.51 (3H, s); δ_C (150 MHz; $CDCl_3$) 187.6, 141.9, 141.1, 138.5, 134.4, 129.3 (2CH), 128.5 (2CH), 82.0, 66.3, 63.0, 53.8, 35.2, 30.9, 21.8; EIHRMS: calcd for $C_{16}H_{18}O_5S$ (M+Na): 345.0773; found: 345.0771 (M+Na). $[\alpha]_D^{25}$ −99.95 (*c* 0.19, $CHCl_3$).

*4.8.3. (1aS,2aS,6aR,Z)-1a-Methyl-5-((phenylsulfonyl)methylene)-1a,2,2a,3,5,6a-hexahydrooxireno[2,3-f]isobenzofuran (**18**).* Yellow oil: ν_{max} (liquid film) 2961, 2928, 1614, 1446, 1304, 1142; δ_H (600 MHz; benzene-d_6) 8.22 (2H, dd, J=7.8, 1.8 Hz), 7.06–6.92 (3H, m), 5.84 (1H, s), 5.51 (1H, t, J=3.7 Hz), 3.71 (1H, t, J=8.7 Hz), 3.00–2.80 (1H, m), 2.47 (1H, d, J=3.7 Hz), 2.19–2.03 (1H, m), 1.18 (1H, dd, J=13.9, 7.5 Hz), 0.91 (3H, s), 0.14 (1H, dd, J=13.9, 11.5 Hz); δ_C (150 MHz; benzene-d_6) 161.5, 144.7, 137.8, 131.9, 128.4 (2CH), 127.5 (2CH), 122.7, 98.2, 76.6, 59.9, 53.1, 34.6, 29.0, 20.5; EIHRMS: calcd for $C_{16}H_{16}O_4S$ (M+H): 305.0848; found: 305.0843 (M+H). $[\alpha]_D^{25}$ +101.61 (*c* 0.31, $CHCl_3$).

4.9. Synthesis of (2*R*,4*R*)-5′-methyl-2,4-bis(phenylsulfonyl)-3′*H*-spiro[cyclobutane-1,1′-isobenzofuran] (19)

Compound **12** (56 mg, 0.19 mmol) and phenyl vinyl sulfone (66 mg, 0.39 mmol) were dissolved in 1 ml of benzene-d_6. The mixture was stirred at reflux for 2.5 h. Flash chromatography (*n*-Hexane/EtOAc, 6:4) afforded **19** as a yellow oil (36.2 mg, 42%). ν_{max} (liquid film) 3062, 2970, 2926, 1714, 1381, 1146, 1319, 1148; δ_H (600 MHz; benzene-d_6) 8.01–7.83 (4H, m), 7.08–6.70 (9H, m), 5.26 (1H, dd, J=9.8, 4.3 Hz), 5.04 (1H, d, J=15.0 Hz, 4.70 (1H, d, J=4.8 Hz), 3.90 (1H, d, J=15.0 Hz), 2.04 (3H, s), 1.90–1.75 (2H, m); δ_C (150 MHz; benzene-d_6) 145.3, 143.7, 142.0 (2C), 138.0, 129.1 (2CH), 128.7 (2CH), 128.2 (2CH), 127.9 (2CH), 127.8 (2CH), 121.4, 119.9, 119.4, 85.5, 78.9, 62.7, 56.2, 33.2, 19.6; EIHRMS: calcd for $C_{24}H_{22}O_5S_2$ (M+NH_4): 472.1247; found: 472.1247 (M+NH_4). $[\alpha]_D^{25}$ −6.67 (*c* 0.81, MeOH).

Acknowledgements

The authors gratefully acknowledge the help of A. Lithgow of Universidad de Salamanca and J. Rodilla of Universidade da Beira Interior for NMRs and C. Raposo (MS) of Universidad de Salamanca. FSE and Junta de Castilla y León (GR 178, BIO/SA74/13) are acknowledged for financial support. J.P. is grateful to the Ministry of Economy and Competitiveness for his FPU fellowship.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.04.076.

