under reduced pressure and analyzed by vpc. The yield of methyl benzoate was 25%.

Carbonylation of α-Bromoacetophenone (5). A mixture of 5.0 g (25 mmol) of **5**, 0.3 g (0.43 mmol) of **1**, 6.0 g (29 mmol) of 1,8-bis(dimethylamino)naphthalene, and 50 ml of methanol was heated at 80° with stirring in a 500 ml autoclave which was pressurized with carbon monoxide at 200 psi. After 48 hr, the reaction mixture was filtered gravimetrically and washed with 50 ml of methanol. The combined filtrates were concentrated under reduced pressure and the residue was extracted with three 50-ml portions of dichloromethane. The combined extracts were washed with 2 *N* hydrochloric acid, aqueous sodium bicarbonate, and saturated aqueous sodium chloride successively. The dichloromethane solution was concentrated under reduced pressure and the residue was distilled using a short path distillation apparatus to afford 3.0 g (16 mmol, 64%) of a liquid which was identified as α-carbomethoxyacetophenone by comparison of its nmr spectrum with that reported for an authentic sample:[11] bp 90–94° (0.4 mm); nmr ($CDCl_3$) δ 3.72 (s, 3), 3.98 (s, 1.7), 5.64 (s, 0.3), 7.2–8.0 (m, 5), and 12.51 ppm (s, 0.3).

Acknowledgment. Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

Registry No.—**1**, 13965-03-2; **4**, 41894-01-3; **5**, 70-11-1; iodobenzene, 591-50-4; benzyl chloride, 100-44-7; α-carbomethoxyacetophenone, 614-27-7.

References and Notes

(1) P. M. Maitlis, "The Organic Chemistry of Palladium," Vol. II, Academic Press, New York, N. Y., (1971), p 18–33.
(2) L. Cassar, G. P. Chiusoli, and F. Guerrieri, *Synthesis*, 509 (1973).
(3) National Distillers and Chemical Corp., British Patent 1,149,259; *Chem. Abstr.*, **67**, 64066s (1967).
(4) R. N. Knowles, U.S. Patent 3,636,082; *Chem. Abstr.*, **76**, 85569j (1972).
(5) M. Hidai, M. Kokura, and Y. Uchida, *J. Organometal. Chem.*, **52**, 431 (1973).
(6) T. Mizoroki, K. Mori, and A. Ozaki, *Bull. Chem. Soc. Jap.*, **44**, 581 (1971).
(7) R. F. Heck and J. P. Nolley, Jr., *J. Org. Chem.*, **37**, 2320 (1972).
(8) P. Fitton and E. A. Rick, *J. Organometal. Chem.*, **28**, 287 (1971).
(9) G. W. Parshall, *J. Amer. Chem. Soc.*, **96**, 2360 (1974).
(10) J. K. Stille, L. F. Hines, R. W. Fries, P. K. Wong, D. E. James, and K. Lau, *Advan. Chem. Ser.*, **132**, 90 (1974).
(11) N. Sugiyama, M. Yamamoto, and C. Kashima, *Nippon Kagaku Zasshi*, **89**, 1268 (1968).

Cleavage–Elimination of 2,3-Decalindione Monothioketals Leading to Vinylic Ester and Lactone Prototypes of Vernolepin

