g) was refluxed vigorously with zinc dust (12 g) in glacial AcOH (70 ml) for 3.5 hr. After cooling to room temperature, the mixture was filtered, and the filtrate was evaporated under reduced pressure until the AcOH was removed. The residue, a thick oil containing some solids, was stirred with $(CH_3)_2CO$ (150 ml) and filtered to remove the last traces of zinc acetate. The resulting solution was evaporated to dryness, leaving a thick oil (3.37 g).

A portion (1.0 g) of this oil was dissolved with $Ac_2O$ (2 ml) in dry pyridine (7 ml). After 16 hr the mixture was poured into ice–water, and the resulting mixture was extracted with ether. The ether extract was dried over anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure to give an oil which slowly crystallized on standing. Recrystallization from $CH_3OH$ gave the product (0.53 g), mp 115–118°. Another recrystallization from $CH_3OH$ provided an analytical sample, mp 120–121°, of 2-(2-acetylaminophenyl)benzothiazole.

*Anal.* Calcd for $C_{15}H_{12}N_2OS$: C, 67.14; H, 4.51; N 10.44; S, 11.95. Found: C, 67.05; H, 4.29; N, 10.22; S, 11.89.

**Registry No.**—**3**, 32612-56-9; **5**, 32612-57-0; **6**, 32827-40-0; **7**, 32675-27-7; **12**, 32722-78-4; **13**, 32675-28-8; **14**, 32722-79-5; **15**, 32675-29-9; **16**, 32675-30-2; **17**, 32675-31-3; **19**, 32675-32-4; **20**, 32675-33-5; **22**, 32675-34-6; **24**, 32675-35-7; **25**, 243-95-8; 2-(2-acetylaminophenyl)benzothiazole, 32675-37-9.

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# Synthesis of 2-Methoxyallyl Chloride, Bromide, and Iodide by Two Independent Routes. The Reaction of *N*-Halosuccinimides with 2-Methoxypropene and the Pyrolysis of 1-Halo-2,2-dimethoxypropanes

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2-Methoxyallyl chloride (**3a**), the corresponding bromide **3b**, and iodide **3c** have been synthesized by two independent routes, and like the series of previously unknown 1-halo-2-methoxypropenes **4a–c** are now readily available for the first time. Our first route is the reaction of 2-methoxypropene (**1**) with the *N*-halosuccinimides (**2a–c**), especially *N*-chlorosuccinimide (**2a**) and *N*-bromosuccinimide (**2b**), to give a series of five products, namely, in the case of **2b**, the desired 2-methoxyallyl bromide (**3b**), 1-bromo-2-methoxypropene (**4b**), 1-bromo-2-methoxy-2-succinimidopropane (**7b**), as well as minor amounts of 1-bromo-2,2-dimethoxypropane (**5b**) and bromoacetone (**6b**). The reaction of *N*-bromosuccinimide (**2b**) and **1** is completely ionic, being insensitive to free-radical donors and inhibitors, and represents the first thoroughly studied example of the reaction of *N*-bromosuccinimide with an enol ether. A second entry into the 2-methoxyallyl system has been provided by the pyrolysis of 1-chloro-2,2-dimethoxypropane (**5a**) above 180° in the presence of Lewis acids. As in the reaction of 2-methoxypropene (**1**) with *N*-chlorosuccinimide (**2a**), not only 2-methoxyallyl chloride (**3a**) is formed in this pyrolysis but also the isomeric 1-chloro-2-methoxypropene (**4a**). Interestingly, even the ratio of **3a**:**4a** is similar to that obtained in the first route. Thermolysis of 1-bromo-2,2-dimethoxypropane (**5b**) proceeds in milder conditions and again produces **3b** as well as **4b**. 2-Methoxyallyl iodide (**3c**) is most readily available from the corresponding bromide **3b** by treatment with NaI in acetone.

2-Alkoxyallyl halides represent a simple class of bifunctional compounds which aside from having intrinsic interest deserve attention in synthesis. For example, we have used **3b** as a precursor in 4 + 3 → 7 cycloadditions,[1,2] and one may easily envisage further applications, for example, in the realm of organometallic chemistry. Curiously, apart from a claim in a dated patent[3] which we have reinvestigated, there is to our knowledge nowhere in the chemical literature any mention of these simple compounds, be it as the parent, *i.e.*, **3a–c**, or more highly substituted, say as part of a ring. As enol ethers[4] and alkyl halides the desired compounds are expected to be electron rich and electron deficient at the same time. Naturally, the confrontation of two such sites within one molecule will not only present problems in synthesis but also new properties, and it seemed to us from the very beginning that neither strongly acidic nor strongly basic conditions could be part of any satisfactory approach and that also some care would be required in working up any potentially interesting reaction mixture.

We now wish to record the synthesis of 2-methoxyallyl chloride (**3a**), bromide **3b**, and iodide **3c** by two efficient routes.

## Results

**A. Product Analysis and Structural Assignments.**—Generally, *N*-halosuccinimides (**2a–c**) have been found to react with 2-methoxypropene (**1**) to give succinimide and five other products as exemplified in Scheme I for the reaction with *N*-bromosuccinimide (**2b**).

(1) (a) H. M. R. Hoffmann, D. R. Joy, and A. K. Suter, *J. Chem. Soc. B*, 57 (1968); (b) H. M. R. Hoffmann and D. R. Joy, *ibid.*, 1182 (1968); (c) H. M. R. Hoffmann and N. F. Janes, *J. Chem. Soc. C*, 1456 (1969); (d) H. M. R. Hoffmann, G. F. P. Kernaghan, and G. Greenwood, *J. Chem. Soc. B*, 2257 (1971); (e) H. M. R. Hoffmann, K. E. Clemens, and R. H. Smithers, *J. Amer. Chem. Soc.*, in press; (f) G. Greenwood, A. E. Hill, and H. M. R. Hoffmann, unpublished work.

(2) Cycloadditions classified according to the ring-size criterion; see R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **7**, 321 (1968). For 4 + 3 → 7 cycloadditions involving oxyallyl, see N. J. Turro, S. S. Edelson, J. R. Williams, T. R. Darling, and W. B. Hammond, *J. Amer. Chem. Soc.*, **91**, 2283 (1969); R. C. Cookson, M. J. Nye, and G. Subrahmanyam, *J. Chem. Soc. C*, 473 (1967), 2009 (1965); A. W. Fort, *J. Amer. Chem. Soc.*, **84**, 2620, 2625, 4979 (1962).

