Table III
Yield of Triphenylphosphine Oxide by GC

Disulfide (mmol)	Ph_3PO formed, mmol (% theory)	Ph_3P recovered, mmol
4 (0.22)	0.15 (68)	0.34
7 (0.28)	0.21 (75)	0.32
10 (0.26)	0.26 (100)	0.22

Ethyl 4-Aminophenyl Disulfide (10). The analytical (and kinetic) sample was prepared by preparative layer chromatography (silica gel–10% ethyl acetate–90% benzene) and Kugelrohr distillation (oven temperature 114–120°, 0.03 Torr): ν_{max} (film) 3390, 3250, and 823 cm^{-1}; ^1H NMR (CCl_4) τ 2.5–3.7 (A_2B_2 pattern, 4 H, ArH), 6.40 (s, 2 H, NH_2), 7.32 (q, J = 7 Hz, 2 H, CH_2), 8.71 (t, J = 7 Hz, 3 H, CH_3).

Anal. Calcd for $C_8H_{11}NS_2$: C, 51.85; H, 5.98; N, 7.56; S, 34.60. Found: C, 52.01, H, 5.98; N, 7.69; S, 34.24.

Products. Triphenylphosphine Oxide (Ph_3PO). A 0.02 M solution of sodium hydroxide in 50% aqueous dioxane, containing 5 × 10^{-4} M disodium ethylenediaminetetraacetic acid, was deoxygenated for 1 hr with oxygen-free nitrogen.[19] Triphenylphosphine (0.50 mmol) and disulfide **4**, **7**, or **10** (0.22–0.28 mmol) were added and the solution was stirred under a nitrogen atmosphere at 40° for 2–10 min. After cooling to room temperature 50 ml of ether was added, the aqueous layer was saturated with sodium chloride, and the organic layer was separated. The aqueous layer was washed with 50 ml of ether and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. A weighed amount of benzophenone was added as an internal standard and the product mixture was analyzed by GC.[21] Peak areas were corrected for detector response by standard methods. Triphenylphosphine sulfide could be detected at the 1% level. The results are summarized in Table III.

Acknowledgment. Financial support of this research by the National Institutes of Health (Grant GM-20674) is gratefully acknowledged.

Registry No.—**3**, 51351-84-9; **4**, 51351-85-0; **5**, 55975-71-8; **6**, 55975-72-9; **7**, 55975-73-0; **8**, 55975-74-1; **9**, 55975-41-2; **10**, 55975-42-3; triphenylphosphine oxide, 791-28-6; triphenylphosphine, 603-35-0.

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(2) (a) Alfred P. Sloan Foundation Fellow, 1975–1977; (b) U. C. President's Undergraduate Fellow, 1974–1975.
(3) The current status of this question is briefly summarized in ref 1. Other recent summaries include (a) J. L. Kice in "Sulfur in Organic and Inorganic Chemistry", Vol. 1, A. Senning, Ed., Marcel Dekker, New York, N.Y., 1971, Chapter 6; (b) E. Ciuffarin and A. Fava, *Prog. Phys. Org. Chem.*, **6**, 81 (1968); (c) L. Senatore, E. Ciuffarin, and A. Fava, *J. Am. Chem. Soc.*, **92**, 3035 (1970); (d) W. A. Pryor and K. Smith, *ibid.*, **92**, 2731 (1970).
(4) An alternate approach, in which one tries to isolate the substituent effect to the sulfur atom undergoing nucleophilic attack, was anticipated to be unsuccessful. Wright and coworkers[5] have previously shown that substituted-phenyl *p*-acetylphenyl disulfides and substituted-phenyl *p*-nitrophenyl disulfides undergo nucleophilic cleavage by cyanide to some extent by attack of cyanide on the *p*-acetylphenyl (or *p*-nitrophenyl) bearing sulfur. In our case, with Ph_3P as the nucleophile, corrections for the cleavage in this direction could not be made.
(5) D. A. R. Happer, J. W. Mitchell, and G. J. Wright., *Aust. J. Chem.*, **26**, 121 (1973).
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(12) M. Behforouz and J. E. Kerwood, *J. Org. Chem.*, **34**, 51 (1969).
(13) The uv change which accompanied the reduction of ethyl phenyl disulfide was so small that the reaction could not be conveniently studied.
(14) A. Fava and G. Pajaro, *J. Am. Chem. Soc.*, **78**, 5203 (1956); R. D. Ritter and J. H. Krueger, *ibid.*, **92**, 2316 (1970).
(15) Unpublished studies from our laboratory show that the hydrolysis of ethanethiolatotriphenylphosphonium hexachloroantimonate in 50% dioxane–water is specific base catalyzed and would be sufficiently fast at pH 13.3 that the first step (k_1) in Scheme II would be clearly rate limiting.
(16) Log k_1 also correlates well with the corresponding benzenethiol pK_a (determined under identical conditions)[1] and affords a Brønsted slope of $\beta = -0.71 \pm 0.07$.
(17) A model for such a process would be the SN2 reaction of carbon compounds. Although substituent effects for the carbon undergoing nucleophilic attack are observed, these effects are small.[18] For example, introducing a meta NO_2 substituent results in rate accelerations (k_X/k_H) in the range of 0.8–3.5.[18] It is also typical for the SN2 reactions of carbon compounds to be accelerated by both electron-withdrawing and electron-donating substituents.[18]
(18) Much of this data is summarized in the following references: A. Steitwieser, Jr., "Solvolytic Displacement Reactions", McGraw-Hill, New York, N.Y., 1962, pp 18–20; R. Fuch and D. M. Carelton, *J. Am. Chem. Soc.*, **85**, 104 (1963).
(19) Nitrogen was deoxygenated by bubbling sequentially through gas traps filled with chromous solution[20] and distilled H_2O.
(20) Cf. A. J. Gordon and R. A. Ford, "The Chemist's Companion", Wiley, New York, N.Y., 1972, p 438.
(21) A 8 ft × 0.12 in. column of 10% SP 2100 on 100/120 Supelcoport operated at 250° with a nitrogen carrier gas (45 ml/min) was used. This column cleanly separated Ph_3P, Ph_3PO, and Ph_3PS.

