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# The Reactions of Sulfur Ylides with Cyclic Carboxyl Compounds and Isocyanates

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It was found that the reactions of dimethyloxosulfoniummethylide (II) with cyclic carboxyl compounds (I), such as lactones, carboxylic anhydrides and imides, gave the corresponding stable oxosulfonium ylides (III). In addition, the reaction of phenyl isocyanate dimer (IX) and dimethylsulfoniummethylide (X) afforded a 1 : 1 adduct (XI), which, on heating, decomposed to give a ring expansion product (XIV). Hydantoin derivatives (XVII) were also produced by treating dimethylsulfonium-α-methylacylmethylide (XVI) with two moles of isocyanates in dimethyl sulfoxide. On the other hand, when the same reactions were carried out in benzene, XVI reacted with an equimolar amount of isocyanates to give acrylamide derivatives (XVIII) in high yields by the rearrangement of the intermediate sulfoniummethylide (XX).

In the previous paper,[1] it was shown that 3-hydroxyfuran derivatives were synthesized in good yields from ketene dimer and stable sulfonium or oxosulfonium[2] ylides accompanied with ring expansion.

In the present paper, in connection with this methylene transfer reaction, the reactions of sul-

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[1] H. Takei, M. Higo, K. Saito and T. Mukaiyama, This Bulletin, **41**, 1738 (1968).

[2] unpublished result.

fonium and oxosulfonium ylides with some cyclic carboxyl compounds (I) such as lactones, imides[3)] or carboxylic anhydrides, and isocyanates[4)] were studied. When I and dimethyloxosulfoniummethylide (II) were allowed to react in tetrahydrofuran (THF), stable oxosulfonium ylides (III)[5)] were produced in high yields instead of the expected ring expansion compounds (IV). The reaction may proceed through an initial formation of a betaine intermediate (V), which in turn changed to III by an intramolecular proton transfer. The results are summarized in Table 1.

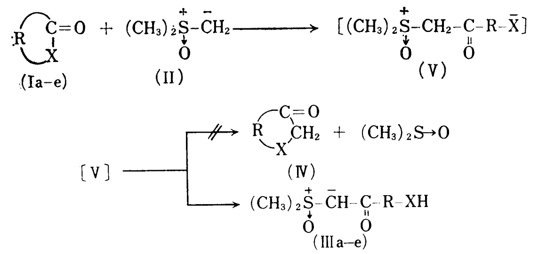
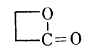
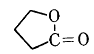
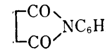
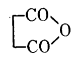
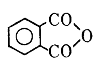
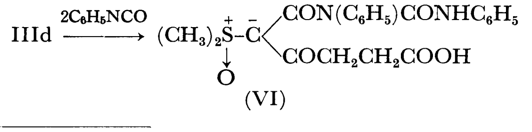


Table 1. Reactions of dimethyloxosulfoniummethylide (II) with cyclic carboxyl compounds (I)

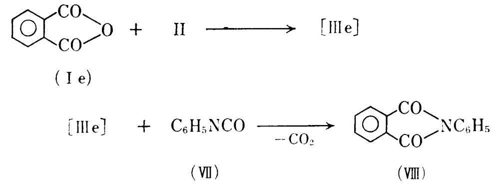
|  | (I) | $(CH_3)_2\underset{\downarrow\atop O}{\overset{+}{S}}-\overset{-}{C}H-\underset{\|\atop O}{C}-R-XH$ (III)<br>-R-X-H | <br>Yield, % |
|---|---|---|---|
|  | (Ia) | $-(CH_2)_2-OH$ | 93 |
|  | (Ib) | $-(CH_2)_3-OH$ | 99 |
|  | (Ic) | $-(CH_2)_2-\underset{\|\atop O}{C}-\overset{H}{N}C_6H_5$ | 94 |
|  | (Id) | $-(CH_2)_2-COOH$ | 69 |
|  | (Ie) | $-o-C_6H_4-COOH$ | 55* |

* IIIe was not isolated but subsequently treated with phenyl isocyanate to give *N*-phenylphthalimide (VIII) in a 55% yield.

