BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 40 2641—2644 (1967)

The Preparation of 1-Dimethylamino-1-ethylthioethylene (Ketene-*N*, *S*-acetal) and Its Reactions with Some Electrophilic Reagents

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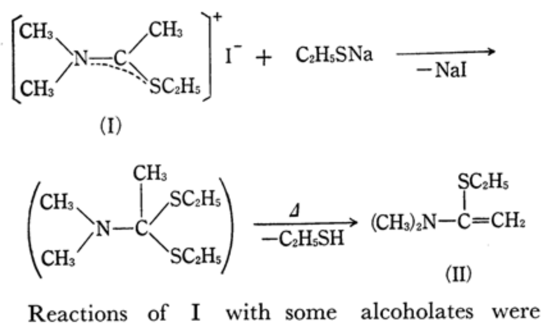
(Received June 2, 1967)

The preparation of 1-dimethylamino-1-ethylthioethylene (ketene-*N*, *S*-acetal) from *N*, *N*-dimethylamino-*S*-ethylthioacetamidium iodide and the reactions of the ketene-*N*, *S*-acetal with some electrophilic reagents were investigated. One equivalent of phenyl isocyanate and two equivalents of diphenylketene reacted with the ketene-*N*, *S*-acetal to produce substituted acrylanilide and 2, 3-dihydro-α-pyrone derivative, respectively. On the other hand, the reactions of the ketene-*N*, *S*-acetal with carbon disulfide in the presence of elemental sulfur and with electrophilic olefins, such as acrylonitrile and methyl acrylate, gave 5-dimethylaminotrithione and substituted cyclobutenes, respectively, by eliminating ethyl mercaptan. Further, it was found that α, β-unsaturated carbonyl compounds, such as acrolein and methyl vinyl ketone, afforded bicyclic compounds, 2, 10-dioxabicyclo[4. 4. 0]decadiene-3, 8 derivatives.

In the preceding papers,[1,2] it has been reported that *N*, *N*-dimethyl-*S*-ethylthioformamidium iodide and *N*, *N*-dimethyl-*S*-ethylthiobenzamidium iodide react with sodium ethylmercaptide to give the corresponding amide diethylmercaptoles in good yields.

It was established in the present experiment that *N*, *N*-dimethylacetamide diethylmercaptole was not isolated by treating *N*, *N*-dimethyl-*S*-ethylthioacetamidium iodide (I) with sodium ethylmercaptide, but 1-dimethylamino-1-ethylthioethylene (ketene-*N*, *S*-acetal) (II) resulted in a fairly good yield. The ketene-*N*, *S*-acetal (II) may be produced by the thermal decomposition of *N*, *N*-dimethylacetamide diethylmercaptole, initially formed, with a loss of ethyl mercaptan during the distillation under reduced pressure.



Reactions of I with some alcoholates were also investigated with the expectation that the ketene-*N*, *S*-acetal (II) would be also produced according to the following equation. Indeed, when potassium *t*-butoxide was treated with I in ether at room temperature, II was prepared in 67% yield.[3] However, it was further found that reactions of other alcoholates, such as sodium isopropoxide, *n*-propoxide and benzyloxide, with (I) gave such undesirable by-products as *N*, *N*-dimethylacetamide and *N*, *N*-dimethylacetamide dialkylacetal along with II.

$$\mathrm{I} + \mathrm{RONa} \xrightarrow[-\mathrm{NaI}]{} \mathrm{II} + \mathrm{ROH}$$

Since II is, formally, the analogue of ketene acetals or enamines, it is expected that β-carbon of the ketene-*N*, *S*-acetal (II) would exhibit a strong nucleophilic character due to the conjugation of the double bond with dimethylamino and ethylthio groups. When phenyl isocyanate, one of the electrophilic reagents, was treated with (II) in cyclohexane at room temperature, a considerable amount of heat was liberated and a white precipitate was separated soon from the reaction mixture. This precipitate was confirmed to be 3-dimethylamino-3-ethylthioacrylanilide (III) by means of its infrared spectrum, which had an absorption band attributable to N–H linkage (3310 cm^{-1}). In this case, the alternative pathway forming β-amino-β-lactam by cyclization of the intermediate (IV), which was observed in the reactions of isocyanates with vinyl ethers,[4,5] was not found. An experiment with phenyl isothiocyanate at room temperature gave a similar result.

