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Asymmetric synthesis of 4-ethoxy-1-*p*-tolylsulfonyl-3,6-dioxabicyclo[3.1.0]hexan-2-ones

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ABSTRACT

Optically pure sulfinylfuranones undergo oxidation at sulfur followed by a totally stereoselective epoxidation at the electron deficient double bond by treatment with MCPBA at room temperature to afford, in good yields, enantiomerically pure 4-ethoxy-5-alkyl-1-*p*-tolylsulfonyl-3,6-dioxabicyclo[3.1.0]hexan-2-ones. These epoxyfuranones are obtained along with cyclopropanefuranones by reaction of 4-ethoxy-6-*p*-tolylsulfinylfuro[3,4-c]pyrazolin-6-ones with MPCBA. In both cases, the formation of the sulfonyl epoxylactones takes place by oxidation of the sulfonylfuran-2(5*H*)-one resulting from the starting materials. This reaction is completely stereoselective (controlled by the configuration of C-5 of furanone) and results from the nucleophilic attack of the peroxycarboxylate generated by interaction of the reagent with weak basic centres at the substrates.

1. Introduction

The α,β-epoxy-γ-lactone (3,6-dioxabicyclo[3.1.0]hexan-2-one) subunit is present in many natural products with biomedical interest (Fig. 1) such as diterpenoides *Lophotoxin*[1] briaranes (cytotoxicity against L1210 murine leukaemia and KB human epidermoid carcinoma cell in vitro),[2] *Bipinnatin* Q (significant cytotoxic activity)[3] or nortriterpenoids (propindilactone L shows anti-HBV activity in vitro).[4]

Simple 3,6-dioxabicyclo[3.1.0]hexan-2-ones have been used as intermediates in synthesis of *Epolactaene* and derivatives[5] and Cerulenin,[6] which exhibit antibiotic activity and are inductors of apoptosis in human cancer cell lines.

The epoxidation of non-activated furan-2(5*H*)-ones has been described as notoriously difficult,[7] and only the specific protocol developed by Tishler and co-workers[6] (NaOCl, pyridine) and other analogous,[8–10] work satisfactorily. Moreover, there are few protocols available for effecting the epoxidation of tri or tetrasubstituted alkenes bearing two electron-withdrawing groups.[11] Therefore 4-alkoxy-3,6-dioxabicyclo[3.1.0]hexan-2-ones are not easily obtained in good yields.[12] We have recently reported that epoxidation of sulfur-deactivated furanones could be accomplished with MCPBA in basic medium.[13] The nature and proportion of the employed base proved to be highly important, especially when starting from furanones, which could be opened by the base. The key for the success of these reactions derived from the nucleophilic character of the epoxidating reagent (perbenzoate anion, instead of the electrophilic attack of the MCPBA), and the strong deactivation of double bonds. In that reference we also reported that MCPBA without base was able to produce the epoxidation of 5-ethoxy-3-*p*-tolylsulfonylfuran-2(5*H*)-one, although such reactions were not investigated in detail. However, the negative influence of the basic reagents, able to interact with the furanone rings and other structural moieties, prompted us to consider the study of scope of MCPBA as reagent for the preparation of epoxyfuranones from

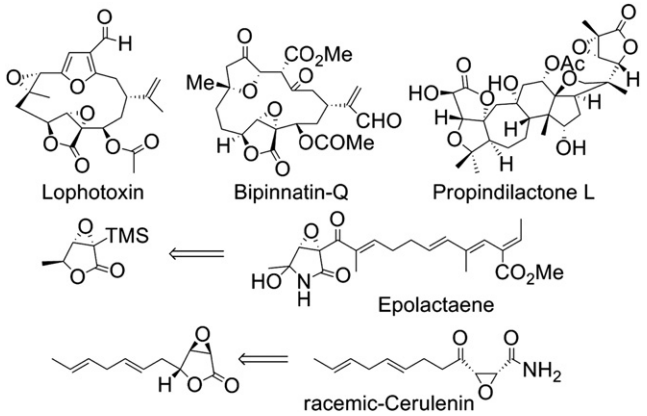

Figure 1. Natural products and synthesis intermediates with epoxyfuranone moiety.

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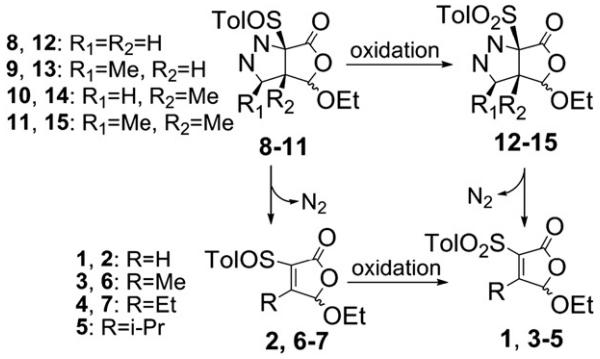
deactivated furanones. The fact that the number of reported processes involving the formation of epoxides by MCPBA oxidation of alkenes bearing two electron-withdrawing groups is rather scarce,[14–17] increased the interest of this research. In this paper we report our studies aiming at establishing the scope of the reactions of 3-sulfinyl and sulfonyl furan-2(5*H*)-ones with MCPBA in the synthesis of enantiomerically pure sulfonyl epoxyfuranones, as well as their competition with other processes affecting the extrusion reactions of furopyrazolines involved in the preparation of the starting products.

2. Results and discussion

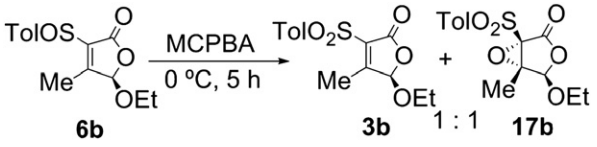
Both enantiomers of 5-ethoxy-3-*p*-tolylsulfonylfuran-2(5*H*)-ones (**1**, R=H in Scheme 1)[13] were obtained by oxidation of the corresponding sulfoxides (**2**). In order to prepare the optically pure sulfonylfuranones R≠H (**3**–**5** in Scheme 1), which will be used as the substrates for our MCPBA oxidation studies, we designed the two strategies shown in Scheme 1. The first route involves the oxidation of the sulfinyl derivatives **6**–**7**, obtained by thermal extrusion of nitrogen from compounds **8**–**11**. In the second one, the order of the steps is inverted and the oxidation of the sulfinyl compounds **8**–**11** into the sulfonyl ones **12**–**15** would be previous to the thermal extrusion of nitrogen.



Scheme 1. Strategies for preparation of 3-sulfonylfuran-2(5*H*)-ones.

Compounds (5*S*,*SS*)-**2a** and (5*R*,*SS*)-**2b**,[18] differ only in the configuration at stereogenic C-5 (Scheme 2). Their reactions with diazomethane were completely stereoselective affording cycloadducts **8a** and **8b**, respectively. They were easily transformed into **6a** and **6b** by thermal extrusion (Scheme 2). A similar procedure has been used for synthesizing 4-ethyl derivatives **7a** and **7b**. These compounds were obtained from pyrazolynes **9** (adducts of furanones **2a** and **2b** with diazoethane) or **10** (adducts of furanones **6a** and **6b** with diazomethane).[19] The best results were obtained from pyrazolines **9**. Compounds **5a** and **5b** were obtained from **11** by reaction with MCPBA.