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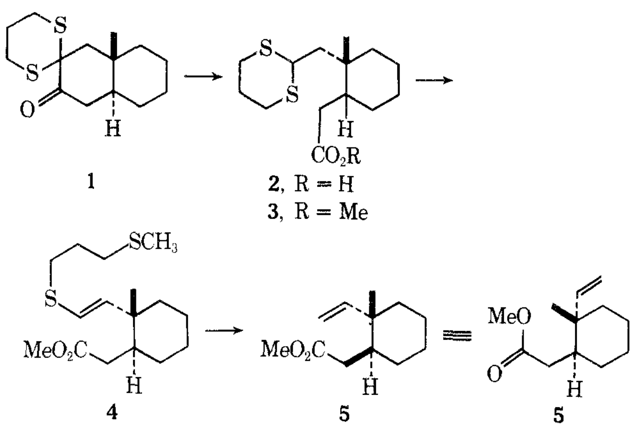
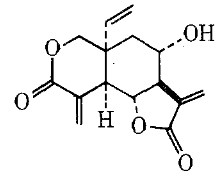
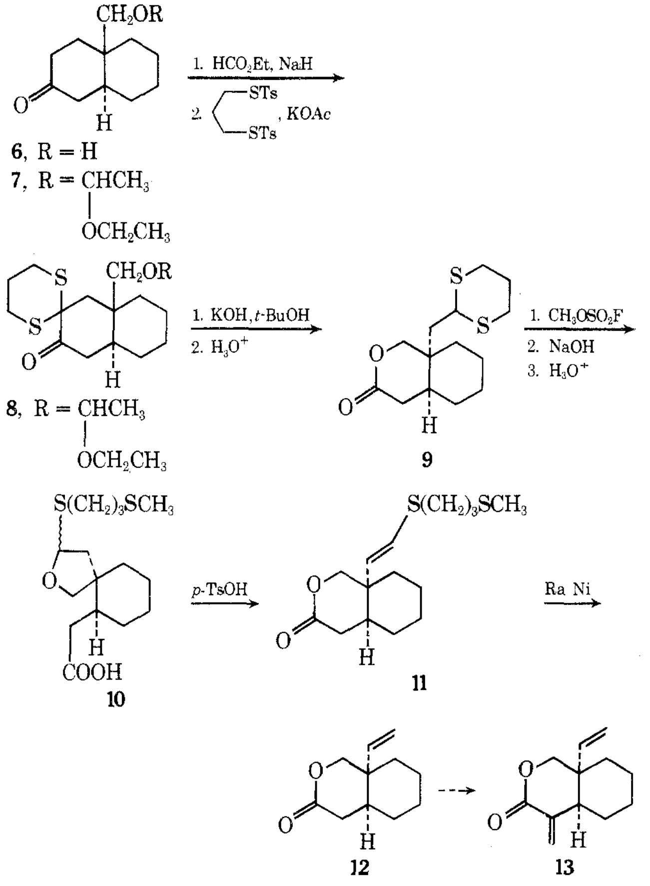
A number of years ago we described a new method for the nonoxidative cleavage of carbon–carbon bonds which involved treatment of α-diketone monothioketals with nucleophilic bases.[1] In the course of subsequent studies aimed at clarifying the reaction pathway we discovered that cleavage of decalone **1** followed by the addition of methyl iodide to the basic reaction mixture led to the vinyl sulfide **4**.[2] This intermediate was smoothly converted to the vinyl compound **5** upon desulfurization with Raney nickel. Alternatively, the intermediate dithianyl acid **2** could be isolated, esterified, and then converted to the sulfonium salt with various methylating agents. Base cleavage was then best effected with sodium hydride. These facile transformations seemed well suited as a potential synthetic entree to the recently discovered growth-inhibitory elemanolide sesquiterpene dilactones vernolepin, vernodalin, and vernomenin.[3] With such goals in mind we directed our attention to the prototype lactone **13** (Scheme I) as our *initial* synthetic objective.[4]


1
2, R = H
3, R = Me
4
5
5

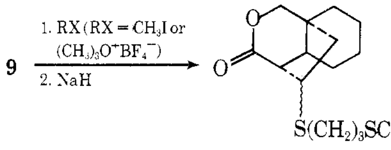

vernolepin

Scheme I


6, R = H
7, R = CHCH$_3$(OCH$_2$CH$_3$)
8, R = CHCH$_3$(OCH$_2$CH$_3$)
9
10
11
12
13

Attempts at dithianylation of hydroxy ketone **6**[5] *via* the hydroxymethylene derivative[6] were unsuccessful presumably because of interactions between the hydroxyl and carbonyl groupings. We therefore examined a number of hydroxyl-protected derivatives of which the mixed acetal **7** proved most suitable.[7] Basic cleavage of the derived thioketal ketone **8** followed by acid hydrolysis yielded the crystalline lactone **9**.[1]