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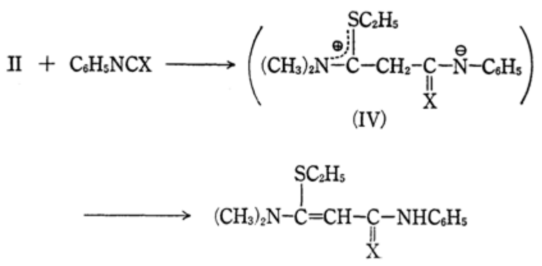
[1] T. Mukaiyama, T. Yamaguchi and H. Nohira, This Bulletin, **38**, 2107 (1965).

[2] T. Mukaiyama and T. Yamaguchi, *ibid.*, **39**, 2005 (1966).

[3] The preparation of some, simple ketene-*N*, *S*-acetals was reported: R. Gompper and W. Elser, *Tetrahedron Letters*, **1964**, 1971, and reactions of ketene *N*, *S*-acetals and 1, 1-dicyanoethylenes appeared in a brief note, after this manuscript had been submitted for publication: R. Gompper, W. Elser and H. J. Müller, *Angew. Chem.*, **79**, 473 (1967).

[4] T. Mukaiyama, R. Yoda and I. Kuwajima, *Tetrahedron Letters*, **1966**, 6247.

[5] F. Effenberger, R. Gleiter and G. Kiefer, *Chem. Ber.*, **99**, 3892 (1966).

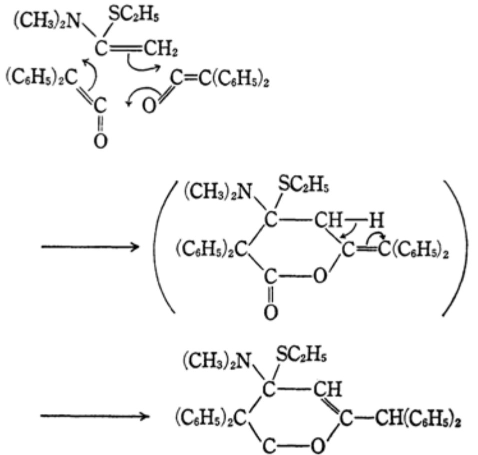


(IIIa) X=O

(IIIb) X=S

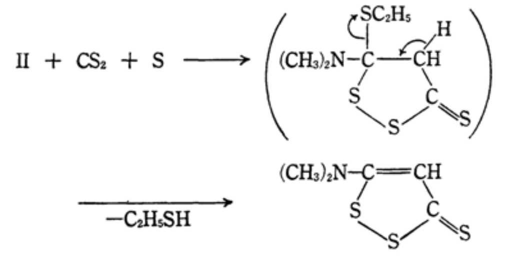
On the other hand, dicyclohexylcarbodiimide did not react with II even in boiling benzene and starting materials were recovered together with a small amount of resinous product.

In the case of diphenylketene, a vigorous reaction took place at room temperature and ice-cooling was necessary. Two moles of the ketene reacted with one mole of II to give 3, 4-dihydro-3, 3-diphenyl-4-dimethylamino-4-ethylthio-6-diphenylmethyl-2*H*-pyran-2-one (V). The structure was confirmed by its elemental analysis, infrared spectroscopy and NMR spectroscopy. Namely, its infrared spectrum had characteristic absorption bands attributable to $-\overset{\overset{\displaystyle O}{\|}}{C}-O-C=C-$ linkage (1740 cm^{-1}) and its NMR spectroscopy indicated that the free rotation of dimethylamino group is inhibited (two singlet peaks at δ 2.63 and 2.46). The reaction may proceed as follows:



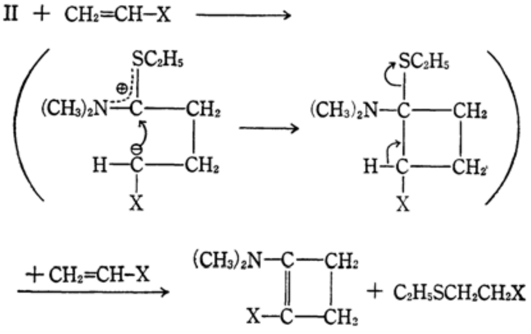
(V)

In the presence of elemental sulfur, carbon disulfide reacted with (II) exothermally in dimethylformamide to afford 5-dimethylamino-3*H*-1, 2-dithiole-3-thione (VI) by eliminating ethyl mercaptan.



(VI)

Further it was established that substituted cyclobutenes were formed by the reactions of II with electrophilic olefins such as acrylonitrile and methyl acrylate. For example, when two equivalents of acrylonitrile were allowed to react with II in boiling dioxane for 10 hr under a nitrogen atmosphere, 73% yield of 1-cyano-2-dimethylaminocyclobutene (VIIa) was obtained together with 39% yield of 3-ethylthiopropionitrile, which resulted from the reaction of the eliminated ethyl mercaptan with another mole of acrylonitrile. In this case a cyanoethylation product, which was observed in the reactions of enamines with acrylonitrile,[6] was not obtained.



(VIIa) X=CN
(VIIb) $X=COOCH_3$

Similarly, VIIb was obtained in 70% yield by treating II and methyl acrylate in boiling dioxane for 10 hr or, better, in 80% yield by refluxing for 4 hr in acetonitrile under a nitrogen atmosphere, together with methyl 3-ethylthiopropionate.

On the other hand, in the case of α, β-unsaturated carbonyl compounds such as acrolein and methyl vinyl ketone, it was found that two moles of the α, β-unsaturated carbonyl compounds reacted with one mole of II, with liberation of heat, to form bicyclic compounds by eliminating ethyl mercaptan. When three equivalents of acrolein was added to II at room temperature, a striking heat liberation was observed and a substance with a chemical formula $C_{10}H_{15}NO_2$ resulted in 48% yield. This product showed negative Tollens' test and its

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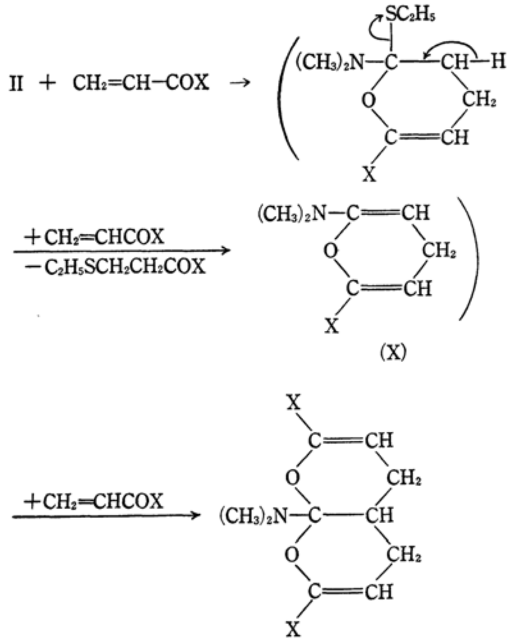
[6] a) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963); b) K. C. Brannock, A. Bell, R. D. Burpitt and C. A. Kelly, *J. Org. Chem.*, **29**, 801 (1964); c) K. C. Brannock, R. D. Burpitt and J. G. Theveatt, *ibid.*, **29**, 940 (1964).

infrared spectrum showed characteristic absorption bands attributable to enol ether linkage and to olefinic C–H linkage. These data indicated that the product is 1-dimethylamino-2, 10-dioxabicyclo[4. 4. 0]decadiene-3, 8 (IXa), which also explained precisely its NMR spectrum.