(3) K. Westphal and H. Klös, German Patent 614,462 [*Chem. Abstr.*, **29**, 5994[4] (1935)]; U. S. Patent 2,119,802 (1938).

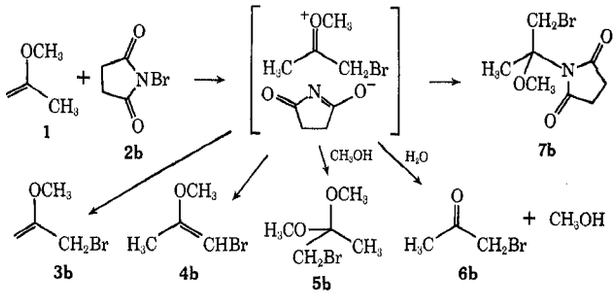
(4) For reviews of enol ethers, see (a) H. Meerwein, "Methoden der Organischen Chemie," Houben–Weyl–Müller, Ed., Vol. 6/3, Thieme, Stuttgart, 1965, p 97; (b) F. Effenberger, *Angew. Chem., Int. Ed. Engl.*, **8**, 295 (1969); (c) M. F. Shostakovskii, A. V. Bogdanova, and G. I. Plotnikova, *Russ. Chem. Rev.*, **33**, 66 (1964); see also M. F. Shostakovskii, B. A. Trofimov, A. S. Atavin, and V. I. Lavrov, *ibid.*, **37**, 907 (1968).

Of the products obtained, compounds **3**, **4**, **5**, and **6** are volatile, lachrymatory liquids, while the adducts **7a–c** proved to be solids. The identification of these products rests on combined glc–nmr, mass spectroscopy, and chemical transformations. Specifically, the peak areas of the volatile products **3**, **4**, **5**, and **6** in gas–liquid chromatograms (*cf.* Table V for retention times) were matched by corresponding intensities of nmr peaks, and preparative glc allowed us to isolate individual compounds whenever desirable. The enol ethers **3a** and **4a**, as well as **3b** and **4b**, were further identified by their reactions with various alcohols. For example, 2-methoxyallyl bromide (**3b**), as well as its isomer **4b**, reacts very smoothly with methanol to give quantitatively the bromo ketal **5b**; not unreasonably, **3b** reacts somewhat faster than **4b**.

*A priori*, the enol ethers **4a**, **4b**, and **4c** could be present as a mixture of cis/trans isomers. That only one respective isomer had been formed could be shown as follows. (1) **4a**, **4b**, and **4c** gave perfectly symmetrical peaks on glc. Specifically, **4a** was examined on five different columns and proved to be a single compound. (2) A cis/trans mixture if present should also be discernible in the nmr spectrum. No additional peaks beyond those ascribable to one isomer were observed. (3) Expansion of the peak at $\tau$ 4.88 in **4a** and at $\tau$ 4.91 in **4b** revealed a broad quartet (coupling to $CCH_3$), while the methyl protons appeared on expansion as a doublet with $J_{H,CH_3} \sim 0.7$ Hz, coupling being confirmed by double irradiation. Whether the halogen atoms in the enol ethers **4a**, **4b**, and **4c** are actually cis or trans to the methoxy grouping can at present not be decided from the magnitude of allylic coupling, since examples are known where $|J_{cis}| > |J_{trans}|$ and vice versa.[5] However, some work in related systems discussed below suggests the formation of cis isomers.[6]

Of the three adducts **7a**, **7b**, and **7c**, 1-bromo-2-methoxy-2-succinimidopropane (**7b**) has been investigated in detail. It is a stable crystalline solid, mp 32–34°, which shows a molecular ion *m/e* 249 for $C_8H_{12}NO_3{}^{79}Br$, provided that the vapor pressure of the sample is sufficiently high, and prominent fragmentation peaks $m - CH_3$ and $m - OCH_3$ in excellent accord with the assigned structure. The nmr spectrum is interesting in that it displays the expected AB quartet for the diastereotopic $CH_2Br$ protons, which are, however, separated rather widely ($\Delta\nu_{AB}$ = 116 Hz), presumably because the neighboring asymmetric carbon is attached to three widely dissimilar groups. Integration shows that the peak at $\tau$ 8.15 has the same area as the sharp methoxy singlet at $\tau$ 6.83; on expansion the downfield half of the quartet appears as two broad quartets, *i.e.*, $H^c$ is coupled further to the $CCH_3$ protons with $J_{H^c,CH_3}$ = 1 Hz. From the "W" rule[5] and also the work of Davis and Roberts[7] it can be concluded with confidence that it is the proton anti to the methyl group which shows long-range coupling. Presumably the conformation of **7b**, in which the succinimidyl grouping is anti to the bromine atom, is preferred.

Scheme I




Adduct **7b** can be heated in chlorobenzene up to 120° and does not suffer any detectable decomposition; only the nmr spectrum changes slightly, with $\Delta\nu_{AB}$ = 104 Hz at 120°. On the other hand, in nitrobenzene solution at room temperature both $\Delta\nu_{AB}$ and $J_{CH_3,H}$ are smaller, being 88 and 0.6 Hz, respectively.

**B. Synthesis of the 2-Methoxyallyl Halides (3a–c). (1) Reaction of 2-Methoxypropene (1) with *N*-Halosuccinimides (2a–c).**—The reaction of 2-methoxypropene (**1**) and *N*-bromosuccinimide (**2b**) gives an array of products and has been investigated in depth (Table I) with the aim of optimizing the formation of 2-methoxyallyl bromide (**3b**), which not unexpectedly is a sensitive compound and is best handled in solution. In the course of our work the conditions detailed in run 9, Table I, have emerged as optimum for the preparation of **3b**. After careful work-up of the reaction mixture a 50% solution in $CCl_4$ of 2-methoxyallyl bromide (**3b**) (68–70%), **4b** (28–30%), and **5b** + **6b** + **7b** (0–4%) is obtained which can be stored over $Na_2CO_3$ in the dark at room temperature. Although neat 2-methoxyallyl bromide (**3b**) and 1-bromo-2-methoxypropene (**4b**) decompose at room temperature, both compounds can be isolated in pure form by preparative glc.