We next explored the conversion of lactone thioacetal **9** to the vinyl sulfide lactone **11** by S-methylation and subsequent basic elimination with sodium hydride under conditions previously optimized for the production of vinyl sulfide **4**. However except for one initial experiment which afforded this substance in about 50% yield, numerous attempts to effect this conversion met with complete failure. The principal product of these many attempts appeared to be the tricyclic lactone **14**, possibly arising *via* internal enolate alkylation or carbene insertion.



14

We eventually discovered a two-step process for the desired conversion which involved methylation of thioacetal **9** with excess methyl fluorosulfate and basic hydrolysis of the resultant (mono)methylsulfonium intermediate to give, after acidification, the hemithioacetal **10**. Previous workers have employed methylation and subsequent aqueous base treatment as a procedure for the hydrolysis of thioacetals.[8] In the present case the inertness of thioacetal **9** toward bismethylation and participation of the lactone-derived hydroxyl group to give a base-stable hemithioacetal must effectively preclude the hydrolysis pathway. Elimination to the vinyl sulfide readily occurred upon heating hemithioacetal **10** with *p*-toluenesulfonic acid in benzene. These conditions also promoted lactonization and the desired lactone sulfide **11** could thus be prepared in over 85% yield. Desulfurization with deactivated W-2 Raney nickel in acetone[9] afforded the vinylated lactone **12**[10] whose conversion to the methylene derivative **13** has been described by Grieco and Hiroi.[4]

Experimental Section[11]

Methyl 1-[2,2-(Propane-1,3-dithio)ethyl]-*cis*-1-methylcyclohex-2-ylacetate (3). An ether solution of 1.15 g (4.0 mmol) of acid **2**[1] was esterified with diazomethane. Isolation with ether afforded 1.20 g (100%) of ester **3**, bp 155° (bath temperature) at 0.02 mm: λ_{max} (film) 5.75 (CO), 6.95, 7.85, 7.90, 8.55, 8.80, 9.95 μm; δ_{TMS} (CCl_4) 4.07 (1 H, t, J = 5 Hz), 3.57 (3 H, s), 0.80 ppm (3 H, s).

Anal. Calcd for $C_{15}H_{26}O_2S_2$: C, 59.56; H, 8.66; S, 21.20. Found: C, 59.44; H, 8.89; S, 20.98.

Methyl 1-(3,7-Dithia-*trans*-1-octenyl)-*cis*-1-methylcyclohex-2-ylacetate (4). A solution of 660 mg (2.2 mmol) of ester **3** and 2 ml (32 mmol) of methyl iodide was stirred at room temperature for 12 hr. The excess methyl iodide was removed *in vacuo* and the crude sulfonium salt in 4 ml of tetrahydrofuran was transferred to a suspension of 186 mg (4.4 mmol) of sodium hydride in 2 ml of tetrahydrofuran. The mixture was stirred for 2.5 hr, water was added, and the product was isolated with ether. Chromatography on 35 g of silica gel with 1:9 ether–benzene as eluent afforded 595 mg (86%) of vinyl sulfide **4**. An analytical sample was secured by preparative layer chromatography on silica gel (1:3 ether–petroleum ether) and distillation, bp 165° (bath temperature) at 0.02 mm: λ_{max} (film) 5.75 (CO), 6.20 (C=C), 6.95, 7.85, 7.95, 8.32, 8.55, 8.75, 9.90, 10.40 μm; δ_{TMS} (CCl_4) 5.60 (2 H, AB, J = 16 Hz, $\Delta\nu_{AB}$ = 22.6 Hz), 3.57 (3 H, s), 2.04 (3 H, s), 0.90 ppm (3 H, s).

Anal. Calcd for $C_{16}H_{28}O_2S_2$: C, 60.71; H, 8.92; S, 20.26. Found: C, 60.68; H, 9.15; S, 20.00.

