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Formation and Reactions of Alkoxydiaminosulfonium Salts

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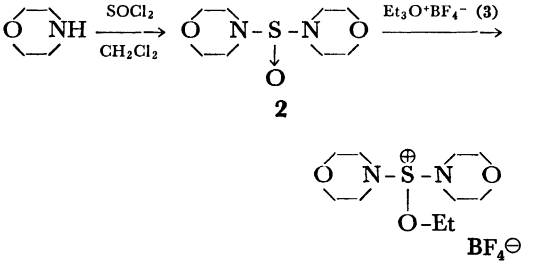
Ethoxydimorpholinosulfonium tetrafluoroborate and tetraphenylborate were prepared by ethylation of dimorpholino sulfoxide. They were readily hydrolyzed with water but did not react with methanol. In the reactions with nucleophiles, they acted as ethylating agent for β-picoline, triethylamine, diethylamine, methoxide ion, and chloride ion. When dimorpholino sulfide, 1-chlorobenzotriazole, and an alcohol were allowed to react at −80 °C, the main products were an alkyl chloride, dimorpholino sulfoxide, and morpholinium chloride. Alkoxydimorpholinosulfonium chloride was presumed to be the intermediate, which decomposed by an S_N2-type nucleophilic attack of chloride ion on the alkyl group. When (+)-2-octanol was used, the 2-chlorooctane formed was of almost completely inverted configuration (enantiomeric excess, 97%). The yield of alkyl chlorides decreased in the order of methyl (80%), isopropyl (51), and *t*-butyl (20).

Dialkoxysulfonium ions,[1-3] alkoxyaminosulfonium ions,[3,4] diaminosulfonium ions[5] were reported, but sulfonium ions possessing three hetero-substituents have not been described in the literature except a short communication from our laboratories.[6] Since alkoxydiaminosulfonium ions appear to be interesting species, we have studied their chemistry, and the results are described in this paper.

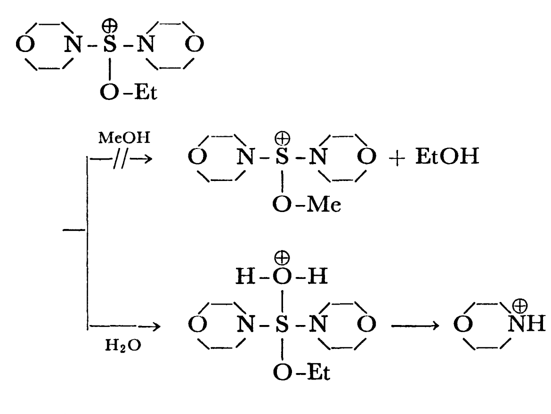
Results and Discussion

The synthesis of alkoxydiaminosulfonium ions was attempted by alkylation of diamino sulfoxides. Diamino sulfoxides were prepared by the reaction of an amine with thionyl chloride. They are readily decomposed by a trace amount of moisture, and must be handled with great care. Ethoxydimorpholinosulfonium tetrafluoroborate (**1a**) was successfully prepared by ethylation of dimorpholino sulfoxide (**2**) with triethyloxonium tetrafluoroborate (**3**) in well-dried dichloromethane in a dry box. The pale-yellow crystals obtained are extremely moisture-sensitive, and all the synthetic procedure must be carried out in a dry box. They are easily decomposed by a small amount of water in solvents or in the atmosphere, and morpholinium salts are produced. However, when crude crystals of **1a** were dissolved in anhydrous methanol and recrystallized, purified crystals were obtained without decomposition or alcohol exchange. Thus, alkoxydiaminosulfonium ions are not affected by alcohols, but extremely sensitive towards water. The reaction with water produces HBF_4, which probably catalyzes the decomposition.