Not unexpectedly, the reaction of *N*-chlorosuccinimide (**2a**) and 2-methoxypropene (**1**) requires slightly more vigorous conditions, *i.e.*, refluxing $CCl_4$ in any case. The product mixture can be worked up as described for the bromo derivatives and it is clear that this reaction provides a simple and satisfactory route to the previously unknown 2-methoxyallyl chloride (**3a**) as well as 1-chloro-2-methoxypropene (**4a**).

In contrast *N*-iodosuccinimide (**2c**) and the enol ether **1** react only incompletely in refluxing $CCl_4$,

(5) (a) S. Sternhell, *Quart. Rev., Chem. Soc.*, **23**, 236 (1969); (b) L. M. Jackman and S. Sternhell, "Applications of Nmr Spectroscopy in Organic Chemistry," 2nd ed, Pergamon Press, Elmsford, N. Y., 1969; (c) M. Barfield and B. Chakrabarti, *Chem. Rev.*, **69**, 757 (1969).

(6) *A priori*, the isomer is either pure *cis*-**4a** (*cis*-**4b**) or pure *trans*-**4a** (*trans*-**4b**). While it would be desirable to obtain the series of both *cis*-**4a–c** and *trans*-**4a–c** in order to reach a firm structural assignment, there are a number of indications which suggest the formation of *cis*-**4a–c**. For example, on pyrolysis over $K_2S_2O_7$ at 140° 1-*chloro*-2,2-*diethoxyethane* has been reported to lose ethanol with formation of mainly cis isomer: J. F. Arens, J. Vegter, and T. de Boer, *Recl. Trav. Chim. Pays-Bas*, **77**, 753 (1958); see also J. F. Arens, *Advan. Org. Chem.*, **2**, 117, 123, 124 (1960); and references cited therein. Similarly, pyrolysis of 1-chloro-2,2-dimethoxyethane over activated carbon at 270° affords 70% *cis*- and 30% *trans*-β-chlorovinyl ether: E. Kobayashi, S. Hattori, and K. Tada, Japanese Patent 158 (1958) [see *Chem. Abstr.*, **52**, 19953*g* (1958)]. Elimination of HCl from 1,2-dichloroethyl ethers with tertiary amine has been reported to yield cis isomers in excess (75–90%) over trans isomers (10–25%): M. Farina, M. Peraldo, and G. Bressan, *Rend. Ist. Lomb. Sci. Lett., A, Cl.* **94**, 600 (1960) [*Chem. Abstr.*, **56**, 7115*e* (1962)].

Generally, the formation of cis isomer follows the cis rule of Viehe [H. G. Viehe, *Chem. Ber.*, **93**, 1697 (1960)], who proposed that, in the case of cis/trans isomers the substituents of which constitute an electron donor–electron acceptor pair, the cis isomer is more stable unless the substituents have particularly large steric requirements. However, that one stereoisomeric β-halovinyl ether can be formed *to the exclusion* of the other, as in our case, is of considerable interest and apparently without precedent.

(7) D. R. Davis and J. D. Roberts, *J. Amer. Chem. Soc.*, **84**, 2252 (1962).

TABLE I

PRODUCTS[a] FROM THE REACTION OF 2-METHOXYPROPENE (1) AND *N*-BROMOSUCCINIMIDE (2b) IN $CCl_4$[b]

| Run | Reagents, mol/l. 1 | Reagents, mol/l. 2b | Temp, °C | Reaction time, min | Product compn, % 3b | 4b | 5b | 6b | 7b |
|---|---|---|---|---|---|---|---|---|---|
| 1[b] | 1.8, *ca.* 3 | 1.8 | 25 | 5 | 30 | 10 | 30 | 5 | 25 |
| 2[b] | 1.6 | *ca.* 2 (excess) | 25 | 90 | 33 | 13 | 7 | 7 | 40 |
| 3[b] | 1.85 | 1.87 | 0 | 120 | 36 | 14 | 7 | 7 | 36 |
| 4 | 1.43 | 1.12 | 25 | 5 | 50 | 17 | 1 | 8 | 24 |
| 5[c] | 1.43 | 1.12 | 25 | 5 | 50 | 17 | 1 | 8 | 24 |
| 6[d] | 1.85 | 1.5 | 25 | 5–75 | 50 | 17 | 1 | 8 | 24 |
| 7[e] | 1.85 | 1.87[f] | 25 | 120 | 46 | 17 | 2 | 8 | 27 |
| 8 | 1.43 | 1.12 | 55–65 | 10 | 48 | 20 | 1 | 7 | 24 |
| 9[g] | 1.85 | 1.87 | 55–65 | 50 | 54 | 18 | 6 | 3 | 19 |
| 10 | 1.85 | 1.87 | 60–70 | 30 | 42 | 16 | 1 | 5 | 36 |
| 11[i] | 1.98 | 1.6 | Reflux–80[h] | 10 | 29 | 14 | 1 | 8 | 48 |
| 12[j] | 1.85 | 1.5 | Reflux–80[h] | 10–15 | 29 | 13 | 1 | 2 | 54 |
| 13 | 1.85 | 1.87 | Reflux–80[h] | 20 | 44 | 17 | 9 | 6 | 24 |

[a] Product distribution determined by glc (**3b**, **4b**, **5b**, and **6b**) and nmr which gave per cent **7b** relative to **3b** and **4b**. The error for measuring peak areas is *ca.* 2.5–4% in general but obviously greater for compounds present in less than 10%. [b] Except for runs 1–3, $CCl_4$ (analytical grade) was dried ($P_4O_{10}$) before use. 2-Methoxypropene was dried ($CaCl_2$) and redistilled except for runs 1–3 and always added to the suspension of **2b** in $CCl_4$ with shaking. *N*-Bromosuccinimide was usually finely ground but otherwise not treated any further (*cf.*, however, run 7). [c] Reaction solution contained 0.01 g of galvinoxyl. In two more runs under the conditions of run 4, but, in the presence of 1 mol % of benzoyl peroxide and 1 mol % of iodine, the composition of product remained unchanged. [d] Product ratios stay constant throughout reaction time. [e] Variation of solvent: $CH_2Cl_2$ (homogeneous) no change, except perhaps more adduct **7b**. In chlorobenzene (semihomogeneous) more **7b** was formed. [f] *N*-Bromosuccinimide dried ($P_4O_{10}$, desiccator). [g] Reaction mixture was stirred. [h] Refluxing causes a slightly yellow coloration of the reaction products. [i] 2,6-Lutidine (*ca.* 0.2 *M*) present. [j] Solid $Na_2CO_3$ (0.5 g) present.