Methyl 1-Vinyl-*cis*-1-methylcyclohex-2-ylacetate (5). A suspension of 5 ml of W-2 Ra Ni, demineralized with ion-exchange resin[12] and deactivated by prior heating at reflux for 25 min in ethyl acetate and for 40 min in acetone, and 150 mg (0.47 mmol) of vinyl sulfide **4** in 30 ml of acetone was heated at reflux for 3 hr. The cooled reaction mixture was filtered through a pad of Celite and the solvent was removed affording 88 mg (95%) of ester **5**. Distillation at 75° (bath temperature) and 0.2 mm afforded 82 mg (89%) of ester **5** which was found to be 82% pure by gc. An analytical sample was secured by preparative gc on a 6 ft × 0.375 in. column packed with 4% DC-550 on Chromosorb G: λ_{max} (film) 5.75 (CO), 6.19 (C=C), 6.90, 10.85 μm; δ_{TMS} (CCl_4) 5.90–4.65 (3 H, m), 3.54 (3 H, s), 0.90 ppm (3 H, s).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.22; H, 10.30.

10-[2,2-(Propane-1,3-dithio)ethyl]-*cis*-3-oxa-2-decalinone (9). A solution of 2.73 g (15 mmol) of alcohol **6**,[5] 1.3 ml (25 mmol) of ethyl vinyl ether, and 120 μl of dichloroacetic acid was stirred at room temperature for 15 hr according to the procedure of Eaton.[7] Solid sodium carbonate was added and stirring was continued an additional 1 hr. The reaction mixture was filtered and the solvents were removed *in vacuo* affording 3.82 g (100%) of acetal **7** as an oil: λ_{max} (film) 5.84 (CO), 6.86, 7.24, 8.80, 9.15, 9.40, 10.65 μm; δ_{TMS} ($CDCl_3$) 4.66 (1 H, q, J = 6 Hz), 3.8–3.0 (4 H, m), 1.28 (3 H, d, J = 5.5 Hz), 1.16 ppm (3 H, t, J = 7 Hz).

A solution of 3.80 g (13.4 mmol) of the hydroxymethylene ketone obtained (92%) from the above acetal **7** by the procedure of Turner,[13] 6.67 g (16 mmol) of propane-1,3-dithiol di-*p*-toluenesulfonate,[14] and 5 g of potassium acetate in 120 ml of absolute ethanol was heated at reflux for 10 hr according to the procedure of Woodward.[6] The ethanol was removed *in vacuo* from the cooled reaction mixture, water was added to the residue, and the products were isolated with ether. The crude product was filtered through 125 g of Fisher alumina with 500 ml of benzene. Removal of the solvent afforded 3.0 g (67%) of thioketal ketone **8** as an oil: λ_{max} (film) 5.90 (CO), 6.90, 7.28, 7.85, 8.11, 8.85, 9.21, 9.50, 10.82 μm; δ_{TMS} ($CDCl_3$) 4.66 (1 H, q, J = 6 Hz), 3.8–3.0 (4 H, m), 1.28 (3 H, d, J = 5.5 Hz), 1.16 ppm (3 H, t, J = 7 Hz).

To a stirred solution of the above thioketal ketone **8** (2.95 g, 8.5 mmol) in 20 ml of *tert*-butyl alcohol was added 1.43 g (25.5 mmol) of powdered potassium hydroxide. The reaction mixture was heated at 60° for 10 hr,[1] water was added, and the mixture was extracted with ether. The aqueous phase was acidified with concentrated hydrochloric acid, acetone was added to make the mixture homogeneous, and the resulting solution was stirred for 3 hr. The acetone was removed *in vacuo* and the product was isolated with ether affording 2.11 g (87%) of lactone **9** as an oil which crystallized on standing. Recrystallization from ether afforded material of mp 75.5–77°: λ_{max} (KBr) 5.80 (CO), 6.84, 7.15, 7.95, 8.10, 8.40, 9.28, 9.50, 11.00, 11.55, 12.55 μm; δ_{TMS} ($CDCl_3$) 4.25 (2 H, AB, J = 11 Hz, $\Delta\nu_{AB}$ = 18.9 Hz), 4.05 ppm (1 H, t, J = 5 Hz).

