δ 2.0 (3 H, d, J = 5.5 Hz), 6.8–7.4 (5 H, m), 7.8 (2 H, m). m/e(%) 146 (36.0), 131 (22.3), 105 (100.0), 77 (50.3), 69 (44.6). This product was not purified (lit.[18] bp 90–95 °C (2 mmHg)).

2-(2-Benzoyl-1-methylethyl)-3,5-diphenylpyrrole (29a). The sublimed product from the pyrolysis of **15a** and **16** (0.12 g) was dissolved in $CDCl_3$ (0.5 mL) and the reaction was monitored by ^1H NMR. After 5–6 days at 25 °C the formation of **28a** was completed. Addition of HBF_4 (48%, 2 drops) gave **29a** in 1 h. Removal of the solvent gave the adduct as a viscous oil: IR ($CHBr_3$) 3430 m (NH), 1672 s (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.5 (3 H, d, J = 7 Hz), 3.4 (2 H, m), 3.6-4.3 (1 H, m), 6.5 (1 H, d, J = 3 Hz), 7.0–8.1 (15 H, m), 8.6 (1 H, d, NH); ^{13}C NMR ($CDCl_3$) 20.3 (q), 27.4 (d), 45.0 (t), 106.35 (d), 123.5–137.1 (aromatic C), 200.4 (s); m/e (%) 365 (24.7), 246 (100.0), 105 (48.0); high-resolution MS, m/e calcd for $C_{26}H_{23}NO$, 365.1772; found, 365.1776.

2-(2-Benzoylethyl)-3,5-diphenylpyrrole (29b). Pyrolysis of **15b** (0.3 g, 0.85 mmol) as above at 170–190 °C (1–5 mmHg) gave 0.18 g of a mixture of **27** and **29b**. The adduct **29b** (50 mg, 17%) was isolated by fractional recrystallization from EtOH: needles; mp 132–133 °C; IR ($CHBr_3$) 3450 m (NH), 1680 s (C=O) cm^{-1}; NMR ($CDCl_3$) δ 3.2 (4 H, m, AA'BB'), 6.5 (1 H, d, J = 3 Hz), 7.0–8.1 (15 H, m), 9.0 (1 H, d, NH); ^{13}C NMR ($CDCl_3$) 19.8 (t), 39.4 (t), 105.9 (d), 123.2–136.5 (aromatic C), 201.25 (s); m/e (%) 351 (32.7), 232 (100), 219 (5.5), 105 (12.0). Anal. Calcd for $C_{25}H_{21}NO$: C, 85.47; H, 5.98; N, 3.98. Found: C, 85.25; H, 6.06; N, 3.94.

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Registry No. **1**, 87803-20-1; **2a**, 73086-81-4; **2b**, 87803-22-3; **3**, 87803-24-5; **4**, 87803-26-7; **5**, 87803-27-8; **6a**, 85018-20-8; **7a**, 87803-29-0; **7b**, 87803-31-4; **8**, 80561-34-8; **9**, 87803-37-0; **15a**, 87803-38-1; **15b**, 87803-39-2; **16**, 87860-09-1; **20a**, 87803-41-6; **23a**, 87803-40-5; **23b**, 87803-42-7; **24**, 87803-43-8; **27**, 3274-56-4; **28a**, 495-41-0; **29a**, 87803-44-9; **29b**, 87803-45-0; 2,6-diisopropyl-4-phenylpyrylium tetrafluoroborate, 87828-74-8; ethanolamine, 141-43-5; 1-(2-hydroxyethyl)-2,6-diisopropyl-4-phenylpyridinium tetrafluoroborate, 87803-33-6; 1-(2-chloroethyl)-2,6-diisopropyl-4-phenylpyridinium tetrafluoroborate, 87803-35-8.

Supplementary Material Available: Table II containing NMR spectra for the *N*-allylpyridinium salts and Scheme III with the MS of **29** (2 pages). Ordering information is given on any current masthead page.

Observation of Intermediates during the Reaction of Linear Alkanesulfinyl Chlorides with Activated Zerovalent Zinc[1]