1a

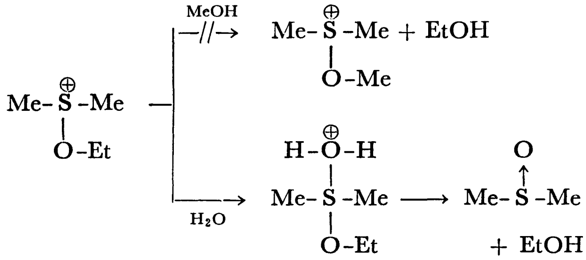
In an attempt to convert **1a** into crystals which can be handled more easily, crystals of **1a** were dissolved in acetone and anion exchange was attempted by addition of an acetone solution of sodium tetraphenylborate. However, such treatment simply hydrolyzed **1a**, and ethoxydimorpholinosulfonium tetraphenylborate (**1b**) was not obtained. After several attempts, crystalline **1b** was successfully prepared when sodium tetraphenylborate was added to the reaction mixture without isolating solid **1a**. In a similar manner, crystalline ethoxybis(diethylamino)sulfonium tetraphenylborate was prepared.



Crystalline **1b** can be handled much more easily than **1a**, and its elemental analyses gave satisfactory results. It was possible to determine its melting point too.

When the reactivity of **1b** with methanol and water was examined, it was found that an equimolar mixture of **1b** and methanol in hexadeuterioacetone did not react at all after 1 day, whereas **1b** was completely hydrolyzed when its hexadeuterioacetone solution was allowed to stand in an uncapped PMR tube for 1 day.

Such remarkable difference in reactivities of **1** with water and methanol appears to be of considerable interest, and we investigated reactions of a simpler alkoxysulfonium salt, dimethylethoxysulfonium tetrafluoroborate. When this alkoxysulfonium salt was



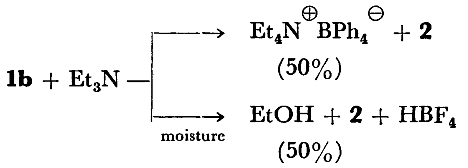
allowed to stand in methanol for 12 h, it did not react at all with methanol, whereas in a hexadeuterioacetone solution containing water (10 equiv.) 65% of the salt was hydrolyzed in 12 h.

Smith and Winstein found that dimethylbenzyloxysulfonium tosylate was not solvolyzed in absolute methanol but yielded benzyl alcohol upon addition of water.[6,7] Thus not only **1** but also dialkylalkoxysulfonium salts are very reactive with water and not reactive with alcohols.

By use of ^{18}O-enriched water[8] and an optically-active alkoxysulfonium salt,[9] Johnson and his coworkers showed that the hydrolysis of alkoxysulfonium salts proceeds by a nucleophilic displacement on sulfur with inversion of configuration of the sulfur atom. It is likely that the hydrolysis of **1** proceeds in a similar manner.

Then the reactions of **1** with nucleophiles were investigated. When **1a** was mixed with an equimolar amount of *β*-picoline at room temperature, **1a** acted as an ethylating agent but only in a 40% yield. The rest of the **1a** used was hydrolyzed by moisture in solvent and atmosphere, and morpholinium tetrafluoroborate was formed.

When equimolar amounts of **1b** and triethylamine were allowed to react in hexadeuterioacetone, the products showed that both ethylation of the amine (50%) and hydrolysis with moisture (50%) took place.



$$\mathbf{1b} + \mathrm{Et_3N} \longrightarrow \overset{\oplus}{\mathrm{Et_4N}}\ \overset{\ominus}{\mathrm{BPh_4}} + \mathbf{2}\quad (50\%)$$

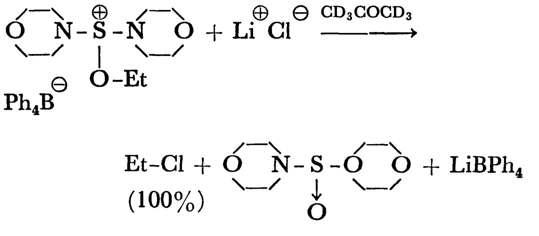
$$\mathbf{1b} + \mathrm{Et_3N} \xrightarrow[\text{moisture}]{} \mathrm{EtOH} + \mathbf{2} + \mathrm{HBF_4}\quad (50\%)$$

In a similar manner, the treatment of **1b** with diethylamine resulted in ethylation of the amine (40%) and hydrolysis with moisture (60%).

