Elution of the adsorbent corresponding to two bands at *Rf* 0.77 and 0.58 with $CHCl_3$ and ether gave two compcunds.

a) Upper band (35 mg, 32%), 3-aza-A-homo-5α-cholest-1-en-4-one (XXVI) as needles, mp 224—225° from MeOH. $[\alpha]_D$ +5.8° (c=1.53, $CHCl_3$). UV λ_{max}^{EtOH} mμ (log ε): 237 (4.03). IR ν_{max}^{Nujol} cm^{-1}: 3330, 1690, 1658, 1643, 1072, 755. NMR τ: 9.32 (18-Me), 9.05 (19-Me), 5.12 (C_1-H, doublet, $J_{1,2}$=10.6 cps), 4.50 (quartet, C_2-H, $J_{2,1}$=10.6 cps, J=5.8 cps), 2.75 (broad, –NH–C(=O)–). *Anal.* Calcd. for $C_{27}H_{45}ON$: C, 81.14; H, 11.35; N, 3.51. Found: C, 81.08; H, 11.42; N, 3.46.

b) Lower band (21 mg, 19%), 4-aza-A-homo-5α-cholest-1-en-3-one (XXV) as needles, mp 230—232°, from MeOH. UV λ_{max}^{EtOH} mμ (log ε): 217.5 (4.14). IR ν_{max}^{Nujol} cm^{-1}: 3165, 3055, 1665, 1642, 1609, 1600, 835. NMR τ: 9.37 (18-Me), 9.01 (19-Me), 6.5—7.0, 7.0—7.6 (broad, 4a-α, β-H), 4.37 (C_2-H, slightly broad doublet, J=13.5 cps), 3.79 (C_1-H, doublet, J=13.5 cps), 3.05 (broad, –NHC(=O)–). *Anal.* Calcd. for $C_{27}H_{45}ON$: C, 81.14; H, 11.35; N, 3.51. Found: C, 80.97; H, 11.31; N, 3.55.

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Synthesis of the Furan Derivatives. XLIV.[1] Oxidation of Dimethyl Sulfonium Bromides in Dimethyl Sulfoxide Solution

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It was shown that the oxidation of seven halides to the corresponding aldehydes could be achieved simply by dissolving the halides in dimethyl sulfoxide[3] (DMSO). In addition, other several papers[4] concerning the reaction of this type which yielded phenyl glyoxal and glyoxalic acid have been reported. In our laboratory,[5] it was found that the oxidation of halides (Ib, Ic, Id) with DMSO at room temperature gave the corresponding glyoxals (IIIb, IIIc, IIId) and thiolformates (IVb, IVc, IVd).

In connection with these experiments, phenacyl dimethylsulfonium bromide (IIa) was isolated unexpectedly from the reaction of phenacyl bromide (Ia) with DMSO under mild condition. This fact suggested that this compound (IIa) wolud be one of the isolable intermediates of this reaction and can be used as starting material, because IIa is readily prepared by the reaction of Ia with dimethyl sulfide.

The object of this work is to investigate the reaction of phenacyl-(IIa),[6a] 4-bromophenacyl-(IIb),[6b] 2-furoylmethyl-(IIc) and 5-nitro-2-furoylmethyl-(IId) dimethylsulfonium bromide with DMSO.

No reaction took place between IIa and DMSO at room temperature (about 15—20°) even after 10 hours. Heating at 40° for 5 hours in a nitrogen atmosphere yielded two com-

1) Part XLIII: H. Saikachi and K. Takai, *Yakugaku Zasshi*, **89**, 34 (1969).
2) Location: *Katakasu, Fukuoka.*
3) N. Kornblum, J.W. Powers, G.J. Anderson, N.J. Jones, H.O. Larson, O. Levand and W.M. Weaver, *J. Am. Chem. Soc.*, **79**, 6562 (1957).
4) *a*) R.T. Mayor and H.J. Hess, *J. Org. Chem.*, **23**, 1563 (1958); *b*) R. Oda and Y. Hayashi, *Tetrahedron Letters*, **1967**, 2181.
5) H. Saikachi and J. Matsuo, *Yakugaku Zasshi*, **88**, 1306 (1968).
6) *a*) A.J. Speziale, C.C. Jung, K.W. Ratts and A. Yao, *J. Am. Chem. Soc.*, **87**, 3460 (1965); *b*) K.W. Ratts and A. Yao, *J. Org. Chem.*, **31**, 1185 (1966).