Fillmore Freeman,* Christos N. Angeletakis, and Monica C. Keindl

Department of Chemistry, University of California, Irvine, California 92717

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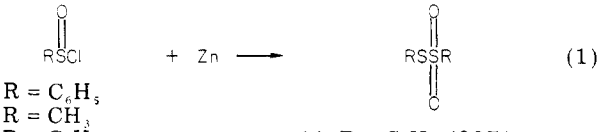
Methane- (**2**), ethane- (**3**), propane- (**4**), butane- (**5**), pentane- (**6**), hexane- (**7**), octane- (**8**), and dodecanesulfinyl chloride (**9**) reacted with activated zerovalent zinc to give the corresponding alkanesulfonothioic *S*-alkyl esters (**12–19**) in 40–89% yield. The reaction of methanesulfinyl chloride (**2**) with activated zerovalent zinc under nitrogen in anhydrous diethyl ether at −30, −20, and 0 °C was investigated by ^1H NMR and ^{13}C NMR spectroscopy. The ^{13}C NMR spectrum of the partially converted −30 °C reaction mixture showed the presence of methanesulfinyl chloride (**2**), *S*-methyl methanesulfonothioate (**12**), methanesulfinic acid (**24**) or zinc methanesulfinate (**25**), methanesulfonyl chloride (**26**), dimethyl sulfide (**27**), *S*-methyl methanesulfinothioate (**28**), and methanesulfinyl methyl sulfone (**29**). *vic*-Dimethyl disulfoxides (**31**) and *OS*-methyl methanesulfino(thioperoxoates) (**32**) are proposed as two of several transient reaction intermediates.

Although it is known that benzenesulfinyl chloride (**1**) and alkanesulfinyl chlorides **2–10** react with zerovalent zinc to give *S*-phenyl benzenesulfonothioate (*S*-phenyl benzenethiosulfonate, **11**; 96%) and symmetrical *S*-alkyl alkanesulfonothioates (**12–20**, 40–89%), respectively (eq 1),



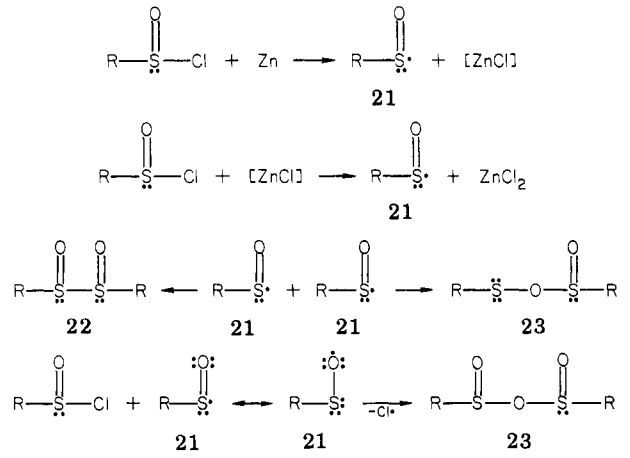
(1)

1, R = C_6H_5
2, R = CH_3
3, R = C_2H_5
4, R = C_3H_7
5, R = C_4H_9
6, R = C_5H_{11}
7, R = C_6H_{13}
8, R = C_8H_{17}
9, R = $C_{12}H_{25}$
10, R = neo-C_5H_{11}

11, R = C_6H_5 (96%)
12, R = CH_3 (55%)
13, R = C_2H_5 (49–54%)
14, R = C_3H_7 (63–68%)
15, R = C_4H_9 (73–89%)
16, R = C_5H_{11} (72–78%)
17, R = C_6H_{13} (68–77%)
18, R = C_8H_{17} (61–78%)
19, R = $C_{12}H_{25}$ (40–46%)
20, R = neo-C_5H_{11} (78%)[3]

very little is known about the mechanism and synthetic potential of this reaction.[2-6] We have investigated the activated zerovalent zinc conversion of linear alkanesulfinyl chlorides **2–9**[8] to symmetrical *S*-alkyl alkanesulfonothioates

Scheme I



(1) Presented at the 186th National Meeting of the American Chemical Society, Washington, DC, Sept 1, 1983; ORGN 242.

(2) (a) Barnard, D. J. *J. Chem. Soc.* **1957**, 4763. (b) de Silva Correa, C. M. M.; Waters, W. A. *J. Chem. Soc. C* **1968**, 1874.
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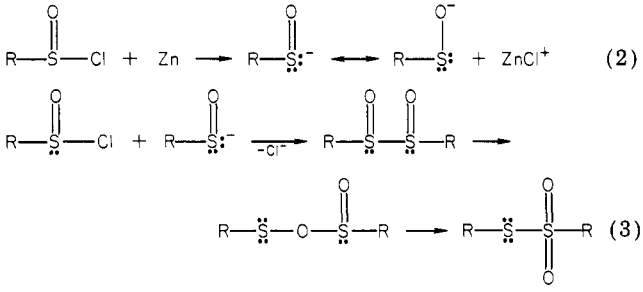
0022-3263/84/1949-0454$01.50/0

12–19 in dry diethyl ether at low temperatures in order to identify transient reaction intermediates and to determine the synthetic scope of the procedure (eq 1).[4,9–12]