The reaction may be explained by considering the intermediate (X), a kind of ketene-*N*, *O*-acetal, which in turns reacts with another mole of acrolein to give the product IXa as sketched below.



(IXa) X = H

(IXb) X = CH_3

Analogously 3, 9-dimethyl-1-dimethylamino-2, 10-dioxabicyclo[4.4.0]decadiene-3, 8 (IXb) was obtained in 57% yield from three equivalents of methyl vinyl ketone and II along with quantitative yield of 4-ethylthiobutanone-2.

Experimental⁷⁾

The Preparation of 1-Dimethylamino-1-ethylthioethylene (II). A suspension of 13.0 g (0.05 mol) of *N*, *N*-dimethyl-*S*-ethylthioacetamidium iodide (I), prepared from *N*, *N*-dimethylthioacetamide and ethyl iodide by the method analogous to that described in the previous paper,¹⁾ and 5.0 g (0.06 mol) of sodium ethylmercaptide in 100 m*l* of dry ether was stirred for 5 hr at room temperature under nitrogen. The precipitate of sodium iodide was then removed by filtration and washed with dry ether. After ether had been evaporated from the filtrate, the residual liquid was distilled under reduced pressure to give 4.9 g (75%) of II. Bp 58—59°C/21 mmHg; n_D^{19} 1.5013.

Found: C, 54.60; H, 10.05; N, 10.71%. Calcd for $C_6H_{13}NS$: C, 54.94; H, 9.99; N, 10.68%.

IR: 3100, 1575 cm^{-1}.

NMR δ_{TMS}: 4.22, 4.02 (s, 2H, $=CH_2$), 2.65 (s, 6H, $(CH_3)_2N$), 2.40 (q, 2H, $S-CH_2$), 1.13 ppm (t, 3H, CH_3).

During the distillation, a considerable amount of ethyl mercaptan was trapped. The ketene-*N*, *S*-acetal (II), thus obtained, turns red brown in a few hours, when it is exposed to air at room temperature.

In a similar way, the reactions of I with some alcoholates were tried. Potassium *t*-butoxide gave II in 67% yield, but other alcoholates, such as sodium isopropoxide, *n*-propoxide and benzyloxide, gave such undesirable by-products as *N*, *N*-dimethylacetamide and *N*, *N*-dimethylacetamide dialkylacetal. The separation of II from these by-products was difficult and one component was always contaminated with others on distillation.

The Reaction of the Ketene-*N*, *S*-acetal (II) with Phenyl Isocyanate. To a stirred solution of II (2.60 g, 0.02 mol) in cyclohexane (10 m*l*) was added drop by drop a solution of phenyl isocyanate (2.40 g, 0.02 mol) in cyclohexane (10 m*l*). The reaction started soon with liberation of heat and in a few minutes a white precipitate was separated from the solution. After the stirring had been continued for 30 min, the white precipitate was filtered and recrystallized from cyclohexane. Yield IIIa, 4.32 g (86%); mp 98—99°C.

Found: C, 62.66; H, 7.16; N, 11.05%. Calcd for $C_{13}H_{18}N_2OS$: C, 62.38; H, 7.25; N, 11.19%.

The infrared spectrum of this compound showed an absorption band at 3310 cm^{-1} assigned to the N–H linkage.

In a similar way, 4.12 g (78%) of IIIb was obtained by treating 2.60 g (0.02 mol) of II and 2.70 g (0.02 mol) of phenyl isothiocyanate in dry ether. Mp 83—84°C.

Found: C, 58.95; H, 6.77; N, 10.81%. Calcd for $C_{13}H_{18}N_2S_2$: C, 58.65; H, 6.77; N, 10.53%.

The infrared spectrum also showed an absorption at 3158 cm^{-1} (N–H).

