J. Org. Chem. 1986, 51, 508-512

[1,4] Addition of (Methylthio)methyl *p*-Tolyl Sulfone to α,β-Unsaturated Carbonyl Compounds

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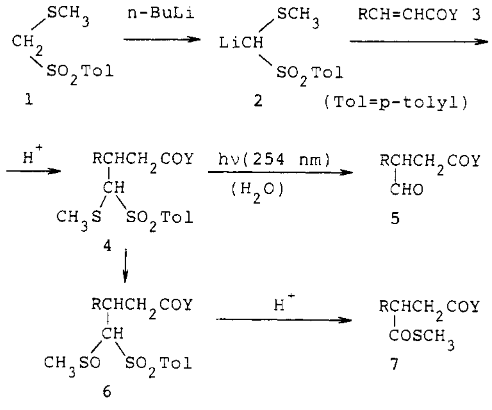
Received June 14, 1985

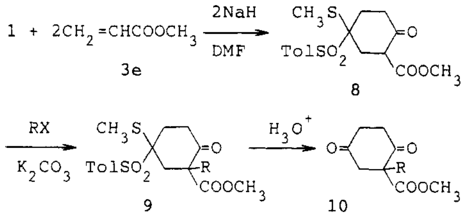
The lithio derivative of (methylthio)methyl *p*-tolyl sulfone (1) reacted with various α,β-unsaturated carbonyl compounds to afford [1,4] adducts in good to high yields. The introduced (methylthio)(*p*-tolylsulfonyl)methyl group was easily converted to a (methylthio)carbonyl group or a formyl group. When the reaction of 1 with methyl acrylate using sodium hydride as a base was performed in DMF at an ambient temperature, 2-(methoxycarbonyl)-4-(methylthio)-4-(*p*-tolylsulfonyl)cyclohexanone (8) was obtained in 81% yield. Furthermore, 8 was shown to be an important intermediate for preparing 2-substituted 2-(methoxycarbonyl)-1,4-cyclohexanediones.

To date, much attention has been paid to the [1,4] addition of the carbanions of dithioacetals and their *S*-oxides to α,β-unsaturated carbonyl compounds mainly because the [1,4] adducts are useful for the preparation of synthetically important 1,4-dicarbonyl compounds. The ratio of the [1,4] and [1,2] adducts has proven to depend on the carbanion nature, the counterion, and the reaction conditions (temperature and solvent).[1-13] In the reaction of α,β-unsaturated carbonyl compounds with highly delocalized or well-stabilized carbanions, reversible additions are normally observed: The [1,2] and [1,4] adducts are usually the results of kinetic and thermodynamic control, respectively. For example, 2-lithio-1,3-dithianes generally react with α,β-unsaturated carbonyl compounds to give only the [1,2] adducts,[14] whereas 2-lithio-2-phenyl-1,3-dithiane affords the [1,4] adduct with 2-cyclohexenone in a thermodynamically controlled manner (at 25 °C).[7] It was also reported that the reaction of [bis(methylthio)(stannyl or silyl)methyl]lithium and [tris(phenylthio)methyl]lithium with α,β-unsaturated ketones resulted in the exclusive formation of [1,4] adducts.[4,5,9] These reports prompted us to investigate the base-induced addition of (methylthio)methyl *p*-tolyl sulfone (1)[15] to α,β-unsaturated carbonyl compounds, where the production of [1,4] adducts (4) is expected because 1 forms a stable carbanion,[17] a synthetic equivalent of formyl carbanion, (methylthio)carbonyl carbanion, or carbonyl dianion.[18,20] This paper reports that the lithio derivative (2) of 1 adds to various α,β-unsaturated carbonyl compounds (3) to give [1,4] adducts (4), which are synthetic precursors for 3-formyl[21] and

Scheme I



Scheme II



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(15) This reagent (1) can be conveniently synthesized by the reaction of acetoxymethyl methyl sulfide with sodium *p*-toluenesulfinate.[12] By our investigations, 1 has proven to be a useful reagent for making various organic compounds such as *S*-methyl α-ketocarbothioate, carboxylic esters, cycloalkanones, α-methoxy-α-arylacetic esters, and aldehydes.[13-15]

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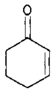
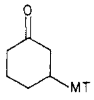
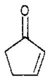
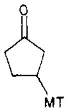
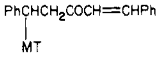
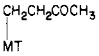
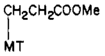
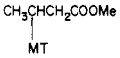
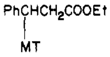
(21) Several reports have been published for converting an α,β-unsaturated ketone into a 4-ketoaldehyde by [1,4] addition of a formyl anion equivalent followed by unmasking to an aldehyde.[8,9,12,22,23]

0022-3263/86/1951-0508$01.50/0

Table I. Reaction of 2 (M = Li) with α,β-Unsaturated Carbonyl Compounds (3)[a]

run	substrate (equiv)[b]	(equiv)[b]	temp, °C/time, h	product 4[c]	yield, %[d]
1	 **3a**	(1.3)	−78/4	 **4a**	trace
2		(1.3)	−78/3 → −25/1 → 0/1		47 (69)
3		(1.2)	−25/3 → −20/1 → 15/3		83 (87)
4	 **3b**	(1.3)	−78/4	 **4b**	trace
5		(1.3)	−78/3 → −25/1 → 0/1		40 (62)
6		(1.2)	−25/3 → −15/1		70 (83)
7	PhCH=CHCOCH=CHPh **3c**	(1.0)	−78/5	 $\underset{\mathrm{MT}}{\mathrm{PhCH}}\mathrm{CH_2COCH{=}CHPh}$ **4c**	71 (81)
8	$CH_2{=}CHCOCH_3$ **3d**	(1.1)	−78/5	 $\underset{\mathrm{MT}}{\mathrm{CH_2}}\mathrm{CH_2COCH_3}$ **4d**	27 (62)
9		(1.2)	−25/3 → −15/3		29 (39)
10	$CH_2{=}CHCOOMe$ **3e**	(1.5)	−78/5	 $\underset{\mathrm{MT}}{\mathrm{CH_2}}\mathrm{CH_2COOMe}$ **4e**	44 (50)[e]
11	$CH_3CH{=}CHCOOMe$ **3f**	(1.2)	−78/4	 $\mathrm{CH_3}\underset{\mathrm{MT}}{\mathrm{CH}}\mathrm{CH_2COOMe}$ **4f**	67
12	PhCH=CHCOOEt **3g**	(1.1)	−78/5	 $\underset{\mathrm{MT}}{\mathrm{PhCH}}\mathrm{CH_2COOEt}$ **4g**	91

