Ring-Opening Reactions of Cyclopropanes. Part 6.[1] A Facile Synthesis of Dialkyl Sulfenylbutanedioates

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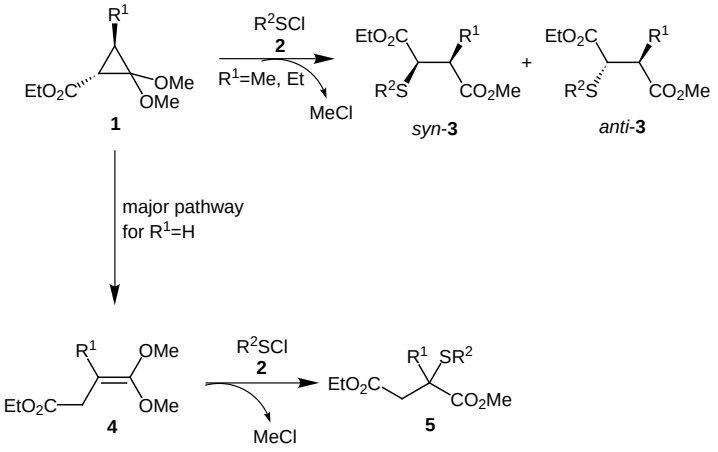
Abstract: The reaction of cyclopropanes **1** with sulfenyl chlorides **2** readily affords 2-sulfenylbutanedioates **3** and/or their 3-sulfenyl analogues **5**, which are compounds of applicative and biological interest.

Key words: cyclopropanes, sulfenyl chlorides, sulfenylbutanedioates, electrophilic bimolecular substitution, selectivity

α-Sulfenylated esters have received considerable attention because the flexibility of sulfur on a carbon adjacent to a carbonyl group allows great diversity in structural modification and elaboration.[2] Among these compounds, sulfenylbutanedioates such as arylthio,[3] phosphonomethylthio[4] and carboxyalkylthio-derivatives[5] have particular applicative and biological interest as they are used as bactericides,[3e] enzyme inhibitors,[4] corrosion inhibitors[5a,b] and components of detergent mixtures[5c] or as intermediates for agrochemicals[3d,f] and bioproducts.[3c] Some of them have been identified by mass spectrometry in the degradation products of widely used pesticides.[6]

The most general method for the synthesis of sulfenylbutanedioates is the addition of thiols to maleates.[3b,3c,4] Here we report the synthesis of dialkyl sulfenylbutanedioates by reaction of sulfenyl chlorides **2** with ethyl 2,2-dimethoxycyclopropanecarboxylates **1** (Scheme 1). The choice of these acceptor–donor substituted cyclopropanes was made by considering their facile regioselective ring opening at the C1–C2 bond by various electrophiles which leads to interesting hetero- and carbocycles.[7] Sometimes, this reaction competes with thermal rearrangement into 1,1-dimethoxyalkenes **4**.[7a,8] The investigation also proved interesting since a survey of the relevant literature on the reaction between sulfenyl halides and cyclopropanes highlighted a paucity of data on the ring cleavage by these electrophilic reagents. In fact, the reaction with alkyl- or aryl-substituted cyclopropanes is generally quite sluggish;[9] it occurs with various methyl 2-(trimethylsiloxy)cyclopropanecarboxylates,[10a] vinylcyclopropanes[10b] or alkylidenecyclopropanes[10c] in the presence of a Lewis acid or in acidic media. Only cy-



1	R^1	**2**	R^2	**3**	R^1	R^2	**5**	R^1	R^2
a	H	**a**	Ph	**a**	Me	Ph	**a**	H	Ph
b	Me	**b**	4-$NO_2C_6H_4$	**b**	Me	4-$NO_2C_6H_4$	**b**	H	4-$NO_2C_6H_4$
c	Et	**c**	Me	**c**	Me	Me	**c**	H	Me
		d	CO_2Me	**d**	Me	CO_2Me	**d**	H	CO_2Me
				e	Et	Ph	**e**	Me	Ph
				f	Et	4-$NO_2C_6H_4$	**f**	Me	4-$NO_2C_6H_4$
				g	Et	Me	**g**	Me	Me
				h	Et	CO_2Me	**h**	Me	CO_2Me

Scheme 1

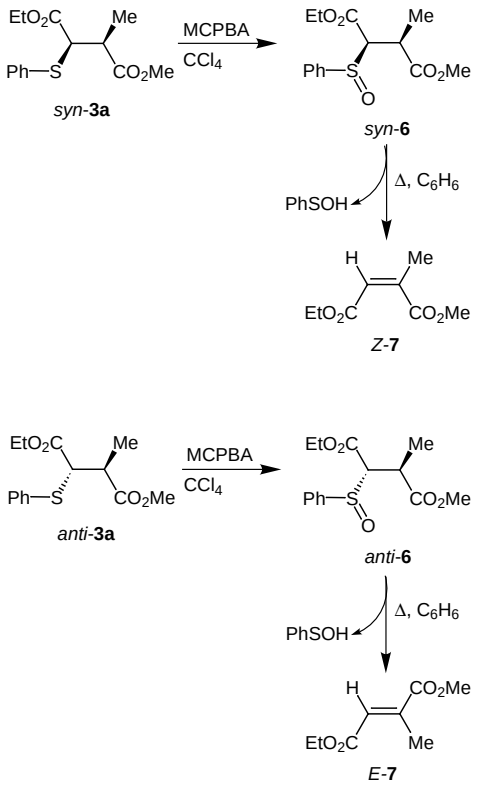
clopropane rings that form part of highly strained molecular framework, such as quadricyclene, undergo uncatalyzed arenesulfenylation.[11]