Aromatic Nucleophilic Substitution. V.[1] Confirmation of the Spiro Janovsky Complex in Base-Catalyzed Rearrangement of *N*-Acetyl-β-aminoethyl-2,4-dinitrophenyl Ether with Simultaneous Migration of Acetyl Group

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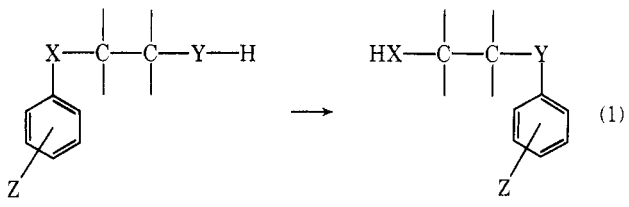
Received January 23, 1975

N-Acetyl-β-aminoethyl-2,4-dinitrophenyl ether readily undergoes a Smiles rearrangement in Me_2SO in the presence of tertiary-butanolic $KOC(CH_3)_3$ to give *N*-β-acetyloxyethyl- and *N*-β-hydroxyethyl-2,4-dinitroaniline. During the reaction, the spiro Janovsky complex is spectrometrically confirmed to exist.

Smiles rearrangements (eq 1) are typical intramolecular nucleophilic substitution reactions. The two carbon atoms joining X and Y may be part of an aliphatic or an aromatic system. It has been well established that aromatic nucleophilic substitution reactions proceed via Bunnett's intermediate.[2] Therefore, Smiles rearrangements can be assumed to be a good model for studying aromatic nucleophilic substitution mechanisms.

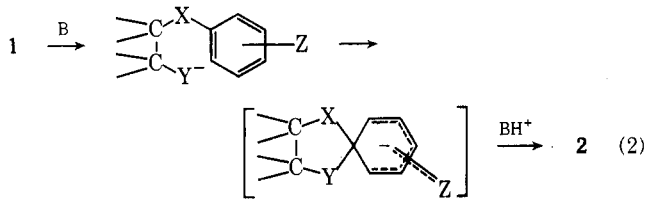


(1)

1 2

Z, activating group

Several pathways are possible for the conversion of 1 to 2. As shown in eq 2, in most cases a nucleophilic function YH may be ionized by a base to give 2 via the intermediate 3. In certain systems, in which aromatic rings are much ac-

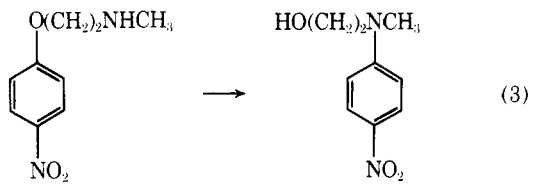


(2)

3

tivated with nitro, cyano, or other electron-withdrawing groups, the intermediates (spiro Meisenheimer or Janovsky complex, hereafter referred to as anionic σ complex), might possibly be confirmed spectrometrically or isolated. This field has been recently reviewed in detail.[3]