[a] In THF. [b] Molar equiv to 1 are in parentheses. [c] MT = (methylthio)(p-tolylsulfonyl)methyl. [d] Yields based on unrecovered 1 are in parentheses. [e] 2:1 adduct (17, n = 2) of 3e and 1 was also produced in 19% yield (see text).

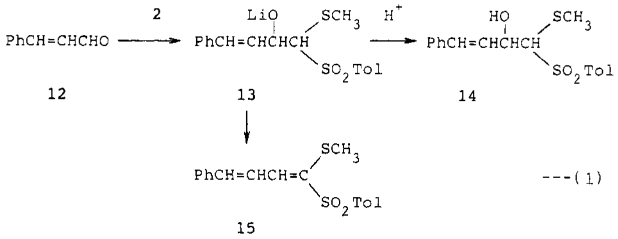
3-(methylthio)carbonyl derivatives (5 and 7 of Scheme I) of 3. We also describe the optimal conditions for a tandem double [1,4] addition–Dieckmann condensation of 1 with methyl acrylate leading to a useful intermediate (8) for synthesizing 2-substituted 2-(methoxycarbonyl)-1,4-cyclohexanedione (10) as depicted in Scheme II.

Results and Discussion

First we examined the reaction of a typical α,β-unsaturated carbonyl compound, 2-cyclohexenone (3a), with the lithio derivative 2 in THF. After 2 was generated by the action of n-butyllithium on 1 at −78 °C → room temperature, 3a was added. The yield of a [1,4] adduct (4a) was found to be crucially dependent on the reaction temperature. At −78 °C, a trace of 4a was formed. When the temperature was slowly raised from −78 °C to 0 °C, the yield of 4a increased to 47%. An NMR analysis showed that the reaction mixture contained a 2:1 adduct of 3a and 1, which was probably formed due to the presence of a large amount of the unreacted 3a in the reaction system. It seems indispensable for the efficient formation of 4a that 3a is consumed as soon as it is introduced into a solution of 2. Indeed, when 3a was added dropwise to a solution of 2 in THF at −25 to −10 °C, 4a was obtained in 83% yield. This is in sharp contrast to the fact that the lithio derivatives of 1,3-dithiane and methyl (methylthio)methyl sulfoxide react with 3a to give the corresponding [1,2] adducts.[11,14] Since the corresponding [1,2]adduct (11) could not be isolated in spite of many efforts, sufficient data are not available for distinguishing possible mechanisms of the present [1,4] addition: thermodynamically and kinetically controlled paths.

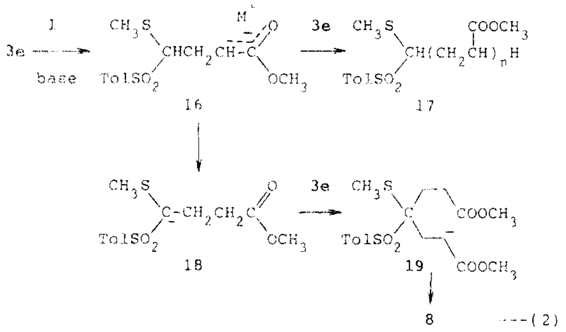
Similar phenomena were observed in the reaction of 2 with 2-cyclopentenone (3b) (Table I, runs 4–6). Acyclic α,β-unsaturated ketones and α,β-unsaturated esters gave the best results when the reaction temperature was kept at −78 °C, as shown in Table I.

In the reaction of 2 with an α,β-unsaturated aldehyde, cinnamaldehyde (12), a [1,2] adduct (14) was exclusively obtained in 85% yield (98% based on the unrecovered 1). In order to obtain the thermodynamically stable [1,4] adduct, the reaction was performed at an elevated temperature (−78 °C → −25 °C → 0 °C → room temperature), but a dehydration product (15) was obtained as the sole product (55%).



---(1)

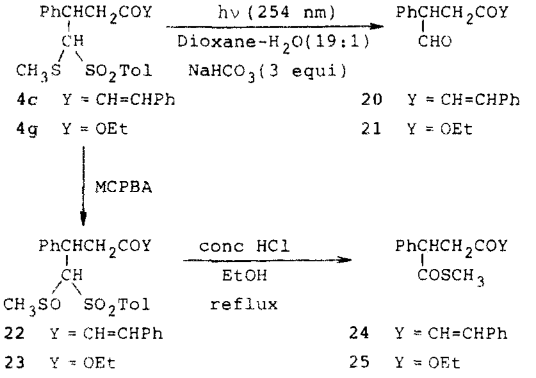
During the course of our study of the conditions for the base-induced [1,4] addition of 1 with methyl acrylate (3e), we discovered that a tandem double [1,4] addition–Dieckmann condensation efficiently occurred in the presence of sodium hydride. In the addition of 2 to 3e, n:1 adducts (17) as well as 4e were formed, indicating that an intermediate carbanion (16, M = Li) derived from 2 and 3e is stable enough to react with another molecule of 3e. The reaction of 1 with 3a (1.5 equiv) in THF using sodium hydride (1 equiv) as a base (0 °C → room temperature) gave 2-(methoxycarbonyl)-4-(methylthio)-4-(p-tolylsulfonyl)cyclohexanone (8) in 42% yield together with 4e (11%). The formation of 8 may be rationalized by the path depicted in eq 2. Since the carbanion 16 (M = Na) is less stable, a proton transfer takes place to give a new car-