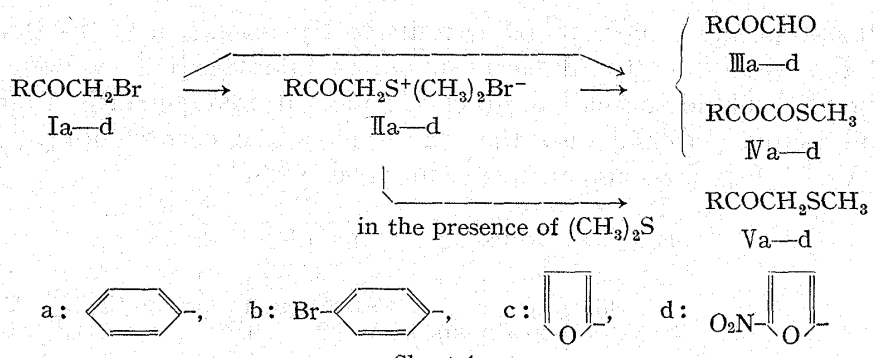


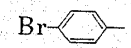
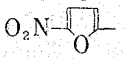
Chart 1

pounds in addition to dimethyl sulfide. One of the compounds had the identical melting point and infrared spectrum with those of authentic phenyl glyoxal[7] prepared by oxidation of selenium dioxide. Another compound was identified as methyl benzoyl thiolformate (IVa) from its elementary analysis, and its infrared (IR ν_{max}^{KBr} cm^{-1}: 1665 (C=O)) and nuclear magnetic resonance spectra (singlet at 2.45 ppm in $CDCl_3$ (3H, $-S-C\underline{H}_3$)), though it has not been clear that the compound IVa is either a precauser of the corresponding glyoxalic acid or not.

Ultimately the above reaction at 80° for one hour gave phenyl glyoxal in 40% yield and phenyl glyoxalic acid in 23% yield.

As can be seen, the above experimental results seemingly propose some complicated possibilities of this reaction mechanisms. In consequence, the reaction of the dimethylsulfonium bromides (IIb, IIc, IId) with DMSO was tentatively carried out at 40° for 5 hours. The above data are listed in Table I.

Table I

	$RCOCH_2S^+(CH_3)_2Br^-$ II R	RCOCHO III Yield (%)	$RCOCOSCH_3$ IV Yield (%)
a:		45[a]	11
b:		70[a]	3
c:		15[b]	10
d:		35[a]	18

a) Isolated as the hydrate. b) Isolated as the 2-(2-furyl)quinoxaline (Lit.[5]).

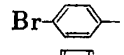
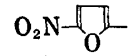
From the results, it was generally suggested that the reaction of dimethylsulfonium bromides (IIa—d) with DMSO promotes the formation of the glyoxals (IIIa—d) and on the other hand, restrains the thiolformates (IVa—d) in comparing with the reaction of bromides (Ia—d) with DMSO.[4a,5]

In the course of this work, F. Banci[8] has reported that the treatment of 5-nitro-2-furoylmethyl dimethylsulfonium bromide (IId) with DMSO in the presence of dimethyl sulfide resulted in the formation of trimethylsulfonium bromide in 94% yield. The fact substantiates partly the side reaction mechanism at the preparation of ethyl glyoxalate by oxidation of ethyl bromoacetate with DMSO.[9]

7) H.A. Riley and A.R. Gray, *Org. Syn.*, Coll. Vol. **2**, 509 (1948).
8) F. Banci, *Ann. Chim.* (Rome), **57**, 549 (1967) [*C. A.*, **67**, 5065 (1967)].
9) I.M. Hunsberger and J.M. Tien, *Chem. Ind.* (London), **1959**, 88.

In an attempt to find a more probable route to the formation of the thiolformates, we reinvestigated the reaction of the dimethylsulfonium bromides (IIa—d) with DMSO in the presence of dimethyl sulfide on trial, and then IId yielded predominantly 5-nitro-2-furyl(methylthio)methyl ketone (Vd) and also the others gave the corresponding (methylthio)methyl ketones (Va,[10] Vb, Vc) comparatively in good yield.

