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2,3-Donor-Acceptor-Substituted 1,3-Butadienes. Synthesis by SO_2-Extrusion from 3-Sulfolenes and Diels-Alder Reactions [1]

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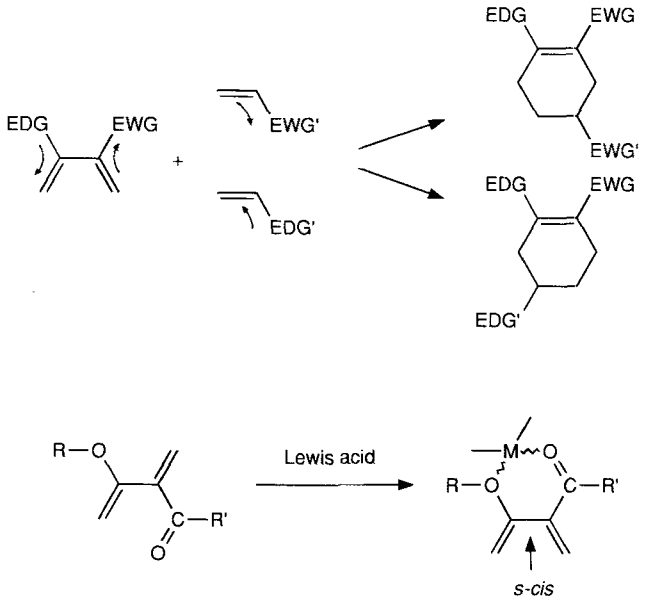
Abstract. The thermal extrusion of SO_2 from disubstituted 3-sulfolenes **3** leads to 2,3-donor-acceptor-substituted 1,3-butadienes **4**. These dienes react with acrylic acid ester and ethyl vinyl ether to the corresponding Diels-Alder adducts **5** and **6** and with themselves to the cyclic dimerization products **7** and **8**. The regiochemistry of the cycloadducts has been determined by chemical- and NMR-methods.

The pyrolysis of 3-sulfolene **11** afforded the thiolactone **13** whose structure has been verified by X-ray diffraction analysis. In addition, the influence of Lewis acid catalysts on the Diels-Alder reaction and an approach to transition state calculation by means of the semiempirical AM 1 method has also been investigated.

The Diels-Alder reaction of 2,3-donor-acceptor-substituted 1,3-butadienes has been of interest in recent years [3]. According to their electronic properties, the substituents influence the FMO-energies and coefficients and thus both the reactivity and the regioselectivity [4]. The electron-donating-group (EDG) and the electron-withdrawing-group (EWG) are expected to reinforce each other in order to contribute to the regioselectivity of the Diels-Alder reaction (Scheme 1). If the substituents include carbonyl functions a fixation of the s-cis-confirmation with Lewis acid catalysts should be possible (Scheme 1). Due to these structural features these butadiene-derivatives should be very useful in regioselective synthesis of six-membered carbocycles.

The requisite dienes can be prepared via pyrolysis of the corresponding disubstituted 3-sulfolenes [5]. In contrast to the unstable dienes the sulfolenes are stable precursors.

A recent communication describing this type of Diels-Alder reaction [6] prompts us to report our investigations in synthesis of new O,C-disubstituted-1,3-dienes and their regioselectivity in Diels-Alder reactions with electron-rich and electron-poor olefins [2].

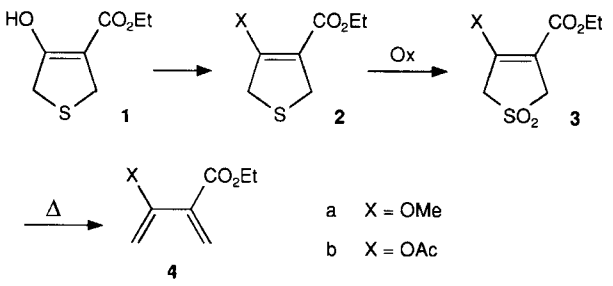


Scheme 1

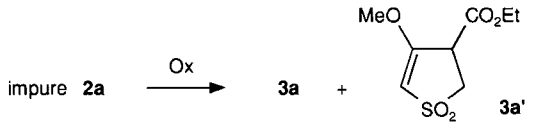
Preparation and Diels-Alder Reactions of the Dienes

The sulfolenes **3a**, **3b** were prepared from the corresponding 2,5-dihydrothiophene by treatment with diazomethane [7] (a) or acetyl chloride (b), respectively, and oxidation with OXONE (potassium hydrogen persulfate) [8]. The crude intermediate 2,5-dihydrothiophene **2b** was used in the oxidation reaction without any further purification to yield pure **3b** after recrystallization.

Compound **2a** had to be purified carefully before oxidation to the sulfolene **3a** to avoid formation of 2-sulfolene **3a'** (Scheme 3). Separation of the isomeric



Scheme 2



Scheme 3

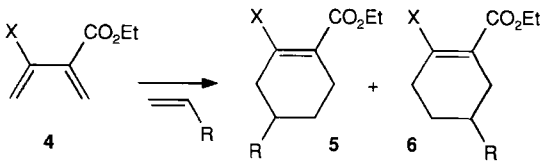
compounds **3a** and **3a'** by recrystallization was not successful.

The thermolysis of **3** in a Kugelrohr-apparatus at 200 °C and low pressure resulted in the extrusion of SO_2. The pyrolysis products consisted of the corresponding dienes **4** and small amounts of complex polymer and dimers **7** and **8**, respectively.

After chromatographic separation the dienes were stable in a cooled 5 % ethyl acetate solution for several days. Fortunately compound **3a'** could also be pyrolysed, however under flash vacuum pyrolysis conditions [5].