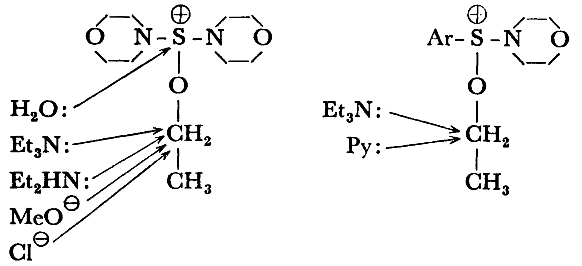
When **1b** was let to react with a slightly excess of potassium methoxide in hexadeuterated DMSO, **1b** ethylated the nucleophile.

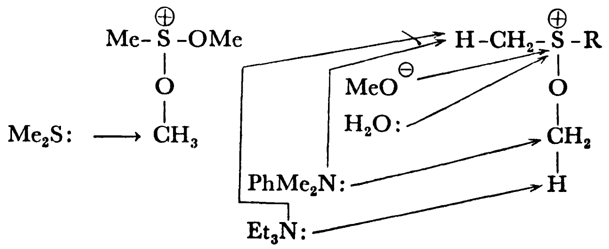
$$\mathbf{1b} + \overset{\oplus\ominus}{\mathrm{K\ \ OMe}} \xrightarrow{\mathrm{CD_3SOCD_3}} \mathrm{Et\text{-}O\text{-}Me} + \mathbf{2}\quad (100\%)$$

When **1b** and lithium chloride were dissolved in hexadeuterioacetone, the PMR spectrum of the solution showed that **1b** was converted to ethyl chloride and **2**.



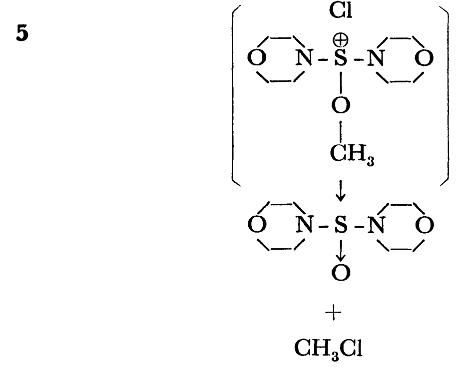
The reactivity of **1** with nucleophiles is summarized below, and compared with those of alkoxyaminosulfonium ions,[3] dialkoxysulfonium ion,[1] and alkoxysulfonium ions.[10,11] The above comparison shows that alkoxysulfonium ions possessing an amino group, two amino groups, or another alkoxy group receive the attack of nucleophiles (except water) on the carbon atom adjacent to the oxygen atom. Thus, the reactions of hetero-atom substituted alkoxysulfonium ions with nucleophiles are simpler than those of alkylarylalkoxysulfonium ions.[11]





Since the main reaction of **1** with nucleophiles has been shown to be ethylation of the nucleophiles, it seems desirable to study the reactions of alkoxydiaminosulfonium salts other than **1**. However, it was not possible to prepare such sulfonium salts by the method used for the preparation of **1**, because trimethyloxonium tetrafluoroborate is not soluble in dichloromethane, and neither triisopropyl- nor tri-*t*-butyloxonium salts are available.