Table II. $RCOCH_2SCH_3$ and $(CH_3)_3S^+Br^-$

Compd. No.	R	Yield (%)	mp (°C) bp (°C/mm)	NMR-signal (ppm in $CDCl_3$) ArH[a]	$-CH_2-$[b]	$-CH_3$[b]	Yield (%) of $(CH_3)_3S^+Br^-$
Va		85	96—98/2[c]	7.65(5H)	3.74(2H)	2.13(3H)	83
Vb		90	45—46	7.75(4H)	3.73(2H)	2.13(3H)	89
Vc		72	35—36	7.10(3H)	3.60(2H)	2.13(3H)	70
Vd		85	67—68	7.40(2H)	3.72(2H)	2.21(3H)	75

a) multiplet centered at value given b) singlet c) lit.[10] bp 136.3—136.8° (11 mmHg)

It is interesting to note that the reaction of sulfonium bromides (IIa—d) with DMSO in the presence of dimethyl sulfide did not give the corresponding glyoxals and glyoxalic acids. It is suggested that dimethyl sulfide in DMSO exert inhibitory effect on oxidation, but not on demethylation of the dimethylsulfonium bromides (IIa—d) in the course of this reaction.

Experimental

5-Nitro-2-furoylmethyl Dimethylsulfonium Bromide (IId)——A solution of 5-nitro-2-furyl bromomethyl ketone (Id, 2.3 g, 0.01 mole) and dimethyl sulfide (1.2 g, 0.02 mole) in EtOH was refluxed for 10 min. The crystals separated were recrystallized from EtOH to give pale yellow prisms of IId (2.2 g, 75%), mp 143—145°. *Anal.* Calcd. for $C_8H_{10}O_4NSBr$: C, 32.45; H, 3.40; N, 4.68. Found: C, 32.26; H, 3.18; N, 4.68.

2-Furoylmethyl Dimethylsulfonium Bromide (IIc)——Colorless needles from MeOH, mp 138—140°. *Anal.* Calcd. for $C_8H_{11}O_2SBr$: C, 38.27; H, 4.42. Found: C, 37.98; H, 4.15.

Reaction between Phenacyl Dimethylsulfonium Bromide (IIa) and DMSO——A solution of IIa (2.6 g, 0.01 mole) in DMSO (8 g, 0.1 mole) was heated in a bubbling N_2 atmosphere at 40° for 5 hr. Evolved dimethylsulfide was collected in a glass tube, which was cooled below −40°. The liquid obtained was distilled to yield 1.2 g of dimethyl sulfide as a colorless oil, bp 30—32°. The reaction mixture was poured into H_2O and exrtacted with ether. The ether extract was treated with $NaHCO_3$ aqueous solution. The ether solution was dried over Na_2SO_4 and the ether was distilled off. The residue was chromatographed on silica gel with benzene to give benzoyl methyl thioformate (IVa) as a yellow crystalline cake (200 mg, 11%), mp 32—35°. Recrystallization from pet. ether gave pale yellow needles of IVa, mp 37—38°. *Anal.* Calcd, for $C_9H_8O_2S$: C, 60.00; H, 4.48. Found: C, 59.99; H, 4.57.

After the further elution of the column with ether, the ether was evaporated and the residue was recrystallized from H_2O to afford IIIa·H_2O (680 mg, 45%) of mp 75—78°.

The bicarbonate solution was acidified with HCl and extracted with ether. The extract was then dried over Na_2SO_4 and the solvent was evaporated to obtaine the phenyl glyoxalic acid. But phenyl glyoxalic acid could not be obtained.

When the above reaction was held at 80° for 1 hr, phenyl glyoxalic acid was obtained from the bicarbonate solution as colorless cake (350 mg, 23%) of mp 50—55°.

Other glyoxals (IIIb, IIIc, IIId) and thiolformates (IVb, IVc, IVd) were reported in our previous paper.[5]

5-Nitro-2-furyl(methylthio)methyl Ketone (Vd)——A mixture of IId (3.0 g, 0.01 mole), dimethyl sulfide (3.1 g, 0.05 mole) and DMSO (20 ml) was heated at 70° for 1 hr. Addition of ether (200 ml) to the reaction mixture gave colorless crystals. Recrystallization from a mixture of MeOH and ether yielded colorless crystalline powder of $(CH_3)_3S^+Br^-$ (1.2 g, 75%) which was sublimated completely at above 198°. The ether solution was washed with water and dried over Na_2SO_4 and the solvent was removed. The residue

10) F. Krollpfeiffer and H. Hartomann, *Chem. Ber.*, **83**, 90 (1950).

was recrystallized from a mixture of benzene and pet. benzine to give yellow needles of Vd (1.7 g, 85%), mp 67—68°. *Anal.* Calcd. for $C_7H_7O_4NS$: C, 41.80; H, 3.51; N, 6.96. Found: C, 41.45; H, 3.87; N, 6.59.