---(2)

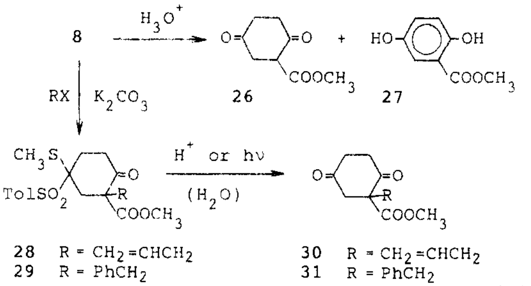
banion (**18**). The subsequent addition of **18** to **3e** followed by the so-called Dieckmann condensation afforded **8**. The use of excess sodium hydride (2.5 equiv) and excess **3e** (2–3 molar equiv) does not improve the yield of **8** (43–48%). After several conditions had been examined, a high yield of **8** was attained in the reaction conducted in DMF which facilitated the proton-transfer step of **16** → **18**: After **1** was treated with sodium hydride (2.6 equiv) in DMF under ice-cooling, **3e** (2.2 equiv) was slowly added at room temperature, and the resulting mixture was stirred at the same temperature. The usual workup gave **8** in 81% yield.

Finally we describe the functionalization of the dithioacetal *S,S*-dioxide part of **4** and **8**. Recently, we reported that hydrolysis of monoalkyl derivatives of **1** to afford aldehydes was photochemically achieved.[20] This photoinduced hydrolysis could be applied to the conversion of **4** to the corresponding formyl derivative. Irradiation of **4c** and **4g** with a low pressure mercury lamp (a Vycor filter) in dioxane–water (19:1) gave aldehydes **20** and **21** in yields of 53% (74% based on the unrecovered **4c**) and 64% (75%), respectively (eq 3). Furthermore, the (methylthio)(*p*-tolylsulfonyl)methyl group of **4** was transformed into a (methylthio)carbonyl group by oxidation leading to a (methylsulfinyl)(*p*-tolylsulfonyl)methyl group, followed by the Pummerer rearrangement and the subsequent removal of *p*-toluenesulfinic acid. Oxidation of **4c** and **4g** with *m*-chloroperbenzoic acid (MCPBA) yielded the corresponding sulfoxides **22** and **23**. On treatment of these sulfoxides with concentrated hydrochloric acid in refluxing ethanol, **24** and **25** were produced in 57%[24] and 70% yields, respectively.



---(3)

Since ketone dithioacetal *S,S*-dioxides are readily converted to the corresponding ketones by hydrolysis with an acid or 254 nm light,[18,20,25,26] the cyclic product **8** is regarded as a synthetic equivalent of 2-(methoxycarbonyl)-1,4-cyclohexanedione (**26**). However, treatment of **8** with concentrated hydrochloric acid in refluxing methanol gave 2-(methoxycarbonyl)-1,4-hydroquinone (**27**, 12%) along with **26** (25%). This suggests that, after **8** has been subjected to various reactions, the dithioacetal *S,S*-dioxide part of the resulting product should be hydrolyzed at the final stage. Reaction of **8** with allyl bromide and benzyl bromide in the presence of potassium carbonate in DMF gave an allylated product (**28**) and a benzylated product (**29**), respectively. When these products were subjected to hydrolysis with concentrated hydrochloric acid in refluxing methanol, the expected cyclohexanediones (**30** and **31**) were obtained in 52% and 46% yields, respectively (eq 4). The photoinduced hydrolysis of **29** with a low pressure mercury lamp in dioxane–water (19:1) raised the yield of **31** to 64%. Thus, **8** has proven to be a useful intermediate in preparation of 2-substituted 2-(methoxycarbonyl)-1,4-cyclohexanediones.



28 R = CH2=CHCH2
29 R = PhCH2
30 R = CH2=CHCH2
31 R = PhCH2

---(4)

Conclusion

In summary, the carbanion of **1** has been revealed to be a good donor in the [1,4] addition to α,β-unsaturated carbonyl compounds. This [1,4] addition can be utilized for introduction of formyl or (methylthio)carbonyl groups into the α-position of α,β-unsaturated carbonyl compounds. Further, a convenient method for the synthesis of 2-substituted 2-(methoxycarbonyl)-1,4-cyclohexanediones was also realized by the use of **1**.

Experimental Section

General Procedures. Melting points were determined on a hot-stage microscope apparatus (Yanagimoto) and are uncorrected. Analytical thin-layer chromatography (TLC) was performed with 0.2-mm silica gel coated plastic sheets (Merck Art. 5748). All column chromatography was done on Wako Gel C-200. Proton magnetic resonance (^{1}H NMR) spectra were recorded on Hitachi R-600 (60 MHz) or JEOL FX-270 (270 MHz) spectrometers in deuteriochloroform. Chemical shifts are reported in parts per million downfield from tetramethylsilane as the internal standard (δ scale). Infrared spectra were determined with JASCO A-200 spectrometer and data are presented in reciprocal centimeters for important diagnostic absorptions. Mass spectra (MS) were determined on Hitachi RMU-6E or RMU-7M spectrometers at 70 eV. Data are presented in the form *m/e* (intensity relative to base peak = 100). Microanalytical data were provided by the Analytical Center of Chiba University.