Although the mechanism of the conversion of alkanesulfinyl chlorides to *S*-alkyl alkanesulfonothioates with zerovalent zinc is not known, the reaction may involve sulfinyl radicals (21, Scheme I), sulfenate anion (eq 2 and 3), *vic*-disulfoxides (22), and/or *OS*-sulfenyl sulfinates (23).[3,4,13–16]



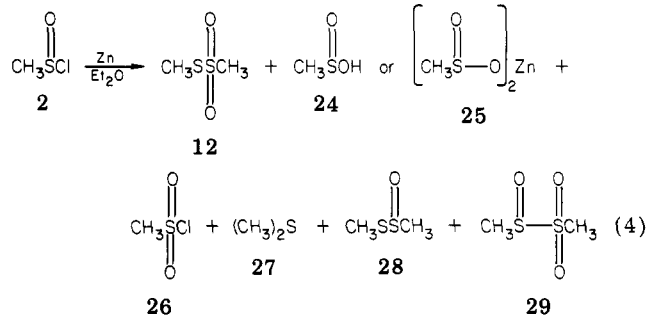
Results and Discussion

The unusual solvent effects with 2,2-dimethylpropanesulfinyl chloride (10) and activated zinc in tetrachloromethane and in diethyl ether[3,4,6] were not observed with linear alkanesulfinyl chlorides 2–9 which gave symmetrical *S*-alkyl alkanesulfonothioates 12–19, respectively, as the major products in both solvents.[4] Moreover, butanesulfinyl chloride (5) and zinc gave *S*-butyl butanesulfonothioate (15) in 79%, 73%, and 89% yields in anhydrous diethyl ether, tetrachloromethane, and benzene, respectively.

Since reduction with zinc cleaves *S*-aryl arenesulfonothioates to the corresponding sulfinic acids and thiols,[17] equimolar quantities of activated zerovalent zinc and *S*-methyl methanesulfonothioate (12) were stirred under dry nitrogen in ether for 1 h at 0 °C. Under these experimental conditions, *S*-methyl methanesulfonothioate (12) was stable to zerovalent zinc. Similarly, no reaction was observed between equimolar quantities of methanesulfinyl chloride (2) and anhydrous zinc chloride[18] under nitrogen in ether at 0 °C during 1 h. This latter result suggests no reaction occurs between methanesulfinyl chloride (2) and zinc chloride during the reaction of 2 and zerovalent zinc.

Proton NMR and ^{13}C NMR analyses were performed on reaction mixtures from the low conversion of methanesulfinyl chloride (2) at low temperatures by activated zinc in a specially designed apparatus[15] in order to observe the initially formed species and to preclude the subsequent reactions of zerovalent zinc and initially formed intermediates and products.

Although the reaction of methanesulfinyl chloride (2) with zerovalent zinc in ether does not proceed at an appreciable rate at −40 °C, it does proceed at reasonable rates at −30 and −20 °C. The reaction is approximately 25% complete in 90 min at −20 °C. The reaction was performed at −20 °C in ether under nitrogen and filtered with nitrogen pressure.[15] The filtrate was evaporated at 22–24 °C and analyzed via ^1H NMR in deuteriochloroform. In addition to the resonance of methanesulfinyl chloride (2) at δ 3.37, five other resonances were observed. Two resonances of equal intensity at δ 2.70 and 3.30 were detected for *S*-methyl methanesulfonothioate (12, [19–23] eq 4). Resonances



for methanesulfinic acid (24, δ 2.86)[19–22] or zinc methanesulfinate (25, δ 2.86), methanesulfonyl chloride (26, δ 3.68),[8,19–21] and dimethyl sulfide (27, δ 2.10)[19,22] were also observed.

The reaction of methanesulfinyl chloride (2) with activated zinc was carried out at −30 °C in ether-d_{10} for 90 min under nitrogen and analyzed by ^{13}C NMR[24–27] to obtain additional information concerning intermediates and products. After 90 min the product mixture was filtered in order to remove unreacted zinc and zinc salts, and the filtrate was thermostated in the NMR spectrometer at −40 °C. Although the filtrate was clear, the ^1H NMR spectrum was not well resolved. The −40 °C ^{13}C NMR spectrum

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(6) Curiously, the reaction of 2,2-dimethylpropanesulfinyl chloride (10) with activated zerovalent zinc in diethyl ether, perdeuterated diethyl ether, or deuterated ethanenitrile (CD_3CN) gave *S*-(2,2-dimethylpropyl) 2,2-dimethylpropanesulfinothioate as the major product.[3]

$$\underset{10}{(CH_3)_3CCH_2\text{-}S(O)Cl} + Zn \rightarrow (CH_3)_3CCH_2\text{-}S(O)S\text{-}CH_2C(CH_3)_3$$