The Diels-Alder reactions were carried out in ethyl acetate solution at room temperature and an excess of acrylic-acid ester or ethyl vinyl ether. After 10 up to 20 days no diene was detectable. Alternatively, some attempts were made to prepare the cycloadducts from the 3-sulfolene **3a** and **3b** by treatment with the dienophiles in a sealed tube at temperatures from 160 °C to 200 °C in toluene. However, gas chromatographic analysis of the reaction mixtures showed the formation of complex product mixtures including the cycloadducts in only poor yields. This observation is in contrast to results reported recently by Chou and coworkers [6].

Diene **4b** reacted faster with acrylic ester than diene **4a**. The cycloadduct formation of **4b** with ethyl vinyl ether to **5d** proceeded very slowly (inverse type Diels-Alder reaction according to Sauer and Sustmann [9]), whereas diene **4a** did not react with this olefin. In all cases the formation of **5** and **6** competed with the dimerization to the side products **7** or **8**. Cycloaddition to **8** was faster than formation of **7**.

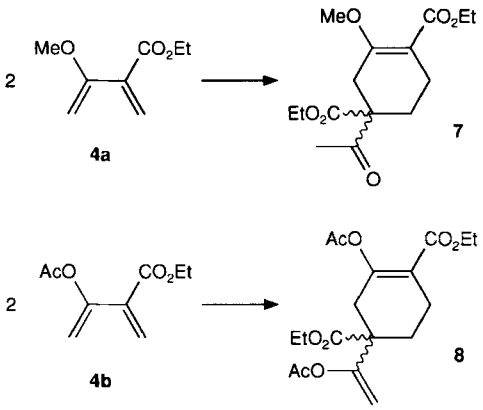


Scheme 4

Table 1 Comparison of Diels-Alder reactions of **4a** and **4b**

Entry	X	R	products[a]	ratio[b]
a	**4a** OMe	CO_2Et	**5a 6a**	40 : 60
b	**4a** OMe	OEt	no product observed	
c	**4b** OAc	CO_2Et	**5c 6c**	75 : 25
d	**4b** OAc	OEt	only **5d**	

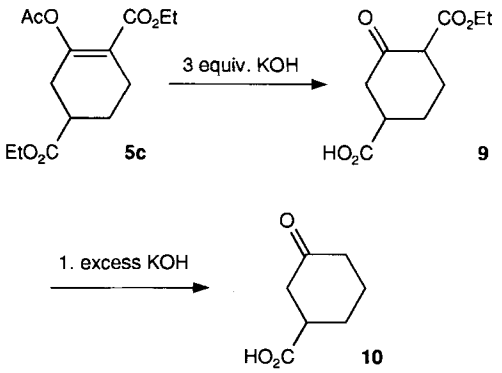
[a] Formation of **5** and **6** accompanied by dimerization of **4a** and **4b**, see experimental section.
[b] Determined by HPLC and confirmed by GLC.



Scheme 5

An attempt was made to correlate the FMO-energies [10] both with the reactivity and the regioselectivity of the Diels-Alder reactions. Whereas this correlation fits perfectly in the former case, we were not able to explain the observed regiochemistry of the cycloaddition yielding the product **5** and **6**. Either the FMO-theory or calculations of transition states with the semi-empirical method AM1 failed. Due to the large number of conformers of the ethoxycarbonyl-butadiene structure which has to be taken into consideration, an approach to this problem was not successful. However, the results correspond with the recent report by Chou about the Diels-Alder reaction with acrylic ester as an electron poor olefin [6]. The 'para'-directing ability of OMe was of larger extent than the influence of OAc. Extremely high selectivities were found in cycloaddition of **4b** with ethyl vinyl ether and in the dimer formation, respectively. This indicates that the regiochemistry of the annelation is controlled by the olefin, too.

The structures of the cycloadducts were determined by a controlled hydrolysis and decarboxylation to monosubstituted cyclohexanones. Treatment of **5c** with an excess of KOH in refluxing EtOH followed by decarboxylation gave 3-oxocyclohexanecarboxylic acid. The use of an equimolar amount of KOH (one equivalent per each ester group) led to the partially hydrolysed product **9** (Scheme 6). Alternatively, we used NMR-methods for determination of the regiochemistry of the cycloadducts.

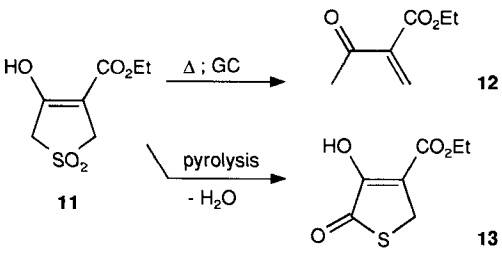


Scheme 6

According to the special substitution pattern a chelating interaction of both dienes with Lewis acid catalysts may be expected to form a six-membered ring complex with a fixed s-cis-structure (Scheme 1). All Lewis acid catalysed reactions ($ZnCl_2$, $AlCl_3$, $TiCl_4$) only lead to the formation of the dimers **7** or **8**. We assume that **7** is formed from the Diels-Alder dimer of **4a** (analogous to **8**) followed by hydrolysis of the enol ether unit during the work-up procedure. These results indicate that the Lewis acid activates **4a** and **4b** as dienophiles rather than as dienes in Diels-Alder reactions.

Pyrolysis of 3-Ethoxycarbonyl-4-hydroxy-3-sulfolene

Oxidation of **1** with OXONE led to 3-sulfolene **11** in low yield. We were also interested in the thermal extrusion of SO_2 from this compound, leading to the reactive olefin **12**, which could react as a hetero-diene or dienophile, respectively. Gas chromatographic analysis of compound **11** followed by mass spectroscopy detected the corresponding butadiene derivative **12** (Scheme 7), indicating that the sulfolene decomposed selectively in the injection block. However an attempt to perform this SO_2-extrusion on a larger scale failed. Instead of **12** only the thiolactone **13** was obtained in 59 % yield leaving small amounts of a polymer and of starting material. To our knowledge a similar type of reacton has not been reported so far.