TABLE II

PRODUCTS FROM THE PYROLYSIS OF 1-CHLORO-2,2-DIMETHOXYPROPANE (5a)

| Run | Catalyst[a] | Column[b] | Temp, °C: Metal bath | Temp, °C: Head | Products,[c] %: 3a | 4a | 5a | 6a |
|---|---|---|---|---|---|---|---|---|
| 1 | $K_2S_2O_7$ | 2 Vigreux | 180–210 | 108 | 26.5 | 43 | 19 | 11.5 |
| 2 | $K_2S_2O_7$ | Vigreux | 180–200 | 110–112 | 25 | 27 | 31.5 | 16 |
| 3 | QP | 2 air condensers | 180–230 | 106–110 | 35.9 | 32.5 | 22.3 | 9.3 |
| 4 | QP, Q[d] | 2 air condensers | 210–250 | 108–112 | 37 | 34.5 | 19 | 9.5 |
| 5 | QP | 2 Vigreux | *ca.* 200 | 120 | 25.5 | 17 | 41 | 16.5 |
| 6 | QP | Air condenser | 200–210 | <124 | 24 | 13.4 | 50 | 12.6 |
| 7 | QOTs | 2 air condensers | 225–235 | 103–105 | 38.2 | 43.6 | 13.4 | 4.7 |
| 8 | $Ac_2O$, AcOH quinaldine | Vigreux | 150–185 | 102–107 | 32 | 56 | 10 | 2 |

[a] QP = quinaldine phosphate; QOTs = quinaldine tosylate. [b] Vigreux column (24 × 1.5 cm) and air condenser (45 × 2 cm) used. [c] Some chloroacetone is present as an impurity in **5a** and could also be formed during the pyrolysis. [d] Quinaldine (1.2%) and phosphoric acid (0.5%) used as catalyst.

iodine being liberated. However, we have found that 2-methoxyallyl iodide (**3c**) can be prepared conveniently from **3b** and NaI in acetone.

**(2) Thermolysis of 1-Chloro-2,2-dimethoxypropane (5a) and 1-Bromo-2,2-dimethoxypropane (5b).**—Having uncovered a simple reaction for preparing the 2-methoxyallyl halides we became aware of a patent according to which the dimethyl ketal of chloroacetone is to break up at 200–270° in the presence of catalytic amounts of quinoline phosphate into **3a** and methanol.[3] Of course, the synthesis of enol ethers from acetals and ketals *via* elimination of alcohols is a well-established reaction,[4] but we noted with more than casual concern that formation of any isomeric enol ether such as **4a** had not been mentioned, although the pyrolysis of **5a** like the reaction of 2-methoxypropene (**1**) with *N*-chlorosuccinimide (**2a**) seemed likely to proceed *via* an ionic mechanism involving similar intermediates. In any event we decided to reinvestigate the patented procedure from the vantage point of modern analytical techniques and our earlier experience with this class of compounds. Accordingly, 1-chloro-2,2-dimethoxypropane (**5a**) which is readily available from chloroacetone was pyrolyzed in the presence of various Lewis acids above 180° (Table II). It became clear immediately that under all conditions, including those cited in the patent,[3] not only methanol and 2-methoxyallyl chloride (**3a**) but also an isomeric enol ether were produced which proved to be a single isomer and identical with 1-chloro-2-methoxypropene (**4a**) characterized previously.

In contrast to **5a** the corresponding bromo ketal **5b** was found to break up more readily, elimination occurring during the preparation of **5b** on distillation and giving rise to 2-methoxyallyl bromide (**3b**) and its isomer **4b** in a ratio of 3:1. Conceivably, HBr was liberated during the distillation and catalyzed the breakup of the ketal. Distillation of chloro ketal **5a** under reduced pressure in the presence of catalytic amounts of $H_2SO_4$ afforded mainly unchanged starting material and only a small quantity of **3a** and **4a**, but the ratio **3a**:**4a** was again rather high, being 3:2.

## Discussion

Turning to the reaction of the enol ether **1** and *N*-bromosuccinimide (**2b**) first, it is striking that dibenzoyl peroxide which is an efficient free-radical initiator and inhibitors such as molecular iodine and galvinoxyl have no effect on the reaction (Table I,

run 5). Clearly, an ionic reaction is indicated and it suffices to invoke an intermediate oxonium succinimidate ion pair (Scheme I), which should be formed on the surface of the *N*-bromosuccinimide before breaking down to the three major products **3b**, **4b**, and **7b**. It should be mentioned explicitly that all products are stable during the reaction (Table I, run 6); *i.e.*, adduct **7b** is not a precursor of either **3b** or **4b**, nor can these two isomeric enol ethers equilibrate under our conditions.

As regards the proportion of the desired 2-methoxyallyl halides **3a–c**, it is of interest that **3b** predominates over **4b** and, even more so, **3c** over **4c** (Table III).

TABLE III
TYPICAL PRODUCT DISTRIBUTION IN THE REACTION OF *N*-HALOSUCCINIMIDES WITH 2-METHOXYPROPENE IN BOILING $CCl_4$

| | | | | |
|---|---|---|---|---|
| **3a** (27%) | **4a** (31%) | **5a** (9%) | **6a** (3%) | **7a** (29%) |
| **3b** (54%) | **4b** (18%) | **5b** (6%) | **6b** (3%) | **7b** (19%) |
| **3c** (36%) | **4c** (3%) | **5c** (15%) | **6c** (6%) | **7c** (40%) |

Apparently, the ratio **3**:**4** is at least partly controlled by the acidity of the $CH_2Hal$ protons, increasing with decreasing acidity (*cf.* nmr of **5a**, **5b**, and **5c** in Table IV).

How are bromoacetone (**6b**) and the corresponding ketal **5b** formed? Although the isomeric enol ethers **3b** and **4b** react readily with solvent methanol and with any traces of moisture, it seems more likely that water and methanol would have to intervene at the earlier ion-pair stage to be effective. A further possible route to bromoacetone (**6b**) is the transfer of the methyl group to succinimidyl anion with release of **6b**. While *N*-methylsuccinimide has not been detected, it cannot be ruled out that this compound if formed would have been precipitated together with succinimide and so escaped detection. Any contaminants such as methanol or water are most likely to be introduced through 2-methoxypropene (**1**), which is difficult to obtain absolutely pure; in any case, drying of *N*-bromosuccinimide did not make any discernible difference to the product composition (run 7).