Anal. Calcd for $C_{14}H_{22}O_2S_2$: C, 58.70; H, 7.74; S, 22.39. Found: C, 58.56; H, 7.70; S, 22.45.

10-(3,7-Dithia-*trans*-1-octenyl)-*cis*-3-oxa-2-decalinone (11). The method of Ho[8] was modified for the preparation of acid **10**. A solution of 620 mg (2.16 mmol) of lactone **9**, 242 μl (3.0 mmol) of methyl fluorosulfonate, and 5 ml of benzene was stirred at room temperature for 3.5 hr whereupon 5 ml of 10% sodium hydroxide was added and stirring was continued an additional 15 min. Water was added and the aqueous phase was extracted with ether and acidified with concentrated hydrochloric acid. The acidic product was isolated by ether extraction affording 672 mg (98%) of acid **10** as an oil: λ_{max} (film) 2.80–4.20 (COOH), 5.88 (CO), 6.90, 7.70, 8.05, 9.55, 10.90 μm; δ_{TMS} (CCl_4) 10.00 (1 H, s), 5.20 (1 H, m), 3.60 (2 H, m), 2.05 ppm (3 H, s).

The above acid **10** was refluxed with 20 mg of *p*-toluenesulfonic acid monohydrate in 20 ml of benzene for 2 hr with removal of water *via* a Dean–Stark trap. Isolation of the product with ether and chromatography on 35 g of silica gel with 1:4 ether–benzene as eluent afforded 545 mg (87%) of lactone **11**: λ_{max} (film) 5.75 (CO), 6.90, 7.90, 8.35, 9.20 μm: δ_{TMS} (CCl_4) 5.75 (2 H, AB, J = 16 Hz, $\Delta\nu_{AB}$ = 55.5 Hz), 4.10 (2 H, AB, J = 11 Hz, $\Delta\nu_{AB}$ = 13.1 Hz), 2.05 ppm (3 H, s). The analytical sample was secured by preparative layer chromatography on silica gel (1:4 ether–benzene) and distillation, bp 180° (bath temperature) at 0.02 mm.

Anal. Calcd for $C_{15}H_{24}O_2S_2$: C, 59.96; H, 8.05; S, 21.34. Found: C, 59.75; H, 8.19; S, 21.18.

10-Vinyl-*cis*-3-oxa-2-decalinone (12). The procedure outlined above for the preparation of ester **5** was followed. A suspension of 7 ml of W-2 Ra Ni, deactivated by prior heating at reflux for 25 min in ethyl acetate and for 4.5 hr in acetone, and 249 mg (0.83 mmol) of lactone **11** in 30 ml of acetone was heated at reflux for 2 hr to give 143 mg (96%) of lactone **12**. Distillation at 115° (bath temperature) and 0.02 mm afforded 135 mg (90%) of lactone **12** which was found to be 85% pure by gc. The infrared and nmr spectra of this material were identical with those of an authentic sample.[10]

Acknowledgment. We are grateful to the National Institutes of Health, Division of Cancer Research, for support of this work through a research grant (5 RO1 CA 11089).

Registry No.—**2**, 27069-39-2; **3**, 53596-99-9; **4**, 53597-00-5; **5**, 53597-01-6; **6**, 24795-49-1; **7**, 53597-02-7; **8**, 53597-03-8; **9**, 53597-04-9; **10**, 53597-05-0; **11**, 53597-06-1; **12**, 42391-78-6; propane-1,3-dithiol di-*p*-toluenesulfonate, 3866-79-3; methyl fluorosulfonate, 421-20-5.