Scheme 7

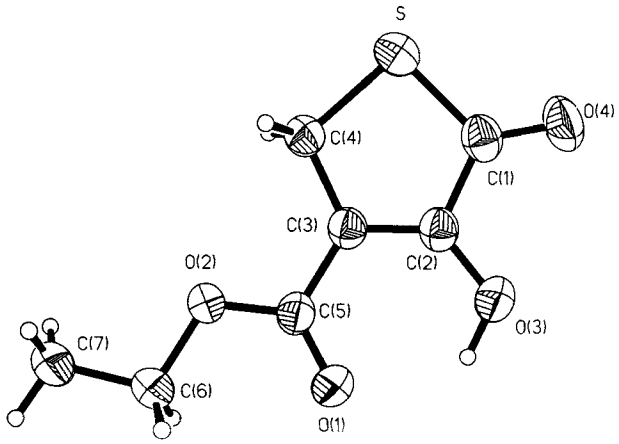


Fig. 1 Solid state structure of the Thiolactone **13**

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Experimental

IR: Shimadzu IR-408 or Perkin Elmer 298 Infrared Spectrophotometer. – ^1H NMR: Bruker WM 300 (300 MHz). – ^{13}C NMR: Bruker WM 300 (75 MHz), Bruker AM 360 (90 MHz). – MS: Varian MAT CH 7A (GLC-MS coupling) or Finnigan MAT 312. – HPLC: Kontron pump 420, RI detector Bischoff RI 8110, column 250 × 20 mm, LiChrosorb Si 60-5 (Fa. Merck). – Column chromatography: Merck Kieselgel 60, Art. 7734. – GLC: Siemens Sichromat 3 with FID and Spectra Physics integrator SP 4290 or Siemens Sichromat 4 with FID and Spectra Physics integrator SP 4400, capillary column Hewlett Packard Ultra 2; Shimadzu GC-9A with FID and Shimadzu integrator C-R3A, capillary column Macherey & Nagel SE 30 – Elemental analyses: Heraeus CHN-O-Rapid or Perkin-Elmer 240 Elemental Analyser. – Melting points: Büchi 510 apparatus, all melting points are uncorrected. Solvents: Diethylether is dried with KOH and distilled. Cyclohexane, chloroform, methanol, dichloromethane and ethyl acetate are distilled at atmospheric pressure. Ethyl acetate is further filtered with basic Al_2O_3. Benzene (Riedel-de Haen, pro analyse) is used without further purification.
Compound **1** was prepared according to ref. [11].

3-Ethoxycarbonyl-4-methoxy-2,5-dihydrothiophene (**2a**)

To a solution of **1** (7.00 g, 40.2 mmol) in 100 ml of dry ether there are added dropwise two equivalents of dry ethereal diazomethane (100 ml solution) at 0 °C. The resultant mixture is kept in an ice bath for 16 h and is then evaporated; the residue is fractionally distilled to give 6.18 g (81.7 %) of **2a** (98 %, GLC). The product is further purified by column chromatography (cyclohexane/ethyl acetate, 2:1) to yield colourless, pure **2a** (5.16 g, 68.2 %), m.p. 35 °C. – IR (KBr): ν = 1670 cm^{-1} (C=O), 1625, 1210, 1050. – ^1H NMR ($CDCl_3$): δ = 1.27 (t, J = 7.1 Hz, 3H, CH_2CH_3), 3.84 (d, J = 3.7 Hz,

1H, CH_2-2), 3.85 (d, J = 3.7 Hz, 1H, CH_2-2), 3.95 (d, J = 3.7 Hz, 1H, CH_2-5), 3.96 (d, J = 3.7 Hz, 1H, CH_2-5), 3.87 (s, 3H, H_3CO), 4.18 (q, J = 7.1 Hz, 2H, $C\underline{H}_2CH_3$). – ^{13}C NMR ($CDCl_3$): δ = 14.15 ($CH_2\underline{C}H_3$), 33.17 (C-2), 34.42 (C-5), 57.83 (H_3CO), 58.66 ($\underline{C}H_2CH_3$), 104.37 (C-3), 163.57 (C=O), 165.21 (C-4). – MS (70 eV), m/z (%): 188 (50) [M^+], 173 (100) [$M^+ - CH_3$], 159 (31) [$M^+ - C_2H_5$].

$C_8H_{12}O_5S$	Calcd. C 51.04	H 6.43
(188.2)	Found C 50.98	H 6.49

4-Acetoxy-3-ethoxycarbonyl-2,5-dihydrothiophene (**2b**)

To an ice-cooled solution of **1** (1.74 g, 10.0 mmol) in 30 ml of dry diethyl ether are added 1.01 g (10.0 mmol) of triethylamine and a solution of acetyl chloride (0.78 g, 10.0 mmol) in 20 ml of dry diethyl ether. After stirring for 2 h at room temperature the mixture is filtered by suction and washed with diethyl ether. The combined organic layers are washed with 0.1 n NaOH, water and brine, dried over $MgSO_4$. Evaporation afforded 2.05 g (88 %) of **2b** (93 %, GLC), which is used without further purification. MS (70 eV), m/z (%): 216 (7) [M^+], 174 [M^+ – ketene], 145 (38), 128 (50), 43 (100).

General procedure for the Oxidation of 2 to 3

10 mmol of **2** are dissolved in 40 ml of methanol and cooled to 0 °C. To this mixture is added a solution of 9.29 g OXONE (15 mmol, 30 mmol $KHSO_5$) in 40 ml of water. The resulting cloudy slurry is stirred for 2 h at room temperature, diluted with water, and extracted with chloroform (3 × 75 ml). The combined organic layers are washed with water and brine and dried with $MgSO_4$. The solvent is evaporated under reduced pressure to give the crude product **3**. The sulfolenes are purified by recrystallization from ethanol.