The reaction of **1a–c** with equimolecular amounts of **2a–d** was performed under strictly anhydrous conditions[12] in carbon tetrachloride at the reaction temperatures and for the times reported in Table 1. 1-Ethyl 4-methyl *syn*-2-sulfenylbutanedioates **3** were obtained in addition to small amounts of their *anti*-isomers starting from *trans*-cyclopropanes **1b**,**c**; for **1b** 3-sulfenyl analogues **5** were also formed and these were the only reaction products starting from 3-unsubstituted **1a**.[15] Control experiments showed that compounds **5** were formed by the sulfenylation of alkenes **4a,b** that derive from the isomerization of **1a,b** (Scheme 1).[15]

As shown in Table 1, the reaction times depend on both reagents; they increase from **1a** to **1c** and by decreasing electrophilicity of **2** from methanesulfenyl chloride (**2c**) up to acyl derivative **2d**. However, the formation of **3** and/or **5** depends only on the starting cyclopropane; thus, **1a** leads to 3-sulfenylbutanedioates **5a–d** via **4a**, **1b** to both 2-sulfenyl- and 3-sulfenyl derivatives **3a–d** and **5e–h** and, finally, **1c** only to **3e–h**. This trend is evidently linked to the tendency of **1** to isomerize into **4**, which is **1a**>**1b**>**1c** and, hence, for **1a**,**b** the isomerization competes with the addition of the sulfenyl chloride to the cyclopropane ring.[16] Reasoning that the isomerization might be favored by the presence of trace amounts of HCl deriving from easily hydrolyzable sulfenyl chloride **2**,[14] we attempted to optimize the reaction, when using **1a**,**b**, by adding pyridine.[17] This expedient proved to be effective for **1b**, leading only to **3** with a similar diastereomeric ratio as is found in the absence of base; for **1a** it was unsuccessful, and the only effect we observed was an increase of the reaction times, showing that the isomerization rate was higher than that of the reaction with **2**.

All of the products were separated and purified by column chromatography followed by HPLC. The structures were assigned on the basis of the analytical and spectroscopic data and, for **5a–d**, they were confirmed by comparing the spectral data with those of authentic samples, which were prepared by the sulfenylation of the alkene **4a** with **2a–d**. The configuration of *syn*- and *anti*-**3** was determined on the basis of the vicinal coupling constants.[18] Confirmation of stereochemistry was performed chemically by stereoselectively obtaining the known[20] alkenes *Z*-**7** and *E*-**7** via the oxidation[21] of *syn*-**3a** and *anti*-**3a** followed by the thermal decomposition of the related sulfoxides *syn*-**6** and *anti*-**6**, respectively (Scheme 2).[22]

The high *syn* diastereoselectivity observed for **3** can be interpreted in terms of a S_E2-type attack at the corner of *trans*-**1b**,**c** which, with inversion of configuration at C1, affords *syn*-**3** via the unstable[23] chloride *syn*-**8**; only to a lesser extent does the edge attack occur, and this leads, with retention at the same carbon, to *anti*-**3** via the corresponding *anti*-**8** (Scheme 3).[24]

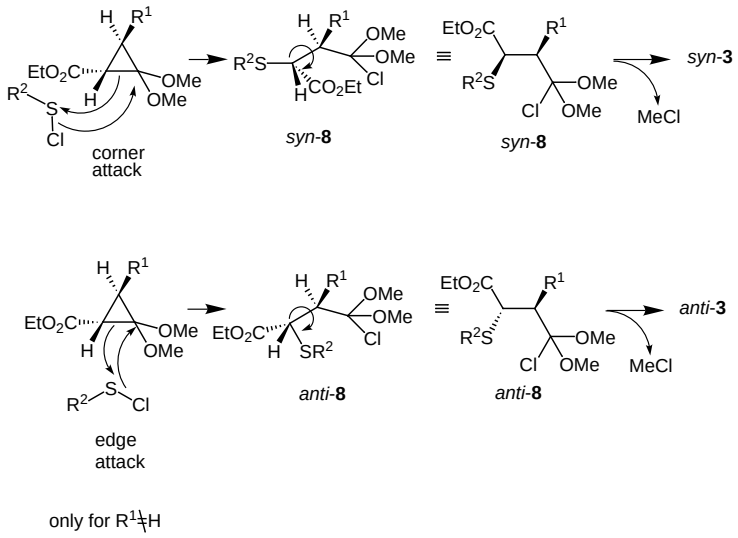


Scheme 2

All attempts to extend the reaction to C3 disubstituted cyclopropanes **1** failed, even in the presence of a Lewis acid.[27]

In conclusion, we report here a facile synthetic method for dialkyl sulfenylbutanedioates **3** and/or **5**, unsubstituted or alkyl-substituted on the carbon bearing the sulfenyl group or on the adjacent one. Formation of **3** occurs regio- and stereoselectively via electrophilic ring opening of **1** while **5** result from the sulfenylation of the alkenes **4** formed by isomerization of the cyclopropane **1**. The reaction can be performed using various sulfenyl chlorides and product distribution depends on the reaction conditions and/or the substitution at C3 of cyclopropane **1**.