In the case of succinic anhydride (Id), IIId was very hygroscopic and identified as its acylurea derivative (VI) by treating with phenyl isocyanate (VII). On the other hand, when the mixture resulted from the reaction of Ie and II was treated with VII, *N*-phenylphthalimide (VIII) was produced with evolution of carbon dioxide.

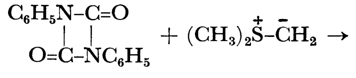


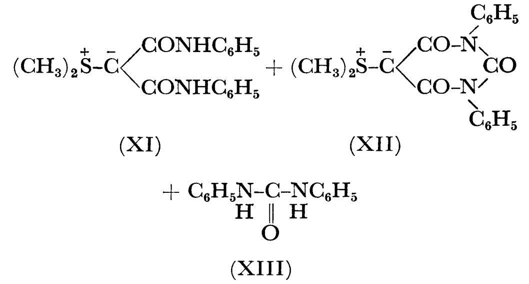
(VI)



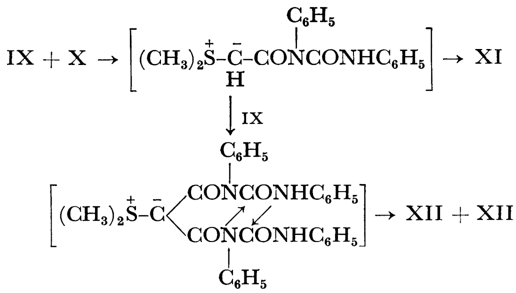
Several attempts to convert III into IV were unsuccessful (See Experimental).

The reaction of phenyl isocyanate dimer (IX) with dimethylsulfoniummethylide (X) was carried out at −15°C, and dimethylsulfonium-bis(phenylcarbamoyl)-methylide (XI), dimethylsulfonium-1,3-diphenylbarbiturylide (XII)[6)] and 1,3-diphenylurea (XIII) were obtained in 15, 4 and 16% yields, respectively.





It seems reasonable to consider that the reaction proceeds *via* such two ylide intermediates as sketched below.



When XI was heated[7)] at 160—170°C in a sealed tube, 1,3-diphenylhydantoin (XIV) was obtained with elimination of dimethyl sulfide probably

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[3)] P. T. Izzo, *J. Org. Chem.*, **28**, 1713 (1963).

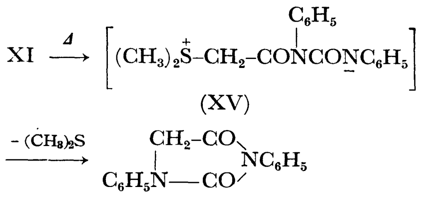
[4)] H. König and H. Metzger, *Chem. Ber.*, **98**, 3733 (1965).

[5)] J. C. Sheehan and J. H. Beeson, *J. Amer. Chem. Soc.*, **89**, 362 (1967).

[6)] a) R. Gompper and H. Euchner, *Chem. Ber.*, **99**, 527 (1966). b) A. Hochrainer, *Monatsh. Chem.*, **97**, 1 and 823 (1966).

[7)] C. Kaiser, B. M. Trost, J. Beeson and J. Neinstock, *J. Org. Chem.*, **30**, 3972 (1965).

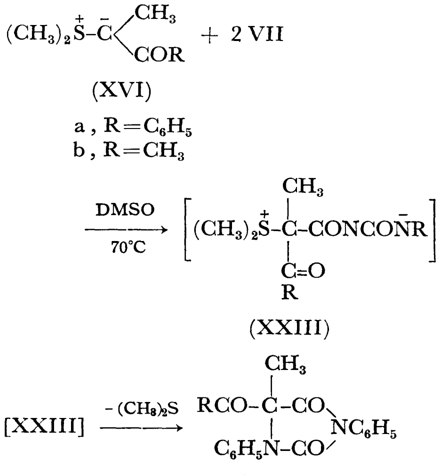
through a betain intermediate (XV), which decomposed to give XIV by an intramolecular nucleophilic displacement.


