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Asymmetric cyclopropanation of (5*S*,S_S)-3-*p*-tolylsulfinyl-5-ethoxyfuran-2(5*H*)-one with sulfonium ylides: influence of the sulfur ylide substituents on stereoselectivity

Jose Luis García Ruano,[a,*] Cristina Fajardo,[a] M. Rosario Martín,[a] Wanda Midura[b] and Marian Mikołajczyk[b,*]

[a]*Departamento de Química Orgánica (C-I), Universidad Autónoma de Madrid, Cantoblanco, Madrid 28049, Spain*
[b]*Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Department of Heteroorganic Chemistry, 90-363 Łódź, Sienkiewicza 112, Poland*

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Abstract—The cyclopropanation of title compound **1** with various sulfur ylides has been examined. A very high π-facial selectivity was observed in the reaction with diphenylsulfonium ylides, $Ph_2S{=}CRR'$ (*anti* attack with respect to the alkoxy group in **1** is clearly preferred) whereas the *endo*-selectivity was found when $R \neq R'$ is dependent on their relative size. Reactions with dimethylsulfonium ylides $Me_2S{=}CRR'$ occurred with a moderate π-facial selectivity and *exo*-selectivity, the former being dependent on the solvent polarity. The stereochemical course of the cyclopropanation reactions is rationalized in terms of steric and electrostatic interactions.

1. Introduction

The occurrence of the cyclopropyl group as a basic structural unit in a wide range of naturally occurring and biologically active compounds, as well as the utility of these small ring compounds as synthetic intermediates, has led to the development of many cyclopropanation strategies.[1,2] While the cyclopropanation of electron rich alkenes can be achieved via carbene insertion,[3] the cyclopropanation of electron deficient alkenes can proceed through an initial Michael type addition of nucleophilic alkylidene transfer agents such as sulfur ylides.[4] There is a great variety of sulfur ylides possessing different structures and stabilities.[5] In sharp contrast to ylides possessing only alkyl, vinyl or aryl substitutents, which can be utilized only at low temperatures, those possessing carbonyl, cyano, sulfonyl and nitro substituents are sufficiently stabilized to be isolable and storable.

The influence of the structure of sulfur ylides on chemoselectivity[6] (epoxidation vs cyclopropanation) and stereoselectivity[7] has been studied with the differences in their behaviour being attributed to kinetic or thermodynamic control of the reaction. However, in the investigations presented so far, not much consideration has been given to the role of the remaining substituents on the sulfur. These substituents have traditionally been phenyl in the alkylides and methyl in others. The effect of these groups on ylide reactivity has been noted in the reactions of ethyl (dimethylsulfuranylidene)acetate (EDSA) and tetrahydrothiophenium carboethoxymethylide with dimethylvinylsulfonium bromide.[8a] The steric bulk of the tetrahydrothiophene ring compared to the methyl groups caused a decrease in the cyclopropanation yield. More recently, Aggarwal et al.[8b] reported a distinct difference in diastereoselectivity of catalytic cyclopropanation of electron deficient alkenes when pentamethylenesulfonium and tetrahydrothiophenium ethoxycabonylmethylides were used.

Great efforts have been made to develop the asymmetric synthesis of cyclopropanes, though mainly based on nonpolarized olefins.[2f] To date, there have only been a few reports on the diastereoselective cyclopropanation of chiral olefins, in which an auxiliary group is attached to the olefinic residue.[9] Only recently, have very efficient and highly stereoselective formations of cyclopropanes

* Corresponding authors. Tel.: +34-914974701; fax: +34-9149-73966 (J.L.G.R.), tel.: +48-42-6815832; fax: +48-42-6847126 (M.M.); e-mail addresses: joseluis.garcia.ruano@uam.es; marmikol@bilbo.cbmm.lodz.pl

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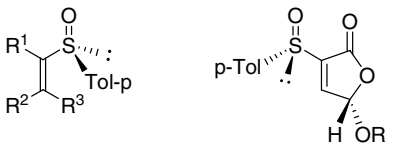
been observed when enantiopure vinyl sulfoxides of the type **A** were reacted with sulfur ylides.[10]



A
R^1=AlkOC(O), $(AlkO)_2P(O)$
R^2,R^3=H, alkyl, aryl

B
R=alkyl

Chiral 5-alkoxy-3-*p*-tolylsulfinylfuran-2(*5H*)-ones **B** containing the reactive vinyl sulfoxide moiety have previously been studied as dienophiles,[11] and dipolarophiles.[12] In many of these reactions, the sulfinyl group exerts highly efficient control over the stereoselectivity. These results prompted us to evaluate the behaviour of furanone **1** in cyclopropanation reactions with sulfonium ylides. The results obtained herein demonstrate the influence of substituents at the sulfonium centre on the stereochemical course of the reactions.