IR spectra were recorded on a Perkin Elmer 1760/X-FT spectrophotometer using $CHCl_3$ as solvent. ^1H and ^{13}C NMR spectra were recorded with a Varian Gemini-200HC spectrometer using $CDCl_3$ as solvent and TMS as internal standard. *J* Values are given in Hz. DEPT techniques were employed to determine the multiplicity in the ^{13}C NMR spectra and gated decoupling methods to obtain quantitative noise-decoupled spectra. Elemental analyses were performed using a Carlo Erba EA 1108-Elemental analyzer. HPLC was performed on a Shimadzu LC-9A instrument equipped with a LCA-Shimadzu UV detector using a Merck Lichrosorb Si-60 (10 μm) column and *t*-BuOMe/hexane (3:17) as eluent with 3 mL/min flow rate of elution unless otherwise stated. CCl_4, CH_2Cl_2, pyridine and C_6H_6 (benzene) used in the reactions were anhydrous. Silica gel [0.063–0.20 mm (Macherey–Nagel)] and light petroleum (bp 40–60 °C) were used for column chromatography. Cyclopropanes **1a,b**,[8]**1c,**[13] alkenes **4a,b**[8] and sulfenyl chloride **2a**[28] were prepared according to literature methods. **2c**[29] was prepared in CCl_4 or CH_2Cl_2 depending on the reaction solvent to be used. Products **2b**,



Scheme 3

2d, *m*-chloroperoxybenzoic acid (MCPBA) and $TiCl_4$ were purchased from Fluka.

Sulfenylation of Cyclopropanes 1; General Procedure

An equimolecular amount of **2a–d** was added to a 0.2 mol/L solution of **1a–c** (1 mmol) in dry CCl_4 and the resulting mixture was kept under strictly anhydrous conditions at the temperature reported in Table 1 until complete conversion of cyclopropane **1** (^{1}H NMR). Then, the solvent was removed under reduced pressure and the residue chromatographed on silica gel. For the residues obtained starting from cyclopropane **1a**, elution with light petroleum/Et_2O (9:1) gave the esters **5a–d**. For the residues obtained starting from cyclopropane **1c**, elution as above led to a mixture of *syn*- and *anti*-**3e–h**, which were separated by HPLC.[30] For the residues obtained in the reaction of cyclopropane **1b** with **2a**,**d**, elution as above gave subsequent fractions containing the esters **5e**,**h** and a mixture of **5e**,**h** and *syn*- and *anti*-**3a**,**d**.[30] Each compound was separated and purified by HPLC except for *anti*-**3d**, which was obtained in mixture with its isomer in ca. 9:1 molar ratio (^{1}H NMR). The work-up as above of the residue derived from **1b** and **2b** afforded only **5f** and *syn*-**3b**; that of **1b** with **2c** led to ester **5g**.

The yield of each compound is reported in Table 1 and the spectral and analytical data are listed in Tables 2 and 3.

Sulfenylation of 4a with 2a–d

The reactions were carried out as above at the temperatures and times reported for **1a** (Table 1). Then, the solvent was removed and chromatography of the residues on silica gel (light petroleum/Et_2O 9:1) led to the esters **5a–d** in similar yields as those starting from **1a**.

Sulfenylation of 4b with 2c

The reaction was carried out at –20 °C for 15 min as above for **1b**. Then, the solvent was removed and chromatography of the residue on silica gel (light petroleum/Et_2O 9:1) followed by HPLC led to the ester **5g** (70%).

Sulfenylation of Cyclopropanes 1 in the Presence of Pyridine

The reaction of **1a** with **2a** was carried out at r.t. as above using **2a**/pyridine in a 1:1.2 molar ratio and dry CH_2Cl_2 as solvent. After completion of the reaction (^{1}H NMR), the solution was washed with H_2O, dried (Na_2SO_4) and evaporated. Chromatography of the residue (light petroleum/ Et_2O 9:1) gave the ester **5a**.

Table 1 Reaction of Cyclopropanes **1a–c** with Sulfenyl Chlorides **2a–d**

Cyclo-propane	Sulfenyl Chloride	Conditions[a] Temp/Time	Product Distribution (%)[b]	
			3 (*syn*/*anti*)	**5**
1a	**2a**	–20 °C/30 min	–	**a** 80
1a	**2b**	r.t./ 2 d	–	**b** 65
1a	**2c**	–20 °C/5 min	–	**c** 70
1a	**2d**	r.t./3 d	–	**d** 60
1b	**2a**	r.t./2 h	**a** 10 (85:15)	**e** 55
1b	**2b**	r.t./2 d	**b** 10 (100:0)	**f** 60
1b	**2c**	–20 °C/5 min	-	**g** 10[c]
1b	**2d**	r.t./7 d	**d** 22 (90:10)	**h** 40
1c	**2a**	r.t./2 d	**e** 60 (85:15)	–
1c	**2b**	r.t./7 d	**f** 50 (85:15)	–
1c	**2c**	–20 °C/15 min	**g** 10 (90:10)	–
1c	**2d**	r.t./16 d	**h** 55 (85 :15)	–
1a	**2a**/py[d]	r.t./12 h	–	**a** 70
1b	**2a**/py[d]	r.t./24 h	**a** 75 (90:10)	–
1b	**2b**/py[d]	r.t./8 d	**b** 30 (100:0)	–
1b	**2c**/py[e]	–20 °C/10 min	**c** 30 (100:0)	–
1b	**2d**/py[d]	r.t./15 d	**d** 65 (90:10)	–
1c	**2c**/py[e]	–20 °C/30 min	**g** 50 (90:10)	–