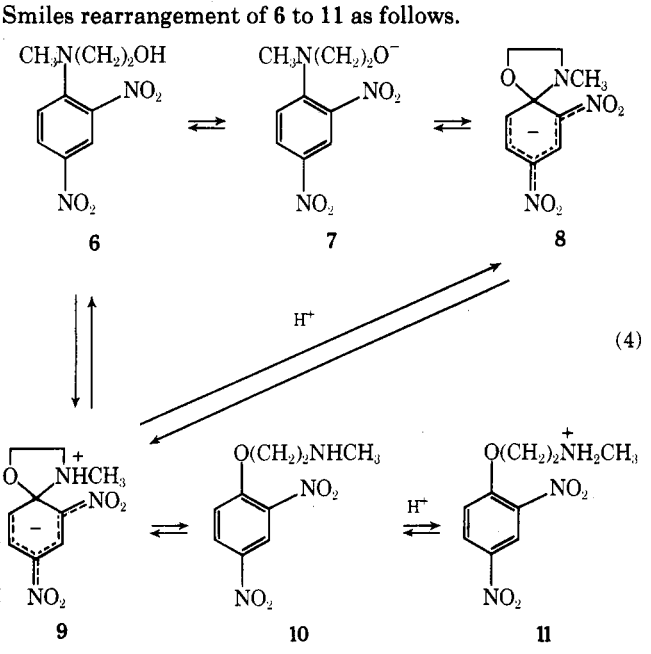
Kleb[4] has reported the rearrangement of 4 to 5, in which the reaction proceeded very rapidly and, therefore, no cyclic intermediate was confirmed by experimental evidence.



(3)

4 5

Bernasconi et al.[5] have recently reported the kinetics of the base-catalyzed formation of 8 from 6 shown in eq 4. Aryl ethers such as 10 or 11 cannot be prepared by ordinary methods. Therefore, they prepared 11 by rapidly acidifying the spiro anionic σ complex (8) and proposed the reverse Smiles rearrangement of 6 to 11 as follows.



(4)

6 7 8

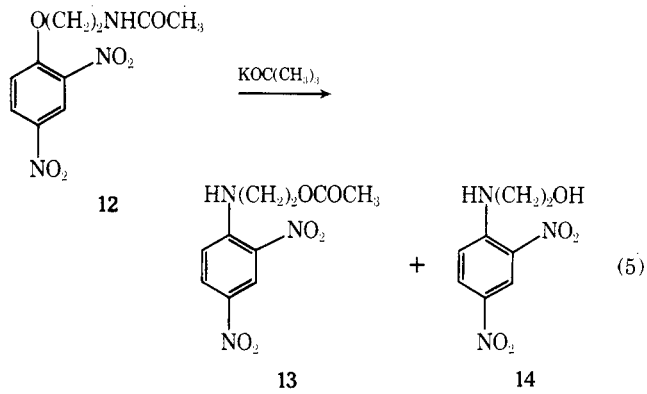
9 10 11

We have more recently carried out the base-catalyzed Smiles rearrangement of *N*-acetyl-β-aminoethyl-2,4-dinitrophenyl ether (12) in Me_2SO, in which the stabilized intermediate (or spiro Janovsky complex) could be spectrometrically confirmed to exist. The compound 12 was selected for study, because pure 12 can be prepared and the life of the anionic σ complex derived from 12 is comparatively longer, so that direct information on the reaction path of the normal Smiles rearrangement can be obtained spectrometrically.

This paper reports the reaction mechanism of the base-catalyzed Smiles rearrangement of 12.

Results and Discussion

Addition of an equivalent amount of tertiary-butanolic $KOC(CH_3)_3$ at room temperature to a Me_2SO solution of 12 immediately led to a red color, and soon to a dark red one. After 1 hr treatment of the colored solution with aqueous HCl solution gave *N*-β-acetyloxyethyl-2,4-dinitroaniline (13) in 78% yield, and a small amount of *N*-β-hydroxyethyl-2,4-dinitroaniline (14), the hydrolysis product of 13, as shown in eq 5. As discussed in the next paragraph, the

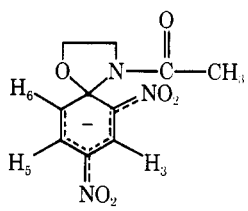


(5)

12 13 14

color change from red to dark red suggests that the reaction in eq 5 proceeds via a spiro anionic σ complex.