2. Results and discussion

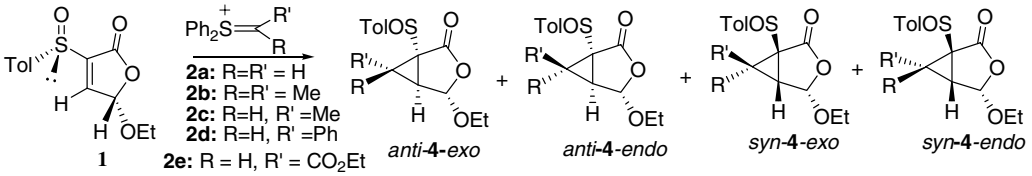
The synthesis of 5-ethoxy-3-*p*-tolylsulfinylfuranone **1** has previously been reported.[11] Diphenylsulfonium ylides, **2** (Ph_2S^+–C^-RR′), were obtained by treatment of the sulfonium tetrafluoroborates with different bases. Ylides **2a** (R = R′ = H) and **2c** (R = H, R′ = Me) were generated with LDA (Method A).[7] This same procedure can be used to prepare ylide **2d** (R = H, R′ = Ph), which can also be generated by using a stronger base such as *t*-BuLi (Method B).[7] Ylide **2b** (R = R′ = Me) was obtained with LHMDS (Method C) and the stabilized ylide **2e** (R = H, R′ = CO_2Et) with DBU (Method D).[13] The preparation of the dimethylsulfonium ylides **3** (Me_2S^+–C^-RR′), turned out to be more troublesome. Ylide **3a** (R = R′ = H) was prepared by reaction of the trimethylsulfonium iodide with NaH according to the previously reported procedure[6] or with LDA (Method A). Ylides **3b** (R = R′ = Me) and **3c** (R = H, R′ = Me) could not be prepared from their corresponding sulfonium salts and bases due to the problems connected with the relative acidity of the protons. A slightly more stabilized ylide **3d** (R = H, R′ = Ph) was obtained from $Me_2S^+CH_2PhBF_4^-$ with *t*-BuLi (Method B) whereas the most stable ylide **3e** (R = H, R′ = CO_2Et) was generated in the reaction of $Me_2S^+CH_2CO_2EtBr^-$ with DBU (Method D) or with a saturated K_2CO_3/NaOH 12.5 N solution (Method E).[14]

The results obtained in the reaction of sulfinyl furanone **1** with ylides **2a–e** are presented in Table 1. The reaction of **2a** with **1** in DME was complete in 5 min at −78 °C (entry 1) yielding *anti*-**4a** as the only diastereoisomer. This compound was isolated in 59% yield after chromatographic purification. Under identical conditions, **2b** and **1** also gave one product, *anti*-**4b**, which was obtained in 91% isolated yield (entry 2). These results clearly show that the reaction of furanone **1** with nonstabilized ylides occurs in a completely stereoselective way via addition of the sulfur nucleophile to the double bond from the opposite face to that occupied by the OEt group (*anti*-adducts).

The reaction of **2c** with **1** afforded a 77:23 mixture of two *anti*-adducts (*anti*-**4c**-*endo* and *anti*-**4c**-*exo*), which were easily separated and purified by chromatography (entry 3). These compounds differ in configuration at C-6, which is (*S*) for the adduct named as *exo* (H-5 and H-6 adopt a *trans* arrangement) and (*R*) for the *endo* one (H-5 and H-6 are in a *cis* arrangement).[15]

As expected, the reaction of **1** with **2d** (more stable than **2a–c**) required a longer reaction time, and occurs with

Table 1. Reactions of the diphenylsulfonium ylides **2** with the sulfinylfuranone **1**



Entry	Ylide **2**		Method[a]	Solvent	Time (min)	*T* (°C)	*anti*[b]		*syn*		*anti*:*syn*
	R′	R					*endo*	*exo*	*endo*	*exo*	
1	H	H	A	DME	5	−78	(59%)				100:0
2	Me	Me	C	DME	5	−78	(91%)				100:0
3	Me	H	A	DME	5	−78	77 (60%)	23 (17%)			100:0
4	Ph	H	A	DME	60	−78	41	56	—	3	97:3
5	Ph	H	B	THF	30	−78	45 (36%)	52 (35%)	—	3	97:3
6	Ph	H	B	DMF	60	−78	56	42	—	2	98:2
7	CO_2Et	H	D	THF	120	−40	80	10	—	10	90:10
8	CO_2Et	H	D	CH_2Cl_2	120	−40	91 (68%)	4	—	5	95:5
9	CO_2Et	H	D	CH_3CN	120	−40	87	11	—	2	98:2
10	CO_2Et	H	D	DMF	180	−40	92	6	—	2	98:2

[a] See text.
[b] Isolated yield in brackets.

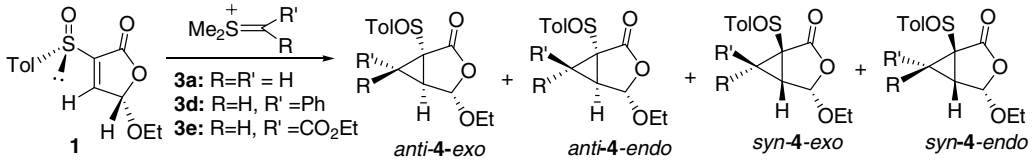
almost complete π-facial selectivity (*syn*-**4d**-*exo* adduct could be detected by NMR of the crude reaction product but the *anti*/*syn* ratio is higher than 97:3) (entries 4–6). The proportion of *anti*-**4d**-*endo* and *anti*-**4d**-*exo* is very similar and essentially independent of the solvent polarity. These compounds were readily separated by chromatography and unequivocally characterized. Finally, the reaction of **2e** with **1** was performed at −40 °C and required 2 h for completion. This reaction afforded a mixture of three products. The *anti*/*syn* and *endo*/*exo* ratios are both very high and increase with the solvent polarity (entries 7–10). The major adduct *anti*-**4e**-*endo* was isolated in 68% yield (entry 8).