Unless otherwise noted, other materials were obtained from commercial suppliers (Aldrich Chemical Co., Tokyo Kasei Chemical Industry Co., Wako Pure Chemical Industries Co., and Kanto Chemical Co.) and used after being purified by distillation and being dried over molecular sieves, 3–4 Å. Tetrahydrofuran (THF) was distilled over lithium aluminium hydride. *n*-Butyllithium (1.6 M in hexane) was purchased from Aldrich Chemical

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(24) As a byproduct, 1-[(methylthio)carbonyl]-1,5-diphenyl-5-(*p*-tolylsulfonyl)-3-pentanone was obtained in 27% yield. This can be converted to **24** by treatment with potassium carbonate in 1,2-dimethoxyethane (see Experimental Section).

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Co. (Methylthio)methyl *p*-tolyl sulfone (**1**) which was purchased from Nissan Chemical Industries Co., was recrystallized from benzene–hexane, and dried over phosphorus pentoxide. Dibenzalacetone (**3c**) was prepared according to the known methods.[27]

Addition of (Methylthio)methyl *p*-Tolyl Sulfone (1) to 2-Cyclohexenone. Typical Procedure. To a solution of **1** (400 mg, 1.85 mmol) in THF (10 mL) was added *n*-butyllithium (1.2 mL, 1.86 mmol) at −78 °C, and the solution was warmed at room temperature and stirred for 1 h. Then the solution was cooled to −25 °C and 2-cyclohexenone (**3a**; 213 mg, 2.22 mmol) was added dropwise over 1 min. The resulting solution was stirred at this temperature for 3 h, at −20 °C for 1 h, and then at −15 °C for 3 h. After workup with saturated aqueous NH_4Cl (50 mL) followed by extraction with dichloromethane (50 mL × 4), the combined extracts were washed with water, dried ($MgSO_4$), and evaporated. The residue was chromatographed [benzene–ethyl acetate (20:1)] to give **4a** (482 mg, 83%) as a mixture of two diastereomers (A:B = 5:3) along with **1** (16 mg, 4%). An analytical sample of **4a** (A:B = 7:8) was obtained by recrystallization from benzene–hexane: mp 128–155 °C; ^1H NMR δ 1.95 (s, CH_3 of A), 2.02 (s, CH_3 of B), 2.46 (s, 3 H), 1.1–3.2 (m, 9 H), 3.56 (br s, CH of B), 3.73 (d, *J* = 2.4 Hz, CH of A), 7.40 (d, *J* = 8 Hz, 2 H), 7.83 (d, *J* = 8 Hz, 2 H); IR (KBr) 1704, 1279, 1138, 1078, 559 cm^{-1}. Anal. Calcd for $C_{15}H_{20}O_3S_2$: C, 57.66; H, 6.45. Found: C, 57.82; H, 6.42.

In a similar manner using the conditions described in Table I, the following [1,4] adducts were obtained. **4b** (a 1:1 mixture of two diastereomers): colorless crystals; mp 112–115.5 °C; ^1H NMR δ 2.02 (s, $^3/_2$ H), 2.08 (s, $^3/_2$ H), 1.6–3.3 (m, 7 H), 2.47 (s, 3 H), 3.78 (d, *J* = 2.4 Hz, $^1/_2$ H), 3.88 (d, *J* = 1.2 Hz, $^1/_2$ H), 7.37 (d, *J* = 8 Hz, 2 H), 7.83 (d, *J* = 8 Hz, 2 H); IR (KBr) 1740, 1298, 1140, 1083, 560, 520 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_3S_2$: C, 56.35; H, 6.08. Found: C, 56.48; H, 6.10.

4c (almost one diastereomer): a colorless glassy solid; ^1H NMR δ 1.96 (s, 3 H), 2.43 (s, 3 H), 3.34 (d, *J* = 7 Hz, 2 H), 3.81 (d, *J* = 2 Hz, 1 H), 4.27 (diffused t, *J* = 7 Hz, 1 H), 6.60 (d, *J* = 16 Hz, 1 H), 7.0–7.7 (m, 13 H), 7.36 (d, *J* = 8 Hz, 2 H); IR (KBr) 1693, 1660, 1609, 1300, 1140, 1081, 698 cm^{-1}; high resolution mass spectrum, *m/e* 295.1176 (24, calcd for $M^+ - SO_2Tol$ 295.1155), 131.0505 (100, calcd for $PhCH{=}CHCO^+$ 131.0487), 103.0559 (17, calcd for $PhCH{=}CH^+$ 103.0548). Anal. Calcd for $C_{26}H_{26}O_3S_2 + CH_2Cl_2$: C, 65.61; H, 5.59. Found: C, 65.79; H, 5.61.

4d: colorless crystals; mp 62–63 °C; ^1H NMR δ 2.14 (s, 3 H), 2.21 (s, 3 H), 2.47 (s, 3 H), 1.4–2.9 (m, 4 H), 3.86 (dd, *J* = 4, 10 Hz, 1 H), 7.39 (d, *J* = 8 Hz, 2 H), 7.83 (d, *J* = 8 Hz, 2 H); IR (KBr) 1715, 1300, 1142, 651, 561, 523 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_3S_2$: C, 54.52; H, 6.33. Found: C, 54.54; H, 6.34.