(XV)

(XIV)

The result indicates that IX was transformed into XIV accompanied with ring expansion *via* XI. In addition, it was found that the intermediate XI was easily obtained from X and two moles of VII. Thus, it will be possible to obtain hydantoin derivatives directly from two moles of isocyanates and sulfur ylides through such intermediates as XV.

Based on the above assumption, the reactions of VII with stable sulfonium ylides having no proton on the ylide carbon atom, *e. g.*, dimethylsulfonium-α-methylphenacylide (XVIa), were investigated. When XVIa was treated in dimethyl sulfoxide (DMSO) with two moles of VII at 70°C, 1,3-diphenyl-5-benzoyl-5-methylhydantoin (XVIIa)[8] was obtained with evolution of dimethyl sulfide, as expected.


(XVI)

a, R=$C_6H_5$

b, R=$CH_3$

(XXIII)

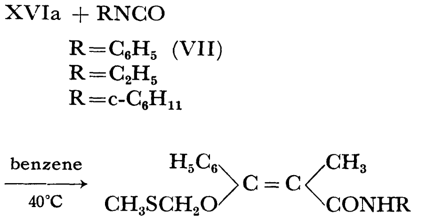
(XVII)

a, R=$C_6H_5$ 52%

b, R=$CH_3$ 49%

On the other hand, when the same reaction of XVIa with VII was carried out in benzene, evolution of dimethyl sulfide was not observed and α-methyl-β-methylthiomethoxy-β-phenylacrylanilide (XVIIIa) was obtained in a good yield along with the recovery of one mole of VII.

The structural assignment was made on the basis


XVIa + RNCO

R=$C_6H_5$ (VII)

R=$C_2H_5$

R=c-$C_6H_{11}$

(XVIII)

a, R=$C_6H_5$ 73%

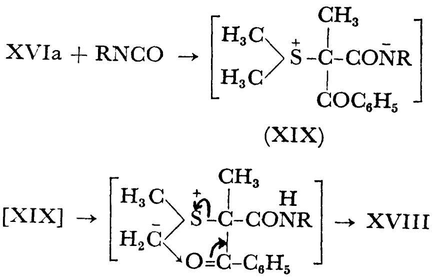
b, R=$C_2H_5$ 86%

c, R=c-$C_6H_{11}$ 80%

of elemental analyses and IR, NMR and mass spectra. The configuration about the carbon-carbon double bond is still not determined, but it is suggested that phenylcarbamoyl and phenyl groups have *trans* relationship because of bulkiness of these two groups.

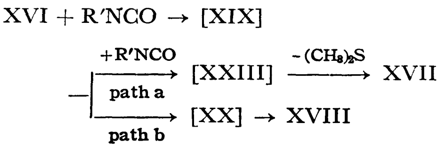
In a similar manner, reactions of XVIa with ethyl and cyclohexyl isocyanates gave XVIIIb and XVIIIc, respectively.

The reaction is considered to proceed through a 1,4-betaine (XIX), which changed to an ylide intermediate (XX) by a proton transfer. The XX in turn undergoes the rearrangement reported by Ruiz[9] and by Ratts and Yao[10] to give XVIII.


(XIX)

(XX)

The difference in the reaction course between the two reactions mentioned above can be explained by considering that the intermediate XIX, formed from XVI and one mole of isocyanate, reacts rapidly with another mole of isocyanate in DMSO to give a 1,6-betaine (XXIII) (path a), and that, in benzene, the formation of XX from XIX by an intramolecular proton transfer proceeds more rapidly (path b) than that of XXIII.



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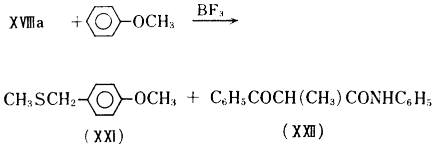
[8] F. Ramirez, S. B. Bhatia and C. P. Smith, *J. Amer. Chem. Soc.*, **89**, 3030 (1967).