The results obtained in the reactions of the dimethylsulfonium ylides **3a**, **3d** and **3e** with the furanone **1** are collected in Table 2. The reaction of **3a** with **1** did not yield the expected cyclopropanes, but caused decomposition of the substrate.[16] In the case of **3d**, the reaction mixture was also very complex but the formation of cyclopropanes could be detected by NMR. However, only the major one could be isolated in 25% yield and completely characterized. Only with **3e** was the reaction found to occur cleanly affording a mixture of three diastereoisomers (entries 3–5). The *syn*/*anti* ratio was 1:2 in CH_2Cl_2 (entry 3) but the facial selectivity increased with the solvent polarity (entries 4–5). By contrast, the *exo* stereoselectivity was very high in CH_2Cl_2 (entry 3) but decreased in more polar solvents (entries 4–5).

The configurational assignment of the obtained adducts was based on their ^{1}H NMR parameters, mainly on the vicinal proton–proton coupling constants. The *syn*- or *anti*-stereochemistry was established from the $J_{4,5}$ values (∼0 Hz for *anti*-adducts[17]). The *endo* or *exo* character can be deduced from the $J_{5,6}$ values, which are related to their *trans* or *cis* arrangement[7] (∼5 and ∼9 Hz, respectively). The ^{1}H NMR parameters of the isolated adducts are collected in Table 3. Compound *anti*-**4a**, with two protons at C-6, exhibited two different $J_{5,6}$ values (8.8 and 5.2 Hz) corresponding to their respective stereochemical arrangements with respect to the proton at C-5. The compounds with the *endo* stereochemistry will have the proton at C-6 in an *exo* arrangement and vice versa. Only one of the compounds depicted in Table 3 (*syn*-**4e**-*exo*) exhibits *syn* stereochemistry.[18]

In order to explain the stereochemical course of the reactions investigated, it is necessary to briefly summarize the results obtained. Thus, the reactions of

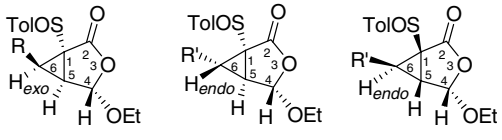
Table 2. Reactions of the dimethylsulfonium ylides **3** with the sulfinylfuranone **1**



Entry	Ylide		Method[a]	Solvent	Time (min)	T (°C)	*anti*[b]		*syn*[b]		*anti*:*syn*
	R′	R					*endo*	*exo*	*endo*	*exo*	
1	H	H	B								
2	Ph	H	B	THF	45	−78	23	77 (25%)	—	—	>90:<10
3	CO_2Et	H	D	CH_2Cl_2	120	−40	4	62 (50%)	—	34 (29%)	66:34
4	CO_2Et	H	E	CH_3CN	120	−40	13	74	—	13	87:13
5	CO_2Et	H	E	DMF	180	−40	20	72	—	8	92:8

[a] See text.
[b] Isolated yield in brackets.

Table 3. Significant ^{1}H NMR parameters for the configurational assignment of the adducts **4**



Compd	R	R′	H_4 (ppm)	H_5 (ppm)	H_{6exo} (ppm)	H_{6endo} (ppm)	$J_{4,5}$ (Hz)	$J_{5,6exo}$ (Hz)	$J_{5,6endo}$ (Hz)
anti-**4a**	H	H	5.26	2.80	1.81	1.17	0	8.8	5.2
anti-**4b**	Me	Me	5.16	2.62	—	—	0	—	—
anti-**4c**-*endo*	Me		5.18	2.77	2.15	—	0	9.1	—
anti-**4c**-*exo*		Me	5.25	2.63	—	1.82	0	—	5.1
anti-**4d**-*endo*	Ph		5.08	3.48	3.13	–	0	9.1	—
anti-**4d**-*exo*		Ph	5.41	3.32	–	3.02	0	—	5.5
anti-**4e**-*endo*	CO_2Et		5.56	3.00	2.92	—	0	9.1	—
anti-**4e**-*exo*		CO_2Et	5.58	3.30	—	2.48	0	—	4.7
syn-**4e**-*exo*	CO_2Et		5.65	3.52	2.78	—	4.0	—	4.5

diphenylsulfonium ylides **2a–e** with sulfinylfuranone **1** occur with very high or complete π-facial selectivity (the *anti* adducts with respect to the ethoxy group are predominant). It was substantially lower for the reactions of **1** with dimethylsulfonium ylide **3e**. An increase of the solvent polarity favoured the formation of the *anti* isomers, which were mainly observed in reactions with **3e**. The *endo*/*exo* selectivity is dependent on the sulfonium sulfur substituents as well as on the nature of the substituent R′ at the ylidic carbon. The *exo* compounds were predominant in both *syn* and *anti* approaches when **3e** was used as the ylide component. For diphenylsulfonium ylides, the *endo* adducts were the major ones for the *anti* approaches, with the *endo*/*exo* selectivity varying in the order **2e** > **2c** > **2d** (it was scarcely significant in the later case). The *exo* adduct was exclusively formed in the *syn* approach of **2e** to the furanone. In polar solvents, the proportion of the *endo* adducts becomes slightly higher in the *anti* approaches.