(7) Shriner, R. L.; Neumann, F. W. "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. III, p 73.
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(9) (a) No attempt was made to exclude air from the reaction apparatus except where noted. (b) Although we have not experienced any difficulities, in view of the frequent problems with chlorinated hydrocarbons and aluminum or magnesium, one should exercise caution in performing the reaction of alkanesulfinyl chlorides and zerovalent zinc on a large scale.
(10) (a) Leandri, G.; Tundo, A. *Ann. Chim. (Rome)* **1954**, *44*, 875; *Chem. Abstr.* **1955**, *49*, 15785e. (b) Allen, P., Jr.; Brook, J. W. *J. Org. Chem.* **1962**, *27*, 1019. (c) Small, L. D.; Bailey, J. H.; Cavallito, C. J. *J. Am. Chem. Soc.* **1949**, *71*, 3565.
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(13) Freeman, F.; Angeletakis, C. N. *J. Am. Chem. Soc.* **1981**, *103*, 6232.
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(27) Oae, S.; Takata, T. *Chem. Lett.* **1981**, 845.

Table I. ^{13}C NMR Chemical Shifts (δ) of Intermediates and Products from the Reaction of Methanesulfinyl Chloride (2) with Activated Zinc at −30 °C in Ether-d_{10}[a,b]

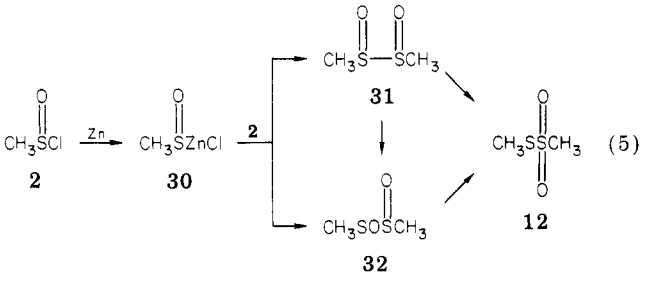
		−40 °C		0 °C		25 °C	
compd	no.	δ_C (114 min)[c]	int,[b] %	δ_C (217 min)[c,d]	int,[b] %	δ_C (312 min)[c,d]	lit,[b] %
$CH_2S(O)Cl$	2	52.84	74	53.11	83[e]	53.24	77
$CH_3SO_2SCH_3$	12	18.56		18.46		18.42	
		48.84	7	49.14	10	49.28	16
CH_3SO_2Cl	26	53.01	9		e	53.45	4
$(CH_3SO_2)_2Zn$	25	43.90	5	44.40	4		
$(CH_3)_2S$	27	20.89	1	20.71	1	20.68	3
$CH_3S(O)SCH_3$	28	16.68					
		41.15	3	41.68[f]	1[f]		
$CH_3SO_2S(O)CH_3$	29	34.13		34.10			
		38.40	1	38.34	<1		

[a] Me_4Si was used as the internal standard. The spectrometer frequency was 62.89 MHz. Two hundred scans were obtained in 15 min with broad-band decoupling. [b] Relative integrals of methyl carbon atoms. [c] Reaction time 0-90 min at −30 °C; 90-105 min temperature lowered to −40 °C, filtration completed, and H NMR spectrum obtained. [d] An unidentified resonance at δ 22.00 (1%) was also present. [e] The resonances of 2 and 26 overlapped. [f] The resonance that can be assigned to the sulfenyl sulfur bonded carbon atom of 28 was not sufficiently intense to be measured.

showed resonances for methanesulfinyl chloride (2), *S*-methyl methanesulfonothioate (12), methanesulfinic acid (24 or 25), methanesulfonyl chloride (26), dimethyl sulfide (27), *S*-methyl methanesulfinothioate (28), and methylsulfinyl methyl sulfone (29).[25,28-30] The resonances for *S*-methyl methanesulfinothioate (28) gradually disappeared, and an unidentified resonance appeared at δ 22.00 (1% of relative integrals) as the temperature of the reaction mixture was raised to 0 °C. The other resonances in the spectrum remained essentially the same (Table I).

Warming the reaction mixture to 22–24 °C led to the disappearance of all peaks except those for methanesulfinyl chloride (2), *S*-methyl methanesulfonothioate (12), and dimethyl sulfide (27). The presence of methanesulfinyl chloride (2) and *S*-methyl methanesulfonothioate (12) in the reaction mixture was also supported by the IR spectrum at 24 °C which showed bands at 1140 cm^{-1} (SO) and at 1170 and 1340 cm^{-1} (SO_2).