[9] E. B. Ruiz, *Acta Salmenticensia, Ser. cienc.*, **2**, 64 (1958); *Chem. Abstr.*, **54**, 7623 (1960).

[10] K. W. Ratts and A. N. Yao, *J. Org. Chem.*, **33**, 70 (1968).

It was found that XVIIIa obtained by the above reaction gave *p*-methylthiomethylanisole (XXI) in a 38% yield along with α-benzoylpropionanilide (XXII) by heating at 60°C with excess anisole in the presence of a catalytic amount of boron trifluoride etherate.



## Experimental

Most of these reactions were carried out in the atmosphere of dry nitrogen. All melting and boiling points are uncorrected.

**Reaction of β-Propiolactone (Ia) with Dimethyloxosulfoniummethylide (II).** To a solution of II (25 mmol) in 40 m*l* of dry tetrahydrofuran (THF), a solution of Ia (1.80 g, 25 mmol) in 18 m*l* of dry THF was added over a period of 10 min with stirring at −15°C. An exothermic reaction soon took place to give a semi-crystalline mush, which, after warming at 50—60°C for 4 hr, afforded 3.80 g (in a 93% yield) of dimethyloxosulfonium-ω-hydroxypropionylmethylide (IIIa), mp 94.5—95.5°C (recrystallized from ethyl acetate). Found: C, 44.09; H, 7.70; S, 19.48%. Calcd for $C_6H_{12}O_3S$: C, 43,90; H, 7.37; S, 19.49%. IR (KBr): 3380, 1030 (OH); 1552 (C=O); 1172 cm$^{-1}$ (S→O). NMR (DMSO-$d_6$): $\delta$=2.20 (2H, t, $CH_2$-CO), 3.43 (6H, s, $2CH_3$), 3.62 (2H, t, $CH_2$-O), 4.40 (1H, s, OH), and 4.78 (1H, s, CH).

In a similar manner, dimethyloxosulfonium-ω-hydroxybutyrylmethylide (IIIb) was obtained from γ-butyrolactone (Ib) and II in a quantitative yield, mp 55—67°C (ethyl acetate). Found: C, 46.91; H, 8.28%. Calcd for $C_7H_{14}O_3S$: C, 47.18; H, 7.96%. IR (KBr): 3400, 1030 (OH); 1552 (C=O); 1172 cm$^{-1}$ (S→O). IIIb was very hygroscopic and decomposed slowly even when stored in a desiccator over phosphorus pentoxide.

**Attempts to Obtain IVa from IIIa.** *1) Thermolysis of IIIa.* When 0.82 g (5.0 mmol) of IIIa was heated in a distilling flask under reduced pressure, decomposition started at 215°C and 0.27 g (70%) of dimethyl sulfoxide (DMSO) was distilled out. The resulting black tar prevented further purification.

*2) Reaction of IIIa with Cupric Chloride.*[11] A mixture of IIIa (1.00 g, 6.1 mmol) and anhydrous cupric chloride (0.82 g, 6.1 mmol) in 20 m*l* of dry dioxane was heated at 90°C for 1.5 hr to give dark brown resinous material which prevented further purification.

*3) Reaction of IIIa with Triphenyl Phosphite.*[12] When 1.64 g (10 mmol) of IIIa was heated in a distilling flask with 3.10 g (10 mmol) of triphenyl phosphite, a vigorous reaction took place at the bath temperature of 120°C. After cooling, 0.84 g (90%) of phenol was distilled from the reaction mixture. The expected IVa (lit. bp 137—138°C) was not obtained.

**Reaction of *N*-Phenylsuccinimide (Ic) with II.** To a solution of II (10 mmol) in 35 m*l* of dry THF, a solution of Ic (1.75 g, 10 mmol) in 30 m*l* of dry THF was added at room temperature with stirring. After stirring for 2 hr, followed by refluxing for 2 hr, the solvent was evaporated. The residue was recrystallized from benzene to give dimethyloxosulfonium-ω-phenylcarbamoylpropionylmethylide (IIIc), 2.52 g (94%), mp 131.5°C. Found: C, 58.27; H, 6.16; N, 5.17%. Calcd for $C_{13}H_{17}NO_3S$: C, 58.42; H, 6.41; N, 5.24%. IR (Nujol): 3320 (NH); 1660, 1534, 1294, 1254 (-CO-NH-); 1572 cm$^{-1}$ (C=O).