It is noteworthy that simply by adding solid $Na_2CO_3$ or 2,6-lutidine to the heterogeneous reaction mixture the proportion of adduct **7b** can be increased to 48% and more (Table I, runs 11 and 12). Although the formation of 1:1 adducts in the reaction of *N*-bromosuccinimide with olefins is not unknown,[8] it seems clear that there have been cases in the past where the formation of adduct has gone undetected, especially when reaction mixtures were analyzed by glc only. Compared with 5–30% adduct in the case of simple olefins,[8b] the proportion of adduct **7b** in the presence of base is, perhaps not surprisingly, large. It should be mentioned that the reaction of *N*-bromosuccinimide with an enol ether, namely dihydropyran, has been studied some time ago by Shelton and his coworkers,[9] who not only reported the formation of an analogous adduct but, in contrast to the results in our system, the formation of a vicinal dibromide and also some effect of free-radical initiators. Altogether, the literature on reactions of *N*-bromosuccinimides seems still in some disarray and need for repair. While it has been recognized that an ionic and a free-radical path may compete,[10] the reaction described herein presents to our knowledge the first clear example of a completely ionic reaction of *N*-bromosuccinimide with an olefin.

In considering the results of the second route to 2-methoxyallyl chloride (**3a**) one should bear in mind that the starting material, *i.e.*, 1-chloro-2,2-dimethoxypropane (**5a**), boils at 132–134°,[3] while the products will be more volatile; furthermore, an estimate based on glc retention indices suggests that the desired 2-methoxyallyl chloride (**3a**) boils about 14° higher than its isomer **4a**. [The same difference in boiling points has been estimated for the isomeric bromides **3b** and **4b** (*cf.* Table V, footnote *c*).] Hence, if a reasonably low proportion of chloro ketal **5a** in the distillate be ensured, it is advisable to maintain the temperature at the column head below 120°. Consistently, the higher the temperature at the column head, the more favorable the ratio **3a**:**4a**, but also the greater the percentage of starting material **5a** (Table II, runs 3–6). A compromise such as the conditions of run 3 and 4 seems optimum for preparing 2-methoxyallyl chloride (**3a**); in point of fact a temperature of 110–112° has been quoted in the patent[3] and it is again evident that the erstwhile product must have contained isomer **4a**.

It is especially interesting that both the first and the second route to 2-methoxyallyl chloride (**3a**) yield this isomer **4a**. Similarly, the first and the second route to 2-methoxyallyl bromide (**3b**) afford **4b** which is isomeric with **3b**.[6] Since the ratio of **3a**:**4a** (**3b**:**4b**) is also comparable for both routes, the ionic path proposed for the two sets of reactions gains additional credence.

## Conclusions

The 2-methoxyallyl system is now readily available by the way of two different reactions. While the first route to **3a** and **3b** is more simple as a laboratory procedure in that the reaction starts from nonlachrymatory materials and involves high conversions, there can be little doubt that the pyrolysis of the halo ketals **5a** and **5b** is adaptable to large-scale preparations and technically attractive.

## Experimental Section

**Preparation of Starting Materials.**—2-Methoxypropene (**1**) was obtained by the published procedure[11] in at least 95% purity, some methyl acetate and 2,2-dimethoxypropane generally being present as well. The *N*-halosuccinimides (**2a–c**) were commercial materials.

1-Chloro-2,2-dimethoxypropane (**5a**)[12] was obtained from chloroacetone (**6a**) (0.9 mol), a redistilled commercial sample being used, and trimethyl orthoformate (1 mol) in methanol

(8) (a) K. Ziegler, A. Späth, E. Schaaf, W. Schumann, and E. Winkelmann, *Justus Liebigs Ann. Chem.*, **551**, 80 (1942); for a reinvestigation, see G. Peiffer, J.-C. Traynard, and A. Guillemonat, *Bull. Soc. Chim. Fr.*, 1910 (1966); (b) A. Guillemonat, G. Peiffer, J.-C. Traynard, and A. Leger, *ibid.*, 1192 (1964); (c) I. Horman, S. S. Friedrich, R. M. Keefer, and L. J. Andrews, *J. Org. Chem.*, **34**, 905 (1969); (d) see also J. M. Landesberg and M. Siegel, *ibid.*, **35**, 1674 (1970); L. H. Zalkow and C. D. Kennedy, *ibid.*, **29**, 1290 (1964).

(9) J. R. Shelton and C. Cialdella, *ibid.*, **23**, 1128 (1958); J. R. Shelton and T. Kasuga, *ibid.*, **28**, 2841 (1963); see also R. Paul and S. Tchelitcheff, *C. R. Acad. Sci.*, **236**, 1968 (1953).

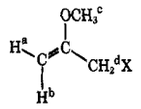
(10) J. H. Incremona and J. C. Martin, *J. Amer. Chem. Soc.*, **92**, 627 (1970); C. W. Jefford and W. Wojnarowski, *Helv. Chim. Acta*, **53**, 1194 (1970); D. I. Davies and L. T. Parfitt, *Tetrahedron Lett.*, 293 (1969); N. A. LeBel, J. E. Huber, and L. H. Zalkow, *J. Amer. Chem. Soc.*, **84**, 2226 (1962); S. D. Ross, M. Finkelstein, and R. C. Petersen, *ibid.*, **80**, 4327 (1958); J. D. Roberts, E. R. Trumbull, W. Bennett, and R. Armstrong, *ibid.*, **72**, 3116 (1950).

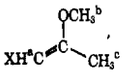
(11) G. Saucy and R. Marbet, *Helv. Chim. Acta*, **50**, 1158 (1967).

(12) Reference 4a, p 199.