3-Ethoxycarbonyl-4-methoxy-3-sulfolene (**3a**)

Yield 1.83 g (83 %), m.p. 70 °C (ethanol). – IR (KBr): ν = 1705 cm^{-1} (C=O), 1605, 1210, 1038. – ^1H NMR ($CDCl_3$): δ = 1.29 (t, J = 7.1 Hz, 3H, $CH_2C\underline{H}_3$), 3.86 (s, 3H, H_3CO), 4.10 (s, 2H, CH_2-2), 4.13 (s, 2H, CH_2-5), 4.21 (q, J = 7.1 Hz, 2H, $C\underline{H}_2CH_3$). – ^{13}C NMR ($CDCl_3$): δ = 14.07 ($CH_2\underline{C}H_3$), 54.65 (C-2), 56.73 (C-5), 58.88 (H_3CO), 60.57 ($\underline{C}H_2CH_3$), 100.47 (C-3), 157.29 (C=O), 161.91 (C-4). – MS (70 eV), m/z (%): no [M^+], 156 (60) [$M^+ - SO_2$], 141 (22) [$M^+ - SO_2 - CH_3$], 113 (100), 99 (39).

$C_8H_{12}O_3S$	Calcd. C 43.63	H 5.49
(220.2)	Found C 43.69	H 5.36

4-Acetoxy-3-ethoxycarbonyl-3-sulfolene (**3b**)

Yield 2.01 g (81 %), m.p. 94 °C (ethanol). – IR (KBr): ν = 1733 cm^{-1} (C=O), 1700 (C=O), 1310 (SO_2). – ^1H NMR ($CDCl_3$): δ = 1.30 (t, J = 7.1 Hz, 3H, $CH_2C\underline{H}_3$), 2.28 (s, 3H, H_3CCO), 4.10 (s, 2H, CH_2-2), 4.18 (s, 2H, CH_2-5), 4.23 (q, J = 7.1 Hz, 2H, $C\underline{H}_2CH_3$). – ^{13}C NMR ($CDCl_3$): δ = 13.69 ($CH_2\underline{C}H_3$), 20.36 ($H_3\underline{C}CO$), 56.43 (C-2), 56.83 (C-5), 61.44 ($\underline{C}H_2CH_3$), 114.29 (C-3), 148.30 ($H_3C\underline{C}O$), 160.41 ($\underline{C}O_2CH_2CH_3$), 166.75 (C-4). – MS (70 eV), m/z (%): no [M^+], 184 (3) [$M^+ - SO_2$], 43 (100) [CH_3CO^+].

$C_9H_{12}O_6S$	Calcd. C 43.54	H 4.87
(248.3)	Found C 43.40	H 4.83

2-Ethoxycarbonyl-3-methoxy-1,3-butadiene (**4a**)

Pure **3a** (200 mg, 0.91 mmol) is mixed with glass beads (2 mm diameter) in a round bottomed flask. This is placed in a Kugelrohr apparatus and subjected to vacuum pyrolysis (200 °C, 2 mbar). The diene **4a** is distilled in 20 min with ice-cooling. The distillate is further purified by column chromatography (cyclohexane / ethyl acetate, 4:1) to give 105 mg (74 %) as a colorless, pleasantly smelling liquid.

A mixture of **3a** and **3a′** is pyrolysed in the following apparatus: 200 mg (0.91 mmol) of the mixture are mixed with glass beads (2 mm diameter) in a round bottomed flask. Evaporated crude product (evaporation at 180 °C, 2 mbar) is led through a pyrolysis tube (30 cm, 1.5 cm diameter) filled with quartz wool and placed in a two-zone oven heated at 350/300 °C. The diene is distilled in 1 h with ice-cooling and purified as above to give 92 mg (65 %) of **4a**. – IR (neat): ν = 1718 cm^{-1} (C=O), 1337, 1240, 1221. – ^1H NMR ($CDCl_3$): δ = 1.32 (t, J = 7.1 Hz, 3H, $CH_2C\underline{H}_3$), 3.63 (s, 3H, H_3CO), 4.25 (q, J = 7.1 Hz, 2H, $C\underline{H}_2CH_3$), 4.33 (s, 1H), 4.71 (s, 1H), 6.03 (s, 1H), 6.06 (s, 1H). – ^{13}C NMR ($CDCl_3$): δ = 14.08 ($CH_2\underline{C}H_3$), 54.90 (H_3CO), 60.92 ($\underline{C}H_2CH_3$), 86.87 (C-4), 124.51 (C-1), 137.30 (C-2), 156.45 (C-3), 166.08 (C=O). – MS (70 eV), m/z (%): 156 (60) [M^+], 141 (22) [$M^+ - CH_3$], 127 (30) [$M^+ - C_2H_5$], 113 (100).

$C_8H_{12}O_3$	Calcd. C 61.52	H 7.75
(156.2)	Found C 61.32	H 7.85

3-Acetoxy-2-ethoxycarbonyl-1,3-butadiene (**4b**)

100 mg (0.40 mmol) **3b** are treated as pure **2b** and pyrolysed at 180 °C/4 mbar. Column chromatography (cyclohexane / ethyl acetate, 7 : 3) yields 67 mg (90 %) of diene **4b** as a colorless liquid. – IR (neat): ν = 1765 cm^{-1} (C=O), 1722 (C=O), 1211, 1099. – ^1H NMR ($CDCl_3$): δ = 1.33 (t, J = 7.2 Hz, 3H, $CH_2C\underline{H}_3$), 2.21 (s, 3H, H_3CCO), 4.26 (q, J = 7.2 Hz, 2H, $C\underline{H}_2CH_3$), 5.10 (s, 1H), 5.70 (d, J = 1.8 Hz, 1H), 5.85 (s, 1H), 6.21 (s, 1H). – ^{13}C NMR ($CDCl_3$): δ = 14.05 ($CH_2\underline{C}H_3$), 20.79 ($H_3\underline{C}CO$), 61.61 ($\underline{C}H_2CH_3$), 107.68 (C-2), 125.73 (C-1), 134.96 (C-4), 148.40 (C-3), 164.63 ($H_3C\underline{C}O$), 168.95 (C=O). – MS (70 eV), m/z (%): 184 (3) [M^+], 43 (100) [CH_3CO^+].