Next we tried to obtain sulfonyl derivative **3b** by oxidation of sulfoxide **6b**[19a] with ≈2.5 equiv amounts of MCPBA at 0 °C for 5 h. Under these conditions a 1:1 mixture of sulfonyl epoxylactone **17b** and sulfonylfuranone **3b** was obtained (Scheme 3). Sulfinyl epoxy lactone was not detected, which suggests that oxidation of the sulfur function is much faster than epoxidation of the sulfinylated double bonds, thus generating the sulfonylfuranones, whose epoxidation must take place at a rate similar to that of the oxidation of the sulfinyl group. This result indicates that MCPBA, without any base, is able to epoxidize 3-sulfonylfuran-2(5*H*)-ones.

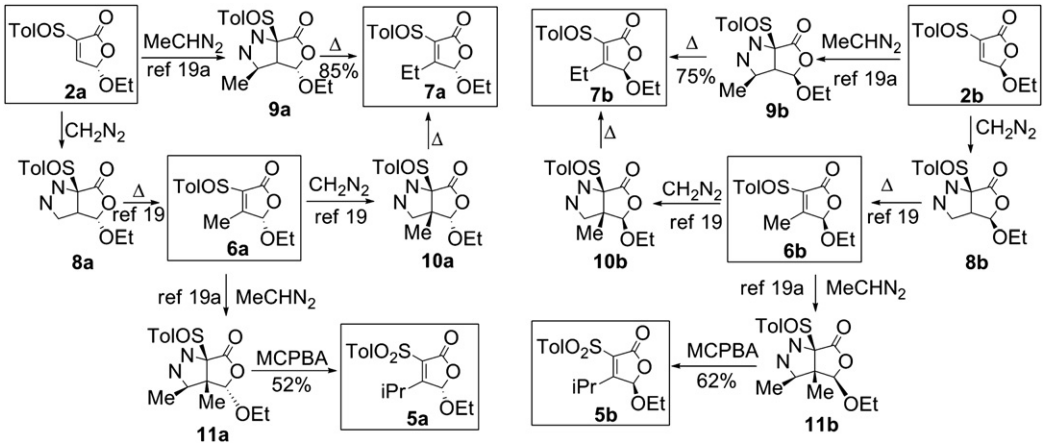


Scheme 3. Reaction of sulfinylfuranone **6b** with MCPBA after 5 h.

In order to develop a good synthetic procedure for preparing epoxysulfonylfuranones (our target molecules), we increased the reaction times. Under the conditions indicated in Table 1 the sulfonylated epoxyfuranones were obtained as the exclusive products from sulfinylfuranones **2**, **6**–**7** and sulfonylfuranones **5**.

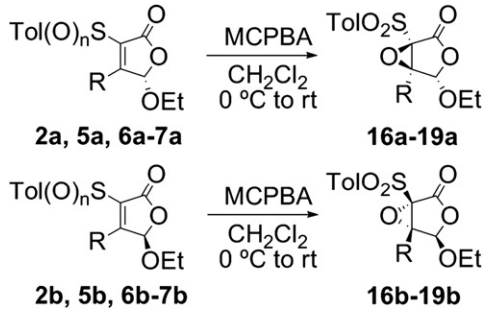
All the reactions were completely stereoselective only yielding the epoxylactones, which exhibit an anti-relationship between the oxirane ring and the OEt group (>98% ee). The yields for compounds **16**–**18** were very high whereas the isopropyl sulfone **5** did not react, presumably due to steric reasons, thus precluding the preparation of compounds **19** by this procedure. 5-Methoxyfuran-2(5*H*)-one[20] was recovered when treated with MCPBA under the conditions indicated in Table 1. Therefore the epoxidation of furanones with this oxidant reagent only evolved when the furanone bear an electron-withdrawing substituent at C-3.

We assume that the transformation of the sulfoxide into sulfonyl group is previous to the epoxidation at the double bond because epoxy sulfoxides were never detected in these reactions (see above). Accordingly, the stereoselectivity control must be exerted by the configuration at C-5 (the only stereogenic element at the intermediate sulfones **1**, **3**–**5**). The approach of the reagent to the



Scheme 2. Synthesis of 5-ethoxy-3-sulfonylfuran-2(5*H*)-ones.

Table 1
Reactions of furan-2(5*H*)-ones **2**, **5**, **6** and **7** with MCPBA (2.5 equiv)

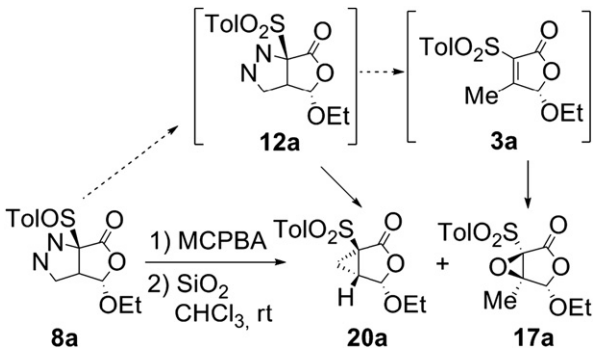


Entry	*n*	Furanone	R	Epoxide	Time (h)	Yield (%)
1	1	**2a**	H	**16a**	3	80
2	1	**2b**	H	**16b**	1.5	75
3	1	**6a**	Me	**17a**	8.5	89
4	1	**6b**	Me	**17b**	8.5	88
5	1	**7a**	Et	**18a**	2.5	86
6	1	**7b**	Et	**18b**	2.5	86
7	2	**5a**	*i*-Pr	(*S*)-**19a**	18	—
8	2	**5b**	*i*-Pr	(*R*)-**19b**	18	—

face opposite to that occupied by the OEt group at C-5, would explain the exclusive formation of the oxiranes exhibiting the anti arrangement with respect to the alkoxy group. This assumption is supported by the fact that epimeric sulfoxides afford enantiomeric sulfonyloxiranes.

Concerning the nature of the actual reagent in these reactions, we propose that it is the *m*-chloroperbenzoate anion, generated by dissociation of MCPBA. In addition to the autoprotolysis, which provides very low concentration of the reagent, the carbonyl oxygen at sulfonylfuranones **1**, **3**–**5** can also act as a basic centre for promoting the dissociation.[21] In any case, as the concentration of these anions must be very small, they will only be able to attack double bonds strongly activated for nucleophilic additions, such as sulfonylfuranones. In order to check the influence of the base on these reactions we have studied the behaviour of compounds **6** in the presence of MCPBA/K_2CO_3, conditions, which had proved optimum in the formation of oxiranes from other cyclic substrates.[13] After 8.5 h the reaction of **6** with MCPBA/K_2CO_3 (1.0:3.2:1.6 ratio **6**:MCPBA:K_2CO_3) afforded epoxysulfones **17** in 67% yield (lower than the yield indicated in Table 1 only with MCPBA).