TABLE IV

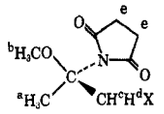
NMR SPECTRA OF PRODUCTS FROM REACTION OF 2-METHOXYPROPENE (1) AND *N*-HALOSUCCIMIMIDES (2a–c) IN $CCl_4$[a]





$CH_3{}^aC(OCH_3{}^b)_2CH_2{}^cX$

$CH_3{}^aCOCH_2{}^bX$



X = Cl

| 3a | 4a | 5a | 6a | 7a |
|---|---|---|---|---|
| a + b 5.79 (d), 5.98 (d, $J_{H^a,H^b}$ = 2.5 Hz), c 6.43 (s), d 6.14 (s) | a 4.88 (broad q), b 6.50 (s), c 8.11 (d, $J_{CH_3,H}$ = 0.7 Hz) | a 8.7 (s), b 6.85 (s), c 6.6 (s) | a 7.75 (s), b 5.7 (s) | a 8.15 (d), b 6.79 (s), c 5.28 (broad q) + 5.47 (broad q, $J_{H^c,H^d}$ = 18 Hz), d 6.48 + 6.66, e 7.4 (s) |

X = Br

| 3b | 4b | 5b | 6b | 7b |
|---|---|---|---|---|
| a + b 5.78 (d), 5.98 (d, $J_{H^a,H^b}$ = 2.5 Hz), c 6.42 (s), d 6.24 (s) | a 4.91 (broad q), b 6.45 (s), c 8.06 (d, $J_{CH_3,H}$ = 0.7 Hz) | a 8.66 (s), b 6.87 (s), c 6.74 (s) | a 7.72 (s), b 6.06 (s) | a 8.15 (d, $J_{CH_3,H^c}$ = 1 Hz), b 6.83 (s), c 5.46 (broad q) + 5.56 (broad q, $J_{CH_3,H^c}$ = 1 Hz), d 6.62 + 6.72 ($J_{H^c,H^d}$ = 10 Hz), e 7.52 (s) |

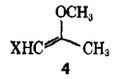
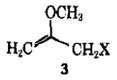
X = I

| 3c | 4c | 5c | 6c | 7c |
|---|---|---|---|---|
| a + b 5.74 (d), 5.98 (d, $J_{H^a,H^b}$ = 2.5 Hz), c 6.42 (s), d 6.20 (s) | a 5.2 (broad), b 6.46 (s), c obscured | a 8.64 (s), b 6.84 (s), c 6.76 (s) | a 7.86 (s), b 6.18 (s) | a 8.12 (d), b 6.79 (s), c 5.48 (broad q) + 5.67 (broad q), d obscured, e 7.41 (s) |

[a] All spectra were recorded at 60 MHz in *ca.* 10% $CCl_4$ solution except for adduct **7b**, which was studied in detail at 100 MHz. Chemical shifts are quoted on the $\tau$ scale. The positions of the $CH_2X$ resonances in **3a–c**, **5a–c**, **6a–c**, and **7a–c** are solvent and concentration dependent. For example, the signals for the $CH_2Cl$ protons of neat **3a** and of a 50% solution in acetone are separated by 0.07 ppm; $CH_2Br$ of **6b** resonates at $\tau$ 6.08 in a *ca.* 50% solution in $CCl_4$ and at $\tau$ 6.18 in 20% solution.

TABLE V

GLC RETENTION TIMES OF 3–6 RELATIVE TO $CCl_4$[a]

| | X = Cl | X = Br | X = I[b] |
|---|---|---|---|
|  4 | 1.6 (941)[c] | 2.4 (1025)[c] | |
|  3 | 2.2 (1009)[c] | 3.6 (1095)[c] | 6.2 |
| $CH_3C(OCH_3)_2CH_2X$ 5 | 2.8 | 4.6 | |
| $CH_3COCH_2X$ 6 | 3.4 | 5.7 | |

[a] Griffin F.I.D. gas chromatograph, 13-ft Carbowax 20M column at 80°. [b] The reaction mixtures of *N*-iodosuccinimide and 2-methoxypropene were analyzed mainly by their nmr spectra. [c] The values in parentheses are retention indices $I_{80°}^{C20M}$ as introduced by E. Kováts, *Helv. Chim. Acta*, **41**, 1915 (1958); *Z. Anal. Chem.*, **181**, 351 (1960). On a nonpolar stationary phase the difference d*I* of retention indices of isomeric compounds can be calculated from the difference d*t* of boiling points and vice versa; since d*I* ~ 5 d*t*, compound **3a** should boil *ca.* 14° higher than **4a**. Similarly, **3b** should boil *ca.* 14° higher than **4b**.

(0.75 mol) in the presence of catalytic amounts (2.5 ml) of concentrated $H_2SO_4$. After the mixture had been refluxed for 2 hr, it was cooled, washed with aqueous $Na_2CO_3$, and taken up in isopentane. Distillation under reduced pressure [38–40° (*ca.* 15 mm)] gave 1-chloro-2,2-dimethoxypropane (**5a**) (*ca.* 55%) in 85–90% purity, the accompanying compound being chloroacetone which can be removed by shaking with dilute aqueous KOH.

1-Bromo-2,2-dimethoxypropane (**5b**) was prepared analogously starting from bromoacetone[13] (**6b**).

**Quinaldine Phosphate.**—Quinaldine was mixed with 85% phosphoric acid in methanol as described for the reaction of related amines with phosphoric acid.[14] A white crystalline solid was precipitated, which melted at least above 216° and gave a satisfactory analysis for $C_{10}H_{12}NO_4P$. Addition of an excess of quinaldine to this compound did not appear to make any difference to the catalytic activity (Table II, run 4).

**Quinaldine Tosylate.**[15]—Quinaldine was added with stirring to a concentrated solution of *p*-toluenesulfonic acid in methanol until in excess which was recognizable by the persistence of the dark orange color of the amine. On slow addition of the resulting solution to ether a white solid precipitated which was collected, redissolved in methanol, and reprecipitated until all impurities had been removed. The solid was washed with ether, acetone, and isopentane and then dried giving quinaldine tosylate, mp 148–150°.

**Reaction of *N*-Bromosuccinimide (2b) and 2-Methoxypropene (1). 2-Methoxyallyl Bromide (3b) and 1-Bromo-2-methoxypropene (4b).**—2-Methoxypropene (1) and *N*-bromosuccinimide (**2b**) were allowed to react under the general conditions for allylic bromination[16] (*cf.* Table I, footnote *b*). The following conditions were found optimum for the preparation and isolation of **3b** (*cf.* Table I, run 9).

(a) The suspension of *N*-bromosuccinimide (50 g) in $CCl_4$ (150 ml) is preheated to *ca.* 55° (temperature measured inside reaction flask) on a water bath. Heating is then stopped, since the heat of the reaction sustains a temperature between 55 and 65°.