To confirm this mechanism, NMR spectra were observed at intervals during the reaction. The results are shown in Figure 1. Immediately after addition of $KOC(CH_3)_3$, the red solution gives the spectrum of Figure 1b; the poor resolution is due to the fast sweep time (500 Hz/50 sec). In Figure 1b, the resonance peak positions of 12 are shifted to a higher magnetic field (H_3 δ 8.72 → 8.57, H_5 δ 8.47 → 7.00, and H_6 δ 7.62 → 5.33), while the amide proton resonance peak (δ 8.03) disappeared. Such chemical shifts are characteristic of 1,1-disubstituted anionic σ complexes of 2,4-dinitrobenzene such as 15.[3,5-11] Figure 1c shows the spectrum scanned (500 Hz/50 sec) immediately after that in 1b. In addition to the signals due to 15, the spectrum shows reso-



15

nance peaks which are the same as those in Figure 1d. Further, several minutes after mixing, the H_3 signal is shifted upfield (δ 8.57 → 8.37) and H_5 and H_6 signals are shifted downfield (H_5 δ 7.00 → 7.52, H_6 δ 5.33 → 6.37) as shown in Figure 1d, and from that time on these peak positions do not change. After the measurement, the solution was already dark red.

In order to clarify what the spectrum of Figure 1d is attributed to, the reaction of 13 with an equivalent amount of $KOC(CH_3)_3$ in Me_2SO was carried out. Immediately after

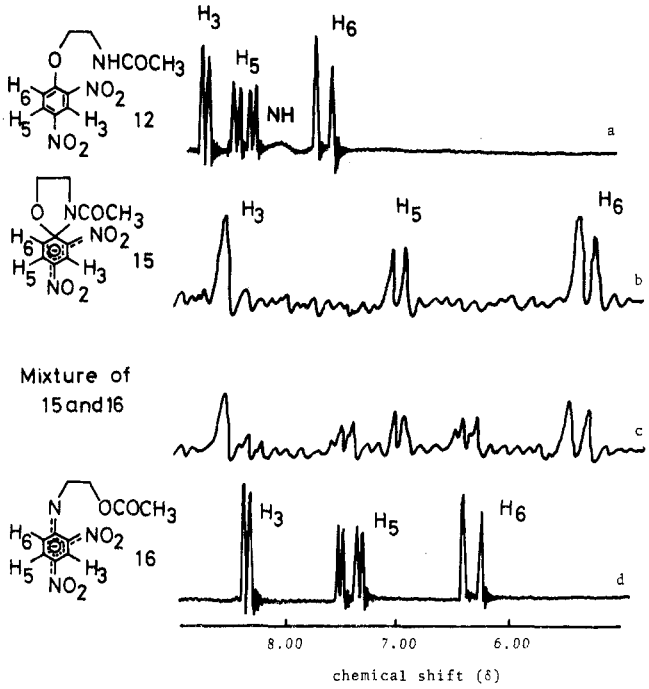
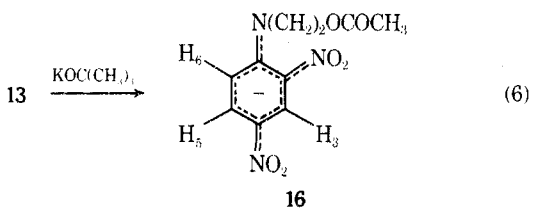


Figure 1. NMR spectra of the reaction of **12** with tertiary-butanolic $KOC(CH_3)_3$ in Me_2SO-d_6: (a) before addition of $KOC(CH_3)_3$; (b) immediately after addition of $KOC(CH_3)_3$; (c) immediately after measurement of Figure 1b; (d) several minutes after addition of $KOC(CH_3)_3$.

addition of $KOC(CH_3)_3$, the dark red solution gives the same spectrum as that in Figure 1d. The H_3, H_5, and H_6 resonance peaks of **13** are shifted upfield (H_3 δ 8.85 → 8.40, H_5 δ 8.28 → 7.57, and H_6 δ 7.28 → 6.38) while the amide proton resonance peak (δ 8.87) disappeared.

From these results it is considered that the following reaction occurs.[5,12]



(6)

Therefore the final product in the rearrangement is assumed to be **16.**

The time-dependent absorption spectral change is shown in Figure 2, when 50 equiv of $KOC(CH_3)_3$ is added to a Me_2SO solution of **12.** The reaction takes place in two distinct stages, indicated by two spectral changes. The first change occurs immediately upon addition of $KOC(CH_3)_3$ to a Me_2SO solution of **12** (from curve a to b). Not only the shape but also the positions and intensities of the spectrum of curve b [λ_{max} 347 nm (ϵ 14,300), 359 (13,800), and 506 (28,000)] are characteristic of 1,1-disubstituted 2,4-dinitrobenzene anionic σ complexes.[3c,5] Furthermore, Hosoya et al.[13] have stated by MO calculation that the shape of an absorption spectrum of 1,1-disubstituted 2,4-dinitrobenzene anionic σ complex does not depend on the substituents at C-1.