The Reaction of the Ketene-*N*, *S*-acetal (II) with Diphenylketene. Into an ice-cooled solution of 3.90 g (0.03 mol) of II in 40 m*l* of dry petroleum ether was added with stirring a solution of 11.50 g (0.06 mol) of diphenylketene⁸⁾ in 10 m*l* of dry petroleum ether. The reaction started soon, and a white precipitate began to separate from the solution. After the stirring had been continued for 4 hr at 3—5°C, the white precipitate was filtered and recrystallized from ethyl acetate. Yield V, 6.70 g (43%); mp 142—143°C.

Found: C, 78.65; H, 6.38; N, 2.84%. Calcd for $C_{34}H_{33}NO_2S$: C, 78.59; H, 6.40; N, 2.70%.

IR: 1740, 1135, 1085 cm^{-1}.

NMR $\delta_{TMS}^{CDCl_3}$: 7.11 (m, 20H, C_6H_5), 5.30—4.85 (m, 2H, CH), 2.63, 2.46 (s, 6H, $(CH_3)_2N$), 2.23 (q, 2H, SCH_2), 1.28—0.76 ppm (m, 3H, CH_3).

The Reaction of the Keten-*N*, *S*-acetal (II) with Carbon Disulfide in the Presence of Elemental Sulfur. Into a stirred suspension of elemental sulfur (0.95 g, 0.03 mol) in carbon disulfide (2.30 g, 0.03 mol) and dimethylformamide (20 m*l*) was added in

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7) All melting points and boiling points are uncorrected.

8) L. I. Smith and H. H. Hoehn, "Organic Syntheses," Coll. Vol. III, p. 356 (1955).

portions a solution of II (4.00 g, 0.03 mol) in dimethylformamide (5 m*l*). The reaction took place exothermally with the evolution of ethyl mercaptan. After a few minutes, pulvered sulfur dissolved completely and a yellowish precipitate was separated slowly from the solution. After the stirring had been continued for 3 hr, the precipitate was filtered and recrystallized from dimethylformamide. Yield VI, 0.90 g (17%); mp 192—194°C.

Found: C, 34.18; H, 3.90; N, 7.97%. Calcd for $C_5H_7NS_3$: C, 33.91; H, 3.98; N, 7.91%.

The Reaction of the Ketene-*N*, *S*-acetal (II) with Acrylonitrile. A solution of 2.60 g (0.02 mol) of II and 2.70 g (0.05 mol) of acrylonitrile in 50 m*l* of dry dioxane was refluxed for 10 hr under nitrogen. Then dioxane was removed *in vacuo* and the residual liquid was distilled under reduced pressure to give 0.90 g (39%) of 3-ethylthiopropionitrile and 1.78 g (73%) of VIIa. Bp 105°C/4 mmHg; n_D^{17} 1.5408.

Found: C, 68.46; H, 8.26; N, 22.80%; mol wt, 126 (cryoscopic in benzene). Calcd for $C_7H_{10}N_2$: C, 68.82; H, 8.25; N, 22.93%; mol wt, 122.

IR: 2180, 1650 cm^{-1}.

NMR $\delta_{TMS}^{CDCl_3}$: 2.88 (s, 6H, $(CH_3)_2N$), 2.45 ppm (m, 4H, CH_2).

3-Ethylthiopropionitrile was identified by comparing its infrared spectrum with that of the authentic sample.[9] VIIa, thus obtained, turns red brown in a few hours, when it is exposed to air at room temperature, but can be stored for several months under nitrogen at low temperature in the crystallized form.

The Reaction of the Ketene-*N*, *S*-acetal (II) with Methyl Acrylate. When 2.60 g (0.02 mol) of II was treated with 1.70 g (0.02 mol) of methyl acrylate in 50 m*l* of refluxing dry dioxane, 2.18 g (70%) of VIIb was obtained with evolution of ethyl mercaptan. Bp 69—71°C/1 mmHg; n_D^{17} 1.5380.

Found: C, 62.20; H, 8.35; N, 8.93%; mol wt, 148 (cryoscopic in benzene). Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03%; mol wt, 155.

IR: 1680, 1620 cm^{-1}.