We have finally attempted the synthesis of sulfonylfuranones **3**–**5** by using the second strategy shown in Scheme 1, consisting in the MPCBA oxidation of cycloadducts **8**,[19b] **9**,[19a] **10**[19b] and **11**[19a] into their sulfonyl derivatives **12**–**15**, followed by thermal extrusion of nitrogen. When compound **8a** (Scheme 4) reacted with MCPBA, sulfonylpyrazoline **12a** was detected by ^{1}H NMR, but it could not be isolated chemically pure. When a chloroform solution of the crude of oxidation was kept at room temperature in the presence of silica gel, surprisingly a 68:32 mixture of epoxy sulfonylfuranone **17a** and cyclopropyl derivative **20a** was obtained in high combined yield.



Scheme 4. Reaction of sulfinylfuropyrazoline **8a** with MCPBA.

The formation of cyclopropanes by extrusion of nitrogen from pyrazolines is a well-known process[22] that we have recently reported from the adducts resulting from the reaction of diazoalkanes with sulfinylcycloalkenones and sulfinyllactones, by treatment with some types of acids.[23] According to these precedents, the obtained results suggest that after oxidation of **8a** into sulfonylpyrazoline **12a**, it is quickly decomposed into cyclopropyl derivative **20a** and the sulfonylfuranone **3a**, which is immediately transformed by MCPBA into the epoxyderivative **17a** (Scheme 4).[24,25]

After these preliminary results, we studied the reactions of the sulfinylfuropyrazolines **8b** and **9**–**11** under the conditions depicted in Scheme 4, to evaluate the influence of the structure of the adducts on the reaction course, mainly on the competition of both extrusion reactions. The results are indicated in Table 2. In all cases mixtures of epoxysulfonylfuranones **17**–**19** and 1-*p*-tolylsulfonyl-3-oxabicyclo[3.1.0]hexan-2-ones **20**–**22** (dimethylcyclopropyl derivative **23** was not detected) or sulfonylfuranones **5** were formed. The composition of the mixture, nature and ratio of the obtained products, depends on the nature of R^1, R^2 and on the stereochemistry of the starting compounds.

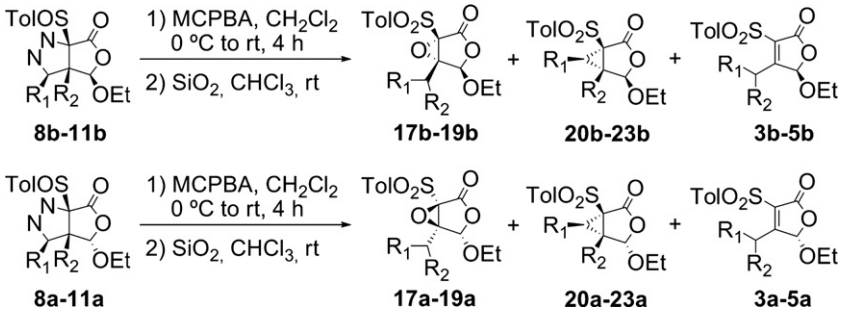
As it can be seen in Table 2, the presence of a methyl group at C-3 of furopyrazoline (entries 3 and 4) diminishes the amount of cyclopropyl derivative, whereas it is completely inhibited when there is an additional methyl group at 3a position (entries 7 and 8). In the latter cases, the major products of the reaction mixtures are the 4-isopropyl-3-sulfonylfuranones **5** (>65%), which is a consequence of their difficult epoxidation (see above). The negative influence of the methyl groups at C-3 and C-3a of the bicyclic systems on the relative rate of cyclopropane or alkene formation by extrusion of nitrogen, had been previously evidenced and explained from steric grounds.[23b,26] A worth mentioning result, is easier formation of cyclopropanes from cycloadducts **8**–**10** with respect to the formation of olefins by extrusion of nitrogen, when they have configuration 4*R* (compare entries 1 and 2, 3 and 4, or 5 and 6 in Table 2).

Another interesting aspect is the formation of compounds **19a** and **19b** starting from pyrazolines **11a** and **11b** (entries 7 and 8, Table 2), whereas they could not be obtained by epoxidation with MCPBA of sulfonylfuranones **5a** and **5b** (entries 7 and 8, Table 1). By assuming that sulfones **5** are the precursors of **19** in both cases, these results could be explained taking into account the higher basicity of pyrazolines **11** that furanones **5**, which increases the concentration of the actual oxidizing reagent.

The structures of both enantiomers of 4-ethoxy-1-(*p*-tolylsulfonyl)-3,6-dioxabicyclo[3.1.0]hexan-2-ones **16**,[13] **17**, **18** and **19**, [(***S*****1**,***S*****4**,***R*****5**)-**a** and (***R*****1**,***R*****4**,***S*****5**)]-**b**] were unequivocally determined from their analysis elemental, [α] values and IR and NMR data (Table 3). The absolute configuration of epoxides **16a**,**b** (Table 3) was determined by the value $J_{4,5}$=0 Hz, indicating that both H are in a trans relationship,[19,27] and the configuration at C-5 of starting furanones.

The absolute configuration at C-1, C-4 and C-5 of epoxides **17a**,**b**, **18a**,**b** and **19a**,**b** was assigned on the assumption that the attack of the oxidant to 5-ethoxy-3-*p*-tolylsulfonylfuran-2(5*H*)-ones is anti with respect to the alkoxy group and the configuration of the acetalic carbon is the same in the epoxide and in the starting furanone. These hypotheses are in agreement with the configuration of epoxides **16** and the observed formation of a different enantiomer from each epimer at C-5 of sulfinylfuranones.

Table 2
Reactions of 4-ethoxy-6a-*p*-tolylsulfinylfuro[3,4-*c*]pyrazolines with MCPBA



Entry	Furopyrazoline	R^1	R^2	Time step 2 (h)	Products (% isolated yield)	Products ratio
1	**8a**	H	H	9	**17a** (53) **20a** (20) **3a** (0)	68:32:0
2	**8b**	H	H	9	**17b** (19) **20b** (43) **3b** (0)	36:64:0
3	**9a**	Me	H	—	**18a** (72) **21a** (8) **4a** (0)	90:10:0
4	**9b**	Me	H	8	**18b** (60) **21b** (11) **4b** (0)	60:11:0
5	**10a**[a]	H	Me	48	**18a** (46) **22a** (23) **4a** (0)	61:39:0
6	**10b**[b]	H	Me	48	**18a** (37) **22b** (40) **4b** (0)	47:53:0
7	**11a**	Me	Me	39	**19a** (21) **23a** (0) **5a** (52)	34:0:66
8	**11b**[c]	Me	Me	90	**19b** (12) **23b** (0) **5b** (62)	21:0:79

[a] From a 95:5 mixture of **9a** ***syn-exo/anti-exo***.
[b] From a 15:85 mixture of ***syn-exo*/9b *anti-exo***.
[c] From a 66:34 mixture of **11b** ***anti-exo/anti-endo***.