The second spectral change is much slower (from curve b to c and d). In order to clarify what curve d is attributed to, absorption spectra were observed immediately after addition of 50 equiv of $KOC(CH_3)_3$ to a Me_2SO solution of **13.** The spectrum is the same as curve d. Accordingly curve d represents the spectrum of **16** [λ_{max} 432 nm (ϵ 19,100) and ca. 490 (sh)].

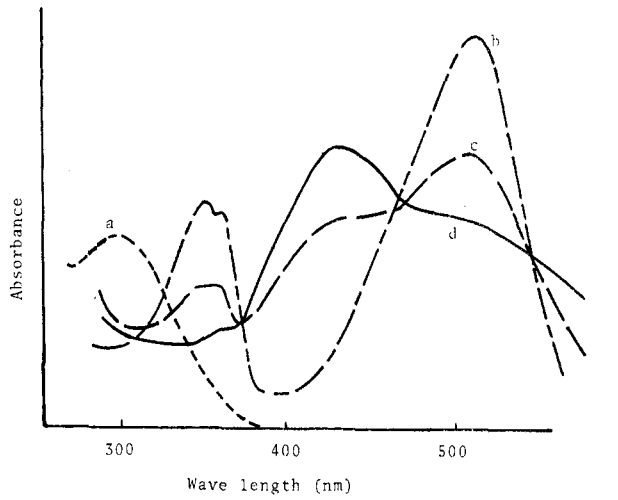
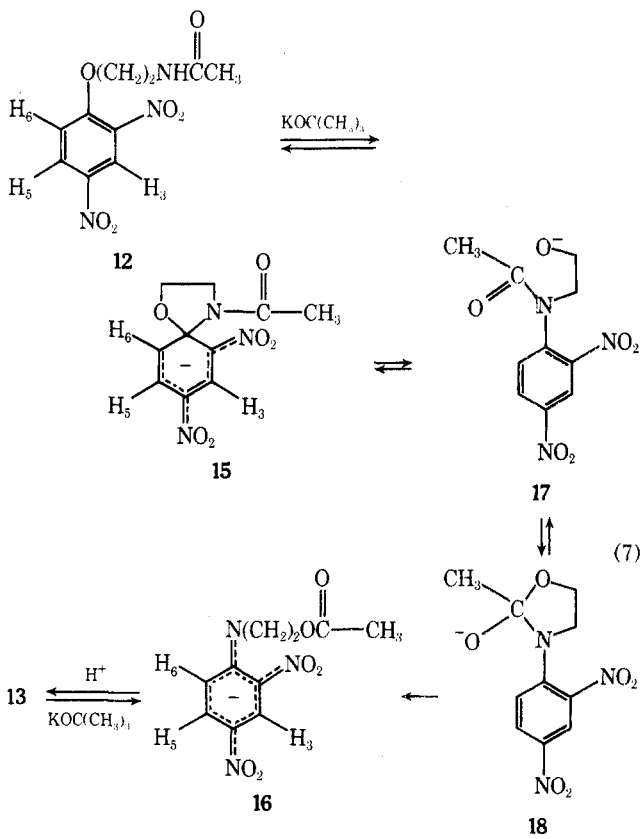


Figure 2. Absorption spectra relevant to the reaction of **12** with $KOC(CH_3)_3$ in Me_2SO: (a) before addition of $KOC(CH_3)_3$; (b, c, and d), immediately, ca. 12, and 40 hr after addition of $KOC(CH_3)_3$.

The following scheme is, therefore, most consistent with these results.