NMR $\delta_{TMS}^{CDCl_3}$: 3.58 (s, 3H, CO_2CH_3), 3.08 (s, 6H, $(CH_3)_2N$), 2.35 ppm (q, 4H, CH_2).

In this case, only a trace amount of methyl 3-ethylthiopropionate was obtained.

The better yield (2.47 g, 80%) of VIIb was obtained, along with 2.20 g (75%) of methyl 3-ethylthiopropionate, when a solution of 2.60 g (0.02 mol) of II and 3.50 g (0.04 mol) of methyl acrylate in 25 m*l* of dry acetonitrile was refluxed for 4 hr under nitrogen. Methyl 3-ethylthiopropionate was identified by comparing its infrared spectrum with that of the authentic sample.[10] VIIb is also unstable, but can be stored for several months under nitrogen at low temperature in the crystallized form.

The Reaction of the Ketene-*N*, *S*-acetal (II) with Acrolein. Into an ice-cooled solution of 5.00 g (0.09 mol) of acrolein in 20 m*l* of dry acetonitrile, 3.90 g (0.03 mol) of II was added dropwise under nitrogen. Then the mixture was stirred for additional 5 hr at room temperature. After acetonitrile had been removed *in vacuo*, the residual liquid was distilled under reduced pressure to give 2.60 g (48%) of IXa. Bp 91—93°C/10 mmHg; n_D^{18} 1.5030.

Found: C, 66.26; H, 8.25; N, 7.86%; mol wt, 174 (cryoscopic in benzene). Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73%; mol wt, 181.

IR: 3074, 1662, 1650, 1235, 1215, 1085—1005 (multiplet) cm^{-1}.

NMR $\delta_{TMS}^{CDCl_3}$: 6.05 (m, 2H, O–CH=), 4.60 (m, 2H, =CH–C), 2.32 (s, 6H, $(CH_3)_2N$), 2.00 ppm (m, 4H, CH_2).

This compound showed negative Tollens' test. IXa easily polymerizes to a resinous material in a few hours even when it was stored under nitrogen at low temperature. In this case, a trace amount of 3-ethylthiopropionaldehyde was yielded and a large amount of undistillable residues resulted.

The Reaction of the Ketene-*N*, *S*-acetal (II) with Methyl Vinyl Ketone. In a manner analogous to that mentioned above, 3.57 g (57%) of IXb, along with quantitative yield of 4-ethylthiobutanone-2, was obtained by the reactions of 3.90 g (0.03 mol) of II and 6.30 g (0.09 mol) of methyl vinyl ketone. Bp 103—106°C/10 mmHg; n_D^{20} 1.4951.

Found: C, 68.57; H, 9.23; N, 7.00%; mol wt, 199 (cryoscopic in benzene). Calcd for $C_{12}H_{19}NO_2$: C, 68.86; H. 9,15; N, 6.69%; mol wt, 209.

IR: 3065, 1690, 1645, 1310—1230 (multiplet), 1180, 1170, 1105—1010 (multiplet) cm^{-1}.

NMR $\delta_{TMS}^{CDCl_3}$: 4.42 (broad, 2H, =CH), 2.37 (s, 6H, $(CH_3)_2N$), 1.94 (broad, 4H, CH_2), 1.70 ppm (s, 6H, CH_3).

This compound showed negative iodoform test. IXb is also unstable, but can be stored for a few weeks under nitrogen at low temperature in the crystallized form. 4-Ethylthiobutanone-2 was identified by comparing its infrared spectrum with that of the authentic sample.[11]

Grateful acknowledgment is made to Miss Mizuko Yoshida for her NMR measurements and to Miss Kazuko Isojima for her microanalyses.

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9) C. D. Hurd and L. L. Gershbein, *J. Am. Chem. Soc.*, **69**, 2328 (1947).

10) M. S. Kharasch and C. F. Fuchs, *J. Org. Chem.*, **13**, 97 (1948).

11) H. Böhme and P. Heller, *Chem. Ber.*, **86**, 443 (1953).