[a] Equimolecular amounts of **1** and **2**; solution of **1** in CCl_4 (0.2 mol/L).
[b] Yields and isomeric ratios were evaluated by chromatography.
[c] To obtain **5g** in higher yield (70%) it is convenient to carry out the methanesulfenylation on the alkene **4b**.
[d] **1**/**2**/py 1:1:1.2; solution of **1** in CH_2Cl_2 (0.2 mol/L).
[e] **1**/**2c**/py 1:1:3; solution of **1** in CH_2Cl_2 (0.2 mol/L).

The reactions of **1b** with **2a**,**b**,**d** were carried out as for **1a** and were similarly worked up. For **2a**,**d** chromatography of the residues, eluting as above, gave subsequent fractions containing *syn*-**3a**,**d** and a mixture of *syn*- and *anti*-**3a**,**d**; each compound was separated and purified by HPLC. For **2b**, the work-up as above gave only the *syn*-**3b**.

The reactions of **1b**,**c** with **2c** were carried out at –20 °C as for **1a** using **2c**/pyridine in a 1:3 molar ratio and were similarly worked up. For **1b** chromatography of the residue as above, followed by HPLC, gave *syn*-**3c**.[30] Chromatography of the residue obtained starting

Table 2 1-Ethyl 4-Methyl 2-Sulfenylbutanedioates (**3**) Prepared

Product[a]	IR ($CHCl_3$) ν (cm^{-1})	t_R (min)	^1H NMR ($CDCl_3$) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$) δ
syn-**3a**	1735	10.4	1.18 (t, *J* = 7.3, 3H, OCH_2CH_3), 1.44 (d, *J* = 7.3, 3H, CH_3), 2.88 (dq, *J* = 10.3, 7.3, 1H, $CHCH_3$), 3.64 (s, 3H, OCH_3), 3.75 (d, *J* = 10.3, 1H, CHS), 4.11 (q, *J* = 7.3, 2H, OCH_2), 7.20–7.55 (m, 5H, ArH)	13.8 (q, CH_2CH_3), 15.2 (q, CH_3), 40.6 (d, $CHCH_3$), 51.9 (q, OCH_3), 53.2 (d, CHS), 61.1 (t, OCH_2), 128.4, 128.9 and 133.6 (3d, CH of Ar), 132.3 (s, C1 of Ar), 171.2 and 174.8 (2s, 2 × CO_2)
anti-**3a**	1735	8.2	1.20 (t, *J* = 7.0, 3H, OCH_2CH_3), 1.26 (d, *J* = 6.7, 3H, CH_3), 2.98 (dq, *J* = 9.8, 6.7, 1H, $CHCH_3$), 3.74 (s, 3H, OCH_3), 3.87 (d, *J* = 9.8, 1H, CHS), 4.14 (q, *J* = 7.0, 2H, OCH_2), 7.25–7.55 (m, 5H, ArH)	14.0 (q, CH_2CH_3), 15.6 (q, CH_3), 42.1 (d, $CHCH_3$), 52.0 (q, OCH_3), 53.5 (d, CH-S), 61.3 (t, OCH_2), 128.3, 128.9 and 133.5 (3d, CH of Ar), 132.8 (s, C1 of Ar), 171.3 and 174.1 (2s, 2 × CO_2)
syn-**3b**	1734	17.7[b]	1.21 (t, *J* = 7.1, 3H, OCH_2CH_3), 1.42 (d, *J* = 7.3, 3H, CH_3), 3.04 (m, *J* = 9.3, 7.3, 1H, $CHCH_3$), 3.71 (s, 3H, OCH_3), 4.02 (d, *J* = 9.3, 1H, CHS), 4.18 (q, *J* = 7.1, 2H, OCH_2), 7.60 and 8.16 (2 d, *J* = 8.2, 4H, C_6H_4)	14.0 (q , CH_2CH_3) , 15.1 (q, CH_3), 40.7 (d, $CHCH_3$), 52.1 and 52.2 (d and q, CHS and OCH_3), 61.6 (t, OCH_2), 123.9 and 130.3 (2 d, CH of Ar), 143.5 and 146.7 (2s, C1 and C4 of Ar), 170.6 and 174.1 (2s, 2 × CO_2)
syn-**3c**	1729	9.3[b]	1.28 (t, *J* = 7.1, 3H, OCH_2CH_3), 1.37 (d, *J* = 7.3, 3H, CH_3), 2.12 (s, 3H, SCH_3), 2.90 (dq, *J* = 10.6, 7.3, 1H, $CHCH_3$), 3.34 (d, *J* = 10.6, 1H, CHS), 3.69 (s, 3H, OCH_3), 4.20 (q, *J* = 7.1, 2H, OCH_2)	13.4 (q, SCH_3), 14.1 (q, CH_2CH_3), 15.2 (q, CH_3), 39.5 and 49.4 (2d, 2 × CH), 52.0 (q, OCH_3), 61.2 (t, OCH_2), 171.4 (s, 2 × CO_2)