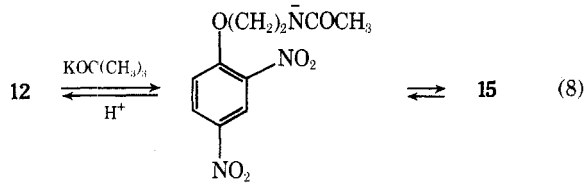


(7)

In order to elucidate the conversion of **12** to **15** or **15** to **12,** absorption spectra were obtained on successive addition of 50, 100, and 200 equiv of $KOC(CH_3)_3$ (1.25 *N*), HCl (1.00 *N*), and $KOC(CH_3)_3$, respectively, to a Me_2SO solution of **12** as shown in Figure 3. The first spectral change (curve a → b) represents the conversion of **12** to **15**[3c,5] and the second one (curve b → c) the conversion of **15** to **12.** A decrease in optical density at λ_{max} 298 nm is attributable to a partial rearrangement of **15** to **16.** The third spectral change (curve c → d) shows that on readdition of $KOC(CH_3)_3$ the spiro anionic σ complex (**15**) is reproduced.

From a consideration on the acidity of the amide hydrogen, the base-catalyzed conversion of **12** to **15** probably

proceeds via the amide ion (19), which is in equilibrium with 15 and the equilibrium lies far to 15, as shown in eq 8.



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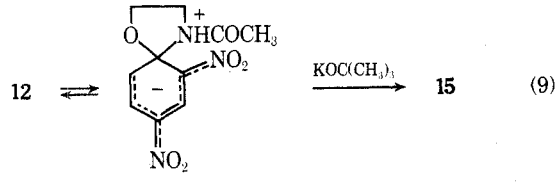
Furthermore, the other conversion of 12 to 15 is possible as shown in eq 9. Spectral change of curve a → b in Figures



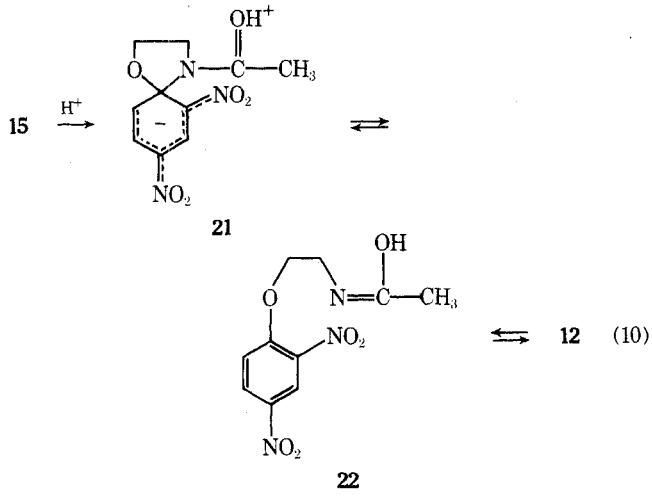
20

2 and 3, however, does not occur in the absence of a base. Bernasconi et al. show that deprotonation of 9 to 8 is very easy.[5] Accordingly, if 20 were spontaneously formed, 20 would change into 15 even in the absence of a base. Accordingly, the conversion in eq 9 is considered to be unlikely.

In the acid-catalyzed conversion of 15 to 12, there are at least two possible paths. One is the process in which 15 returns to 19, and, in turn, 19 is protonated to change into 12 as shown in eq 8.

The other is the process in which 15 directly changes to 12 by protonation of the amide group, in which protonation occurs on the amide nitrogen or the carbonyl oxygen. However, much available evidence supports the conclusion that O-protonation on carbonyl oxygen predominates over N-protonation on amide nitrogen in acidification of amide groups.[14]

Therefore, the other process in the acid-catalyzed conversion of 15 to 12 is considered to be as follows.



21

22

It is not clear at present which path (reverse of eq 8, and eq 10) is predominant.

Experimental Section

Melting points are uncorrected. The NMR spectra were recorded on a Varian A-60D spectrometer. Elemental analyses were performed at the Microanalytical Center of Gunma University. The absorption spectra were measured in Me_2SO on a Hitachi-124 uv–visible spectrophotometer. All reagents were purified by recrystallization or by distillation prior to use.

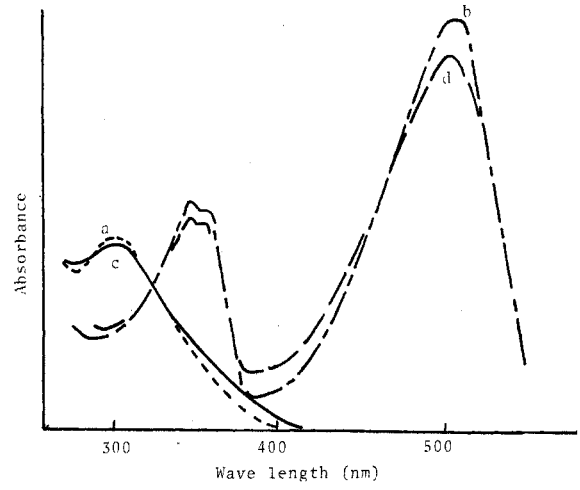


Figure 3. Absorption spectral change in successive addition of $KOC(CH_3)_3$, HCl, and $KOC(CH_3)_3$ to a Me_2SO solution of 12: (a) 12 before addition of $KOC(CH_3)_3$; (b) immediately after addition of $KOC(CH_3)_3$; (c) immediately after addition of HCl to 15 (anionic σ complex); (d) immediately after addition of $KOC(CH_3)_3$ to reproduced 12.