(b) An equimolar amount of 2-methoxypropene (20 ml), the purity of which is crucial for reducing the amount of undesirable by-products, is stirred into the reaction flask over a period of 30 min. Slow addition and vigorous stirring ensure a high conversion of enol ether.

(c) The reaction mixture is cooled to *ca.* 10–20° by immersion of the flask into ice for 15 min. Very little *N*-bromosuccinimide remains and any dissolved succinimide is precipitated.

(13) J. R. Catch, D. F. Elliott, D. H. Hey, and E. R. H. Jones, *J. Chem. Soc.*, 272 (1948).

(14) K. H. Engel, U. S. Patent 2,408,975 (1946) [*Chem. Abstr.*, **41**, 999*b* (1947)].

(15) A. F. Thomas, *J. Amer. Chem. Soc.*, **91**, 3282 (1969).

(16) L. Horner and E. H. Winkelmann, "Newer Methods of Preparative Organic Chemistry," Vol. 3, W. Foerst, Ed., Academic Press, New York, N. Y. 1964, p 151; C. Djerassi, *Chem. Rev.*, **43**, 271 (1948).

(d) The suspension is filtered quickly. Rapid removal of any remaining *N*-bromosuccinimide and the following step (e) prevent any undesirable consecutive reactions of the products.

(e) The filtered solution is concentrated at the water pump for *ca.* 15 min by immersion of the flask into warm water. This step removes any excess of 2-methoxypropene, methanol (which can be formed through adventitious water), any methyl acetate, and 2,2-dimethoxypropane (present as impurities in 2-methoxypropene) as well as some of the solvent $CCl_4$.

(f) The remaining solution is washed with dilute aqueous KOH (two 300-ml portions) and then with ice-cold water (two 100-ml portions). Shaking with dilute alkali destroys the adduct **7b**, any bromoacetone (**6b**), and any harmful traces of acid. Alkaline conditions also discourage the hydrolysis of any bromo ketal **5b** to bromoacetone and methanol and suppress the addition of water to enol ethers. Washing with ice-cold water neutralizes the solution and removes any methanol which in any event is unlikely to be present (also any acetone and 2,2-dimethoxypropane).

(g) The organic layer is dried immediately over $CaCl_2$ (enol ethers react with water!) and stored over anhydrous $Na_2CO_3$ in the dark as a *ca.* 50% solution of product in $CCl_4$ [neat 2-methoxyallyl bromide (**3b**) and 1-bromo-2-methoxypropene (**4b**) decompose at room temperature]. The solution so prepared contains **3b** (68–70%), **4b** (28–30%), and **5b** + **6b** + **7b** (0–4%). Pure **3b** as well as pure **4b** was isolated by preparative glc (Hewlett-Packard 776 preparative gas chromatograph, 20 ft × 0.75 in. Carbowax 20M column at 100°). 2-Methoxyallyl bromide (**3b**): *m/e* 152 ($C_4H_7O^{81}Br$), 150 ($C_4H_7O^{79}Br$); nmr (Table IV); glc retention time and retention index (Table V); and chemical transformations (see below). 1-Bromo-2-methoxypropane (**4b**): *m/e* 152 ($C_4H_7O^{81}Br$), 150 ($C_4H_7O^{79}Br$); nmr (Table IV); glc retention time and retention index (Table V); and its reaction with methanol (see below).

**1-Bromo-2-methoxy-2-succinimidopropane (7b).**—On removal of the bulk of the volatile products from the reaction mixture of **1** and **2b**, a dark brown residue remained which was kept for several days in a refrigerator. The impurity was absorbed on filter paper, and on standing for 2–3 weeks one obtained 1-bromo-2-methoxy-2-succinimidopropane (**7b**) as white, needle-like crystals: mp 32–34°; very soluble in acetone, benzene, $CCl_4$, $CHCl_3$, ethanol, furan, and glyme; slightly soluble in $CH_2Cl_2$, 1-pentene, chlorobenzene, and nitrobenzene; insoluble in isopentane, hexane, and petroleum ether (bp 40°); mass spectrum at 70 eV *m/e* 249 (at high pressure), 233.9775 (*m* − $CH_3$) (calcd for $C_7H_9NO_3{}^{79}Br$ 233.9776), 217.9818 (*m* − $OCH_3$) (calcd for $C_7H_9NO_2{}^{79}Br$ 217.9817), 170 (*m* − $^{79}Br$), 156 (base peak) (*m* − $CH_2{}^{79}Br$), 151 (*m* − $C_4H_4NO_2$), 150 (*m* − $C_4H_5NO_2$).

The nmr spectrum (*cf.* Table IV) was recorded in chlorobenzene solution from 27 to 120°. While the succinimido and the methoxy resonances showed no change, those of the $CH^cH^dBr$ and $CCH_3$ protons were temperature dependent. Specifically, the peaks at $\tau$ 5.38 and 5.48 (broad quartets) shifted upfield by 10 Hz, the peaks at $\tau$ 6.58 and 6.68 downfield by 2.2 Hz, and that at $\tau$ 8.13 upfield by 3.5 Hz. Also, the two broad quartets showed a small decrease in coupling, although the main part of this coupling was still present at 120°. All spectral changes were reversible over this temperature range. Nmr (100-MHz) in nitrobenzene solution (*ca.* 10%) at 27° was c 5.34 (broad quartet) + 5.44 (broad quartet, $J_{CH_3,H^c} \sim 0.6$ Hz), d 6.22 + 6.32 ($J_{H^c,H^d} = 10$ Hz), b 6.66 (s), e 7.22 (s), a 7.96 (d, $J_{CH_3,H^c} \sim 0.6$ Hz).

**Reaction of *N*-Chlorosuccinimide (2a) and 2-Methoxypropene (1). 2-Methoxyallyl Chloride (3a) and 1-Chloro-2-methoxypropene (4a).**—The reaction of 2-methoxypropene with *N*-chlorosuccinimide was very clean and carried out as that with *N*-bromosuccinimide, the only difference being that refluxing was required. The product mixture was analyzed (*cf.* Table III for a typical product distribution) and worked up as before yielding **3a** and **4a**. 2-Methoxyallyl chloride (**3a**): *m/e* 108 ($C_4H_7O^{37}Cl$), 106 ($C_4H_7O^{35}Cl$); nmr (*cf.* Table IV); glc retention times and retention indices (Table V); and chemical transformations (see below). 1-Chloro-2-methoxy propene (**4a**): *m/e* 108 ($C_4H_7O^{37}Cl$), 106 ($C_4H_7O^{35}Cl$); nmr (Table IV); glc retention times and retention indices (Table V); and its reaction with methanol (*cf.* below).