The structures of cyclopropanefuranones (4-ethoxy-1-*p*-toly lsulfonyl-3-oxabicyclo[3.1.0]hexan-2-ones) **20**–**22** were determined from their analysis elemental, and their IR and NMR data (Table 3). The cis or trans relationship of H_5 with respect to H_4 and H_6 of cyclopropanes **20** and **21** is based on the value of $J_{4,5}$ and $J_{5,6}$. Accordingly, $J_{4,5}$=0 Hz showed a trans relationship between these protons[19,27] (compounds **20b** and **21b**), whereas $a \sim 4$ Hz value indicated a cis relationship (**20a** and **21a**). Taking into account that the relative stereochemistry of these cyclopropanefuranones is the same that of the starting furopyrazolines, we can assume that the configuration of acetalic carbon of furanone remains unaltered. Both facts allowed us to assign the absolute configuration of above-mentioned cyclopropanes and that of **22a** and **22b**, with no proton at C-5.

In summary, we have reported that sulfonylepoxyfuranones can be obtained by MCPBA oxidation of the corresponding sulfinylfuranones. Additionally, we have demonstrated that this reagent is efficient only for oxidizing strongly deactivated double bonds, which suggests that it is acting as a nucleophile and therefore is indicative that the *m*-chloroperbenzoate anion, generated by dissociation of the acid with some basic centre at the substrate, is the actual oxidizing agent.

3. Experimental section

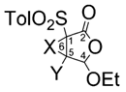
3.1. General methods

Flash chromatography was carried out with silica gel Merck 60 (230–400 mesh ASTM). NMR spectra were determined in $CDCl_3$ solutions at 300 and 75 MHz for ^1H and ^{13}C NMR, respectively; *J* values are given in hertz. Melting points were measured using a Gallenkamp apparatus in open capillary tubes and are uncorrected. The optical rotations were measured at room temperature (20–23 °C) using a Perkin–Elmer 241 MC polarimeter (concentration in g/100 mL). Compounds **1**,[13] **2**,[18] **6**[19] and **8**–**11**,[19] were synthesized and purified following the reported procedures. The ee's of compounds **16**–**19** were determined by chiral HPLC on Chiralcel OD column using *i*-PrOH/hexane (13:87) as the eluent.

3.2. 3-Ethyl-5-ethoxy-3-*p*-tolylsulfinylfuran-2(5*H*)-ones (7)

A 0.03 M solution of furopyrazolines **9** or **10** in toluene was heated at 100 °C for 60 min or 24 h, respectively. The evolution of the reaction was followed by TLC. After evaporation of the solvent

Table 3
NMR data for compounds of structure



No	X	Y	^1H NMR							^{13}C NMR				
			H_4	H_5	H_{6ex}	H_{6en}	$J_{4,5}$	$J_{5,6en}$	$J_{5,6ex}$	C_1	C_2	C_4	C_5	C_6
16	O	H	5.42	4.67	—	—	0	—	—	65.8	163.1	99.0	62.6	—
17	O	Me	5.25	—	—	—	—	—	—	73.6	164.4	101.4	68.1	—
18	O	Et	5.34	—	—	—	—	—	—	77.0	164.6	100.5	68.9	—
19	O	*i*-Pr	5.36	—	—	—	—	—	—	79.1	164.8	101.8	69.4	—
20a	CH_2	H	5.63	3.18	2.04	1.86	4.1	5.2	8.8	48.0	165.9	100.0	29.2	17.1
20b	CH_2	H	5.24	3.06	2.16	1.44	0	5.5	8.8	45.2	166.9	100.2	31.7	18.5
21a	CHMe	H	5.66	3.00	—	2.11	4.0	5.3	—	52.6	166.9	100.9	34.1	26.6
21b	CHMe	H	5.25	2.94	—	1.71	0	5.5	—	49.9	167.9	100.4	36.8	28.9
22a	CH_2	Me	5.26	—	2.07	1.88	—	—	—	49.9	166.5	104.0	38.7	22.4
22b	CH_2	Me	5.13	—	2.11	1.50	—	—	—	47.7	167.8	102.2	39.7	24.3

under reduced pressure the residue was purified by column chromatography (hexane/ethyl acetate 3:1).

*3.2.1. (5S,SS)-4-Ethyl-5-ethoxy-3-p-tolylsulfinylfuran-2(5H)-one (**7a**).* It was obtained after heating for 1 h a 95:5 mixture of ***syn-exo*-9a**:***anti-exo*-9a**. Yield 85%. Colourless oil. IR (film) 1760, 1639, 1084, 1060. ^{1}H NMR δ: 7.69 and 7.33 (AA′BB′ system, 4H), 5.71 (s, 1H, H_5), 3.90 (m, 1H), 3.74 (m, 1H), 3.22 (m, 1H), 2.67 (m, 1H), 2.40 (s, 3H), 1.28 (t, 3H, J=7.0), 1.22 (t, 3H, J=7.6). ^{13}C NMR δ: 169.4 (C), 165.5 (C), 142.2 (C), 138.6 (C) 132.3 (C), 130.0 (CH), 124.7 (CH), 101.8 (C_5), 66.4 (CH_2), 21.4 (CH_3), 18.9 (CH_2), 14.8 (CH_3), 12.5 (CH_3). $[\alpha]_D$=+195.5 (c=1.35, $CHCl_3$). Anal. Calcd for $C_{15}H_{18}O_4S$: C 61.20, H 6.16, S 10.89. Found: C 61.48, H 6.50, S 11.17.

*3.2.2. (5R,SS)-4-Ethyl-5-ethoxy-3-p-tolylsulfinylfuran-2(5H)-one (**7b**).* It was obtained after heating for 30 min a 15:85 mixture of ***syn-exo*-9b**:***anti-exo*-9b**. Yield 75%. Colourless oil. IR (film): 1765, 1639, 1084, 1058. ^{1}H NMR δ: 7.69 and 7.33 (AA′BB′ system, 4H), 5.74 (s, 1H, H_5), 3.88 (m, 1H), 3.73 (m, 1H), 3.24 (m, 1H), 2.66 (m, 1H), 2.41 (s, 3H), 1.25 (t, 3H, J=7.0), 1.23 (t, 3H, J=7.6). ^{13}C NMR δ: 169.1 (C), 165.7 (C), 142.3 (C), 138.9 (C), 132.3 (C), 130.2 (CH), 125.0 (CH), 101.9 (C_5), 66.7 (CH_2), 21.5 (CH_3), 18.8 (CH_2), 14.9 (CH_3), 12.4 (CH_3). $[\alpha]_D$=+140.6 (c=0.35, $CHCl_3$). Anal. Calcd for $C_{15}H_{18}O_4S$: C 61.20, H 6.16, S 10.89. Found: C 61.12, H 6.28, S 11.18.

3.3. Oxidation of 5-ethoxy-3-*p*-tolylsulfinyllfuran-2(5*H*)-ones. General procedure

To a stirred solution of 0.38 mmol of sulfinylfuranone (**2**, **6** or **7**), in dichloromethane (5 mL) under argon atmosphere at 0 °C, was added dropwise a solution of MCPBA (162 mg, 0.84 mmol, ~90%) in dichloromethane (10 mL). The reaction mixture was stirred at room temperature for the time indicated in each case, and then it was washed with saturated aqueous sodium bicarbonate until pH 7. The aqueous layer was extracted with several portions of dichloromethane. The combined organic layers were dried over dry sodium sulfate and the solvent removed in vacuo. The crude product was chromatographied on silica gel (hexane/CH_2Cl_2/Et_2O in the ratio indicated in each case) to give the pure epoxide.