syn-**3d**	1733	14.1[b]	1.27 (t, *J* = 7.1, 3H, OCH_2CH_3), 1.32 (d, *J* = 7.3, 3H, CH_3), 3.08 (m, *J* = 8.4, 7.3, 1H, $CHCH_3$), 3.71 and 3.85 (2s, 6H, 2 × OCH_3), 4.21 (q, *J* = 7.1, 2H, OCH_2), 4.35 (d, *J* = 8.4, 1H, CHS)	14.0 and 14.7 (2q, CH_2CH_3 and CH_3), 41.2 (d, $CHCH_3$), 50.2 (d, CHS), 52.2 and 54.8 (2q, 2 × OCH_3), 61.9 (t, OCH_2), 169.6, 170.3 and 173.9 (3s, 3 × CO_2)
anti-**3d**[c]	1734	14.7[b]	1.27 (t, *J* = 7.0, 3H, OCH_2CH_3), 1.31 (d, *J* = 7.2, 3H, CH_3), 3.24 (m, *J* = 7.2, 5.7, 1H, $CHCH_3$), 3.71 and 3.86 (2s, 6H, 2 × OCH_3), 4.21 (q, *J* = 7.0, 2H, OCH_2), 4.42 (d, *J* = 5.7, 1H, CHS)	14.0 and 14.5 (2q, CH_2CH_3 and CH_3), 41.4 (d, $CHCH_3$), 50.7 (d, CHS), 52.6 and 54.6 (2q, 2 × OCH_3), 62.0 (t, OCH_2), 169.9, 170.3 and 173.6 (3s, 3 × CO_2)
syn-**3e**	1734	9.8	0.91 (t, *J* = 7.3, 3H, CH_2CH_3), 1.17 (t, *J* = 7.1, 3H, OCH_2CH_3), 1.80–2.20 (m, 2H, CH_2), 2.80 (m, 1H, $CHCH_2$), 3.66 (s, 3H, OCH_3), 3.78 (d, *J* = 11.2, 1H, CHS), 4.10 (q, *J* = 7.1, 2H, OCH_2), 7.28–7.55 (m, 5H, ArH)	10.3 (q, CH_2CH_3), 13.8 (q, OCH_2CH_3), 22.4 (t, CH_2), 46.8 (d, $CHCH_2$), 51.2 and 51.4 (d and q, CHS and OCH_3), 61.0 (t, OCH_2), 128.6, 128.9 and 133.6 (3d, CH of Ar), 132.2 (s, C1 of Ar), 171.3 and 174.0 (2s, 2 × CO_2)
anti-**3e**	1735	6.8	0.90 (t, *J* = 7.3, 3H, CH_2CH_3), 1.19 (t, *J* = 7.1, 3H, OCH_2CH_3), 1.55–1.75 (m, 2H, CH_2), 2.85 (m, 1H, $CHCH_2$), 3.75 (s) and 3.78 (d, *J* = 11.2[d]) (4H, OCH_3 and CHS), 4.25 (q, *J* = 7.1, 2H, OCH_2), 7.28–7.55 (m, 5H, ArH)	11.7 (q, CH_2CH_3), 14.0 (q, OCH_2CH_3), 24.4 (t, CH_2), 49.4 (d, $CHCH_2$), 51.8 (d, CHS), 52.9 (q, OCH_3), 61.3 (t, OCH_2), 128.5, 128.9 and 133.7 (3d, CH of Ar), 130.0 (s, C1 of Ar), 170.6 and 173.5 (2s, 2 × CO_2)
syn-**3f**	1735	12.9	0.91 (t, *J* = 7.3, 3H, CH_2CH_3), 1.20 (t, *J* = 7.1, 3H, OCH_2CH_3), 1.75–2.10 (m, 2H, CH_2), 2.92 (m, 1H, $CHCH_2$), 3.71 (s, 3H, OCH_3), 4.03 (d, *J* = 10.8, 1H, CHS), 4.16 (q, *J* = 7.1, 2H, OCH_2), 7.64 and 8.20 (2d, *J* = 8.2, 4H, C_6H_4)	10.5 (q, CH_2CH_3), 13.9 (q, OCH_2CH_3), 22.5 (t, CH_2), 46.8 (d, $CHCH_2$), 49.8 (d, CHS), 51.9 (q, OCH_3), 61.7 (t, OCH_2), 123.9 and 130.2 (2d, CH of Ar), 143.2 and 146.5 (2s, C1 and C4 of Ar), 170.6 and 173.4 (2s, 2 × CO_2)
anti-**3f**	1735	10.2	0.94 (t, *J* = 7.1, 3H, CH_2CH_3), 1.24 (t, *J* = 7.1, 3H, OCH_2CH_3), 1.55–1.75 (m, 2H, CH_2), 2.89 (m, 1H, $CHCH_2$), 3.74 (s, 3H, OCH_3), 3.99 (d, *J* = 10.5, 1H, CHS), 4.20 (q, *J* = 7.1, 2H, OCH_2), 7.57 and 8.15 (2d, *J* = 8.2, 4H, C_6H_4)	11.6 (q, CH_2CH_3), 14.1 (q, OCH_2CH_3), 24.4 (t, CH_2), 49.1 (d, $CHCH_2$), 51.4 (d, CHS), 52.0 (q, OCH_3), 61.9 (t, OCH_2), 123.9 and 130.4 (2d, CH of Ar), 143.6 and 146.7 (2s, C1 and C4 of Ar), 169.9 and 173.0 (2s, 2 × CO_2)
syn-**3g**	1735	15.0[b,e]	0.90 (t, *J* = 7.3, 3H, CH_2CH_3), 1.28 (t, *J* = 7.1, 3H, OCH_2CH_3), 1.70–2.10 (m) and 2.11 (s) (5H, CH_2 and SCH_3), 2.85 (m, 1H, $CHCH_2$), 3.40 (d, *J* = 11.4, 1H, CHS), 3.69 (s, 3H, OCH_3), 4.20 (q, *J* = 7.1, 2H, OCH_2)	10.3 (q, CH_2CH_3), 13.2 (q, SCH_3), 14.1 (q, OCH_2CH_3), 22.2 (t, CH_2), 45.4 (d, CH), 47.0 (d, CHS), 51.7 (q, OCH_3), 61.1 (t, OCH_2), 171.4 and 174.4 (2s, 2 × CO_2)