$C_9H_{12}O_4$	Calcd. C 58.69	H 6.57
(184.2)	Found C 58.15	H 6.50

Procedures for the Diels-Alder Reactions of the Dienes to 5,6

1. 250 mg (1.60 mmol) of **4a** are dissolved in 10 ml of acrylic acid ester and heated at 80 °C for some hours until the reaction is complete (TLC). The mixture is evaporated *in vacuo*. The residue is filtered by column chromatography (cyclohexane / ethyl acetate, 4 : 1) to give 336 mg (82 %) of the Diels-Alder adducts **5a** and **6a** (ratio 1 : 1.5). The pure regioisomers are separated by HPLC (same eluent).

The percentage of dimer is about 3 % in the crude reaction mixture (GLC). The same adduct-ratio is found for the reaction carried out at room temperature. Therefore a solution of **4a** (250 mg, 1.60 mmol) and acrylic acid ester (3.20 g, 32 mmol) in 30 ml of ethyl acetate is allowed to stand for 10 to 14 days (TLC).

2. A solution of **4b** (295 mg, 1.60 mmol) and acrylic acid ester (3.20 g, 32 mmol) in 30 ml of ethyl acetate is allowed to stand for 7 to 10 days at room temperature (TLC). Evaporation of the solvent under reduced pressure and column

chromatography (cyclohexane / ethyl acetate, 9 : 1) affords 328 mg (72 %) of **5c** and **6c** and 65 mg (22 %) of the dimer **8**. The pure regioisomers are separated by HPLC.

3. A solution of **4b** (295 mg, 1.60 mmol) and ethyl vinyl ether (2.30 g, 32 mmol) in 30 ml of ethyl acetate is allowed to stand at room temperature for three weeks (TLC). Evaporation of the solvent and column chromatography (cyclohexane / ethyl acetate, 6:1) yielded 111 mg (27 %) **5d** and 173 (59 %) dimer **8**.

All cycloadducts are colorless oils.

1,4-Diethoxycarbonyl-2-methoxy-cyclohex-1-ene (**5a**)

IR ($CDCl_3$): ν = 1726 cm^{-1} (C=O), 1279, 1185. – ^1H NMR ($CDCl_3$): δ = 1.20 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.21 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.72 (m_c, 1H), 2.13 (m_c, 1H), 2.29 (m_c, 1H), 2.43 (m_c, 3H), 2.60 (m_c, 1H), 3.65 (s, 3H, H_3CO), 4.08 (q, J = 7.1 Hz, 2H, CH_2CH_3), 4.11 (q, J = 7.1 Hz, 2H, CH_2CH_3). – ^{13}C NMR ($CDCl_3$): δ = 14.11 (CH_2CH_3), 14.24 (CH_2CH_3), 24.59 (cyclic CH_2), 25.16 (cyclic CH_2), 27.59 (cyclic CH_2), 38.73 (CH), 55.88 (H_3CO), 59.79 (CH_2CH_3), 60.45 (CH_2CH_3), 105.58 (C-1), 161.89 (C-2), 166.89 (C=O), 174.58 (C=O). – MS (70 eV), m/z (%): 256 (4) [M^+], 241 (3) [M^+ – CH_3], 210 (22) [M^+ – EtOH], 137 (18), 109 (100).

$C_{13}H_{20}O_5$ Calcd. 256.1311 Found 256.1305 (MS)

2-Acetoxy-1,4-ethoxycarbonylcyclohex-1-ene (**5c**)

IR ($CDCl_3$): ν = 1756 cm^{-1} (C=O), 1716 (C=O), 1185. – ^1H NMR ($CDCl_3$): δ = 0.94 (t, J = 7.2 Hz, 3H, CH_2CH_3), 0.95 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.55 (m_c, 1H), 1.81 (m_c, 1H), 1.95 (s, 3H, H_3CCO), 2.20 (m_c, 1H), 2.41 (m_c, 3H), 2.67 (m_c, 1H), 3.94 (q, J = 7.2 Hz, 2H, CH_2CH_3), 3.95 (q, J = 7.2 Hz, 2H, CH_2CH_3). – ^{13}C NMR ($CDCl_3$): δ = 14.15 (CH_2CH_3), 14.15 (CH_2CH_3), 20.86 (H_3CCO), 24.31 (cyclic CH_2), 25.52 (cyclic CH_2), 31.11 (cyclic CH_2), 38.95 (CH), 60.45 (CH_2CH_3), 60.73 (CH_2CH_3), 117.33 (C-1), 153.66 (C-2), 165.04 (C=O), 168.40 (C=O), 173.78 (C=O). – MS (70 eV), m/z (%): no [M^+], 241 (4) [M^+ – CH_3CO], 196 (6), 123 (18), 95 (31), 43 (100).