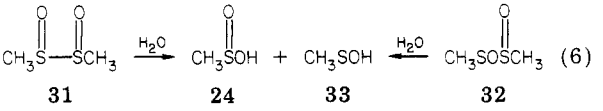
The reaction of methanesulfinyl chloride (2) with zerovalent zinc can give sulfinyl zinc chloride (30, eq 5) which



(5)

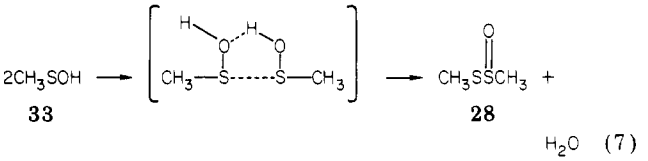
can react with 2 to give *vic*-dimethyl disulfoxide (31) and/or *OS*-methyl methanesulfino(thioperoxoate) (32).[31,32] Alternately, *vic*-dimethyl disulfoxide (31) and *OS*-methyl methansulfino(thioperoxoate) (32) may also be formed from sulfinyl radicals (Scheme I).[13-16,31,33-36]

vic-Disulfoxide 31 or *OS*-sulfenyl sulfinate 32[37] can react with traces of water to give methanesulfinic acid (24) and methanesulfenic acid (33,[13-16] eq 6). Unstable methane-



(6)

sulfenic acid (33) can undergo dehydration to afford *S*-methyl methanesulfinothioate (28,[38,39] eq 7). The water



(7)

generated in this reaction can react with methanesulfinyl chloride (2), *vic*-dimethyl disulfoxide (31), and/or *OS*-sulfenyl sulfinate (32, eq 6).

Warming the reaction mixture to 0 °C can lead to the reaction of methanesulfinic acid (24) with *S*-methyl methanesulfonothioate (28) to yield *S*-methyl methanesulfonothioate (12) and methanesulfenic acid (33, [13-16,40-42] eq 8). The absence of methanesulfinic acid (24), *S*-methyl methanesulfinothioate (28), and methanesulfenic acid (33) in the final product mixture is consistent with eq 6 and 7.

Methanesulfinyl chloride (2) can react with methanesulfinic acid (24) to afford methylsulfinyl methyl sulfone (29, eq 9) which reacts with 2 to give methanesulfonyl

(28) The methanesulfinyl chloride (2) used in these experiments contained less than 3% methansulfonyl chloride (26) which could not be always be completely removed, owing to photolytic disproportionation of 2 and/or inadventitious moisture. Hexanesulfinyl chloride (7) contained approximately 5% hexanesulfonyl chloride.

(29) (a) Douglass, I. B.; Koop, D. A. *J. Org. Chem.* **1964**, *29*, 951. (b) Douglass, I. B. *Ibid.* **1959**, *24*, 2004.

(30) The inevitable presence of some zinc chloride in the ether filtrate could cause some unexpected NMR shifts.

(31) Diastereomeric *vic*-disulfoxides (22) and *OS*-sulfenyl sulfinates (23) are possible (Scheme I).

(32) (a) The reaction of lithium benzenesulfenate with benzenesulfinyl chloride (1) gives *S*-phenyl benzenesulfonothioate (11).[32b,c] (b) Vinkler, E.; Klivenyi, F.; Lazar, J.; Kozakiewicz, I. *Acta Chem. Acad. Sci. Hung.* **1969**, *10*, 167. (c) Vinkler, E.; Klivenyi, F. *Int. J. Sulfur Chem.* **1973**, *8*, 11.

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(40) It is known that sulfinic acids react with thiosulfinates to give thiosulfonates.[13-16,41,42]

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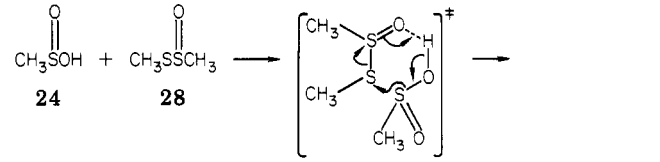
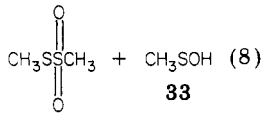
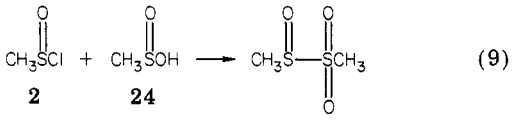


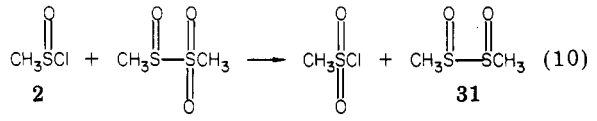
24 28



12 (8)