**Thermolysis of IIIc.** When 0.82 g (3 mmol) of IIIc was heated in a distilling flask under reduced pressure, decomposition occurred at the bath temperature of 180°C and DMSO was distilled out, bp 75—76°C/11 mmHg, 0.23 g (quantitative yield). The resulting solid was recrystallized from ethanol to give Ic, 0.29 g (53%), mp and mmp 154°C.

**Reaction of Succinic Anhydride (Id) with II.** A solution of Id (1.00 g, 10 mmol) in 24 m*l* of dry THF was added to a solution of II (10 mmol) in 35 m*l* of dry THF over a period of 30 min with stirring at −15°C. The reaction started at once with evolution of heat to afford colorless precipitates. After stirring for 1.5 hr with the cooling bath removed, the precipitates were filtered and washed with dry THF. The resulting precipitates were very hygroscopic and prevented further purification. However, they were identified as dimethyloxosulfonium-ω-carboxypropionylmethylide (IIId), 1.30 g (69%), by the following manner. Thus, to a suspension of IIId in dry THF prepared from Id (10 mmol) and II (10 mmol) by the method described above, a solution of phenyl isocyanate (VII) (1.19 g, 10 mmol) in 30 m*l* of dry dioxane was added dropwise. The reaction mixture turned to a clear solution by warming at 30—60°C for 2 hr. After removal of the solvents, the resulting colorless solid was submitted to a silica gel column to afford 1,3-diphenylurea (XIII), 0.42 g (40%), and dimethyloxosulfonium-ω-carboxypropionyl-(2,4-diphenylallophanyl)-methylide (VI), 0.35 g (17%), mp 135—136°C (benzene). Found: C, 58.92; H, 5.13; N, 6.27%. Calcd for $C_{21}H_{22}N_2O_6S$: C, 58.60; H, 5.15; N, 6.51%. IR (KBr): 3320 (NH); 1700 (COOH); 1667 (C=O); 1614, 1545 cm$^{-1}$ (C=O).

**Reaction of Phthalic Anhydride (Ie) and II.** When a solution of Ie (1.26 g, 8.5 mmol) in 25 m*l* of dry THF was added dropwise to a solution of I (8.5 mmol) in 32 m*l* of dry THF with stirring at −15°C, the reaction soon took place to give colorless precipitates, to which, after stirring for 2 hr with the cooling bath removed, VII (1.01 g, 8.5 mmol) in 20 m*l* of dry dioxane was added dropwise at room temperature. The mixture was stirred at 60—70°C for 3 hr and turned to a clear solution. During the time, 145 m*l* (15°C, 760 mmHg) of carbon dioxide (76%) was evolved. The solvents were evaporated and the residue was recrystallized from methanol to give *N*-phenylphthalimide (VIII), 1.05 g (55%), mp 205.5—206.5°C.

**Reaction of Phenyl Isocyanate Dimer (IX) with Dimethylsulfoniummethylide (X).** A solution of IX (2.14 g, 9.0 mmol) in 75 m*l* of dry THF was added to a solution of X (10 mmol) in dry DMSO with stirring at −15°C. Stirring was continued for 40 min, followed by an additional two hours' stirring with the cooling bath removed. The reaction mixture was poured into

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[11] J. Selbin, W. E. Bull and L. H. Holmes, Jr., *J. Inorg. Nucl. Chem.*, **16**, 219 (1961).

[12] E. H. Amonoo-Neizer, S. K. Ray, R. A. Shaw and B. C. Smith, *J. Chem. Soc.*, **1965**, 4296.