$C_{14}H_{20}O_6$	Calcd. C 59.14	H 7.09
(284.3)	Found C 59.35	H 7.12

2-Acetoxy-1-ethoxycarbonyl-4-ethoxycyclohex-1-ene (**5d**)

IR ($CDCl_3$): ν = 1760 cm^{-1} (C=O), 1711 (C=O), 1272, 1185. – ^1H NMR ($CDCl_3$): δ = 1.20 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.27 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.70 (m_c, 1H), 1.92 (m_c, 1H), 2.19 (s, 3H, H_3CCO), 2.34 (m_c, 2H), 2.58 (m_c, 2H), 3.52 (dq, J = 7.1 Hz and 3.2 Hz, 2H, C-4OCH_2CH_3), 3.68 (m_c, 1H, HC-4), 4.16 (q, J = 7.1 Hz, 2H, CH_2CH_3). – ^{13}C NMR ($CDCl_3$): δ = 14.00 (CH_2CH_3), 15.33 (CH_2CH_3), 20.71 (H_3CCO), 22.08 (cyclic CH_2), 26.83 (cyclic CH_2), 35.40 (cyclic CH_2), 60.17 (CH_2CH_3), 63.42 (CH_2CH_3), 72.37 (CH), 117.21 (C-1), 152.63 (C-2), 164.92 (C=O), 168.26 (C=O). – MS (70 eV), m/z (%): 256 (3) [M^+], 214 (39), 168 (49), 122 (100).

$C_{13}H_{20}O_5$	Calcd. C 60.94	H 7.81
(256.3)	Found C 60.89	H 7.82

2,4-Diethoxycarbonyl-1-methoxy-cyclohex-1-ene (**6a**)

IR ($CDCl_3$): ν = 1730 cm^{-1} (C=O), 1260, 1184. – ^1H NMR ($CDCl_3$): δ = 1.20 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.21 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.53 (m_c, 1H), 1.97 (m_c, 1H), 2.23 (m_c, 1H), 2.48 (m_c, 4H), 3.66 (s, 3H, H_3CO), 4.10 (q, J = 7.1 Hz, 2H, CH_2CH_3), 4.11 (q, J = 7.1 Hz, 2H, CH_2CH_3). – ^{13}C NMR ($CDCl_3$): δ = 14.12 (CH_2CH_3), 14.23 (CH_2CH_3), 24.45 (cyclic CH_2), 24.93 (cyclic CH_2), 28.04 (cyclic CH_2), 39.38 (CH), 55.97 (H_3CO), 59.80 (CH_2CH_3), 60.67 (CH_2CH_3), 107.39 (C-2), 160.54 (C-1), 167.08 (C=O), 174.27 (C=O). – MS (70 eV), m/z (%): 256 (16) [M^+], 241 (26) [M^+ – CH_3], 210 (53) [M^+ – EtOH], 137 (100), 95 (27).

$C_{13}H_{20}O_5$ Calcd. 256.1311 Found 256.1305 (MS)

1-Acetoxy-2,4-diethoxycarbonylcyclohex-1-ene (**6c**)

IR ($CDCl_3$): ν = 1757 cm^{-1} (C=O), 1718 (C=O), 1185. – ^1H NMR ($CDCl_3$): δ = 1.27 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.28 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.85 (m_c, 1H), 2.08 (m_c, 1H), 2.19 (s, 3H, H_3CCO), 2.36 (m_c, 2H), 2.59 (m_c, 2H), 2.85 (m_c, 1H), 4.16 (q, J = 7.2 Hz, 2H, CH_2CH_3), 4.17 (q, J = 7.2 Hz, 2H, CH_2CH_3). – ^{13}C NMR ($CDCl_3$): δ = 14.05 (CH_2CH_3), 14.09 (CH_2CH_3), 20.76 (H_3CCO), 24.29 (cyclic CH_2), 27.21 (cyclic CH_2), 28.32 (cyclic CH_2), 38.47 (CH), 60.36 (CH_2CH_3), 60.52 (CH_2CH_3), 116.01 (C-2), 154.90 (C-1), 164.75 (C=O), 168.26 (C=O), 174.08 (C=O). – MS (70 eV), m/z (%): no [M^+], 241 (18) [M^+ – CH_3CO], 197 (43), 168 (100), 95 (56).

$C_{14}H_{20}O_6$	Calcd. C 59.14	H 7.09
(284.3)	Found C 59.10	H 7.16

4-Acetyl-1,4-ethoxycarbonyl-2-methoxycyclohex-1-ene (**7**)

A solution of **4b** (156 mg, 1 mmol) in 2 ml of CH_2Cl_2 are added to a suspension of aluminium trichloride (120 mg, 0.9 mmol) in 5 ml of the same solvent at 0 °C. The reaction is complete after 15 min. The mixture is poured into ice-water and extracted with diethylether. The organic phases are dried with $MgSO_4$ and evaporated under reduced pressure. Isolation by HPLC (cyclohexane / ethyl acetate, 2 : 1) yields 94 mg (66 %) of **7** as a colorless oil. The Lewis acids $ZnCl_2$, $SnCl_4$, $TiCl_4$ were used, too. – IR ($CDCl_3$): ν = 1715 cm^{-1} (C=O), 1220, 1171. – ^1H NMR ($CDCl_3$): δ = 1.23 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.26 (t, J = 7.2 Hz, 3H, CH_2CH_3), 2.12 (m_c, 2H, CH_2-5), 2.19 (s, 2H, CH_3CO), 2.39 (m_c, 2H, CH_2-6), 2.78 (ddd, ^2J = 16.7 Hz, ^4J = 1.6 Hz, ^5J = 1.6 Hz, 1H, CH_2-3), 2.91 (ddd, ^2J = 16.7 Hz, ^4J = 1.6 Hz, ^5J = 1.6 Hz, 1H, CH_2-3), 3.66 (s, 3H, H_3CO), 4.16 (q, J = 7.1 Hz, 4H, CH_2CH_3). – ^{13}C NMR ($CDCl_3$): δ = 13.88 (CH_2CH_3), 14.21 (CH_2CH_3), 23.25 (cyclic CH_2), 25.92 (H_3CCO), 26.21 (cyclic CH_2), 29.88 (cyclic CH_2), 55.52 (H_3CO), 56.22 (C-4), 59.89 (CH_2CH_3), 61.58 (CH_2CH_3), 103.41 (C-1), 162.10 (C-2), 166.36 (C=O), 171.07 (C=O), 204.17 (C=O). – MS (70 eV), m/z (%): 298 (4) [M^+], 255 (25) [M^+ – CH_3CO], 253 (21) [M^+ – EtOH], 181 (31), 43 (100).