4e: a colorless viscous oil; ^1H NMR δ 2.22 (s, 3 H), 2.46 (s, 3 H), 1.6–2.8 (m, 4 H), 3.66 (s, 3 H), 3.89 (dd, *J* = 4, 10 Hz, 1 H), 7.40 (d, *J* = 8 Hz, 2 H), 7.82 (d, *J* = 8 Hz, 2 H); IR (KBr) 1722, 1302, 1297, 1195, 1141, 1126, 1092 cm^{-1}. The disulfone derivative of **4e** was obtained by Na_2WO_4-catalyzed oxidation with H_2O_2 in methanol: colorless crystals; mp 112–113 °C (from methanol); ^1H NMR δ 2.1–3.0 (m, 4 H), 2.48 (s, 3 H), 3.28 (s, 3 H), 3.67 (s, 3 H), 4.52 (t, *J* = 6 Hz, 1 H), 7.37 (d, *J* = 8 Hz, 2 H), 7.87 (d, *J* = 8 Hz, 2 H); IR (KBr) 1724, 1312, 1148, 699, 586, 513 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_4S_2$: C, 46.69; H, 5.43. Found: C, 46.72; H, 5.38.

4f (one diastereomer): mp 112–113 °C (from benzene–hexane); ^1H NMR δ 1.17 (d, *J* = 7 Hz, 3 H), 2.11 (s, 3 H), 2.47 (s, 3 H), 1.88–3.12 (m, 3 H), 3.64 (d, *J* = 2.3 Hz, 1 H), 3.67 (s, 3 H), 7.36 (d, *J* = 8 Hz, 2 H), 7.84 (d, *J* = 8 Hz, 2 H); IR (KBr) 1720, 1290, 1260, 1140, 660, 579 cm^{-1}. Anal. Calcd for $C_{14}H_{20}O_4S_2$: C, 53.14; H, 6.37. Found: C, 53.29; H, 6.35.

4g (almost one diastereomer): a colorless oil; ^1H NMR δ 1.04 (t, *J* = 7 Hz, 3 H), 1.87 (s, 3 H), 2.45 (s, 3 H), 2.7–3.1 (m, 2 H), 3.6–4.3 (m, 4 H), 7.21 (s, 5 H), 7.38 (d, *J* = 8 Hz, 2 H), 7.84 (d, *J* = 8 Hz, 2 H); IR (liquid film) 1733, 1301, 1141 cm^{-1}. Anal. Calcd for $C_{20}H_{24}O_4S_2$: C, 61.20; H, 6.16. Found: C, 61.29; H, 6.17.

In the reaction of **2** with **3e**, **17** (*n* = 2) was also isolated in almost pure form. Its physical properties were obtained after oxidation leading to its disulfone derivative which consisted of two diastereomers (11:10): mp 61–65 °C; ^1H NMR δ 1.7–2.05 (m, 2 H), 2.1–2.3 (m, 2 H), 2.38 (t, *J* = 7 Hz, 2 H), 2.47 (s, 3 H), 2.85–3.0 (m, 1 H), 3.27 + 3.69 + 3.70 (three CH_3 singlets of the minor isomer), 3.30 + 3.66 + 3.68 (three CH_3 singlets of the major isomer), 4.56 + 4.58 (two triplets, 1 H), 7.40 (d, *J* = 8 Hz, 2 H), 7.86 (d, *J* = 8 Hz, 2 H); IR (KBr) 1730, 1310, 1150 cm^{-1}. Anal. Calcd for $C_{17}H_{24}O_8S_2$: C, 48.56; H, 5.75. Found: C, 48.83; H, 5.73.

Reaction of 1 with *trans*-Cinnamaldehyde. To a solution of **1** (500 mg, 1.85 mmol) in THF (10 mL) was added *n*-butyllithium (1.5 mL, 2.31 mmol) at −78 °C, and the solution was warmed at room temperature and stirred for 1 h. Then the solution was cooled at −78 °C and **12** (336 mg, 2.55 mmol) was dropwise added. After the resulting solution was stirred at the same temperature, saturated aqueous NH_4Cl (100 mL) was added, and extraction with dichloromethane (40 mL × 4) was performed. The combined extracts were washed with water, dried ($MgSO_4$), and evaporated. The residue was chromatographed [benzene–ethyl acetate (20:1)] to give two diastereomers (A:B = 1:1) of **14** (688 mg, 85%) along with **1** (65 mg, 13%). **14A**: mp 106–107 °C (from 95% ethanol); ^1H NMR δ 2.02 (s, 3 H), 2.38 (s, 3 H), 3.31 (d, *J* = 3 Hz, 1 H, OH), 3.86 (d, *J* = 2 Hz, 1 H), 4.95–5.3 (br peak which becomes diffused d in the presence of D_2O, *J* = 5 Hz) 6.25 (dd, *J* = 5, 16 Hz, 1 H), 6.63 (d, *J* = 16 Hz, 1 H), 7.26 (s, 5 H), 7.32 (d, *J* = 8 Hz, 2 H), 7.83 (d, *J* = 8 Hz, 2 H); IR (KBr) 3470, 1281, 1138, 1080, 571 cm^{-1}. Anal. Calcd for $C_{18}H_{20}O_3S_2$: C, 62.04; H, 5.78. Found: C, 62.16, H, 5.81. **14B**: mp 90–91 °C (from benzene–hexane); ^1H NMR δ 2.09 (s, 3 H), 2.35 (s, 3 H), 3.86 (d, *J* = 5 Hz, 1 H, OH), 4.01 (d, *J* = 5 Hz, 1 H), 4.88 (q which becomes t in the presence of D_2O, *J* = 5 Hz), 6.24 (dd, *J* = 5, 16 Hz, 1 H), 6.61 (d, *J* = 16 Hz, 1 H), 7.24 (s, 5 H), 7.27 (d, *J* = 8 Hz, 2 H), 7.83 (d, *J* = 8 Hz, 2 H); IR (KBr) 3480, 1284, 1137, 1080, 574 cm^{-1}. Anal. Calcd for $C_{18}H_{20}O_3S_2$: C, 62.04; H, 5.78. Found: C, 62.19; H, 5.80.