Therefore, preparation of alkoxydiaminosulfonium salts was attempted from other routes. Johnson *et al.*[13] prepared alkoxysulfonium salts by treating dialkyl sulfides with 1-chlorobenzotriazole, an alcohol and silver tetrafluoroborate. If diamino sulfides react in a similar manner, formation of alkoxydiaminosulfonium salts is expected. Therefore, equimolar amounts



of dimorpholino sulfide (**4**) and 1-chlorobenzotriazole (**5**) were mixed in dichloromethane at −80 °C, and to the yellow solution formed (a sulfurane[13)]) an equimolar amount of methanol was added. When the mixture was warmed up, its PMR spectrum suggested that the reaction shown above occurred. Methoxydimorpholinosulfonium chloride is the product expected from the results of Johnson *et al.*[13)] Since we have already shown that **1b** is readily converted by chloride ion to **2** and ethyl chloride, the scheme shown above probably represents the main reactions taking place in a mixture of **4**, **5**, and an alcohol. In order to determine the stereochemistry of this nucleophilic reaction on the carbon atom adjacent to the oxygen atom, (+)-2-octanol was treated in a similar manner. The 2-chlorooctane obtained was found to be of almost completely inverted configuration (enantiomeric excess, 97%). Thus the nucleophilic attack of chloride ion on an alkoxydiaminosulfonium ion is an S_N2-type reaction with inversion of configuration.

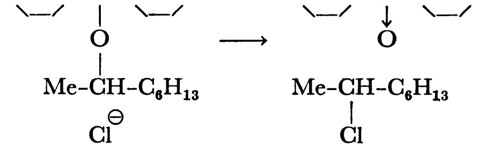


Table 1 summarizes the results of reactions of diamino sulfide (**4** or bis(dimethylamino) sulfide (**6**)) with **5** (or *N*-chlorosuccinimide (**7**)) and an alcohol (MeOH, *i*-Pr–OH, or *t*-BuOH).

As shown in Table 1, the yields of alkylation of chloride by alkoxydiaminosulfonium ions decrease in the order of Me, *i*-Pr, and *t*-Bu. This fact is probably ascribable to greater tendency for S_N1-type reaction of alkoxydiaminosulfonium ions when the alkyl group is secondary or tertiary. When **7** was used in place of **5**, yields were not improved, but when **6** was used in place of **4**, the yields were improved. Even with isopropyl alcohol, S_N2-type alkylation of chloride took place in an 85% yield.

Table 1. Products of the reaction of diamino sulfides with 5 (or 7) and alcohols

Reactants	Products (mol %)
4 + **5** + MeOH	MeCl(80), **2**(80)
4 + **5** + *i*-PrOH	*i*-PrCl(51), *i*-PrOH(21), **2**(60)
4 + **5** + *t*-BuCl(20)	*t*-BuCl(20), *t*-BuOH(10)
4 + **5** + (+)-2-octanol	(−)-octylCl (25)[a)]
4 + **7** + MeOH	MeCl(45),
4 + **7** + *i*-PrOH	*i*-PrCl(47), Me_2CO(6)
4 + **7** + *t*-BuOH	*t*-BuCl(18), *t*-BuOH(16)
6 + **7** + MeOH	many products
6 + **7** + *i*-PrOH	*i*-PrCl(51), *i*-PrOH(40), Me_2CO(8.7)
6 + **7** + *t*-BuOH	*t*-BuCl(35)
6 + **5** + MeOH	MeCl(83), $(Me_2N)_2S{\rightarrow}O$ (90)
6 + **5** + *i*-PrOH	*i*-PrCl(85), $(Me_2N)_2S{\rightarrow}O$ (78)
6 + **5** + *t*-BuOH	*t*-BuCl(40)
6 + **5** + 2-octanol	2-octylCl (51),[a,b)] $(Me_2N)_2S{\rightarrow}O$ (95)

a) Yield after isolated. b) By PMR, the yield was 70%.

Corey et al. treated succinimidodimethylsulfonium ion with benzyl and allyl alcohols, and obtained the corresponding chloride.[14)] However, their reaction works only with benzyl and allyl alcohols, and not with ordinary primary or secondary alcohols. It is of interest that in our system a primary alcohol or a secondary alcohol is transformed into chloride in much better yield than a tertiary alcohol.