$C_{15}H_{22}O_6$	Calcd. C 60.39	H 7.43
(298.3)	Found C 59.94	H 7.68

2-Acetoxy-1,4-diethoxycarbonyl-4-[1-(acetoxy)ethenyl]-cyclohex-1-ene (**8**)

4b (100 mg, 0.54 mmol) is dissolved in 4 ml of ethyl acetate and allowed to stand at room temperature until no diene is found by TLC. Evaporation of the solvent and column chromatography (cyclohexane / ethyl acetate, 2 : 1) affords 89 mg (89 %) of dimer **8** as a colorless oil. – IR ($CDCl_3$): ν = 1745 cm^{-1} (C=O), 1700 (C=O), 1649 (C=C), 1238. – ^1H NMR ($CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.26 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.98 (m_c, 1H, CH_2-5), 2.12 (m_c, 1H, CH_2-5), 2.14 (s, 3H, CH_3CO), 2.21 (s, 3H,

CH_3CO), 2.45 (m_c, 2H, CH_2-6), 2.57 (ddd, ^2J = 18.5 Hz, ^4J = 2.0 Hz, ^5J = 2.0 Hz, 1H, CH_2-3), 2.78 (ddd, ^2J = 18.5 Hz, ^4J = 2.0 Hz, ^5J = 2.0 Hz, 1H, CH_2-3), 4.15 (q, J = 7.1 Hz, 2H, $C\underline{H}_2CH_3$), 4.16 (q, J = 7.1 Hz, 2H, $C\underline{H}_2CH_3$), 5.03 (d, J = 2.9 Hz, 1H, H_2C=C), 5.22 (d, J = 2.9 Hz, 1H, H_2C=C). – ^{13}C NMR ($CDCl_3$): δ = 13.66 ($CH_2\underline{C}H_3$), 14.08 ($CH_2\underline{C}H_3$), 20.81 ($H_3\underline{C}CO$), 20.85 ($H_3\underline{C}CO$), 22.15 (cyclic CH_2), 26.76 (cyclic CH_2), 26.81 (C-4), 35.12 (cyclic CH_2), 50.57 (H_2C=$\underline{C}$), 60.42 ($\underline{C}H_2CH_3$), 61.59 ($\underline{C}H_2CH_3$), 103.69 ($H_2\underline{C}$=C), 116.66 (C-1), 152.55 (C-2), 152.85 (C=O), 164.62 (C=O), 166.32 (C=O), 171.49 (C=O). – MS (70 eV), m/z (%): no [M^+], 325 (20) [M^+ – CH_3CO], 283 (100) [M^+ – CH_3CO – ketene], 192 (54), 43 (100).

$C_{18}H_{24}O_8$	Calcd. C 58.69	H 6.57
(368.4)	Found C 58.32	H 6.89

4-Ethoxycarbonyl-3-oxocyclohexanecarboxylic acid (**9**)

Compound **9** is obtained similarily to **10** but using one equivalent of KOH per each ester group, m.p. 90–92 °C, yield 25 %. ^1H NMR ($CDCl_3$): δ = 0.95 (t, J = 7.1 Hz, 3H, CH_3), 1.43 (m_c, 1H), 1.54 (m_c, 1H), 1.80 (m_c, 1H), 2.07 (m_c, 1H), 2.35 (m_c, 3H), 2.63 (m_c, 1H), 3.94 (q, J = 7.1 Hz, 2H, $C\underline{H}_2CH_3$), 11.49 (s, 1H, CO_2H). – ^{13}C NMR ($CDCl_3$): δ = 14.12 ($CH_2\underline{C}H_3$), 21.53 (cyclic CH_2), 25.02 (cyclic CH_2), 30.78 (cyclic CH_2), 38.70 (CH), 42.74 (CH), 60.28 ($\underline{C}H_2CH_3$), 97.19 (C=O), 170.33 (C=O), 172.45 (C=O).

3-Oxocyclohexanecarboxylic acid (**10**)

440 mg (1.55 mmol) of **5c** and 0.54 g (9.64 mmol) of KOH are refluxed for 2 h in a mixture of 5 ml of ethanol and 2 ml of water. Evaporation of the solvent and treating with 0.8 ml of concd. HCl decarboxylated the β-oxo-ester. An additional portion of 0.8 ml of concd. HCl and heating to 50 °C completed the reaction. The aqueous solution is extracted with diethylether (4 × 20 ml), dried over $MgSO_4$ and evaporated. Column chromatography ($CHCl_3$ / MeOH / HAc, 100 : 10 : 1) affords 170 mg (77.4 %) of **10** as a colorless oil which crystallizes slowly, m.p. 75 °C. – IR ($CDCl_3$): ν = 3155 cm^{-1}, 1711 (C=O), 1282. – ^1H NMR ($CDCl_3$): δ = 1.08 (m_c, 1H), 1.41 (m_c, 2H), 1.60 (m_c, 1H), 1.73 (m_c, 1H), 1.96 (m_c, 1H), 2.31 (m_c, 3H), 10.95 (s, 1H, $CO_2\underline{H}$). – ^{13}C NMR ($CDCl_3$): δ = 24.11, 27.34, 40.57, 42.70, 42.84 (CH), 178.92 (C=O), 208.96 (C=O). – MS (70 eV), m/z (%): 142 (40) [M^+], 97 (83), 55 (100). Spectroscopic data are in accordance to those obtained from 3-oxocyclohexanecarboxylic acid prepared from 3-hydroxybenzoic acid after reduction of the aromatic ring and oxidation of the hydroxy group [12].