Preparation of N-Acetyl-β-aminoethyl-2,4-dinitrophenyl Ether (12), N-β-Acetyloxy- (13) and N-β-Hydroxyethyl-2,4-dinitroaniline (14). After 0.69 g (0.030 mol) of metallic sodium had been added to a stirred solution of 4.6 g (0.045 mol) of N-acetylethanolamine in 50 ml of dioxane, the mixture was refluxed for 5 hr so that sodium might be completely dissolved. After a solution of 5.6 g (0.030 mol) of 2,4-dinitrofluorobenzene in 30 ml of dioxane had been added thereto under stirring, the mixture was stirred for an additional 4 hr at 30°. Then the mixture was poured into 200 ml of ice–water and extracted with chloroform. After the organic layer had been dried over anhydrous Na_2SO_4, the solvent was evaporated to produce the crude products, which were separated by column chromatography on silica gel with benzene–acetone mixture as a developing solvent. After the solvent had been distilled off, recrystallization of each crude product from benzene or benzene–ligroin gave each analytical sample: **12**, 14%, mp 105–105.5°, λ_{max} 298 nm (ε 11,300); **13**, 9%, mp 131–132°, λ_{max} 358 nm (ε 17,400), ca. 410 (sh); **14**, 37%, mp 91–92°, λ_{max} 362 nm (ε 17,700), ca. 390 (sh). Anal. Calcd for $C_{10}H_{11}N_3O_6$ (12): C, 44.61; H, 4.12. Found: C, 44.33; H, 4.05. Anal. Calcd for $C_{10}H_{11}N_3O_6$ (13): C, 44.61; H, 4.12. Found: C, 44.76; H, 4.40. Anal. Calcd for $C_8H_9N_3O_5$ (14): C, 42.29; H, 3.99. Found: C, 42.20; H, 3.80%.

Reaction of N-Acetyl-β-aminoethyl-2,4-dinitrophenyl Ether (12) with Tertiary-Butanolic $KOC(CH_3)_3$. To a stirred solution of 0.778 g (2.89×10^{-3} mol) of 12 in 10 ml of Me_2SO was added at room temperature 2.37 ml (2.89×10^{-3} mol) of tertiary-butanolic $KOC(CH_3)_3$ (1.22 *N*). After the mixture had been stirred for 1 hr and then 2.89 ml of 2.00 *N* HCl solution added thereto, it was poured into 100 ml of water, extracted with chloroform, and dried over anhydrous Na_2SO_4. The solvent was evaporated to produce the crude products, which were separated by column chromatography on silica gel with benzene as a developing solvent and purified. 13 and 14 were obtained in 78% yield and in a small amount, respectively.

NMR and Absorption Spectra Measurement. In NMR measurement a certain amount of a sample (ca. 42 mg) was dissolved in a small amount of Me_2SO-d_6 (ca. 0.5 ml) in a NMR tube. After an equivalent amount of $KOC(CH_3)_3$ (0.840 *N*) had been added to the solution through a microsyringe, shaken vigorously, and filtered if necessary, the spectra of the mixture were observed.

In absorption spectra measurement of the rearrangement reaction, 3.66 μl of tertiary-butanolic $KOC(CH_3)_3$ (1.25 *N*) was added to 3 ml of a Me_2SO solution of 12 (3.05×10^{-5} *M*), and then the spectra of the mixture were observed (Figure 2). In absorption spectra measurement on successive addition (Figures 3), at first 3.66 μl (50 equiv) of tertiary-butanolic $KOC(CH_3)_3$ (1.25 *N*) was added to 3 ml of a Me_2SO solution of 12 (3.05×10^{-5} *M*), the spectra of the mixture were observed, and then 9.15 μl (100 equiv) of HCl solution (1.00 *N*) was added to the mixture. Immediately after the spectrum had been observed, 14.6 μl (200 equiv) of tertiary-butanolic $KOC(CH_3)_3$ was again added to the mixture, and, the spectrum was observed.