200 m*l* of cold water, and the suspension was extracted with three 80 m*l* portions of ether, and then with three 100 m*l* portions of chloroform. The ethereal extract was dried over anhydrous sodium sulfate and the solvent was evaporated to give slight yellow crystals, to which a small amount of dichloromethane was added. The undissolved crystals were filtered, washed and recrystallized from ethanol to give XIII, 0.30 g (16%), mp 238°C (dec.). The filtrate was chromatographed over silica gel. Elution with dichloromethane gave dimethylsulfonium-bis(phenylcarbamoyl)-methylide (XI), 0.43 g (15%), mp 165°C (dec.) (benzene). IR (KBr): 3290, 1632, 1570, 1530, and 1510 cm$^{-1}$. NMR ($CDCl_3$): $\tau$=6.95 (6H, s, $2CH_3$) and 2.45—3.00 (12H, m, $2C_6H_5$ and 2NH). The chloroform extract was dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. The resulting red-brown oil was chromatographed over silica gel. By elution with methylene chloride, dimethylsulfonium-1,3-diphenylbarbiturylide (XII) was obtained, 0.06 g (4%), mp 289°C (dec.) (methanol). Found: C, 63.50; H, 4.74; N, 8.49; S, 9.78%. Calcd for $C_{18}H_{16}N_2O_3S$: C, 63.52; H, 4.74; N, 8.23; S, 9.40%. IR (KBr): 3020, 1705, 1640, 1610, and 1595 cm$^{-1}$.

**Thermolysis of XI.** When XI (1.50 g) was heated in a sealed tube at 160—170°C for 2 hr, formation of dimethyl sulfide was observed by its characteristic odour. The resulting slight yellow solid was dissolved in a small amount of dichloromethane and chromatographed over silica gel to give 1,3-diphenylhydantoin (XIV), 0.15 g (13%), mp 137.0—137.5°C (ligroin). Found: C, 71.45; H, 4.99; N, 11.43%. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.41; H, 4.80; N, 11.11%.

**Reaction with VII and X.** To a solution of X (30 mmol) in dry DMSO, a solution of VII (3.57 g, 30 mmol) in 10 m*l* of dry THF was added with stirring at −15°C. An exothermic reaction started at once. After stirring for 50 min with the cooling bath removed, the reaction mixture was treated in the same way as described for the reaction of IX and X to give XI (26%), XII (10%) and XIII (4%). From the water layer, kept standing after extraction with ether and chloroform, colorless precipitates were deposited, which were recrystallized from ligroin and identified as XIV, 0.17 g (5%).

In a similar way, the reaction of X with 2 mol of VII gave XI, XII and XIII in 32, 22 and 23% yields, respectively. The reaction of X with 4 mol of VII also gave XII (24%) and XIII (22%).

**Reaction of Dimethylsulfonium-$\alpha$-methylphenacylide (XVIa) with 2 mol of VII in DMSO.** XVIa,b were newly prepared from the corresponding bromides by a method similar to that described for the preparation of dimethylsulfoniumcarbethoxymethylide.[13] To a suspension of XVIa (0.97 g, 5 mmol) in 18 m*l* of dry DMSO, VII (1.19 g, 10 mmol) was added portionwise. The mixture was stirred for a while, and then turned to a clear solution. When the solution was heated at 70°C, evolution of dimethyl sulfide was observed. After heating for 6 hr, the solvent was removed under reduced pressure at 50°C to give a slight yellow viscous oil, which was chromatographed over silica gel. Elution with benzene afforded XIII, 0.45 g (43%), and 1,3-diphenyl-5-benzoyl-5-methylhydantoin (XVIIa), 0.97 g (52%), mp 138.5—140°C (ligroin). Found: C, 74.84; H, 4.84; N, 7.72%. Calcd for $C_{23}H_{18}N_2O_3$: C, 74.58; H, 4.90; N, 7.56%. IR (KBr): 1775, 1716, and 1685 cm$^{-1}$. NMR ($CDCl_3$): $\tau$=8.16 (3H, s, $CH_3$) and 2.15—2.90 (15H, m, $3C_6H_5$).