3-Ethoxycarbonyl-4-hydroxy-3-sulfolene (**11**)

Oxidation of 1.74 g (10 mmol) of **1** with OXONE following the method mentioned above yields 0.39 g (19 %) of **11** as colorless needles, m.p. 87 °C (ethanol). – IR (KBr): ν = 3400 cm^{-1} (OH), 1670 (C=O), 1307 (SO_2). – ^1H NMR ($CDCl_3$): δ = 1.33 (t, J = 7.2 Hz, 3H, CH_3), 3.99 (s, 2H, CH_2-2), 4.05 (s, 2H, CH_2-5), 4.29 (q, J = 7.2 Hz, 2H, $C\underline{H}_2CH_3$), 11.37 (s, 1H, OH). – ^{13}C NMR ($CDCl_3$): δ = 14.09 (CH_3), 55.10 (C-2), 56.05 (C-5), 61.71 ($\underline{C}H_2CH_3$), 95.83 (C-3), 163.47 (C-4), 167.92 (C=O). – Ms (70 eV), m/z (%): no [M^+], 142 (7) [M^+ – SO_2], 99 (15), 43 (100) [CH_3CO^+].

$C_7H_{10}O_5$	Calcd. C 40.77	H 4.89
(206.2)	Found C 40.75	H 4.71

3-Ethoxycarbonyl-4-hydroxy-2-oxo-2,5-dihydrothiophene (**13**)

300 mg (1.46 mmol) of **11** are placed in a horizontal mounted Kugelrohr-apparatus and heated at 160 °C/3 mbar for 2 hours. The product is distilled with ice-cooling and cristallizes in the refrigerator. Recrystallization from cyclohexane affords 162 mg (59 %) of **13** as colorless crystals, m.p. 83 °C (cyclohexane). – IR (KBr): ν = 3225 cm^{-1} (OH), 1665 (C=O), 1625. – ^1H NMR ($CDCl_3$): δ = 1.39 (t, J = 7.2 Hz, 3H, CH_3), 3.99 (s, 2H, SCH_2), 4.40 (q, J = 7.2 Hz, 2H, $C\underline{H}CH_3$), 9.88 (s, 1H, OH). – ^{13}C NMR ($CDCl_3$): δ = 14.01 (CH_3), 28.05 (C-5), 62.03 ($\underline{C}H_2CH_3$), 116.39 (C-4), 161.07 (C-3), 166.89 (CO_2), 191.84 (C-2). – MS (70 eV), m/z (%): 188 (14) [M^+], 160 (100) [M^+ – CO].

$C_7H_8O_4S$	Calcd. C 44.68	H 4.26
(188.2)	Found C 44.59	H 4.39

X-Ray Structure Analysis of Thiolactone (**13**)

Single crystals of sufficient quality have been obtained from benzene. Cristallographic data: $C_7H_8O_4S$, M_r = 188.2, monoclinic space group $P2_1/n$ with a = 4.2540(10), b = 17.681(4), c = 10.864(2) Å, β = 93.66(3)°, Z = 4, D_{cal} = 1.533 g/cm^3, V = 815.5(3) $Å^3$, absorption coefficient 0.35 mm^{-1}, F(000) = 392.

Data collection at room temperature: crystal size ~0.075 × 0.125 × 0.400 mm; Turbo cAD4 (Enraf-Nonius) diffractometer used; highly oriented graphite crystal monochromatized Mo-K_α radiation (λ = 0.71073 Å); 3982 reflections have been collected in the range of $-5 \leq h \leq 5$, $0 \leq k \leq 22$, $-14 \leq l \leq 14$; 2Θ Range from 4.0 to 55.0°; scan type 2Θ – Θ; variable scan speed from 1.03 to 4.12°/min in ω; scan range (ω) = 1.50° plus K_α-separation; 2 standard reflections measured every 120 minutes; 1875 independent reflections ($R_{int.}$ = 0.46 %); 1322 observed reflections ($F > 4.0\sigma(F)$).

Solution and refinement: The structure has been solved by direct methods as implemented in the Siemens SHELXTL PLUS (VMS) system; refinement method – Full-Matrix Least-Squares; quantity minimized – $\Sigma w (F_o - F_c)^2$; absolute structure – N/A; extinction correction – χ = 0.0017(3), where $F^* = F [1 + 0.002 \chi F^2/\sin(2\Theta)^2]^{-1/4}$; Hydrogen Atoms – Riding model, fixed isotropic U; weighting scheme – $w^{-1} = \sigma^2(F) + 0.0001F^2$; 110 parameters were refined; final R indices (obs. data) – R = 3.32 %, wR = 3.48 %; R indices (all data) – R = 5.78 %, wR = 3.78 %; Goodness-of-Fit – 1.58; largest and mean Δ/σ – 0.003, 0.001; Data-to-Parameter ratio – 12.0:1; largest difference peak – 0.19 $eÅ^{-3}$; largest difference hole – –0.17 $eÅ^{-3}$.

Table 2 Atomic coordinates ($\times 10^{-4}$) and equivalent isotropic displacement coefficients ($pm^2 \times 10^{-1}$)

	x	y	z	U(eq)
S	2368(1)	2570(1)	3369(1)	50(1)
O1	–3414(4)	4972(1)	3950(1)	62(1)
O2	–1234(3)	4919(1)	2137(1)	44(1)
O3	–2386(4)	3807(1)	5543(1)	52(1)
O4	705(4)	2428(1)	5662(1)	60(1)
C1	669(5)	2814(1)	4741(2)	44(1)
C2	–877(5)	3564(1)	4591(2)	39(1)
C3	–536(4)	3894(1)	3492(2)	37(1)
C4	1175(5)	3436(1)	2590(2)	41(1)
C5	–1863(5)	4641(1)	3230(2)	40(1)
C6	–2524(6)	5670(1)	1853(2)	51(1)
C7	–1881(6)	5857(1)	565(2)	55(1)

Further details of the structure are deposited at Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen. These data are available with quotation of the registry number CSD-57473, the authors, and the reference to this publication.

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