3.3.1. (5R)-5-Ethoxy-4-methyl-3-p-tolylsulfonylfuran-2(5H)-one (3b). It was obtained by reaction of (5*R*,*SS*)-5-ethoxy-4-methyl-3-*p*-tolylsulfinylfuran-2(5*H*)-one (6b) with MCPBA for 5 h at room temperature. It was isolated by column chromatography (6:1 hexane/ethyl acetate). ^{1}H NMR δ: 7.95 and 7.35 (AA′BB′ system, 4H), 5.62 (s, 1H, H_5), 3.90 (m, 1H), 3.75 (m, 1H), 2.50 (s, 3H), 2.44 (s, 3H), 1.26 (t, 3H, J=7.0).

*3.3.2. (1S,4S,5R)-4-Ethoxy-1-p-tolylsulfonyl-3,6-dioxabicyclo[3.1.0]-hexan-2-one [(+)-**16a**]*[9]. It was obtained from **2a** after 3 h, purified by column chromatography (60:35:5 hexane/CH_2Cl_2/Et_2O) and isolated in 80% yield. White solid, mp 152–153 °C. IR (KBr) 1796, 1596, 1158. ^{1}H NMR δ: 7.99 and 7.43 (AA′BB′ system, 4H), 5.42 (s, 1H, H_4), 4.67 (s, 1H, H_5), 3.96 (m, 1H), 3.72 (m, 1H), 2.48 (s, 3H), 1.29 (t, 3H, J=7.1); ^{13}C RMN δ: 163.1 (C_2), 146.8 (C), 132.6 (C), 130.0 (CH), 129.8 (CH), 99.0 (C_4), 66.7 (CH_2), 65.8 (C_1), 62.6 (C_5), 21.8 (CH_3), 14.7 (CH_3). $[\alpha]_D$=+184.8 (c 0.5, $CHCl_3$), ee 99.4% (flow 0.8 mL/min, t_R=12.36 min). Anal. Calcd for $C_{13}H_{14}O_6S$: C 52.34, H 4.73, S 10.75. Found: C 52.38, H 4.66, S 10.99.

*3.3.3. (1R,4R,5S)-4-Ethoxy-1-p-tolylsulfonyl-3,6-dioxabicyclo[3.1.0]-hexan-2-one [(−)-**16b**].* It was obtained from **2b** after 1.5 h, purified by column chromatography (60:35:5 hexane/CH_2Cl_2/Et_2O) and isolated in 75% yield. White solid, mp 150–152 °C. $[\alpha]_D$=−162.6 (c 0.5, $CHCl_3$), ee 87% (from a 95:5 mixture of **3b**:**3a**) (flow 0.8 mL/min, t_R=10.28 min). Anal. Calcd for $C_{13}H_{14}O_6S$: C 52.34, H 4.73, S 10.75. Found: C 52.37, H 4.63, S 10.99.

*3.3.4. (1S,4S,5R)-4-Ethoxy-5-methyl-1-p-tolylsulfonyl-3,6-dioxabicyclo[3.1.0]hexan-2-one [(+)-**17a**].* This compound was obtained from **6a** after 8.5 h, purified by column chromatography (75:20:5 hexane/CH_2Cl_2/Et_2O) and isolated in 89% yield. It was also obtained from sulfinylpyrazoline **8a** in 53% yield. White solid, mp 114–115 °C. IR (KBr) 1790, 1596, 1190. ^{1}H NMR δ: 7.99 and 7.41 (AA′BB′ system, 4H), 5.25 (s, 1H, H_4), 3.93 (m, 1H), 3.68 (m, 1H), 2.47 (s, 3H), 2.02 (s, 3H), 1.27 (t, 3H, J=7.0). ^{13}C NMR δ: 164.4 (C_2), 146.6 (C), 133.8 (C), 129.9 (CH), 129.8 (CH), 101.4 (C_4), 73.6 (C_1), 68.1 (C_5), 66.5 (CH_2), 21.8 (CH_3), 14.7 (CH_3), 10.0 (CH_3). $[\alpha]_D$=+226.8 (c 1, $CHCl_3$), ee 98.4% (flow 0.8 mL/min, t_R=12.10 min). Anal. Calcd for $C_{14}H_{16}O_6S$: C 53.84, H 5.16, S 10.27. Found: C 53.84, H 5.15, S 10.55.

*3.3.5. (1R,4R,5S)-4-Ethoxy-5-methyl-1-p-tolylsulfonyl-3,6-dioxabicyclo[3.1.0]hexan-2-one [(−)-**17b**].* It was obtained from **6b** after 8.5 h, purified by column chromatography (75:20:5 hexane/CH_2Cl_2/Et_2O) and isolated in 88% yield. It was also obtained from sulfinylpyrazoline **8b** in 19% yield. White solid, mp 114–115 °C. $[\alpha]_D$=−220.0 (c 0.5, $CHCl_3$), ee 96% (flow 0.8 mL/min, t_R=8.67 min). Anal. Calcd for $C_{14}H_{16}O_6S$: C 53.84, H 5.16, S 10.27. Found: C 53.93, H 5.24, S 10.53.

*3.3.6. (1S,4S,5R)-4-Ethoxy-5-ethyl-1-p-tolylsulfonyl-3,6-dioxabicyclo[3.1.0]hexan-2-one [(+)-**18a**].* It was obtained from sulfinylfuranone **7a** after 2.5 h, purified by column chromatography (80:15:5 hexane/CH_2Cl_2/Et_2O) and isolated in 86% yield. It was also obtained from sulfinylpyrazolines **9a** or **10a** in 72% and 46% yields, respectively. White solid, mp 141–143 °C. IR (KBr) 1794, 1594, 1150. ^{1}H NMR δ: 7.99 and 7.41 (AA′BB′ system, 4H), 5.34 (s, 1H, H_4), 3.94 (m, 1H), 3.69 (m, 1H), 2.50 (q, 2H, J=7.6), 2.47 (s, 3H), 1.29 (t, 3H, J=7.0), 1.24 (t, 3H, J=7.6). ^{13}C NMR δ: 164.6 (C_2), 146.5 (C), 133.8 (C), 130.0 (CH), 129.8 (CH), 100.5 (C_4), 77.0 (C_1), 68.9 (C_5), 66.6 (CH_2), 21.8 (CH_3), 17.9 (CH_2), 14.7 (CH_3), 9.5 (CH_3). $[\alpha]_D$=+233.6 (c 0.5, $CHCl_3$), ee 98.8% (flow 0.7 mL/min, t_R=11.79 min). Anal. Calcd for $C_{15}H_{18}O_6S$: C 55.20, H 5.56, S 9.83. Found: C 55.21, H 5.58, S 10.22.