Experimental

Dimorpholino sulfide (mp 125—126°; lit,[15)] 125—126 °C), and bis(dimethylamino) sulfide (bp 30—32 °C/15 Torr; lit,[15)] 33.5—36 °C/14 Torr) were prepared by the methods described in the literature.[15)] (+)-2-Octanol was purchased from Fluka AG; $[\alpha]^{20}_{546}=+11°$.

Dimorpholino sulfoxide was prepared from morpholine and thionyl chloride; mp 52 °C.[16)] Bis(diethylamino) sulfoxide was prepared in a similar manner.

1-Chlorobenzotriazole was prepared from benzotriazole and a 10% aq NaOCl solution according to the method in the literature.[13)]

*Formation of Ethoxydimorpholinosulfonium Tetrafluoroborate (**1a**).* After a dichloromethane solution of **2** (40 mmol) and **3** (42 mmol) was refluxed for 2 h, ether was added. The brown-black oil which precipitated was recrystallized from methanol in a dry box. Pale yellow crystals of **1a** were obtained (24.6%). PMR (CD_3COCD_3), δ 1.52 (t, 3, CH_3), 3.50—3.71 (m, 8, N-CH_2), 3.74—4.00 (m, 8, O-CH_2), 4.61 (q, 2, $C\underline{H}_2CH_3$). Because of its instability, it was not possible to carry out successful elemental analysis.

*Reaction between **1a** and β-Picoline.* An equimolar mixture of the reactants were allowed to stand in CD_3COCD_3 at room temperature for 2 h, and *N*-ethylpicolinium salt was found in a 40% yield (identified by comparison with an authentic sample). PMR(CD_3COCD_3), δ 1.71 (t, $C\underline{H}_3$-CH_2), 2.60 (s, CH_3–Py), 4.80 (q, $C\underline{H}_2CH_3$).

*Formation of Ethoxydimorpholinosulfonium Tetraphenylborate (**1b**).* A dichloromethane solution (30 ml) of **2** (10 mmol) and **3** (10.6 mmol) was refluxed for 2 h, and to this orange-red solution an acetone solution (25 ml) of $NaBPh_4$(9.36 mmol) was added. Addition of some ether and acetone precipitated $NaBF_4$, and further addition of ether precipitated **1b**: 3.85 g (67.7%). Repeated crystallizations from acetone–ether yielded white prisms, mp 113 °C (dec). Found: C, 71.78; H, 7.54; N, 5.02%. Calcd for $C_{34}H_{41}N_2O_3BS$: C, 71.82; H, 7.27; N, 4.93%. PMR(CD_3COCD_3) δ 1.47 (t, 3, *J*=7.2 Hz, $C\underline{H}_3CH_2O$), 3.30—3.57 (m, 8, $NC\underline{H}_2$), 3.63—3.90 (m, 8, $NCH_2C\underline{H}_2O$), 4.46 (q, 2, *J*=7.2 Hz, $OC\underline{H}_2CH_3$), 6.82—7.53 (m, 20, C_6H_5); ^{13}CMR(CD_3COCD_3) δ 15.34 ($\underline{C}H_3CH_2O$), 47.07 ($NCH_2\underline{C}H_2O$), 66.88 ($N\underline{C}H_2$), 72.07 ($O\underline{C}H_2CH_3$).

Ethoxybis(diethylamino)sulfonium Tetraphenylborate was prepared in a similar manner; yield, 60.0%, mp 119 °C (dec). Found: C, 75.39; H, 8.85; N, 4.90%. Calcd for $C_{34}H_{45}N_2OBS$: C, 75.54; H, 8.39; N, 5.18%. PMR(CD_3COCD_3) δ 1.22 (t, 12, *J*=7.0 Hz, $C\underline{H}_3CH_2N$), 1.45 (t, 3, *J*=6.5 Hz, $C\underline{H}_3CH_2O$), 3.46 (q, 8, *J*=7.0 Hz, $CH_3C\underline{H}_2N$), 4.28 (q, 2, *J*=6.5 Hz, $CH_3C\underline{H}_2O$); ^{13}CMR(CD_3COCD_3) δ 13.72 ($\underline{C}H_3CH_2N$), 15.18 ($\underline{C}H_3CH_2O$), 42.45 ($CH_3\underline{C}H_2N$), 70.29 ($CH_3\underline{C}H_2O$).