2 24 29 (9)



2 29 26 31 (10)

chloride (**26**) and *vic*-dimethyl disulfoxide (**31**,[15,19] eq 10). Rearrangement of *vic*-dimethyl disulfoxide (**31**) can afford *S*-methyl methanesulfonothioate (**12**).[13-16,37,43-45]

Experimental Section

NMR spectra were obtained on Perkin-Elmer EM-360, Varian FT-80A, Bruker WH-90, and Bruker WM-250 spectrometers. The Bruker WH-90 and WM-250 FT NMR spectrometers were controlled by Burker Model B-NC-12 and Bruker Aspect 2000 computers, respectively. The NMR assignments were made based on the chemical shifts of previously reported compounds.[6,18-21,23,27,31]

Reagents and solvents were purified by standard procedures. Nitrogen was dried by passing it through a column of Drierite and 5-Å molecular sieves. Commercial $CDCl_3$ and $(C_2D_5)_2O$ were used without further purification.

Thin layer chromatography was performed on silica gel GF (250 μm thick) glass plates which were developed in a solvent mixture of ethyl acetate–hexanes (1:9 by volume). A solvent mixture of ether–hexanes (3:7 by volume) was used for analysis of the products from the reaction of methanesulfinyl chloride (**2**) and zerovalent zinc. After the solvent had risen to the top, the plates were immersed in phosphomolybdic acid and charred.

Flash Column Chromatography.[46] The product mixtures containing alkanesulfonothioic *S*-alkyl esters were placed on a 46 cm × 5 cm diameter column which contained 15 cm of Mallinckrodt silica AR CC-4 100–200-mesh silica gel covered with 0.3 cm of sand. The *S*-alkyl alkanesulfonothioates were eluted with 1 L of ethyl ethanoate–hexanes (1:9 by volume) solution at a rate such that the eluant in the column fell ca. 2 cm/min. Fractions (50 mL) were collected and combined on the basis of TLC analysis. Removal of solvent gave pure *S*-alkyl alkanesulfonothioates.

Activation of Zinc Metal.[7] To a 25-mL Erlenmeyer flask were added 2.0 g (0.03 mmol) of Mallinckrodt zinc metal dust (97.1%) and 20 mL of 2% (v/v) hydrochloric acid. The mixture was stirred (ca. 5 min) until the zinc became silver colored. After suction filtration, the zinc was washed successively with 50 mL of water, 20 mL of 95% ethanol, 20 mL of 2-propanone, and 20 mL of anhydrous ether. The zinc was transferred to a 25-mL round-bottomed flask which was heated in a water bath at 90 °C while the excess solvent was removed under reduced pressure (ca. 20 min at 2 torr). The purified zinc was used within 20 min after drying.

Anhydrous Zinc Chloride.[18] To a 10-mL round-bottomed flask containing a magnetic stirring bar was added 0.61 g (4.1 mmol) of zinc chloride. The flask was evacuated to 0.2 mm, heated, and cooled three times. The anhydrous zinc chloride was used immediately after the third cooling at 0.2 mm.

Alkanesulfinyl chlorides 2–10 were prepared as previously described.[8] The boiling points agreed with literature values.

Synthesis of *S*-Alkyl Alkanesulfonothioates: General Procedure (Inverse Addition). Into a 25-mL round-bottomed flask which was equipped with a calcium chloride drying tube and contained a magnetic stirring bar was added 4.23 g (30 mmol) of butanesulfinyl chloride (**5**) in 12 mL of anhydrous ether. The solution was stirred at 0 °C while 3.24 g (49.5 mmol) of activated zerovalent zinc was added (inverse addition) via a powder funnel during a 60-min period. After the mixture was stirred at 0 °C for an additional 23 h, the organic layer was decanted from the zinc and metal salts and washed with 25 mL of a saturated ammonium chloride solution, the layers were separated, and the organic layer was dried (Na_2SO_4). After gravity filtration, the solvent was removed in vacuo, and the *S*-butyl butanesulfonothioate (**15**) was isolated via flash chromatography.[46] For alkanesulfonothioic *S*-alkyl esters **12–19** the zinc metal and zinc salts were removed via suction filtration instead of decantation. *S*-Dodecyl dodecanesulfonothioate (**19**)[10b,47] was purified by recrystallization from hexane instead of via flash chromatography.

The asymmetric and symmetric IR SO_2 bands, ^{13}C NMR spectra, and boiling and melting points of the *S*-alkyl alkanesulfonothioates **12–19** agreed with literature values.[4]

Reaction of Methanesulfinyl Chloride (2) with Activated Zinc in Ether at −20 °C. The reaction was performed under nitrogen as described above for the 0 °C reaction, except a solution of methanesulfinyl chloride (**2**) in ether was added to zerovalent zinc in ether, and the reaction mixture was filtered with nitrogen pressure.