Table 2 (continued)

Product[a]	IR ($CHCl_3$) ν (cm^{-1})	t_R (min)	^1H NMR ($CDCl_3$) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$) δ
anti-**3g**	1734	9.9[b,e]	0.91 (t, *J* = 7.3, 3H, CH_2CH_3), 1.28 (t, *J* = 7.1, 3H, OCH_2CH_3), 1.50–1.70 (m, 2H, CH_2), 2.16 (s, 3H, SCH_3), 2.90 (m, 1H, $CHCH_2$), 3.34 (d, *J* = 11.4, 1H, CHS), 3.74 (s, 3H, OCH_3), 4.22 (q, *J* = 7.1, 2H, OCH_2)	11.7 (q, CH_2CH_3), 13.6 (q, SCH_3), 14.1 (q, OCH_2CH_3), 24.6 (t, CH_2), 48.2 and 48.5 (2d, 2 × CH), 51.7 (q, OCH_3), 61.2 (t, OCH_2), 170.4 and 173.5 (2s, 2 × CO_2)
syn-**3h**	1735	11.3	0.92 (t, *J* = 7.3, 3H, CH_2CH_3), 1.27 (t, *J* = 7.1, 3H, OCH_2CH_3), 1.70–1.90 (m, 2H, CH_2), 2.91 (m, 1H, $CHCH_2$), 3.71 and 3.86 (2s, 6H, 2 × OCH_3), 4.20 (q, *J* = 7.1, 2H, OCH_2), 4.33 (d, *J* = 9.2, 1H, CHS)	11.0 (q, CH_2CH_3), 14.0 (q, OCH_2CH_3), 22.6 (t, CH_2), 47.7 and 48.6 (2d, 2 × CH), 51.9 and 54.7 (2q, 2 × OCH_3), 61.9 (t, OCH_2), 170.3, 173.4 and 173.9 (3s, 3 × CO_2)
anti-**3h**	1734	11.7	0.97 (t, *J* = 7.3, 3H, CH_2CH_3), 1.27 (t, *J* = 7.1, 3H, OCH_2CH_3), 1.55–1.90 (m, 2H, CH_2), 3.02 (m, 1H, $CHCH_2$), 3.70 and 3.85 (2s, 6H, 2 × OCH_3), 4.20 (q, *J* = 7.1, 2H, OCH_2), 4.37 (d, *J* = 6.7, 1H, CHS)	11.9 (q, CH_2CH_3), 14.0 (q, OCH_2CH_3), 23.3 (t, CH_2), 48.3 and 49.1 (2d, 2 × CH), 51.9 and 54.6 (2q, 2 × OCH_3), 62.0 (t, OCH_2), 170.2, 170.3 and 173.1 (3s, 3 × CO_2)

[a] Satisfactory microanalyses obtained: C±0.34; H±0.13; N±0.28.
[b] Using a differential refractometric detector RID-10A (Shimadzu).
[c] Obtained in mixture with *syn*-isomer in 9:1 molar ratio (^1H NMR).
[d] Measured by recording the spectrum in C_6D_6 where the signals of CH and OCH_3 are split at δ 4.05 and 3.39, respectively.
[e] 2.5 mL/ min flow rate of elution and *t*-BuOMe/hexane (3:22) as eluent.

from **1c**, eluting as above, gave subsequent fractions containing *syn*-**3g** and a mixture of *syn*- and *anti*-**3g**.[30] Each compound was separated and purified by HPLC.

The reaction times and yields are reported in Table 1. The analytical and spectral data for *syn*-**3c** are reported in Table 2.