The *anti* selectivity observed in all these reactions can be best explained in terms of the repulsive steric effects exerted by the 5-ethoxy group of the furanone ring, determining the preferential approach of the attacking nucleophile from the opposite face. The steric hindrance exerted by the *p*-tolylsulfinyl group at C-3 is much less important in spite of the fact that in the most stable conformation of **1** the *p*-tolyl substitutent occupies the face from which the attack of ylide takes place. During the initial approach of the sulfur ylide **2**, the large pyramidal diphenyl sulfonium moiety would prefer to be directed away from the furanone ring to minimize steric interactions.[19] However, electrostatic attractions between the ethoxy oxygen and the positively charged sulfur could minimize the steric repulsion. This effect must be more important for dimethylsulfonium ylides (lower size and higher charge density at sulfur than in diphenylsulfonium analogues), thus resulting in the formation of a significant amount of the *syn*-**4e**-*exo* adduct (Fig. 1). In polar solvents it is produced in much smaller amounts.

Rationalization of the *endo*/*exo* selectivity is not easy. Based on the results obtained so far, it is reasonable to propose two different *anti* approaches, depicted in Figure 1, for reactions of **1** with **2e** and **3e**. By assuming the antiperiplanar arrangement of the sulfur function with respect to the C-3 of the furanone ring, the transition state, **TS-I**, yielding the *anti*-**4e**-*endo*, would be more favoured than **TS-II** due to the steric interactions of the CO_2Et and sulfinyl groups in the latter. These repulsive interactions will be more distinct in the less populated conformer of butenolide **1** with the *p*-tolyl group *syn*-coplanar with the endocyclic double bond. On the other hand, by assuming a *gauche* arrangement of the R_2S^+ with respect to C-3 and C-4 of the furanone ring, **TS-II**′, yielding the *anti*-**4e**-*exo* isomer, would be preferred for the same reasons. According to these criteria, the reaction of **1** with **2e** should mainly occur via **TS-I** (*anti*-**4e**-*endo* is obtained as the major isomer, entries 7–10, Table 1) whereas with **3e** through **TS-II**′ (it mainly yielded the *anti*-**4e**-*exo* isomer, entries 3–5, Table 2). Electrostatic interactions (maybe intramolecular hydrogen bonds) between the positively charged methyl group and the carbonyl oxygen could be responsible for the stabilization of **TS-II**′ for **3e**. The lower stereoselectivity observed in the more polar solvents supports this explanation. As these electrostatic interactions are not possible for **2e**, the steric effects are predominant and transition states such as **TS-I** are now favoured. A similar model could be used to explain the results obtained with **2c**. In the case of **2d**, the stabilization of **TS-II** as a consequence of the existence of π-stacking interactions between the aromatic rings (see Fig. 1), could be taken into account to explain the low *endo*/*exo* selectivity, determining the formation of a significant amount of *anti*-**4d**-*exo* (Table 1, entries 4–6).

3. Conclusion

In summary, we have observed that stereochemistry of the cyclopropanation of furanone **1** with sulfonium ylides is highly dependent on the substituents bonded to the ylidic sulfur atom. The stereochemistry of the 5-ethoxy group of the furanone **1** is the main factor controlling the facial selectivity, which is governed by steric and in some cases electrostatic interactions with the attacking ylide. In this sense, the charge density on the sulfur atom related to the substituents at sulfur, plays a significant role. The formation of the *endo* or *exo* adducts depends on the face of the ylide, which is attacked by the electrophiles and is completely dependent on the substituents at sulfur. Dimethylsulfonium derivatives yield mainly the *exo* adducts while with the diphenylsulfonium ylides the *endo* products predominate. Steric and electrostatic factors account for these results. The reaction of ylides **2** and **3** with acyclic sulfinyl acrylates and the derivatization of the resulting cyclopropanes are currently under study in our research groups.

4. Experimental

4.1. General

All moisture sensitive reactions were performed in flame-dried glasswares equipped with rubber septa under positive pressure of argon. THF was distilled from sodium-benzophenone under argon and CH_2Cl_2 over P_2O_5. Silica gel 60 (230–400 mesh ASTM) and DC-Alufolien 60 F_{254} were used for flash column chromatography and analytical TLC, respectively. Melting points were determined in 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 photopolarimeter (concentration in g/100 mL). NMR spectra were determined in a $CDCl_3$ solutions at 300 and 75 MHz for ^1H and ^{13}C NMR, respectively; chemical shifts (δ) are reported in ppm and J values given in hertz. The IR spectra frequencies are given in cm^{-1}.