*3.3.7. (1R,4R,5S)-4-Ethoxy-5-ethyl-1-p-tolylsulfonyl-3,6-dioxabicyclo[3.1.0]hexan-2-one [(−)-**18b**].* It was obtained from **7b** after 2.5 h, purified by column chromatography (80:15:5 hexane/CH_2Cl_2/Et_2O) and isolated in 86% yield. It was also obtained from sulfinylpyrazolines **9b** and **10b** in 60% and 37% yields, respectively. White solid, mp 142–143 °C. $[\alpha]_D$=−234.0 (c 0.3, $CHCl_3$), ee 99.5% (flow 0.7 mL/min, t_R=8.51 min). Anal. Calcd for $C_{15}H_{18}O_6S$: C 55.20, H 5.56, S 9.83. Found: C 55.16, H 5.35, S 10.13.

3.4. Transformation of 6-*p*-tolylsulfinylfuro[3,4-*c*]pyrazolin-6-ones to sulfonylcyclopropanefuranones and sulfonylepoxyfuranones. General procedure

To a stirred ice-cooled solution of furopyrazoline **8**–**11** (0.75 mmol) in dichloromethane (16 mL), was added dropwise a solution of MCPBA (360 mg, ≈90%, 1.9 mmol) in dichloromethane (15 mL). The mixture was stirred under argon atmosphere at room temperature for 4 h, and then it was washed with saturated aqueous sodium bicarbonate until pH 7. The aqueous layer was extracted several times with dichloromethane. The combined organic layers were dried over dry sodium sulfate and the solvent removed at reduced pressure. The residue was dissolved in 23 mL of chloroform and then 954 mg of silica gel were added. The mixture was stirred at room temperature for the time indicated in each case, and the evolution of reaction was followed by TLC. The silica gel was filtered off and the solvent was removed under reduced pressure. ^{1}H NMR analysis of the crude product showed the

presence of compounds indicated in Table 2. The products were separated by flash column chromatography and purified as indicated in each case.

*3.4.1. (1R,4S,5S)-4-Ethoxy-1-p-tolylsulfonyl-3-oxabicyclo[3.1.0]hexan-2-one (**20a**).* Compound **20a** was obtained from **8a** and purified by column chromatography (5:1 hexane/ethyl acetate). Yield 20%. White solid, mp 130–131 °C. IR (KBr) 1770, 1596, 1155, 1085. ^{1}H NMR δ: 7.92 and 7.38 (AA′BB′ system, 4H), 5.63 (d, 1H, H_4, $J_{4,5}$=4.1), 3.81 (m, 1H), 3.66 (m, 1H), 3.18 (ddd, 1H, H_5, $J_{5,4}$=4.1, $J_{5,6endo}$=5.2 and $J_{5,6exo}$=8.8), 2.46 (s, 3H), 2.04 (dd, 1H, H_{6exo}, $J_{6exo,6endo}$=5.3 and $J_{6exo,5}$=8.8), 1.86 (t, 1H, H_{6endo}, J=5.2), 1.22 (t, 3H, J=7.1). ^{13}C NMR δ: 165.9 (C_2), 145.6 (C), 135.1 (C), 129.8 (CH), 129.1 (CH), 100.0 (C_4), 67.0 (CH_2), 48.0 (C_1), 29.2 (C_5), 21.7 (CH_3), 17.1 (C_6), 14.8 (CH_3); $[\alpha]_D^{20}$ −16.6 (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{14}H_{16}O_5S$: C 56.74, H 5.44, S 10.82. Found C 56.56, H 5.44, S 10.80.

*3.4.2. (1R,4R,5S)-4-Ethoxy-1-p-tolylsulfonyl-3-oxabicyclo[3.1.0]hexan-2-one (**20b**).* Compound **20b** was obtained from **8b** and purified by column chromatography (50:45:5 hexane/dichloromethane/ethyl ether). Yield 43%. White solid, mp 128–129 °C. IR (KBr) 1782, 1598, 1150. ^{1}H NMR δ: 7.93 and 7.37 (AA′BB′ system, 4H), 5.24 (s, 1H, H_4), 3.81 (m, 1H), 3.58 (m, 1H), 3.06 (dd, 1H, H_5, $J_{5,6endo}$=5.5 and $J_{5,6exo}$=8.8), 2.46 (s, 3H, CH_3), 2.16 (dd, 1H, H_{6exo}, $J_{6exo,6endo}$=5.5 and $J_{6exo,5}$=8.8), 1.44 (t, 1H, H_{6endo}, J=5.5), 1.18 (t, 3H, J=7.1). ^{13}C NMR δ: 166.9 (C_2), 145.5 (C), 135.0 (C), 129.7 (CH), 129.0 (CH), 100.2 (C_4), 65.0 (CH_2), 45.2 (C_1), 31.7 (C_5), 21.7 (CH_3), 18.5 (C_6), 14.7 (CH_3). $[\alpha]_D^{20}$ −121.2 (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{14}H_{16}O_5S$: C 56.74, H 5.44, S 10.82. Found: C 56.78, H 5.31, S 11.08.

*3.4.3. (1R,4S,5S,6R)-4-Ethoxy-6-methyl-1-p-tolylsulfonyl-3-oxabicyclo[3.1.0]hexan-2-one (**21a**).* Compound **21a** was obtained from a 95:5 mixture of **9a-*syn-exo*:*anti-exo*** furopyrazolines and purified by column chromatography (60:35:5 hexane/dichloromethane/ethyl ether). Yield 8%. White solid, mp 100–103 °C. IR (KBr) 1777, 1595, 1322, 1153. ^{1}H NMR δ: 7.99 and 7.37 (AA′BB′ system, 4H), 5.66 (d, 1H, H_4, $J_{4,5}$=4.0), 3.80 (m, 1H), 3.66 (m, 1H), 3.00 (dd, 1H, H_5, $J_{4,5}$=4.0 and $J_{5,6}$=5.3), 2.46 (s, 3H), 2.11 (qd, 1H, H_6, $J_{6,5}$=5.3 and $J_{6,Me}$=6.5), 1.50 (d, 3H, CH_3-6, $J_{Me,6}$=6.5), 1.22 (t, 3H, J=7.1). ^{13}C NMR δ: 166.9 (C_2), 145.3 (C), 136.3 (C), 129.7 (CH), 128.8 (CH), 100.9 (C_4), 66.9 (CH_2), 52.6 (C_1), 34.1 (C_5), 26.6 (C_6), 21.7 (CH_3), 14.8 (CH_3), 10.6 (CH_3). $[\alpha]_D$=+15.2 (*c* 0.25, $CHCl_3$). Anal. Calcd for $C_{15}H_{18}O_5S$: C 58.05, H 5.85, S 10.33. Found: C 58.06, H 5.83, S 10.56.