Similarly, 1,3-diphenyl-5-acetyl-5-methylhydantoin (XVIIb),[8] mp 135—137°C (ligroin), was obtained from XVIb and 2 mol of VII in a 49% yield along with XIII (24%). Found: C, 70.22; H, 4.90; N, 9.11%. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.11; H, 5.23; N, 9.09%. IR (KBr): 1780 and 1720 cm$^{-1}$.

**Reaction of XVIa with 1 mol of VII in Benzene.** When 0.60 g (5.0 mmol) of VII was added portionwise to a suspension of XVIa (0.97 g, 5. 0mmol) in 20 m*l* of dry benzene, an exothermic reaction took place and the mixture turned into a clear solution. The solution was warmed at 40°C for 4 hr and the solvent was removed *in vacuo*. The residue was chromatographed over silica gel. Elution with benzene gave 1.13 g (73%) of $\alpha$-methyl-$\beta$-methylthiomethoxy-$\beta$-phenylacrylanilide (XVIIIa), mp 118.5—119°C (ligroin). Found: C, 69.25; H, 5.85; N, 4.32; S, 10.11%. Calcd for $C_{18}H_{19}NSO_2$: C, 68.99; H, 6.11; N, 4.47; S, 10.22%. IR (KBr): 3300, 1640, 1535, 1340, and 1112 cm$^{-1}$. NMR ($CDCl_3$): $\tau$=8.16 (3H, s, $CH_3$-C), 7.86 (3H, s, $CH_3$-S), 5.28 (2H, s, S-$CH_2$-O), 2.20—3.05 (10H, m, $2C_6H_5$), and 0.24 (1H, s, NH). Mass: *m*/*e* 251, 222, 146, 119, 105, and 77.

In a similar manner, *N*-ethyl- and *N*-cyclohexyl-$\alpha$-methyl-$\beta$-methylthiomethoxy-$\beta$-phenylacrylamide, (XVIIIb) and (XVIIIc), were obtained by the reactions of XVIa with ethyl and cyclohexyl isocyanates, respectively. XVIIIb (in an 80% yield), mp 77—78°C (petroleum ether). Found: C, 67.50; H, 8.10; N, 4.35; S, 9.99%. Calcd for $C_{18}H_{25}NO_2S$: C, 67.69; H, 7.89; N, 4.39; S, 10.02%. XVIIIc (in an 86% yield), bp 141.0°C/0.073 mmHg. Found: C, 63.37; H, 7.13; N, 5.29; S, 11.83%. Calcd for $C_{14}H_{19}NO_2S$: C, 63.38; H, 7.22; N, 5.28; S, 12.06%.

**Reaction of XVIIIa with Anisole.** To a solution of XVIIIa (1.57 g, 5.0 mmol) in 25 m*l* of anisole, several drops of boron trifluoride etherate were added. Evolution of heat was observed and the color of the solution turned slightly yellow. After stirring for 1.5 hr at room temperature, followed by warming at 60°C for 6 hr, anisole was evaporated and dry ether was added to the residue to precipitate $\alpha$-benzoylpropionanilide (XXII), 0.70 g (67%), mp 137.0—138.5°C (benzene). Found: N, 5.53%. Calcd for $C_{16}H_{15}NO_2$: N, 5.58%. From the filtrate, *p*-methylthiomethylanisole (XXI) was obtained, 0.31 g (38%), bp 80—81°C/1.6 mmHg. Found: C, 63.98; H, 7.43; S, 18.83%. Calcd for $C_9H_{12}OS$: C, 64.27; H, 7.19; S, 19.03%. NMR ($CDCl_3$): $\tau$=8.08 (3H, s, $CH_3$-S), 6.43 (2H, s, -$CH_2$-), 6.28 (3H, s, $CH_3$-O), 3.22 and 2.85 (4H, a pair of doublets with a coupling constant of 8.5 Hz, -$C_6H_4$-).

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[13] G. B. Payne, *J. Org. Chem.*, **32**, 3351 (1967).