4.2. (1*S*,4*S*,5*R*,S_S)-4-Ethoxy-1-[(4-methylphenyl)sulfinyl]-3-oxabicyclo[3.1.0]hexan-2-one *anti*-4a

This was obtained as the only compound following Method A[7] from diphenylmethylsulfonium tetrafluoro-

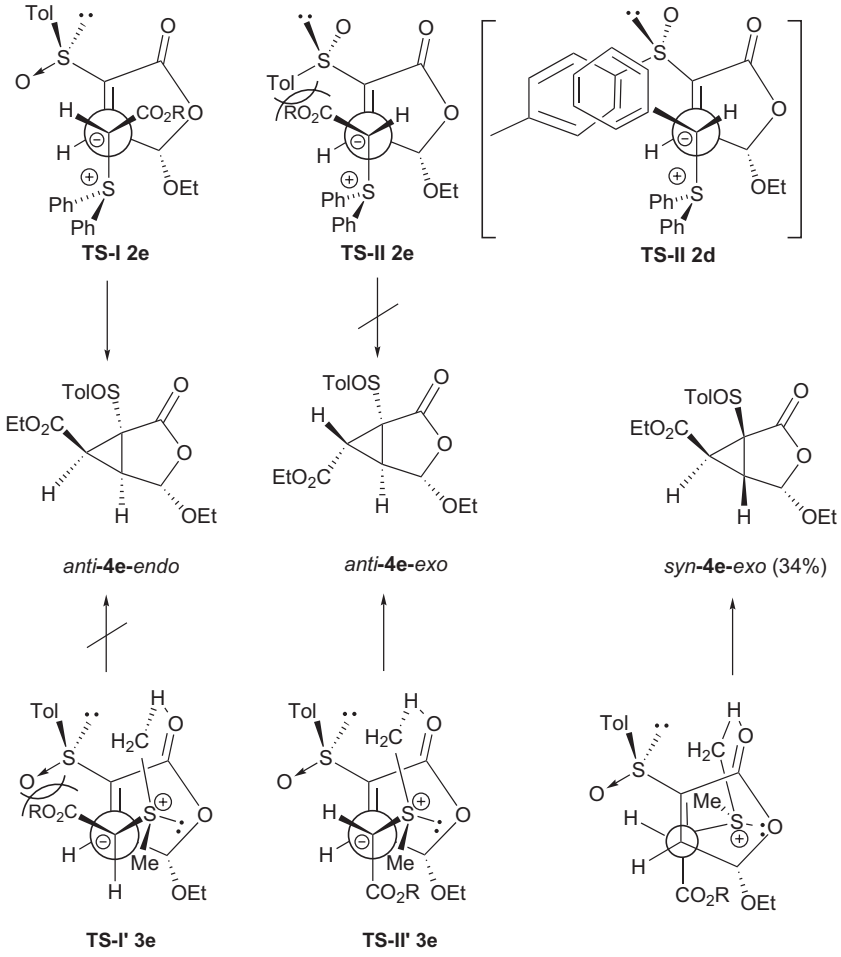


Figure 1. Possible transition states for the first step of the cyclopropanation.

borate and was purified by column chromatography (ethyl acetate–hexane, 1:3) and subsequent precipitation in hexane. Yield 59%, white solid, mp = 63–64 °C. $[\alpha]_D$ = +310.1 (*c* 0.25, $CHCl_3$). IR (KBr): 1756, 1344, 1081. ^{1}H RMN δ 7.69 and 7.33 (AA′BB′ system, 4H), 5.26 (s, 1H, H_4), 3.91 (dq, *J* = 7.1 and 9.4, 1H, CH_2), 3.64 (dq, *J* = 7.1 and 9.4, 1H, CH_2), 2.80 (dd, *J* = 5.2 and 8.8, 1H, H_5), 2.41 (s, 3H, CH_3 *p*-tol), 1.81 (dd, *J* = 5.4 and 8.8, 1H, H_{6exo}), 1.26 (t, *J* = 7.1, 3H, CH_3), 1.17 (dd, *J* = 5.2 and 5.4, 1H, H_{6endo}); ^{13}C NMR δ 169.7 (CO), 142.3 and 138.7 (C arom), 129.8 and 124.8 (CH arom), 101.6 (C_4), 65.3 (CH_2), 44.5 (C_1), 30.3 (C_5), 21.4 (CH_3 *p*-tol), 14.8 (CH_3), 12.8 (C_6); Anal. Calcd for $C_{14}H_{16}O_4S$: C, 59.98; H, 5.75; S, 11.44. Found: C, 60.08; H, 5.93; N, 0.06; S, 11.02.