Reaction of Methanesulfinyl Chloride (2) with Activated Zinc at −10 °C. At −40 °C in a flame-dried, nitrogen-flushed, three-necked, 2.5-mL, round-bottomed flask fitted with septa inlets, a magnetic stirring bar, and a powder addition funnel was added, via a syringe, a solution of 2.96 g (30 mmol) of methanesulfinyl chloride (**2**) in 12 mL of anhydrous ether. To this solution was added via the addition funnel 3.24 g (49.5 mmol) of activated zinc during 30 min. The reaction mixture was warmed to −10 °C with stirring (0.5 h) and maintained at −10 °C for 2 h. The product mixture was filtered via suction, the filtrate was washed with 25 mL of saturated ammonium chloride solution, and the layers were separated. The organic layer was dried (Na_2SO_4) and filtered. The filtrate was flash chromatographed (ether–hexanes; 3:7 by volume) after solvent removal.

Reaction of Methanesulfinyl Chloride (2) with Activated Zinc in Ether-d_{10} at −30 °C. The apparatus described in ref 15 was used except an evacuated stopcock was placed immediately below the glass frit in order to avoid leakage of solvent.

In a dry nitrogen atmosphere, methanesulfinyl chloride (**2**) (0.60 g, 6.1 mmol) in 1.5 mL of ether-d_{10} was slowly added to activated zinc (0.66 g, 10.1 mmol) in 1.5 mL of ether-d_{10} at −30 °C with mechanical stirring. Stirring was continued for 90 min, and the reaction mixture was filtered at −30 °C. The clear filtrate was kept at −40 °C during transfer with nitrogen pressure to an NMR tube, which was cooled to −40 °C. Table I shows the results of the ^{13}C NMR analysis at −40 °C.

Attempted Reaction of Methanesulfonyl Chloride (26) with Activated Zinc at 0 °C. To a solution of 30 mmol (3.44 g) of methanesulfonyl chloride (**26**) in 12 mL of dry ether in a 25 mL round-bottomed flask was added 3.24 g (49.5 mmol) of activated zinc with magnetic stirring at 0 °C. After 1 h, the zinc was removed by suction filtration, the filtrate was washed with 25 mL of saturated ammonium chloride solution, and the organic layer was dried over Na_2SO_4. After filtration, the solvent was removed in vacuo. Proton NMR analysis in $CDCl_3$ of the resiude

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(45) Although the proposed mechanisms for the hydrolysis of methanesulfinyl chloride (**2**) must also be considered for the reaction of **2** with activated zerovalent zinc, the anhydrous experimental conditions of these low-temperature experiments militate against their involvement in the reduction reaction. Moreover, **2** is not affected by moisture at −40, −30, −20, and 0 °C under the experimental conditions used for the zinc reaction.
(46) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(47) Wilson, A. R. N.; van de Ven, L. J. M.; de Haan, J. W. *Org. Magn. Reson.* **1974**, *6*, 601.

(3.26 g of **26**; 95% recovery) showed a resonance (δ 3.68) only for methanesulfonyl chloride (**26**). Treatment of the aqueous phase with benzylthiuronium chloride gave neither benzylthiuronium methanesulfinate nor benzylthiuronium methanesulfonate (absence of methanesulfinic acid (**24**) and methanesulfonic acid).[48,49]

Attempted Reaction of *S*-Methyl Methanesulfonothioate (12) with Activated Zinc at 0 °C. The experimental procedure described above for zinc and methanesulfonyl chloride (**26**) at 0 °C for 1 h was repeated except thiosulfonate **12** was substituted for **26**.[9a] After the workup, ^{1}H NMR analysis showed the presence of **12** (92% recovery). Treatment of the aqueous phase with benzylthiuronium chloride did not produce a precipitate (absence of methanesulfinic acid (**24**) and methanesulfonic acid).[48,49]

Attempted Reaction of *S*-Methyl Methanesulfonothioate (12) with Anhydrous Zinc Chloride at 0 °C. A 10-mL round-bottomed flask fitted with a serum stopper and containing 0.61 g (4.10 mmol) of anhydrous zinc chloride[18] and a magnetic stirring bar was placed in an ice bath. Dry ether (1 mL) was added via syringe to the flask. To this solution was added via syringe under nitrogen flow 0.51 g (4.10 mmol) of *S*-methyl methanesulfonothioate (**12**) in 2 mL of dry ether. The solution was stirred 1 h at 0 °C, the reaction solution was washed with 15 mL of saturated ammonium chloride salution, and the organic layer was dried (Na_2SO_4). After removal of the solvent in vacuo, ^{1}H NMR showed only the presence of thiosulfonate **12**. No compounds were detected in the aqueous layer from the saturated ammonium chloride wash.