References and Notes

(1) J. A. Marshall and H. Roebke, *Tetrahedron Lett.*, 1555 (1970); J. A. Marshall, C. T. Buse, and D. E. Seitz, *Syn. Commun.*, **3**, 85 (1973); J. A. Marshall and D. E. Seitz, *J. Org. Chem.*, **39**, 1814 (1974).

(2) H. Roebke, unpublished observations.

(3) S. M. Kupchan, R. J. Hemingway, D. Werner, A. Karim, A. T. McPhail, and G. A. Sim, *J. Amer. Chem. Soc.*, **90**, 3596 (1968).

(4) *Two routes to this lactone have recently been described:* P. A. Grieco and K. Hiroi, *Tetrahedron Lett.*, 1831 (1973): R. D. Clark and C. H. Heathcock, *ibid.*, 1713 (1974).

(5) L. S. Minckler, A. S. Hussey, and R. H. Baker, *J. Amer. Chem. Soc.*, **78**, 1009 (1956).

(6) R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. Ives, and R. B. Kelly, *J. Chem. Soc.*, 1131 (1957).

(7) P. E. Eaton, G. F. Cooper, R. C. Johnson, and R. H. Mueller, *J. Org. Chem.*, **37**, 1947 (1972).

(8) T. L. Ho and C. M. Wong, *Synthesis*, 561 (1972): T. Oishi, K. Kamemoto, and Y. Ban, Tetrahedron Lett., 1085 (1972).

(9) *Cf.* M. Tomoeda, M. Ishizaki, H. Kobayashi, S. Kanatomo, T. Koga, M. Inuzuka, and T. Furuta, *Tetrahedron*, **21**, 733 (1965).

(10) We thank Professor C. H. Heathcock for kindly supplying us with the spectra of this compound.

(11) The apparatus described by W. S. Johnson and W. P. Schneider ["Organic Syntheses," Collect. Vol. IV, New York, N.Y., 1963, p 132] was used to maintain an argon atmosphere. The isolation procedure consisted of thorough extractions with the specified solvent, washing the combined extracts with saturated brine solution, and drying the extracts over anhydrous magnesium sulfate. The solvent was removed from the filtered extracts under reduced pressure on a rotary evaporator. Microanalyses were performed by Micro-Tech Laboratories, Inc., Skokie, Ill. Infrared spectra were obtained with a Perkin-Elmer 137 spectrophotometer. Infrared absorption are reported in wavelengths (μm) and are *standardized with reference* to the 6.24-μm peak of polystyrene. Nuclear magnetic resonance spectra were recorded with a Varian T-60 spectrometer. Signals are reported as the chemical shift downfield from tetramethylsilane (TMS) in parts per million (ppm) of the applied field. The multiplicity of the peak is abbreviated: singlet, s; doublet, d; triplet, t; quartet, q; multiplet, m. Coupling constants are reported in hertz (Hz). Melting points were determined on a calibrated Thomas capillary melting point apparatus. Melting points are not corrected.

(12) H. v. Driel, J. W. v. Reijendam, J. Buter and H. Wynberg, *Syn. Commun.*, **1**, 25 (1971).

(13) R. B. Turner, K. H. Gänshirt, P. E. Shaw, and J. D. Tauber, *J. Amer. Chem. Soc.*, **88**, 1776 (1966).

(14) J. C. A. Chivers and S. Smiles, *J. Chem. Soc.*, 697 (1928): R. B. Woodward, I. J. Pachter, and M. L. Scheinbaum, *Org. Syn.*, **52**, unchecked procedure 1815 (1972).