References and notes

1. (a) Audran, S.; Brérmond, P.; Feuerstein, M.; Marque, S. R. A.; Santelli, M. *Tetrahedron* **2013**, *69*, 8325; (b) Lepage, O.; Stone, C.; Deslongchamps, P. *Org. Lett.* **2002**, *4*, 1091.
2. (a) Patai, S.; Rappoport, Z.; Stirling, C. *The Chemistry of Sulphones and Sulfoxides*; John Wiley and Sons: Chichester, UK, 1988; (b) Simpkins, N. S. *Sulphones in Organic Synthesis*; Pergamon: Oxford, UK, 1993; (c) Paquette, L. A. *Synlett* **2001**, 1; (d) Nájera, C.; Sansano, J. M. *Recent Res. Dev. Org. Chem.* **1998**, *2*, 637; (e) Chinchilla, R.; Nájera, C. *Recent Res. Dev. Org. Chem.* **1997**, *1*, 437.
3. (a) Ravindar, K.; Caron, P.-Y.; Deslongchamps, P. *Org. Lett.* **2013**, *15*, 6270; (b) Barroso, S.; Blay, G.; Al-Midfa, L.; Muñoz, M. C.; Pedro, J. R. *J. Org. Chem.* **2008**, *73*, 6389; (c) Pei, W.; Wang, Y.-G.; Wang, Y.-J.; Sun, L. *Synthesis* **2008**, 3383.
4. Peña, J.; Antón, A. B.; Moro, R. F.; Marcos, I. S.; Garrido, N. M.; Díez, D. *Tetrahedron* **2011**, *67*, 8331.
5. Peña, J.; Moro, R. F.; Basabe, P.; Marcos, I. S.; Díez, D. *RSC Adv.* **2012**, *2*, 8041.
6. (a) Feldgitscher, C.; Peterlik, H.; Puchberger, M.; Kickelbick, G. *Chem. Mater.* **2009**, *21*, 695; (b) Arboré, A.; Dujardin, G.; Maignan, C. *Eur. J. Org. Chem.* **2003**, 4118.
7. (a) Dalko, P. I. *Enantioselective Organocatalysis, Reactions and Experimental Procedures*; Wiley-VCH: Weinheim, Germany, 2007; (b) Giacalone, F.; Gruttadauria, M.; Agrigento, P.; Noto, R. *Chem. Soc. Rev.* **2012**, *41*, 2406; (c) Bertelsen, S.; Marigo, M.; Brandes, S.; Dinér, P.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2006**, *128*, 12973.
8. (a) Serebryakov, E. P.; Shcherbakov, M. A.; Gamalevich, G. D.; Struchkova, M. I. *Russ. Chem. Bull. Int. Ed.* **2003**, *52*, 734; (b) Serebryakov, E. P.; Nigmatov, A. G.; Shcherbakov, M. A.; Struchkova, M. I. *Russ. Chem. Bull. Int. Ed.* **1998**, *47*, 82; (c) Nigmatov, A. G.; Serebryakov, E. P. *Russ. Chem. Bull. Int. Ed.* **1996**, *45*, 623; (d) Nigmatov, A. G.; Kornilova, I. N.; Serebryakov, E. P. *Russ. Chem. Bull. Int. Ed.* **1996**, *45*, 144; (e) Nigmatov, A. G.; Serebryakov, E. P. *Russ. Chem. Bull. Int. Ed.* **1993**, *42*, 213.
9. Bench, B. J.; Liu, C.; Evett, C. R.; Watanabe, C. M. H. *J. Org. Chem.* **2006**, *71*, 9458.
10. (a) Marqués-López, E.; Herrera, R. P.; Marks, T.; Jacobs, W. C.; Konning, D.; de Figueiredo, R. M.; Christmann, M. *Org. Lett.* **2009**, *11*, 4116; (b) de Figueiredo, R. M.; Fröhlich, R.; Christmann, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 1450 see too; (c) Yamada, S.-I.; Shibasaki, M.; Terashima, S. *Tetrahedron Lett.* **1973**, *5*, 381.
11. Haindl, M. H.; Schmid, M. B.; Zeitler, K.; Gschwind; Ruth, M. *RSC Adv.* **2012**, *2*, 5941.
12. (a) Watanabe, C. M. H.; Bench, B. J. U.S. Patent 2,007,232,813, 2007; Watanabe, C. M. H.; Bench, B. J. *Chem. Abstr.* **2007**, *147*, 427217. (b) Hong, B.-C.; Wu, M.-F.; Tseng, H.-C.; Huang, G.-F.; Su, C.-F.; Liao, J.-H. *J. Org. Chem.* **2007**, *72*, 8459; (c) Ye, L.-W.; Wang, S.-B.; Wang, Q.-G.; Sun, X.-L.; Tang, Y.; Zhou, Y.-G. *Chem. Commun.* **2009**, 3092; (d) Moreno-Clavijo, E.; Moreno-Vargas, A. J.; Carmona, A. T.; Robina, I. *Org. Biomol. Chem.* **2013**, *11*, 7016; (e) See complete volume*Chem. Rev.* **2005**, *105*, 3433; (f) Alizadeh, A.; Rezvanian, A.; Mokhtari, J. *Synthesis* **2011**, 3491.
13. (a) Gu, Q.; You, S.-L. *Chem. Sci.* **2011**, *2*, 1519; (b) Rueping, M.; Kuenkel, A.; Atodiresei, I. *Chem. Soc. Rev.* **2011**, *40*, 4539; (c) Díez, D.; Núñez, M. G.; Benéitez, A.; Moro, R. F.; Marcos, I. S.; Basabe, P.; Broughton, H. B.; Urones, J. G. *Synlett* **2009**, 390.
14. Ramachary, D. B.; Reddy, Y. V. *Eur. J. Org. Chem.* **2012**, 865.