4.3. (1*R*,4*S*,5*S*,S_S)-4-Ethoxy-6,6-dimethyl-1-[(4-methylphenyl)sulfinyl]-3-oxabicyclo[3.1.0]hexan-2-one *anti*-4b

Method C. A solution 1 M LHMDS in THF (0.75 mmol) was added dropwise to a suspension of diphenylisopropylsulfonium tetrafluoroborate[20] (0.75 mmol) in freshly distilled DME (9 mL) at −78 °C. After 30 min, vinyl sulfoxide **1** (0.5 mmol) was added as a solution in DME (6.7 mL). After 5 min the reaction was quenched with saturated aqueous NH_4Cl and allowed to warm to room temperature. The aqueous layer was separated and extracted with CH_2Cl_2. The combined organic fractions were dried over Na_2SO_4 and concentrated. Purification by column chromatography (ethyl acetate–hexane, 1:3) gave the cyclopropane *anti*-**4b** in 91% yield. White solid, mp = 136–137 °C (CH_2Cl_2–hexane). $[\alpha]_D$ = +114.6 (*c* 0.25, $CHCl_3$). IR (KBr): 1770, 1594, 1493, 1330, 1057. ^{1}H NMR δ 7.67 and 7.30 (AA′BB′ system, 4H), 5.16 (s, 1H, H_4), 3.78 (dq, *J* = 7.1 and 9.3, 1H, CH_2), 3.56 (dq, *J* = 7.1 and 9.3, 1H, CH_2), 2.62 (s, 1H, H_5), 2.41 (s, 3H, CH_3 *p*-tol), 1.45 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.19 (t, *J* = 7.1, 3H, CH_3); ^{13}C NMR δ 168.4 (CO), 141.2 and 138.3 (C arom), 129.6 and 124.6 (CH arom), 99.8 (C_4), 65.0 (CH_2), 53.8 (C_1), 40.7 (C_5), 33.3 (C_6), 21.4 (CH_3 *p*-tol), 20.6 (CH_3), 17.2 (CH_3), 14.9 (CH_3); Anal. Calcd for $C_{16}H_{20}O_4S$: C, 62.31; H, 6.54; S, 10.40. Found: C, 62.10; H, 6.62; N, 0.05; S, 10.85.

4.4. (1*S*,4*S*,5*S*,6*R*,S_S)-4-Ethoxy-6-methyl-1-[(4-methylphenyl)sulfinyl]-3-oxabicyco[3.1.0]hexan-2-one *anti*-4c-*endo*

This was obtained as the major compound (77%) following Method A[7] from diphenylethylsulfonium tetrafluoroborate.[21] It was purified by column chromatography (ethyl acetate–hexane, 1:3) and subsequent precipitation

in hexane. Yield 60%, white solid, mp = 108–109 °C. $[\alpha]_D$ = +231.0 (*c* 0.5, acetone). IR (KBr): 1768, 1349, 1123, 1091, 1051. ^{1}H NMR δ 7.68 and 7.32 (AA′BB′ system, 4H), 5.18 (s, 1H, H_4), 3.92 (dq, J = 7.1 and 9.3, 1H, CH_2), 3.64 (dq, J = 7.1 and 9.3, 1H, CH_2), 2.77 (d, J = 9.1, 1H, H_5), 2.41 (s, 3H, CH_3 *p*-tol), 2.15 (dq, J = 6.7 and 9.1, 1H, H_{6exo}), 1.27 (t, J = 7.1, 3H, CH_3), 1.01 (d, J = 6.7, 3H, CH_3); ^{13}C NMR δ 168.6 (CO), 142.1 and 138.9 (C arom), 129.8 and 124.7 (CH arom), 99.9 (C_4), 65.4 (CH_2), 49.7 (C_1), 34.9 (C_5), 21.4 (CH_3 *p*-tol), 19.2 (C_6), 14.9 (CH_3), 7.8 (CH_3); Anal. Calcd for $C_{15}H_{18}O_4S$: C, 61.20; H, 6.16; S, 10.89. Found: C, 61.15; H, 6.08; N, 0.01; S, 11.29.

4.5. (1*S*,4*S*,5*S*,6*S*,S_S)-4-Ethoxy-6-methyl-1-[(4-methylphenyl)sulfinyl]-3-oxabicyclo[3.1.0]hexan-2-one *anti*-4c-*exo*

This was obtained as the minor compound (23%) following the same procedure as for *anti*-**4c**-*endo*. It was purified by column chromatography (ethyl acetate–hexane, 1:3). Yield 17%, white solid, mp = 74–76 °C (ethyl ether–hexane). $[\alpha]_D$ = +137.7 (*c* 0.2, acetone). IR (KBr): 1770, 1339, 1088, 1059, 1040. ^{1}H NMR δ 7.71 and 7.30 (AA′BB′ system, 4H), 5.25 (s, 1H, H_4), 3.77 (dq, J = 7.0 and 9.3, 1H, CH_2), 3.55 (dq, J = 7.0 and 9.3, 1H, CH_2), 2.63 (d, J = 5.1, 1H, H_5), 2.40 (s, 3H, CH_3 *p*-tol), 1.82 (dq, J = 5.1 and 6.3, 1H, H_{6endo}), 1.40 (d, J = 6.3, 3H, CH_3), 1.17 (t, J = 7.0, 3H, CH_3); ^{13}C NMR δ 169.5 (CO), 141.3 and 137.9 (C arom), 129.6 and 124.7 (CH arom), 101.0 (C_4), 64.9 (CH_2), 47.9 (C_1), 35.8 and 28.1 (C_5 and C_6), 21.4 (CH_3 *p*-tol), 14.8 (CH_3), 11.4 (CH_3); Anal. Calcd for $C_{15}H_{18}O_4S$: C, 61.20; H, 6.16; S, 10.89. Found: C, 60.95; H, 6.40; N, 0.01; S, 10.55.