*3.4.4. (1R,4R,5S,6R)-4-Ethoxy-6-methyl-1-p-tolylsulfonyl-3-oxabicyclo[3.1.0]hexan-2-one (**21b**).* It was obtained from a 85:15 mixture of **9b-*anti-exo*:*syn-exo*** and purified by column chromatography (50:45:5 hexane/dichloromethane/ethyl ether). Yield 11%. White solid, mp 129–131 °C. IR (KBr) 1775, 1595, 1332, 1156. ^{1}H NMR δ: 7.98 and 7.35 (AA′BB′ system, 4H), 5.25 (s, 1H, H_4), 3.80 (m, 1H), 3.58 (m, 1H), 2.94 (d, 1H, H_5, $J_{5,6}$=5.5), 2.45 (s, 3H), 1.71 (qd, 1H, H_6, $J_{6ndo,5}$=5.5 and $J_{6,Me}$=6.3), 1.53 (d, 3H, $J_{Me,6}$=6.3), 1.19 (t, 3H). ^{13}C NMR δ: 167.9 (C_2), 145.2 (C), 136.3 (C), 129.5 (CH), 128.9 (CH), 100.4 (C_4), 64.9 (CH_2), 49.9 (C_1), 36.8 (C_5), 28.9 (C_6), 21.7 (CH_3), 14.8 (CH_3), 10.8 (CH_3). $[\alpha]_D$=−74.0 (*c* 0.25, $CHCl_3$). Anal. Calcd for $C_{15}H_{18}O_5S$: C 58.05, H 5.85, S 10.33. Found: C 58.08, H 5.86, S 10.53.

*3.4.5. (1R,4S,5S)-4-Ethoxy-5-methyl-1-p-tolylsulfonyl-3-oxabicyclo[3.1.0]hexan-2-one (**22a**).* Compound **22a** was obtained from **10a** and purified by column chromatography (50:45:5 hexane/dichloromethane/ethyl ether). Yield 23%. White solid, mp 82–84 °C. IR (KBr) 1777, 1599, 1155, 1071. ^{1}H NMR δ: 7.90 and 7.36 (AA′BB′ system, 4H), 5.26 (s, 1H, H_4), 3.82 (m, 1H), 3.64 (m, 1H), 2.46 (s, 3H), 2.07 (d, 1H, H_{6exo}, J=5.1), 1.88 (d, 1H, H_{6endo}, J=5.1), 1.77 (s, 3H), 1.22 (t, 3H, J=7.1). ^{13}C NMR δ: 166.5 (C_2), 145.4 (C), 136.1 (C), 129.7 (CH), 129.1 (CH), 104.0 (C_4), 67.1 (CH_2), 49.9 (C_1), 38.7 (C_5), 22.4 (C_6), 21.7 (CH_3), 14.8 (CH_3), 13.1 (CH_3). $[\alpha]_D$=−17.8 (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{15}H_{18}O_5S$: C 58.05, H 5.85, S 10.33. Found: C 58.13, H 5.72, S 10.68.

*3.4.6. (1R,4R,5S)-4-Ethoxy-5-methyl-1-p-tolylsulfonyl-3-oxabicyclo[3.1.0]hexan-2-one (**22b**).* It was obtained from **10b** and purified by column chromatography (4:1 hexane/ethyl acetate). Yield 40%. White solid, mp 80–82 °C. IR (KBr) 1780, 1597, 1159, 1060. ^{1}H NMR δ: 7.89 and 7.35 (AA′BB′ system, 4H), 5.13 (s, 1H, H_4), 3.78 (m, 1H), 3.54 (m, 1H), 2.44 (s, 3H), 2.11 (d, 1H, H_{6exo}, J=5.1), 1.71 (s, 3H), 1.50 (d, 1H, H_{6endo}, J=5.1), 1.16 (t, 3H, J=7.0). ^{13}C NMR δ: 167.8 (C_2), 145.2 (C), 135.9 (C), 129.6 (CH), 128.9 (CH), 102.2 (C_4), 65.2 (CH_2), 47.7 (C_1), 39.7 (C_5), 24.3 (C_6), 21.6 (CH_3), 14.7 (CH_3), 11.0 (CH_3). $[\alpha]_D$=−160.0 (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{15}H_{18}O_5S$: C 58.05, H 5.85, S 10.33. Found: C 58.18, H 5.90, S 10.78.

*3.4.7. (1S,4S,5R)-4-Ethoxy-5-isopropyl-1-p-tolylsulfonyl-3,6-dioxabicyclo[3.1.0]hexan-2-one [(+)-**19a**].* It was obtained from sulfinylfuropyrazoline **11a** and purified by column chromatography (85:10:5 hexane/dichloromethane/ethyl ether). Yield 21%. White solid, mp 149–151 °C. IR (KBr) 1796, 1595, 1341, 1160, 1123, 1006. ^{1}H NMR δ: 8.00 and 7.40 (AA′BB′ system, 4H), 5.36 (s, 1H, H_4), 3.95 (m, 1H), 3.67 (m, 1H), 2.78 (sept, 1H, J=7.1), 2.47 (s, 3H), 1.42 (d, 3H, J=7.2), 1.31 (t, 3H, J=7.1), 1.30 (d, 3H, J=7.0). ^{13}C NMR δ: 164.8 (C_2), 146.5 (C), 133.9 (C), 130.1 (CH), 129.7 (CH), 101.8 (C_4), 79.1 (C_1), 69.4 (C_5), 66.9 (CH_2), 28.3 (CH), 21.8 (CH_3), 19.6 (CH_3), 17.9 (CH_3), 14.8 (CH_3). $[\alpha]_D$=+258.8 (*c* 0.25, $CHCl_3$), ee 97.6% (flow 1 mL/min, t_R=10.93 min). Anal. Calcd for $C_{16}H_{20}O_6S$: C 56.46, H 5.92, S 9.42. Found: C 56.63, H 6.03, S 9.11.

*3.4.8. (1R,4R,5S)-4-Ethoxy-5-isopropyl-1-p-tolylsulfonyl-3,6-dioxabicyclo[3.1.0]hexan-2-one [(−)-**19b**].* It was obtained from a mixture of sulfinylfuropyrazolines **11b-*anti-exo*:*anti-endo*** and purified by column chromatography (85:10:5 hexane/dichloromethane/ethyl ether). Yield 12%. White solid, mp 148–150 °C; $[\alpha]_D$=−259.9 (*c* 0.24, $CHCl_3$), ee 98% (flow 1 mL/min, t_R=7.29 min). Anal. Calcd for $C_{16}H_{20}O_6S$: C 56.46, H 5.92, S 9.42. Found: C 56.75, H 6.02, S 9.11.

*3.4.9. (5S)-5-Ethoxy-4-isopropyl-3-p-tolylsulfonylfuran-2(5H)-one [(+)-**5a**].* It was obtained from **11a** in 52% yield. Colourless oil. IR (film) 1778, 1626, 1597, 1158. ^{1}H NMR δ: 7.93 and 7.33 (AA′BB′ system, 4H), 5.78 (s, 1H, H_5), 4.03 (sept, 1H, J=7.0), 3.91 (m, 1H), 3.74 (m, 1H), 2.41 (s, 3H), 1.32 (d, 3H, J=7.0), 1.25 (t, 3H, J=7.1), 1.22 (d, 3H, J=7.0). ^{13}C NMR δ: 175.7 (C), 164.1 (C), 145.6 (C), 135.9 (C), 129.7 (CH), 129.0 (C), 128.8 (CH), 101.2 (C_5), 67.2 (CH_2), 27.2 (CH), 21.6 (CH_3), 21.4 (CH_3), 19.0 (CH_3), 14.8 (CH_3).