Acknowledgment. We thank the Asahi Glass Foundation for the Contribution to Industrial Technology and the Ministry of Education for their financial support.

Registry No.—**12**, 55759-61-0; **13**, 19289-04-4; **14**, 1945-92-2; $KOC(CH_3)_3$, 865-47-4; *N*-acetylethanolamine, 142-26-7; 2,4-dinitrofluorobenzene, 70-34-8.

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Cleavage Reaction of Cyclic Ethers by Alkyl Chlorosulfinates

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The reaction of alkyl chlorosulfinates with tetrahydrofuran (THF) produced predominantly 4-chlorobutylalkyl ethers, but with ethylene oxide β-chloroethylalkyl sulfites were the main product. The kinetic study on the formation of 4-chlorobutylalkyl ethers revealed that the nucleophilic attack of THF on the carbon atom of alkyl chlorosulfinates is the rate-determining step, followed by simultaneous fission of C–O and S–Cl bonds of alkyl chlorosulfinates.

Of the various classes of organic reactions, nucleophilic substitution reactions on carbon have, to date, been studied most intensively. On the formation of alkyl chlorides from the reactions of the corresponding alcohols with thionyl chloride, Hughes and Ingold[1] proposed a mechanism involving the formation of intermediate alkyl chlorosulfinates, followed by the loss of sulfur dioxide, and simultaneously with it formed the carbon–chlorine bond, presumably by way of a cyclic transition state due to their stereochemical reasons. They called this reaction the SNi mechanism. Since then, Boozer and Lewis[2] showed by the study dealing with the decomposition of alkyl chlorosulfinates that intermediates in the formation of alkyl chlorides must have much ionic character. Cram[3] concluded that the SNi reaction proposed by Hughes and Ingold for the decomposition of alkyl chlorosulfinates differs from the SN1 reaction only in the sense that the leaving group is complex, and that the anion of the first ion pair can decompose internally under some conditions faster than a potential anion can react at the carbon undergoing substitution. However, the study on the reactions employing the alkyl chlorosulfinates as the substrate is lacking compared with those of the alkyl chloroformates[4] except for the studies on the interactions of alkyl chlorosulfinates and pyridine by Gerrard.[5,6] We will report the cleavage reaction of cyclic ethers by alkyl chlorosulfinates.

Results

The reaction of ethylene oxide with methyl chlorosulfinate in benzene at 0° gave 70.8% of β-chloroethylmethyl sulfite[7] for 20 min. The results obtained from a variety of epoxides are shown in Table I; the preferential attack of the sulfinyl sulfur of methyl chlorosulfinate by epoxides seems to be predictable from the fact that methanesulfinyl chloride is known to react with ethylene oxide yielding the corresponding sulfinate ester.[8] However, from the five-membered ether, tetrahydrofuran (THF), 4-chlorobutylmethyl ether is obtained as the main reaction product. As shown in Figure 1 this reaction proceeded with an exceedingly slow rate at 30°. At this temperature, the yield of methyl chloride formed by a side reaction is less than about 5% of that of 4-chlorobutylmethyl ether.

These interesting results by the use of THF caused us to elucidate the mechanism of the reaction of THF with alkyl chlorosulfinates yielding 4-chlorobutylalkyl ethers. As shown in Scheme I it is possible to consider two mechanisms containing different modes of attack: (1) THF as the nucleophilic reagent attacks the carbon atom of alkyl chlorosulfinates (C-attack) forming both *O*-alkyl tetrahydrofuranium ion and chlorosulfinate anion (I), followed by the loss of SO_2 to produce the chloride anion. On the other hand, (2) the nucleophilic attack of THF on the sulfur atom of alkyl chlorosulfinates (S-attack) may lead to the formation of an intermediate *O*-alkoxysulfinyl tetrahydrofuranium ion (II), followed by the formation of *O*-alkyl tetrahydrofuranium ion[9] by way of a cyclic transition state.

It is conceivable that the intramolecular reaction of an intermediate (II) may proceed more rapidly than the attack of the chloride ion on an intermediate oxonium ion (II) because of the high stability of such an oxonium ion compared with that of the three-membered oxonium ions. Thus, we elucidate at first the distinction between the C-attack and S-attack of THF and then the feature of this reaction. The reaction rate of methyl chlorosulfinate with THF was followed by gas–liquid partition chromatography (GLC) determining the concentration of methyl 4-chlorobutyl ether formed by the use of *p*-cymene as an internal reference. The reactions were carried out at the temperatures below 50° in order to avoid the side reactions probably due to thermal instability of alkyl chlorosulfinates.