*Decomposition of **1b** in CD_3COCD_3.* When a CD_3COCD_3 solution of **1b** was allowed to stand in an uncapped PMR tube at room temperature for 1 day, **1b** was hydrolyzed and morpholinium tetraphenylborate precipitated, which was identified by determining its PMR spectrum in CD_3SOCD_3.

*Treatment of **1b** with Methanol in CD_3COCD_3.* When equimolar amounts of **1b** and well-dried methanol were dissolved in CD_3COCD_3 and allowed to stand in a capped PMR tube at room temperature for 1 day, no change was observed in its PMR spectrum.

Reaction between Dimethylethoxysulfonium Tetrafluoroborate and D_2O or CD_3OD. When a CD_3COCD_3 solution of the salt (1 equiv.) and D_2O (10 equiv.) was allowed to stand for 12 h at 34 °C, its PMR spectrum showed that 65% of the salt was hydrolyzed, forming CH_3SOCH_3 (δ 2.67) and EtOD (δ 1.10(t) and 3.56(q)). When a CD_3OD solution of the salt was allowed to stand for 12 h at 34 °C, no CD_3O–EtO exchange was observed and about 10% of the salt was hydrolyzed probably by the moisture in CD_3OD, forming CH_3SOCH_3 and EtOD.

*Reaction between **1b** and Triethylamine.* When equimolar amounts of **1b** and triethylamine were mixed in CD_3COCD_3 at room temperature, reaction was complete in 3 h, and tetraethylammonium tetraphenylborate precipitated. It was filtered and identified by determining its PMR spectrum in CD_3SOCD_3; δ 1.22 (t, 3, CH_3), 3.21 (q, 2, CH_2); yield, 50%. In the filtrate, ethanol (50%) and **2**(100%) (PMR-(CD_3COCD_3), δ 2.90—3.12 (NCH_2), 3.60—3.78 (OCH_2)) were found.

*Reaction between **1b** and Diethylamine.* When equimolar amounts of **1b** and diethylamine were mixed in CD_3COCD_3 at room temperature, reaction was complete in 20 min; its PMR spectrum showed complete disappearance of **1b** and formation of **2**. The precipitates formed were filtered, and their PMR spectrum in CD_3SOCD_3 showed the presence of $Et_3NH^+BPh_4^-$ (40%) (δ 1.34(t, 9, CH_3), 3.16 (q, 6, CH_2), and 6.80—7.50 (m, 20, C_6H_5)) and $Et_2NH_2^+BPh_4^-$ (60%) (δ 1.27 (t, 6, CH_3), 3.12 (q, 4, CH_2), and 6.80—7.50 (m, 20, C_6H_5)).

*Reaction between **1b** and Potassium Methoxide.* When CD_3SOCD_3 solutions of **1b** (0.53 mmol) and KOMe (0.93 mmol) were mixed at room temperature the PMR spectrum of the mixture showed that **1b** was quantitatively converted to ethyl methyl ether; δ 1.08 (t, 3, $\underline{CH_3}CH_2$), 3.18 (s, 3, CH_3O), and 3.47 (q, 2, CH_2).

*Reaction between **1b** and Chloride Ion.* When **1b** (1 equiv.) and lithium chloride (4 equiv.) were mixed in CD_3COCD_3 at room temperature, the PMR spectrum of the solution showed that **1b** was quantitatively converted to **2** and ethyl chloride (δ 1.47 (t, 3, $J=7.2$ Hz, CH_3), and 3.63 (q, 2, $J=7.2$ Hz, CH_2).