*3.4.10. (5R)-5-Ethoxy-4-isopropyl-3-p-tolylsulfonylfuran-2(5H)-one [(−)-**5b**].* It was obtained from a 66:34 mixture of sulfinylfuropyrazoline **11b-*anti-exo*:*anti-endo*** and purified by column chromatography (60:35:5 hexane/dichloromethane/ethyl ether). Yield 62%. Colourless oil, $[\alpha]_D$=−40.5 (*c* 1.68, $CHCl_3$).

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References and notes

1. Ortega, M. J.; Zubía, E.; Sánchez, M. C.; Carballo, J. L. *J. Nat. Prod.* **2008**, *71*, 1637–1639 and references cited therein.
2. (a) Sung, P.; Lin, M.; Hwang, T.; Fan, T.; Su, W.; Ho, C.; Fang, L.; Wang, W. *Chem. Pharm. Bull.* **2008**, *56*, 930–935 and references cited therein; (b) Sung, P.; Lin, M.; Su, Y.; Chiang, T.; Hu, W.; Su, J.; Cheng, M.; Sheu. *Tetrahedron* **2008**, *64*, 2596–2604.

3. Marrero, J.; Benítez, J.; Rodríguez, A. D.; Zhao, H.; Raptis, R. G. *J. Nat. Prod.* **2008**, *71*, 381–389.
4. Lei, C.; Pu, J.; Huang, S.; Chen, J.; Liu, J.; Yang, L.; Ma, Y.; Xiao, Y.; Li, X.; Sun, H. *Tetrahedron* **2009**, *65*, 164–170.
5. (a) Kuramochi, K.; Nagata, S.; Itaya, H.; Matsubara, Y.; Sunoki, T.; Uchiro, H.; Takao, K.; Kobayashi, S. *Tetrahedron* **2003**, *59*, 9743–9758; (b) Kuramochi, K.; Yukizawa, S.; Ikeda, S.; Sunoki, T.; Arai, S.; Matsui, R.; Morita, A.; Mizushina, Y.; Sakaguchi, K.; Sugawara, F.; Ikekita, M.; Kobayashi, S. *Biorg. Med. Chem.* **2008**, *16*, 5039–5049.
6. Jakubowski, A. A.; Guziez, F. S., Jr.; Sugiura, M.; Tam, C. C.; Tishler, M. *J. Org. Chem.* **1982**, *47*, 1221–1228.
7. Boeckman, R. K., Jr.; Thomas, E. W. *J. Am. Chem. Soc.* **1979**, *101*, 987–994.
8. Cardellach, J.; Font, J.; Ortuño, R. M. *Tetrahedron Lett.* **1985**, *26*, 2815–2816.
9. Reed, A. D.; Hegedus, L. S. *J. Organomet. Chem.* **1995**, *60*, 3787–3794.
10. Renard, M.; Ghosez, L. A. *Tetrahedron* **2001**, *57*, 2597–2608.
11. For tetrasubstituted epoxides see Rozen, S.; Golan, E. *Eur. J. Org. Chem.* **2003**, 1915–1917.
12. Optically active epoxylactones have also been synthesized by the oxiranyl anion methodology: see Capriati, V.; Degennaro, L.; Favia, R.; Florio, S.; Luisi, R. *Org. Lett.* **2002**, *4*, 1551–1554.
13. García Ruano, J. L.; Fajardo, C.; Fraile, A.; Martín, M. R. *J. Org. Chem.* **2005**, *70*, 4300–4306. The reaction of **1a** with 2:1 MCPBA/K_2CO_3 at room temperature for 5 min afforded the corresponding sulfonyl epoxide in good yield.
14. For 4a,9a-epoxy-4a,9a-dihydroanthracene-1,4,9,10-tetrone see: Chandler, M.; Stoodley, R. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1007–1012.
15. For epoxypyridazinone see: Fariña, F.; Martín, M. V.; Romañach, M.; Sánchez, F. *An. Quim., Ser. C* **1988**, *84*, 173–175.
16. For epoxydisulfone see: Ogura, K.; Takahashi, S.; Kawamoto, Y.; Suzuki, M.; Fujita, M.; Suzuki, Y.; Sugiyama, Y. *Tetrahedron Lett.* **1993**, *34*, 2649–2652.
17. For methylidenemalonates see: De Cock, C. J. C.; De Keyser, J.; Poupaert, J. H.; Dumont, P. *Bull. Soc. Chim. Belg.* **1987**, *96*, 783–786.
18. Carretero, J. C.; García Ruano, J. L.; Lorente, A.; Yuste, F. *Tetrahedron: Asymmetry* **1993**, *4*, 177–180.
19. (a) García Ruano, J. L.; Fraile, A.; González, G.; Martín, M. R.; Clemente, F. R.; Gordillo, R. *J. Org. Chem.* **2003**, *68*, 6522–6534; (b) García Ruano, J. L.; Fraile, A.; Martín, M. R. *Tetrahedron: Asymmetry* **1996**, *7*, 1943–1950.
20. The preparation of 5-methoxyfuran-2(5*H*)-one was readily accomplished, following the procedure reported by Schenck, Schenck, G. O. *Ann. Chem.* **1953**, *584*, 156–176, by photooxygenation of furfural using methanol as the solvent.
21. One of the reviewers has suggested that the oxygen-atom transfer reaction on the sulfinyl group leads to formation of metachlorobenzoic acid and traces of base can generate the metachlorobenzoate anion, which is able to catalyze the epoxidation reaction through general basic catalysis process.
22. (a) McGreer, D. E.; Chiu, N. W. K.; Vinje, M. G. *Can. J. Chem.* **1965**, *43*, 1407–1416; (b) Clarke, T. C.; Wendinling, L. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1977**, *99*, 2740–2750; (c) Fariña, F.; Martín, M. V.; Paredes, M. C.; Tito, A. *Heterocycles* **1988**, *27*, 365–370.
23. (a) Ruano, J. L.; Alonso, M.; Cruz, D.; Peromingo, M. T.; Fraile, A.; Martín, M. R.; Tito, A.; Yuste, F. *Tetrahedron* **2008**, *64*, 10546–10551; (b) García Ruano, J. L.; Peromingo, M. T.; Martín, M. R.; Tito, A. *Org. Lett.* **2006**, *8*, 3295–32988.
24. The extrusion of nitrogen from the sulfinylpyrazoline cannot be ruled out.
25. Reactions of **8a** with $YbTf_3$, which was the Lewis acid affording the higher yield in the corresponding cyclopropyl derivative starting from the adducts derived from sulfinylfuranones and cycloalkenones, were unsuccessful, presumably due to its preferent association to the acetalic moiety instead of to the sulfinyl one.
26. Cruz, D.; Yuste, F.; Martín, M. R.; Tito, A.; Yuste, F.; García Ruano, J. L. *J. Org. Chem.* **2009**, *74*, 3820–3826.
27. García Ruano, J. L.; Fraile, A.; Martín, A. M.; Martín, M. R. *J. Org. Chem.* **2005**, *70*, 8825–8834.