4.6. (1*S*,4*S*,5*S*,6*R*,S_S)-4-Ethoxy-1-[(4-methylphenyl)sulfinyl]-6-methyl-3-oxabicyclo[3.1.0]hexan-2-one *anti*-4d-*endo*

This was obtained following Method B[11] from diphenylbenzylsulfonium tetrafluoroborate.[22] It was purified by column chromatography (ethyl acetate–hexane, 1:4). Yield 36%. White solid, mp = 111–112 °C (ethyl acetate–hexane). $[\alpha]_D$ = −37.7 (*c* 0.25, $CHCl_3$). IR (KBr): 1778, 1594, 1489, 1450, 1337, 1112, 1049. ^{1}H NMR δ 7.84 and 7.38 (AA′BB′ system, 4H), 7.19 (m, 3H, Ph), 6.76 (m, 2H, Ph), 5.08 (s, 1H, H_4), 3.82 (m, 1H, CH_2), 3.56 (m, 1H, CH_2), 3.48 (d, J = 9.1, 1H, H_5), 3.13 (d, J = 9.1, 1H, H_6), 2.44 (s, 3H, CH_3 *p*-tol), 1.25 (t, J = 7.1, 3H, CH_3); ^{13}C NMR δ 168.6 (CO), 142.6, 139.2 and 130.4 (C arom), 130.0, 129.0, 128.7, 128.1 and 124.8 (CH arom), 99.8 (C_4), 65.5 (CH_2), 50.9 (C_1), 35.7 and 27.2 (C_5 and C_6), 21.6 (CH_3 *p*-tol), 14.9 (CH_3); Anal. Calcd for $C_{20}H_{20}O_4S$: C, 67.39; H, 5.66; S, 9.00. Found: C, 66.96; H, 5.73; N, 0.09; S, 9.60.

4.7. (1*S*,4*S*,5*R*,6*S*,S_S)-4-Ethoxy-1-[(4-methylphenyl)sulfinyl]-6-methyl-3-oxabicyclo[3.1.0]hexan-2-one *anti*-4d-*exo*

This was obtained following Method B[11] from diphenylbenzylsulfonium tetrafluoroborate or dimethylbenzylsulfonium tetrafluoroborate.[23] It was purified by column chromatography (ethyl acetate–hexane, 1:2). Yield 35% and 25%, respectively. White solid, mp = 104–106 °C (hexane). $[\alpha]_D$ = +117.2 (*c* 0.25, $CHCl_3$). IR (KBr): 1771, 1493, 1341, 1160, 1088, 1063. ^{1}H NMR δ 7.47 and 7.19 (AA′BB′ system, 4H), 7.32 (m, 5H, Ph), 5.41 (s, 1H, H_4), 3.79 (m, 1H, CH_2), 3.60 (m, 1H, CH_2), 3.32 (d, J = 5.5, 1H, H_5), 3.02 (d, J = 5.5, 1H, H_6), 2.37 (s, 3H, CH_3 *p*-tol), 1.18 (t, J = 7.0, 3H, CH_3); ^{13}C NMR δ 168.6 (CO), 141.4, 137.4 and 135.2 (C arom), 129.6, 129.3, 128.6, 128.5 and 124.5 (CH arom), 100.8 (C_4), 65.0 (CH_2), 49.6 (C_1), 36.1 and 32.9 (C_5 and C_6), 21.3 (CH_3 *p*-tol), 14.9 (CH_3); Anal. Calcd for $C_{20}H_{20}O_4S$: C, 67.39; H, 5.66; S, 9.00. Found: C, 66.95; H, 5.79; N, 0.09; S, 8.66.

4.8. Method D.[13] General procedure

A mixture of the corresponding salt (1 mmol) and vinyl sulfoxide **1** (0.5 mmol) in the solvent indicated in Table 1 or 2 (13 mL) was cooled at −40 °C. DBU (1 mmol) was added and the reaction stirred at this temperature for 2 h. A saturated solution of NH_4Cl was added, and allowed to warm to room temperature. The aqueous layer was separated and extracted with CH_2Cl_2. The combined organic fractions were dried over Na_2SO_4 and concentrated. The ratios of the products obtained are indicated in Table 1 or 2. Purification and yields are given in each case.

4.9. Method E[14]

A solution of vinyl sulfoxide **1** (0.3 mmol) in the solvent indicated in Table 2 (3 mL) was added to ethyl (dimethylsufuranylidene)acetate[14] (0.75 mmol) as a solution in the same solvent (4.3 mL) and then reaction mixture stirred for 2 h at −40 °C. Saturated aqueous NH_4Cl was added and allowed to warm to room temperature. The aqueous layer was separated and extracted with CH_2Cl_2. The combined organic fractions were dried over Na_2SO_4 and concentrated. The ratios of the products obtained are indicated in Table 2. Purification and yields are given in each case.