When the temperature of the above reaction was raised slowly (at −78 °C for 3 h, at −25 °C for 1 h, at 0 °C for 1 h, and then at room temperature for 1 d), 1-(methylthio)-4-phenyl-1-(*p*-tolylsulfonyl)-1,3-butadiene (**15**) was obtained in 55% yield together with **1** (23%). **15**: a yellow oil; ^1H NMR δ 2.31 (s, 3 H), 2.43 (s, 3 H), 7.15 (d, *J* = 15.8 Hz, 1 H), 7.25–7.47 (m, 6 H), 7.50–7.58 (m, 2 H), 7.84 (d, *J* = 8.2 Hz, 2 H), 7.96 (d, *J* = 10.6 Hz, 1 H);[28] IR (KBr) 1613, 1314, 1291, 1140, 1086, 683 cm^{-1}. Anal. Calcd for $C_{18}H_{18}O_2S_2$: C, 65.42; H, 5.49. Found: C, 65.49; H, 5.50.

Synthesis of 2-(Methoxycarbonyl)-4-(methylthio)-4-(*p*-tolylsulfonyl)cyclohexanone (8). To a solution of **1** (3.27 g, 15.1 mmol) in DMF (100 mL) was added NaH (60% dispersion in an oil, 1.54 g, 38.6 mmol) under cooling with ice, and the resulting suspension was stirred at room temperature for 1 h. Then, methyl acrylate (2.87 g, 33.3 mmol) was added dropwise at room temperature over a period of 30 min. The resulting mixture was further stirred at same temperature for 30 min. After addition of a saturated aqueous NH_4Cl (200 mL) and extraction with diisopropyl ether (50 mL × 5), the combined organic layers were washed with brine, dried ($MgSO_4$), and evaporated. The residue was separated by column chromatography [benzene–ethyl acetate (25:1)] to give **8** (4.36 g, 81%) as a pale yellow oil which crystallized: mp 87–88 °C (from dichloromethane–hexane); ^1H NMR δ 2.18 (s, 3 H), 2.44 (s, 3 H), 2.98 (d, *J* = 16 Hz, 1 H), 3.73 (3 H, s), 7.35 (d, *J* = 8 Hz, 2 H), 7.86 (d, *J* = 8 Hz, 2 H), 9.10 (s, 1 H, OH); IR (KBr) 3450, 1657, 1620, 1285, 1214, 1137, 1080 cm^{-1}. Anal. Calcd for $C_{16}H_{20}O_5S_2$: C, 53.91; H, 5.66. Found: C, 53.97; H, 5.65.

Photoinduced Hydrolysis of 4c. A mixture containing **4c** (258 mg, 0.55 mmol) and sodium hydrogen carbonate (138 mg, 1.64 mmol) in dioxane–water (19:1, 200 mL) was irradiated by using a 10-W low pressure mercury lamp with Vycor housing under bubbling N_2 under cooling with tap water for 1 h. Then, after brine (200 mL) was added, the mixture was extracted with dichloromethane (100 mL × 4). The extracts were combined, washed with water (100 mL × 3), and dried ($MgSO_4$). Evaporation of the solvent and the subsequent column chromatography [benzene–hexane (1:3)] gave **20** (94 mg, 64%) as a mixture of its geometric isomers [*E*:*Z* = 85:15]. The *E* isomer was isolated by rechromatography to a colorless oil which soon crystallized: mp 68–72 °C; ^1H NMR δ 2.91 (dd, *J* = 18, 5 Hz, 1 H), 3.59 (dd, *J* = 18, 8 Hz, 1 H), 4.32 (dd, *J* = 8, 5 Hz, 1 H), 6.70 (d, *J* = 16 Hz,

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[27] Conard, C. R.; Dolliver, M. A. "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, p 167.

[28] Two small singlets were also observed at δ 2.23 and 2.39. These might be attributable to the geometric isomer of 15.

1 H), 7.0–7.7 (m, 11 H), 9.70 (1 H, s); IR (KBr) 1720, 1642, 984, 744, 696, 528 cm^{-1}. Anal. Calcd for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.57; H, 6.15. The *Z* isomer showed its ^{1}H NMR signals at δ 2.77 (dd, *J* = 18, 5 Hz, 1 H), 3.40 (dd, *J* = 18, 8 Hz, 1 H), 4.27 (dd, *J* = 8, 5 Hz, 1 H), 6.20 (d, *J* = 16 Hz, 1 H), 9.68 (1 H, s).

Ethyl 3-Formyl-3-phenylpropionate (21). In a similar manner to that described above, irradiation of **4g** afforded **21** (111 mg, 49%) together with the unreacted **4g** (27 mg). **21**: a colorless oil: ^{1}H NMR δ 1.20 (t, *J* = 7 Hz, 3 H), 2.61 (dd, *J* = 16, 6 Hz, 1 H), 3.15 (dd, *J* = 16, 8 Hz, 1 H), 3.8–4.4 (3 H, m), 7.29 (diffused s, 5 H), 9.67 (1 H, s); IR (KBr) 1740, 1373, 1246, 1190, 1030, 700 cm^{-1}; MS (70 eV), *m/e* 178 (44, M$^+$ – CO), 161 (23), 135 (15), 107 (51), 106 (17), 105 (100), 104 (94), 103 (14), 91 (23), 79 (14), 77 (19), 29 (13).