1-Ethyl 4-Methyl (*E*)- and (*Z*)-3-Methylbutenedioates 7[20]

A solution of *syn*-**3a** (70 mg, 0.25 mmol) in CH_2Cl_2 (5 mL) was treated with MCPBA (48 mg, 0.25 mmol) and the resulting mixture kept at r.t. under stirring. After completion of the reaction (2 h, ^1H NMR), the mixture was poured onto 10% aq $NaHCO_3$ (2 mL). The organic layer was washed with brine (2 mL) and dried (Na_2SO_4). After removal of the solvent, the residue was chromatographed on silica gel (light petroleum/Et_2O 1:1) and gave the diastereomeric mixture of sulfoxide *syn*-**6**[31] (60 mg with a purity of 90%, ^1H NMR). The latter (60 mg) was dissolved in dry C_6H_6 (6 mL) and refluxed. After 12 h, the solvent was removed and chromatography of the residue on silica gel (light petroleum/Et_2O 9:1) afforded *Z*-alkene **7** (25 mg, 58% based on *syn*-**3a**) which was identified by comparing its ^1H NMR spectrum with that reported.[20]

The same procedure was carried out for *anti*-**3a** (50 mg, 0.18 mmol) and led to the sulfoxide *anti*-**6**[31] (43 mg with a purity of 90%, ^1H NMR) which, treated as *syn*-**6**, afforded *E*-**7** (20 mg, 67% based on *anti*-**3a**). This was identified by comparing its ^1H NMR spectrum with that reported.[20]

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Table 3 1-Ethyl 4-Methyl 3-Sulfenylbutanedioates (**5**) Prepared

Product[a]	IR ($CHCl_3$) ν (cm^{-1})	t_R (min)	^1H NMR ($CDCl_3$) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$) δ
5a	1734		1.24 (t, *J* = 7.0, 3H, CH_3), 2.73 (dd, *J* = 16.5, 6.2) and 2.94 (dd, *J* = 16.5, 9.3) (2H, CH_2), 3.69 (s, 3H, OCH_3), 4.01 (dd, *J* = 9.3, 6.2) and 4.13 (q, *J* = 7.0) (3H, CH and OCH_2), 7.30–7.55 (m, 5H, ArH)	14.0 (q, CH_3), 36.6 (t, CH_2), 45.6 (d, CH), 52.4 (q, OCH_3), 60.9 (t, OCH_2), 128.7, 129.0 and 134.1 (3d, CH of Ar), 131.6 (s, C1 of Ar), 170.4 and 171.5 (2s, 2 × CO_2)
5b	1734		1.26 (t, *J* = 7.3, 3H, CH_3), 2.80 (dd, *J* = 17.1, 6.2) and 3.06 (dd, *J* = 17.1, 8.8) (2H, CH_2), 3.75 (s, 3H, OCH_3), 4.17 (q, *J* = 7.3) and 4.25 (dd, *J* = 8.8, 6.2) (3H, OCH_2 and CH), 7.57 and 8.16 (2d, *J* = 8.2, 4H, C_6H_4)	14.1 (q, CH_3), 36.3 (t, CH_2), 44.4 (d, CH), 52.8 (q, OCH_3), 61.3 (t, OCH_2), 124.0 and 130.4 (2d, CH of Ar), 142.7 and 146.7 (2s, C1 and C4 of Ar), 169.9 and 170.9 (2s, 2 × CO_2)
5c	1734		1.26 (t, *J* = 7.3, 3H, CH_3), 2.18 (s, 3H, SCH_3), 2.67 (dd, *J* = 17.1, 5.5) and 3.01 (dd, *J* = 17.1, 9.9) (2H, CH_2), 3.64 (dd, *J* = 9.9, 5.5, 1H, CH), 3.77 (s, 3H, OCH_3), 4.15 (q, *J* = 7.3, 2H, OCH_2)	13.7 and 13.9 (2q, CH_3 and SCH_3), 35.8 (t, CH_2), 41.9 (d, CH), 52.2 (q, OCH_3), 60.8 (t, OCH_2), 170.5 and 171.6 (2s, 2 × CO_2)
5d	1734		1.26 (t, *J* = 7.0, 3H, CH_3), 2.93 (dd, *J* = 17.2, 5.7) and 3.07 (dd, *J* = 17.2, 7.6) (2H, CH_2), 3.77 and 3.86 (2s, 6H, 2 × OCH_3), 4.15 (q, *J* = 7.0, 2H, OCH_2), 4.38 (dd, *J* = 7.6, 5.7, 1H, CH)	14.0 (q, CH_3), 36.9 (t, CH_2), 43.0 (d, CH), 53.0 and 54.6 (2q, 2 × OCH_3), 60.9 (t, OCH_2), 169.4, 170.0 and 170.3 (3s, 3 × CO_2)
5e	1733	10.9	1.23 (t, *J* = 7.0, 3H, OCH_2CH_3), 1.58 (s, 3H, CH_3), 2.63 and 3.06 (2d, *J* = 16.6, 2H, CH_2), 3.66 (s, 3H, OCH_3), 4.11 (q, *J* = 7.0, 2H, OCH_2), 7.30–7.55 (m, 5H, ArH)	14.1 (q, CH_2CH_3), 22.6 (q, CH_3), 43.0 (t, CH_2), 51.5 (s, C-S), 52.2 (q, OCH_3), 60.7 (t, OCH_2), 128.8 and 129.9 (2d, CH of Ar), 137.4 (s + d, CH and C1 of Ar), 170.1 and 172.6 (2s, 2 × CO_2)
5f	1733	14.8[b]	1.24 (t, *J* = 7.2, 3H, OCH_2CH_3), 1.63 (s, 3H, CH_3), 2.68 and 3.04 (2d, *J* = 16.4, 2H, CH_2), 3.71 (s, 3H, OCH_3), 4.12 (q, *J* = 7.2, 2H, OCH_2), 7.64 and 8.19 (2d, *J* = 8.2, 4H, C_6H_4)	14.0 (q, CH_2CH_3), 22.8 (q, CH_3), 42.8 (t, CH_2), 52.1 (s, C-S), 52.5 (q, OCH_3), 60.9 (t, OCH_2), 123.5 and 137.1 (2d, CH of Ar), 138.8 and 148.5 (2s, C1 and C4 of Ar), 169.5 and 172.1 (2s, 2 × CO_2)
5g	1735	14.8[b,c]	1.25 (t, *J* = 7.0, 3H, OCH_2CH_3), 1.60 (s, 3H, CH_3), 2.10 (s, 3H, SCH_3), 2.55 and 3.16 (2d, *J* = 16.3, 2H, CH_2), 3.75 (s, 3H, OCH_3), 4.13 (q, *J* = 7.0, 2H, OCH_2)	12.6 (q, SCH_3), 14.1 (q, CH_2CH_3), 22.1 (q, CH_3), 42.2 (t, CH_2), 46.9 (s, C-S), 52.4 (q, OCH_3), 60.7 (t, OCH_2), 170.2 and 172.5 (2s, 2 × CO_2)
5h	1734	16.2[b]	1.26 (t, *J* = 7.0, 3H, OCH_2CH_3), 1.79 (s, 3H, CH_3), 2.98 and 3.21 (2d, *J* = 15.6, 2H, CH_2), 3.78 and 3.79 (2s, 6H, 2 × OCH_3), 4.15 (q, *J* = 7.0, 2H, OCH_2)	14.1 (q, CH_2CH_3), 23.6 (q, CH_3), 42.0 (t, CH_2), 52.9 (s, C-S), 53.1 and 54.0 (2q, 2 × OCH_3), 60.8 (t, OCH_2), 169.1, 169.6 and 172.4 (3s, 3 × CO_2)