4.10. Ethyl (1*R*,4*S*,5*R*,6*S*,S_S)-4-ethoxy-1-[(4-methylphenyl)sulfinyl]-2-oxo-3-oxabicyclo[3.1.0]hexan-6-carboxylate *anti*-4e-*endo*

This was obtained as the major compound following Method D from (carbethoxymethyl)diphenylsulfonium tetrafluoroborate[3b] and purified by column chromatography (ethyl acetate–hexane, 1:3). Colourless oil, yield 68%. $[\alpha]_D$ = +80.1 (*c* 0.85, acetone). IR (film): 1774, 1737, 1597,1447, 1119, 1056. ^{1}H NMR δ 7.74 and 7.34 (AA′BB′ system, 4H), 5.56 (s, 1H, H_4), 3.98 (m, 3H), 3.68 (dq, J = 7.0 and 9.2, 1H, CH_2), 3.00 (d, J = 9.1, 1H, H_5), 2.92 (d, J = 9.1, 1H, H_6), 2.42 (s, 3H, CH_3 *p*-tol), 1.28 (t, J = 7.0, 3H, CH_3), 1.08 (t, J = 7.0, 3H, CH_3); ^{13}C NMR δ 166.7 and 165.7 (CO), 138.1 and 135.2 (C arom), 129.8 and 125.1 (CH arom), 99.8 (C_4), 65.9 and 62.0 (CH_2), 50.5 (C_1), 35.9 and 24.2 (C_5 and C_6), 21.5 (CH_3 *p*-tol), 14.9 and 13.7 (CH_3); Anal. Calcd for $C_{17}H_{20}O_6S$: C, 57.94; H, 5.72; S, 9.10. Found: C, 58.23; H, 5.85; N, 0.01; S, 8.86.

4.11. Ethyl (1*R*,4*S*,5*R*,6*R*,S_S)-4-ethoxy-1-[(4-methylphenyl)sulfinyl]-2-oxo-3-oxabicyclo[3.1.0]hexan-6-carboxylate *anti*-4e-*exo*

This was obtained as the major compound following Method D from (carbethoxymethyl)dimethylsulfonium bromide[14] or Method E. The product was purified by column chromatography (ethyl acetate–hexane, 1:3). Yield 50%. Colourless oil, $[\alpha]_D = +139.6$ (*c* 0.25, acetone). IR (film): 1775, 1729, 1354, 1300, 1200, 1087. ^{1}H NMR δ 7.64 and 7.32 (AA′BB′ system, 4H), 5.28 (s, 1H, H_4), 4.28 (m, 2H, CH_2), 3.70 (dq, $J = 7.0$ and 9.1, 1H, CH_2), 3.55 (dq, $J = 7.0$ and 9.1, 1H, CH_2), 3.30 (d, $J = 4.7$, 1H, H_5), 2.48 (d, $J = 4.7$, 1H, H_6), 2.40 (s, 3H, CH_3 *p*-tol), 1.32 (t, $J = 7.0$, 3H, CH_3), 1.14 (t, $J = 7.0$, 3H, CH_3); ^{13}C NMR δ 166.4 and 165.3 (CO), 141.7 and 137.2 (C arom), 129.6 and 124.8 (CH arom), 99.8 (C_4), 65.3 and 62.8 (CH_2), 48.4 (C_1), 34.4 and 30.2 (C_5 and C_6), 21.4 (CH_3 *p*-tol), 14.8 and 13.9 (CH_3).

4.12. Ethyl (1*S*,4*S*,5*R*,6*S*,S_S)-4-ethoxy-1-[(4-methylphenyl)sulfinyl]-2-oxo-3-oxabicyclo[3.1.0]hexan-6-carboxylate *syn*-4e-*exo*

This was obtained following Method E using dichloromethane as solvent and purified by column chromatography (ethyl acetate–hexane, 1:3). Yield 29%. Colourless oil, $[\alpha]_D = +507.8$ (*c* 0.95, $CHCl_3$). IR (film): 1783, 1734, 1167, 1057. ^{1}H NMR δ 7.62 and 7.33 (AA′BB′ system, 4H), 5.65 (d, $J = 4.0$, 1H, H_4), 4.26 (m, 2H, CH_2), 3.81 (dq, $J = 7.3$ and 9.7, 1H, CH_2), 3.67 (dq, $J = 7.3$ and 9.7, 1H, CH_2), 3.52 (dd, $J = 4.0$ and 4.5, 1H, H_5), 2.78 (d, $J = 4.5$, 1H, H_6), 2.42 (s, 3H, CH_3 *p*-tol), 1.32 (t, $J = 7.3$, 3H, CH_3), 1.21 (t, $J = 7.3$, 3H, CH_3); ^{13}C NMR δ 165.4 and 165.0 (CO), 142.5 and 137.5 (C arom), 129.8 and 125.3 (CH arom), 100.1 (C_4), 67.1 and 62.5 (CH_2), 51.1 (C_1), 31.7 and 29.6 (C_5 and C_6), 21.5 (CH_3 *p*-tol), 14.9 and 14.1 (CH_3); Anal. Calcd for $C_{17}H_{20}O_6S$: C, 57.94; H, 5.72; S, 9.10. Found: C, 57.92; H, 5.77; N, 0.04; S, 8.59.

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