Phenyl (Methylthio) methyl Ketone (Va): colorless oil, bp 96—98° (2 mmHg). *Anal.* Calcd. for $C_9H_{10}OS$: C, 65.05; H, 6.07. Found: C, 64.77; H, 6.19.

4-Bromophenyl(methylthio)methyl Ketone(Vb): colorless needles from pet. ether, mp 45—46°. *Anal.* Calcd. for C_9H_9OSBr: C, 44.10; H, 3.70. Found: C, 44.02; H, 3.65.

2-Furyl(methylthio)methyl Ketone (Vc): colorless needles from a mixture of ether and pet. ether, mp 35—36°. *Anal.* Calcd. for $C_7H_8O_2S$: C, 53.84; H, 5.16. Found: C, 53.55; H, 5.00.

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UDC 547.892.5.04.07

Benzodiazepines. III.[1] A Novel Synthesis of a 1-Cyclopropylmethyl-1,4-benzodiazepine Derivative

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(Received July 4, 1968)

Recently it has been reported[3] that a new benzodiazepine derivative, 7-chloro-1-(cyclopropylmethyl)-1,3-dihydro-5-phenyl-2H-1,4-benzodiazepin-2-one (VI) was a potent drug for the relief of tension and anxiety, which had qualities different from chlordiazepoxide and diazepam.

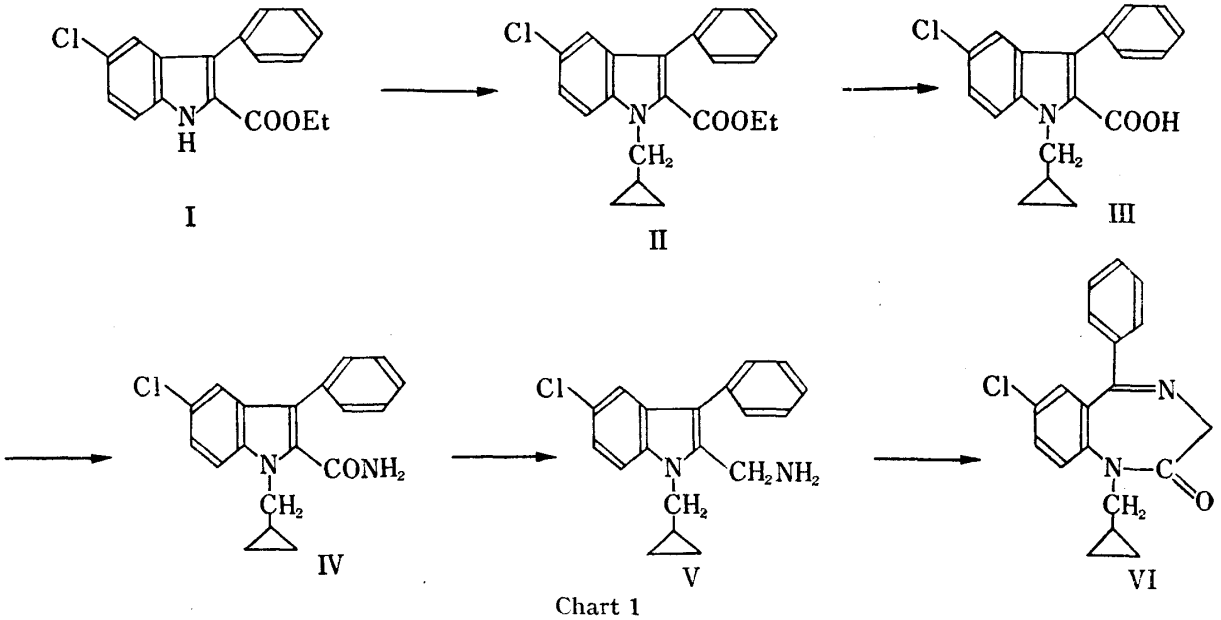

Chart 1

1) Part II: *Chem. Ber.*, **101**, 4245 (1968).
2) Location: *278, Kasugade-cho, Konohana-ku, Osaka.*
3) E. Kingstone, A. Villeneuve and I. Kassay, *Current Therapeutic Reserch*, **8**, 159 (1966).