*Reaction of **4** with **5** and MeOH.* A dichloromethane solution (3 ml) of **4** (3.0 mmol) and dichloromethane solution (4 ml) of **5** (3.0 mmol) were cooled to −18 °C, and then mixed. To this yellow solution, a cooled dichloromethane solution (2 ml) of methanol (3.0 mmol) was added at −80 °C. Mixing of these three solutions must be done with exclusion of moisture either in a glass apparatus sealed from the atmosphere or in a dry box. The mixture was warmed up to room temperature. Distillation gave a distillate and a residue. The distillate contained CH_3Cl (δ 3.00; yield, 80%). The residue contained **2** [δ 3.00—3.20 (N-CH_2) and 3.60—3.80 (OCH_2); yield, 80%] and an unidentified methyl compound (δ 3.50; yield, 20%).

Reactions with other alcohols were carried out in a similar manner with equimolar mixtures.

The reaction of **6** with **5** and 2-propanol gave *i*-PrCl (δ 1.46 (d); yield 85%) and acetone (δ 2.13(s); yield 15%) in the distillate, and $(Me_2N)_2S\rightarrow O$ (δ 2.61 (s); yield 78%) and an unidentified compound (δ 2.81(s); yield 22%) in the residue.

*Reaction of **4** with **5** and (+)-2-Octanol.* An equimolar mixture (10 mmol each) of the reactants was treated as described above. 2-Chlorooctane was collected at 51—52°/14 Torr; yield, 25%. $[\alpha]_D^{22}=-34.91°$ (*c* 7.38, CH_2Cl_2); enantiomeric excess $\% = -34.91/-36.15^{17)} \times 100 = 96.6\%$.

References

1) H. Minato, K. Yamaguchi, and M. Kobayashi, *Chem. Lett.*, **1975**, 307.

2) H. Warthmann and A. Schmidt, *Chem. Ber.*, **108**, 520 (1975).

3) H. Minato, K. Yamaguchi, K. Okuma, and M. Kobayashi, *Bull. Chem. Soc. Jpn.*, **49**, 2590 (1976).

4) H. Minato, K. Yamaguchi, and M. Kobayashi, *Chem. Lett.*, **1975**, 991.

5) J. L. Richards and D. S. Tarbell, *J. Org. Chem.*, **35**, 2079 (1970).

6) H. Minato, K. Okuma, and M. Kobayashi, *J. Chem. Soc., Chem. Commun.*, **1975**, 868.

7) S. G. Smith and S. Winstein, *Tetrahedron*, **3**, 317 (1958).

8) S. G. Smith, Ph. D. Thesis, University of California, Los Angeles, Calif., 1959.

9) N. J. Leonard and C. R. Johnson, *J. Am. Chem. Soc.*, **84**, 3701 (1962).

10) C. R. Johnson and D. McCants, Jr., *J. Am. Chem. Soc.*, **87**, 5404 (1965).

11) K. Tsumori, H. Minato, and M. Kobayashi, *Bull. Chem. Soc. Jpn.*, **46**, 3503 (1973).

12) C. R. Johnson and W. G. Phillips, *Tetrahedron Lett.*, **1965**, 2101.

13) C. R. Johnson, C. C. Bacon, and W. D. Kingsbury, *Tetrahedron Lett.*, **1972**, 501.

14) E. J. Corey, C. U. Kim, and M. Takeda, *Tetrahedron Lett.*, **1972**, 4339.

15) E. S. Blake, *J. Am. Chem. Soc.*, **65**, 1267 (1943).

16) G. Zinner and W. Kollig, *Naturwissenschaften*, **46**, 354 (1959).

17) I. Heilbron and H. M. Bunberry, Ed., "Dictionary of Organic Compounds," Oxford Univ. Press, Vol. 4, New York (1953), p. 15.