Transformation of 4c into 5-[(Methylthio)carbonyl]-1,5-diphenyl-1-penten-3-one (24). To a solution of **4c** (250 mg, 0.55 mmol) in dichloromethane (10 mL) was added MCPBA (370 mg, 2.15 mmol) under ice-cooling, and the resulting mixture was stirred at the same temperature for 2 h. After addition of water (50 mL) and extraction with dichloromethane (40 mL × 4), the combined organic layers were washed with aqueous $NaHCO_3$ (50 mL) and water (50 mL), dried ($MgSO_4$), evaporated, and chromatographed [benzene–ethyl acetate (9:1)] to give the corresponding sulfoxide (**22**) (238 mg, 92%) as a diastereomeric mixture. A solution of **22** (230 mg, 0.49 mmol) and concentrated hydrochloric acid (1 mL) in ethanol (5 mL) was heated under reflux for 2 h. The aqueous workup followed by column chromatography [hexane–benzene (1:3)] afforded **24** (88 mg, 57%) as colorless crystals along with 1-[(methylthio)carbonyl]-5-(*p*-tolylsulfonyl)-1,5-diphenyl-3-pentanone (61 mg), the structure of which was deduced by its ^{1}H NMR and IR spectra. Treatment of this product with potassium carbonate (35 mg) in DME (5 mL) at room temperature for 6 days gave **24** (28 mg) after the usual workup and subsequent column chromatography. The total yield of **24** amounted to 67%. **24**: colorless crystals; mp 110–111 °C (from 95% ethanol); ^{1}H NMR δ 2.23 (s, 3 H), 2.99 (dd, *J* = 17, 5 Hz, 1 H), 3.66 (dd, *J* = 17, 9 Hz, 1 H), 4.97 (dd, *J* = 9, 5 Hz, 1 H), 6.70 (d, *J* = 16 Hz, 1 H), 7.09–7.22 (m, 11 H); IR (KBr) 1683, 1608, 1059, 940, 717, 686 cm^{-1}. Anal. Calcd for $C_{19}H_{18}O_2S$: C, 73.52; H, 5.84. Found: C, 73.48; H, 5.88.

Transformation of 4g into Ethyl 3-[(Methylthio)-carbonyl]-3-phenylpropanoate (25). Oxidation of **4g** (804 mg, 2.05 mmol) and MCPBA (371 mg, 2.15 mmol) was carried out in the manner analogous to the transformation of **4c** to give the corresponding sulfoxide **23** (721 mg, 86%) as a diastereomeric mixture. This sulfoxide (290 mg, 0.71 mmol) was dissolved in ethanol (5 mL), and concentrated hydrochloric acid (1 mL) was added. After the resulting solution was heated under reflux for 5 h, water (50 mL) was added and extraction with diethyl ether (50 mL × 4) was performed. The combined extracts were washed with brine, dried ($MgSO_4$), and evaporated. The residue was separated by column chromatography [benzene–hexane (2:1)] to give **25** (126 mg, 70%) as a colorless oil: ^{1}H NMR δ 1.17 (t, *J* = 7 Hz, 3 H), 2.21 (s, 3 H), 2.69 (dd, *J* = 16, 6 Hz, 1 H), 3.20 (dd, *J* = 16, 8 Hz, 1 H), 4.08 (q, *J* = 7 Hz, 2 H), 4.27 (dd, *J* = 6, 8 Hz, 1 H), 7.22 (s, 5 H); IR (liquid film) 1740, 1688, 1240, 1186, 1094, 704 cm^{-1}; MS, *m/e* 207 (23, M$^+$ – OEt), 205 (93, M$^+$ – SCH_3), 137 (42), 136 (24), 135 (100), 107 (31), 105 (61), 104 (45), 103 (35), 91 (26), 77 (25), 75 (23), 30 (40).

Acid Hydrolysis of 8. A mixture of **8** (1.20 g, 3.36 mmol) and concentrated hydrochloric acid (1 mL) in methanol (20 mL) was heated under reflux for 8 h. After addition of water (100 mL) and extraction with dichloromethane (40 mL × 5), the combined extracts were washed with brine, dried ($MgSO_4$), and evaporated. The residue was chromatographed [hexane–benzene (5:7)] to give 2-(methoxycarbonyl)-1,4-cyclohexanedione (**26**) (125 mg) along with a 19:81 mixture (83 mg) of **26** and methyl 2,5-dihydroxybenzoate (**27**). **26**: a colorless oil; ^{1}H NMR δ 2.35–2.9 (m, 4 H), 3.09 (s, 2 H), 3.80 (s, 3 H), 7.32 (s, 1 H, OH); IR (liquid film) 1728, 1667, 1442, 1240, 1181 cm^{-1}; MS, *m/e* 170.0568 (88, M$^+$, calcd for $C_8H_{10}O_4$ 170.0578). The structure of **27** was assigned by comparison of its ^{1}H NMR signals and the R_f value of its TLC with those of an authentic sample which was prepared by esterification of commercially available 2,5-dihydroxybenzoic acid with hydrogen chloride–methanol.

2-Allyl-2-(methoxycarbonyl)-4-(methylthio)-4-(*p*-tolylsulfonyl)cyclohexanone (28). After the mixture of **8** (500 mg, 1.4 mmol) and potassium carbonate (291 mg, 2.11 mmol) in DMF (15 mL) was stirred at room temperature for 30 min, allyl bromide (543 mg, 3.74 mmol) was added under ice-cooling, and the resulting mixture was further stirred at the same temperature for 30 min and then at room temperature for 17 h. After being quenched with aqueous NH_4Cl (20 mL), the resulting mixture was extracted with diethyl ether (40 mL × 4). The combined extracts were dried ($MgSO_4$), evaporated, and subjected to column chromatography [benzene–ethyl acetate (20:1)] to give two diastereomers (A and B) (500 mg, 90% yield) of **28** in the ratio of 79:21 (A:B). **28A**: colorless crystals; mp 104–105 °C (from hexane–benzene); ^{1}H NMR δ 2.29 (s, 3 H), 2.44 (s, 3 H), 1.8–3.2 (m, 8 H), 3.60 (s, 3 H), 4.8–5.3 (m, 2 H), 5.4–6.2 (m, 1 H), 7.35 (d, *J* = 8 Hz, 2 H), 7.73 (d, *J* = 8 Hz, 2 H); IR (KBr) 1743 (sh), 1721, 1291, 1220, 1141, 1081, 572 cm^{-1}. ,Anal. Calcd for $C_{19}H_{24}O_5S_2$: C, 57.55; H, 6.10. Found: C, 57.74; H, 6.09. **28B**: a colorless oil; ^{1}H NMR δ 1.70 (diffused d, *J* = 15.5 Hz, 1 H), 2.24 (s, 3 H), 2.47 (s, 3 H), 1.9–3.0 (m, 6 H), 3.72 (s, 3 H), 4.75–5.25 (m, 2 H), 5.3–6.1 (m, 1 H), 7.35 (d, *J* = 8 Hz, 2 H), 7.82 (d, *J* = 8 Hz, 2 H); IR (KBr) 1739, 1721, 1289, 1221, 1141, 1081, 574 cm^{-1}; MS, *m/e* 365 (1, M$^+$ – OCH_3), 241 (82, M$^+$ – SO_2Tol), 209 (44), 200 (62), 199 (100), 193 (45), 181 (61), 168 (63), 167 (47), 161 (37), 139 (50), 105 (32), 100 (21), 92 (37), 91 (69), 65 (32).