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(49) Stirling, C. J. M. *Int. J. Sulfur Chem., Part B* **1971**, *6*, 277.

Attempted Reaction of Methanesulfinyl Chloride (2) with Anhydrous Zinc Chloride at 0 °C. A small amount of anhydrous zinc chloride[18] was added to a solution of methanesulfinyl chloride (**2**) in $CDCl_3$ in a 5-mm NMR tube. The ^{1}H NMR and ^{13}C NMR spectra were taken as soon as possible after addition. The ^{1}H NMR spectrum was taken again after the solution was kept at 22-24 °C for several hours. All spectra showed the presence of only methanesulfinyl chloride (**2**).

Stability of Methanesulfinyl Chloride (2) in the Absence of Activated Zinc. A solution of 2.96 g (30 mmol) of methanesulfinyl chloride (97.5% **2** and 2.5% **26**) in 12 mL of dry ether was syringed into a flame-dried, nitrogen-flushed, 25-mL, round-bottomed flask containing a magnetic stirring bar. After the solution was stirred for 1 h at 0 °C under dry nitrogen, the ether was removed in vacuo. Proton NMR analysis of the residue in $CDCl_3$ showed the presence of only methanesulfinyl chloride (**2**, 97.5%) and **26** (2.5%).

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Registry No. **2**, 676-85-7; **3**, 1718-44-1; **4**, 23267-68-7; **5**, 13455-88-4; **6**, 23267-70-1; **7**, 41892-39-1; **8**, 72394-49-1; **9**, 70936-25-3; **12**, 2949-92-0; **13**, 682-91-7; **14**, 1113-13-9; **15**, 1118-40-7; **16**, 78630-48-5; **17**, 88130-84-1; **18**, 7651-62-9; **19**, 37784-86-4; **25**, 19186-23-3; **26**, 124-63-0; **27**, 75-18-3; **28**, 13882-12-7; **29**, 14128-56-4; Zn, 7440-66-6.

Rotational Selectivity in Cyclobutene Ring Openings. Model Studies Directed toward a Synthesis of Verrucarin A

Barry M. Trost* and Patrick G. McDougal

McElvain Laboratories of Organic Chemistry, Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706

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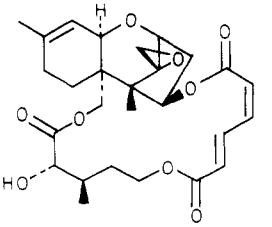
The rotational selectivity in the opening of dissymmetric cyclobutenes to the corresponding dienes is described. In the opening of the monoesters of *cis*-3,4-cyclobutenedicarboxylic acid, an unusual solvent effect on the ring opening is noted. Switching from Me_2SO to 1,2-dichloroethane leads to a 3:1 ratio of the (*E*,*Z*)-muconates, favoring the ester on the *E* double bond. The two isomers can be differentiated by ^{13}C NMR spectroscopy in which the above isomer shows a $\Delta\delta$ for the α,α' carbons of only $\sim$2.5 ppm but a $\Delta\delta$ of 5-6 ppm for the isomer having the ester on the *Z* double bond. Inclusion of the cyclobutene as part of a macrotriolide related to verrucarin A imparts conformational control on the rotational selectivity to favor the *E*,*Z* isomer corresponding to the natural products. These relatively simple models inhibit protein synthesis in a fashion reminiscent of the natural products.

Introduction

Verrucarin A is a representative example of a class of macrocyclic compounds, the macrocyclic trichothecanes, which display a wide array of biological activity including significant cytotoxicity.[1] Verrucarin A itself causes 50% inhibition of mouse tumor cell (P-815) growth at a concentration of 0.6 ng/mL, making it one of the most active cytostatic agents known.[2] As is usual with potent cytostatic agents, verrucarin A is also extremely toxic, possessing an LD_{50} (mouse) of 0.5 mg/kg (ip).[1c] Along with the verrucarins, the roridins and baccharins, both dilactides, comprise this important class of fungal metabolites. In all cases a macrocyclic "ribbon" joins the C-4 and C-15 hydroxy groups of a trichothecanoid backbone, most often



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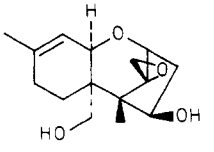

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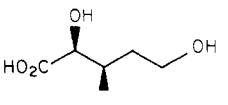

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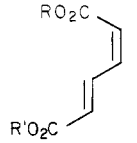

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