15. Crystal data for **10**: CCDC 975368. See http://www.ccdc.cam.ac.uk/Community/Requestastructure/Pages/DataRequest.aspx for crystallographic data in cif or other electronic format.
16. (a) Williams, I.; Reeves, K.; Kariuki, B. M.; Cox, L. R. *Org. Biomol. Chem.* **2007**, *5*, 3325; (b) Ley, S. V.; Armstrong, A.; Díez-Martín, D.; Ford, M. J.; Grice, P.; Knight, J. G.; Kolb, H. C.; Madin, A.; Marby, C. A.; Mukherjee, S.; Shaw, A. N.; Slawin, A. M. Z.; Vile, S.; White, A. D.; Williams, D. J.; Woods, M. *J. Chem. Soc., Perkin Trans. 1* **1991**, 667; (c) Romanski, S.; Kraus, B.; Guttentag, M.; Schlundt, W.; Rücker, H.; Adler, A.; Neudörfl, J.-M.; Alberto, R.; Amslinger, S.; Schmalz, H.-G. *Dalton Trans.* **2012**, *41*, 13862.
17. Cordes, J.; Harms, K.; Koert, U. *Org. Lett.* **2010**, *12*, 3808.
18. Lorbach, V.; Franke, D.; Niegerb, M.; Müller, M. *Chem. Commun.* **2002**, 494.
19. Cuendet, M.; Pezzuto, J. M. *J. Nat. Prod.* **2004**, *67*, 269.
20. Hill, K. W.; Taunton-Rigby, J.; Carter, J. D.; Kropp, E.; Vagle, K.; Pieken, W.; McGee, D. P. C.; Husar, G. M.; Leuck, M.; Anziano, D. J.; Sebesta, D. P. *J. Org. Chem.* **2001**, *66*, 5352.
21. Basabe, P.; de Román, M.; Díez, D.; Marcos, I. S.; Bodero, O.; Blanco, A.; Molinedo, F.; Urones, J. G. *Synlett* **2008**, 1149.
22. Ishihara, K.; Ishibashi, H.; Yamamoto, H. *J. Am. Chem. Soc.* **2002**, *124*, 3647.
23. Xie, S.; Uesato, S.; Fujita, T.; Inouye, H. *J. Nat. Prod.* **1989**, *52*, 701.

Please cite this article in press as: Peña, J.; et al., Tetrahedron (2014), http://dx.doi.org/10.1016/j.tet.2014.04.076