[a] Satisfactory microanalyses obtained: C±0.18; H±0.10; N±0.22.
[b] Using a differential refractometric detector RID-10A (Shimazdu).
[c] 2 mL/min flow rate of elution and *t*-BuOMe/hexane (1:7) as eluent.

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(12) Both cyclopropanes **1**[8,13] and sulfenyl chlorides **2**[14] hydrolyze very easily; in particular, the former lead to the corresponding ethyl methyl butanedioates, which may be present occasionally in the reaction mixtures.

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(15) For all reactions ^1H NMR of a sample of the CCl_4 solution, recorded in $CDCl_3$, indicated the presence of MeCl. This could not be quantified owing to its volatility.

(16) By heating at 130 °C **1a** isomerizes quantitatively into **4a** within 4 h while **1b** isomerizes into **4b** within 10 h.[8] Control experiments showed that under above conditions **1c** was recovered unchanged even after 10 h.

(17) CH_2Cl_2 was used as solvent since in CCl_4 a pyridine–sulfenyl chloride complex precipitated.[14] However, control experiments showed that the reaction of **1b** with **2a** in the absence of pyridine carried out in this solvent gave the same results as in CCl_4.

(18) The values for the *syn* isomers are larger than those for their *anti* counterparts.[19] Since the diastereomeric pairs **3e** and **3g** exhibited the same value for both isomers, configuration was assigned on the basis of straightforward comparison of ^1H NMR spectral data with those of pairs **3f**,**h**; in particular, *syn*-**3e**,**g** show signals due to chain methylenes in the δ range 1.7–2.2 and *anti*-**3e**,**g** in the δ range 1.5–1.7 as observed for *syn*-**3f**,**h** and *anti*-**3f**,**h**, respectively. In the reactions of **1b** with **2b**,**c** only one isomeric 2-sulfenyl-3-methylbutanedioate was

obtained in moderate amount; thus, configuration of *syn*-**3b** and *syn*-**3c** was assigned on the basis of the general stereochemical course which leads to *syn*-**3** as by far the main products.
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(24) These modes of attack on the cyclopropane ring have been found both in bromination[25] and in reactions with other electrophiles[26]. However, for cyclopropanes **1** hitherto only a S_E2-type attack has been observed as reported in ref 7a.
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(27) Control experiments showed that ethyl 2,2-dimethoxy-3,3-dimethylcyclopropanecarboxylate[8] was recovered unchanged under the above reaction conditions, even after prolonged times. When the sulfenylation was carried out in the presence of either catalytic[10a] or equimolecular amount of $TiCl_4$ at –70 or 0 °C, ethyl methyl 3,3-dimethylbutanedioate and/or mixtures of unidentified products were obtained. It is to be noted that the low reactivity of C3 disubstituted cyclopropanes **1** was already observed.[7a,8,13]
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(30) In the reactions of **1b**,**c** with **2c** a prevailing unidentified product was present which did not interfere in the chromatographic procedures as it is more polar than the reaction products.
(31) Spectral data are consistent with the structural assignment. Selected IR data: ν (S=O) = 1057 and 1059 cm^{-1} for *syn*-**6** and *anti*-**6**, respectively.

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