2-Benzyl-2-(methoxycarbonyl)-4-(methylthio)-4-(*p*-tolylsulfonyl)cyclohexanone (29). In a manner analogous to the preparation of **28**, **29** was produced as the sole diastereomer (74% yield): colorless crystals; mp 143–144 °C (from hexane–benzene); ^{1}H NMR δ 2.28 (s, 3 H), 2.40 (s, 3 H), 1.8–2.8 (m, 6 H), 3.09 (s, 2 H), 3.52 (s, 3 H), 7.19 (s, 5 H), 7.29 (d, *J* = 8 Hz, 2 H), 7.65 (d, *J* = 8 Hz, 2 H); IR (KBr) 1740 (sh), 1723, 1283, 1230, 1139, 1081, 578 cm^{-1}. Anal. Calcd for $C_{23}H_{26}O_5S_2$: C, 61.86; H, 5.87. Found: C, 61.96; H, 5.84.

2-Allyl-2-(methoxycarbonyl)-1,4-cyclohexanedione (30). A solution of **28** (520 mg, 1.31 mmol) and concentrated hydrochloric acid (2 mL) in methanol (20 mL) was heated under reflux for 1 day. Then, brine (200 mL) was added, and the resulting mixture was extracted with dichloromethane (40 mL × 5). The combined extracts were washed with brine (100 mL × 2), dried ($MgSO_4$), and evaporated. The residue was subjected to column chromatography [benzene–ethyl acetate (15:1)] to give **30** (147 mg, 52%): a colorless oil; ^{1}H NMR δ 2.40–2.93 (m, 6 H), 2.70 (d, *J* = 17 Hz, 1 H), 2.99 (d, *J* = 17 Hz, 1 H), 3.74 (s, 3 H), 5.05–5.18 (m, 2 H), 5.64 (ddt, *J* = 17, 10, 7 Hz, 1 H); IR (liquid film) 1718, 1640 cm^{-1}; MS, *m/e* 210.0899 (8, calcd for $C_{11}H_{14}O_4$ 210.0891).

2-Benzyl-2-(methoxycarbonyl)-1,4-cyclohexanedione (31). The above-described procedure was applied to **29** and **31** was afforded in 46% yield. **31**: colorless crystals; mp 107.5–108.5 °C (from 95% ethanol); ^{1}H NMR δ 2.37–2.81 (m, 4 H), 2.66 (d, *J* = 17 Hz, 1 H), 2.90 (d, *J* = 17 Hz, 1 H), 3.10 (d, *J* = 14 Hz, 1 H), 3.45 (d, *J* = 14 Hz, 1 H), 3.74 (s, 3 H), 7.06–7.33 (m, 5 H); IR (KBr) 1720(sh), 1710, 1259, 1198, 1132, 701, 599 cm^{-1}. Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20. Found: C, 68.97; H, 6.23.

Registry No. **1**, 59662-65-6; **3a**, 930-68-7; **3b**, 930-30-3; **4a** (isomer 1), 99765-62-5; **4a** (isomer 2), 99765-63-6; **4b** (isomer 1), 99765-64-7; **4b** (isomer 2), 99765-65-8; **4c**, 99765-66-9; **4d**, 99765-67-0; **4e**, 94816-49-6; **4e** (disulfone, 99765-86-3; **4f**, 99765-68-1; **4g**, 99764-03-1; **8**, 99765-76-1; **12**, 14371-10-9; **17** (isomer 1), 99765-69-2; **17** (isomer 2), 99765-70-5; **14** (isomer 1), 99765-73-8; **14** (isomer 2), 99765-74-9; **15**, 99765-75-0; **17** (*n* = 1 disulfone) (isomer 1), 99765-71-6; **17** (*n* = 1 disulfone) (isomer 2), 99765-72-7; (*E*)-**20**, 99764-06-4; (*Z*)-**20**, 99764-07-5; **21**, 2016-01-5; **22**, 99765-77-2; **23**, 99765-80-7; **24**, 99765-78-3; **25**, 99765-81-8; **26**, 27024-89-1; **27**, 2150-46-1; **28** (isomer 1), 99765-82-9; **28** (isomer 2), 99765-83-0; **29**, 99765-84-1; **30**, 99765-85-2; **31**, 99783-12-7; PhCH=CHCOCH=CHPh, 538-58-9; CH_2=CHCOOMe, 96-33-3; CH_3CH=CHCOOMe, 18707-60-3; PhCH=CHCOOEt, 103-36-6; 1-[(methylthio)carbonyl]-5-(*p*-tolysulfonyl)-1,5-diphenyl-3-pentanone, 99765-79-4; 3-butenone, 78-94-4.