The Effect of Substituents on the Addition of Thiophenol to α-Methylstyrene[1]

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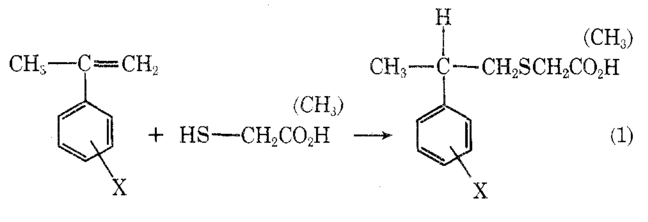
The additions of free radicals in general,[2] and of thiyl radicals in particular,[3] to carbon–carbon double bonds have been studied extensively over the years. Examples of the application of Hammett-type linear free-energy treatments to such a reaction, however, are rather rare.[4] In the case of thiyl radical addition, previous work[4b,c] tended to indicate that electron-donating substituents enhanced the rate of addition, while electron-withdrawing substituents retarded it. However, these studies, which dealt with the reaction (eq 1) between thioglycolic acid (or its methyl ester) and substituted α-methylstyrenes, suffer due to the small number of different substituted compounds examined and the possibility of competing ionic addition in certain cases. It was felt that a more extensive Hammett study of this reaction might be of interest.



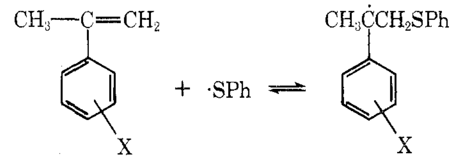
(1)

Table I
Relative Reactivities of Substituted α-Methylstyrenes toward Thiyl Radicals at 70°

Substituent	Registry no.	σ^a	σ^{+a}	k_X/k_H
p-CH_3O	1712-69-2	−0.27	−0.778	1.85 ± 0.13
p-CH_3	1195-32-0	−0.17	−0.311	1.36 ± 0.18
m-CH_3	1124-20-5	−0.07	−0.066	1.15 ± 0.09
H	98-83-9	0.00	0.00	1.00
m-CH_3O	25108-57-0	0.12	0.047	1.02 ± 0.07
p-Cl	1712-70-5	0.23	0.114	0.98 ± 0.04
m-Cl	1712-71-6	0.37	0.399	0.69 ± 0.10
m-CF_3	368-79-6	0.47	0.52	0.58 ± 0.07
p-NO_2	1830-68-8	0.78	0.790	0.99 ± 0.10

[a] Reference 5.

The system chosen for study involved photoinduced competitive reactions of pairs of substituted α-methylstyrenes with thiophenol under nitrogen at reduced pressure. It was felt that the possible reversibility of addition step[2,3] (eq 2) should not affect the validity of the result from the linear free-energy treatment under these conditions. In support of this assumption was an experiment of Cadogan and Sadler[4c] in which they found that the relative reactivity ratio for a pair of substituted α-methylstyrenes toward the thiyl radical derived from methyl thioglycolate remained constant as the relative initial concentration of methyl thioglycolate was varied.



(2)

Our results for the relative reactivities of substituted α-methylstyrenes toward the thiyl radical from thiophenol in benzene at 70° are listed in Table I. Nearly identical reactivity ratios were obtained when thiyl radicals were thermally, rather than photolytically, generated. In the former case, however, a lessened total reactivity was observed. When a linear free-energy treatment is applied using the Hammett σ constants, a ρ value of -0.57 ± 0.03 (correlation coefficient, $r = -0.962$) is obtained, while using the Okamoto–Brown σ^+ parameters gives ρ equal to -0.38 ± 0.02 ($r = -0.984$).[5] Both of these ρ values were obtained using all of the data points except that corresponding to the para nitro compound. A graphic presentation of the linear free-energy treatment using the σ^+ parameters is shown in Figure 1.

The anomalously high reactivity of p-nitro-α-methylstyrene observed in this study has also been noted in previous work[4c,d] for strongly electron-withdrawing substituents in the para position. It has been attributed to enhanced resonance stabilization of the benzylic free radical by such groups. An alternative explanation is suggested by the work of Walling, *et al.*[6] In a copolymerization study, the relative reactivities of a series of substituted styrenes toward styrene radical were determined. These results show rate enhancement by *electron-withdrawing* substituents and tend to correlate with the σ^- parameters. Thus, the high reactivity of the para nitro compound in the present study could be due to copolymerization taking place preferentially to,