*N*-Iodosuccinimide (**2c**) and 2-methoxypropene (**1**) were refluxed in dry $CCl_4$ for 10 min, giving rise to a pink violet solution and a low conversion to products (*cf.* Table III), which included 2-methoxyallyl iodide (**3c**) and 1-iodo-2-methoxypropene (**4c**). **3c** can be prepared more conveniently from **3b** and NaI in acetone solution (*cf.* below).

**Reaction of 2-Methoxyallyl Bromide (3b) and 1-Bromo-2-methoxypropene (4b) with Alcohols.**—A 50% solution of **3b** and the isomeric enol ether **4b** in $CCl_4$ was mixed with methanol at room temperature and the ensuing reaction followed by nmr. After about 20 min the formation of 1-bromo-2,2-dimethoxypropane (**5b**) was complete, **3b** reacting somewhat faster than **4b**. The reaction time of the enol ethers toward ethanol was about the same (*ca.* 20 min) and *ca.* 40 min toward isopropyl alcohol, mixed ketals being formed. With *tert*-butyl alcohol 50% reaction occurred after 30 min at room temperature.

**2-Methoxyallyl Chloride (3a) and 1-Chloro-2-methoxypropene (4a) by Pyrolysis of 1-Chloro-2,2-dimethoxypropane (5a).**—The pyrolysis of 1-chloro-2,2-dimethoxypropane (**5a**) under the conditions of run 3 (Table II) may serve to illustrate our general procedure. **5a** (20 ml) and quinaldine phosphate (0.5 g) in a 50-ml flask attached to an air condenser (90 × 2 cm) were heated on a metal bath (180–250°), the temperature at the column head being kept below 111°.[17] The distillate was collected in a flask containing a stirred solution of aqueous $Na_2CO_3$. Methanol came over first and the fraction collected (106–110°) was found to contain unchanged starting material as well as *two* products rather than one[3] which were recognized and separated as described above and shown to be identical with authentic 2-methoxyallyl chloride (**3a**) and **4a** obtained by the reaction of *N*-chlorosuccinimide and 2-methoxypropene.

Except for the case of the acetic anhydride–acetic acid–quinaldine combination (Table II, run 8), elimination of methanol was found to require temperatures above 170°. Obviously, even then and in the presence of catalysts, loss of methanol was not instantaneous but a slow process. It commenced at about 180° with $K_2S_2O_7$ and at around 200° with quinaldine phosphate, while quinaldine tosylate seemed to have intermediate activity. Although $K_2S_2O_7$ and the conditions of run 8 produced the highest conversions of starting material at comparatively low temperature, the less acidic quinaldine phosphate appeared to give a higher proportion of 2-methoxyallyl chloride (**3a**). Addition of free quinaldine to the catalyst (run 4) made no discernible difference. Distillation of 1-chloro-2,2-dimethoxypropane (**5a**) under reduced pressure (bath temperature below 150°) in the presence of catalytic amounts of $H_2SO_4$ gave, aside from unchanged starting material **5a** (67%) and chloroacetone (**6a**) (16%), the desired 2-methoxyallyl chloride (**3a**) (10%) and **4a** (7%) (*cf.* also Table II, footnotes).

As regards the possible condenser types it would appear that a simple air condenser is more effective for pyrolysis than a Vigreux column, possibly because mixing of the components in the open tube will be minimized and recombination of methanol with the enol ether becomes less likely.

**2-Methoxyallyl Bromide (3b) and 1-Bromo-2-methoxypropene (4b) by Thermolysis of 1-Bromo-2,2-dimethoxypropane (5b).**—1-Bromo-2,2-dimethoxypropane (**5b**) was distilled for 2 hr under reduced pressure (bath temperature below 150°) and found to lose methanol readily, giving apart from starting material **5b** (53%), bromoacetone (**6b**) (12%), an unknown compound (6.3%), and the desired 2-methoxyallyl bromide (22%) and **4b** (7%).

**Interconversion of 2-Methoxyallyl Halides *via* Halide Ion Displacement in Acetone.**—2-Methoxyallyl chloride (**3a**) was dissolved in an excess of a saturated solution of LiBr in acetone and refluxed for *ca.* 6 hr. A 15% conversion into 2-methoxyallyl bromide (**3b**) occurred.

**2-Methoxyallyl Iodide (3c).**—A 50% solution (25 ml) of 2-methoxyallyl bromide (**3b**) and **4b** in $CCl_4$ was added dropwise at room temperature to an excess of a stirred saturated solution of NaI (40g) in acetone (400 ml). After 1 hr the mixture was washed with water (two 400-ml portions) and the lower dark brown layer separated and dried ($CaCl_2$). Swift distillation from mercury at reduced pressure gave a forerun of solvent and then a light yellow liquid [bp 18–20° (0.5–1 mm)] which proved to be pure 2-methoxyallyl iodide (**3c**) (2.5 ml, *ca.* 20% yield), mp −18 to −20°. **3c** is highly lachrymatory and decomposes

(17) Recently, Mr. C. Gatford has shown that **5a** can be pyrolyzed by dropwise addition to a mixture of catalyst in high-boiling solvent, *e.g.*, decalin (bp 189–196°). This method provides a convenient control of the pyrolysis and is more easily adaptable to a large-scale preparation.

rapidly at room temperature to give a thick black tar and was therefore stored at −80° in the dark.

**Registry No.**—**1**, 116-11-0; **2**, 128-08-5; **3a**, 32730-64-6; **3b**, 26562-24-3; **3c**, 32730-66-8; **4a**, 32730-67-9; **4b**, 26562-25-4; **4c**, 32730-69-1; **5a**, 32730-70-4; **5b**, 126-38-5; **5c**, 32730-72-6; **6a**, 78-95-5; **6b**, 598-31-2; **6c**, 3019-04-3; **7a**, 32827-44-4; **7b**, 32730-75-9; **7c**, 32730-76-0.

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# Alkaline Hydrolysis of Phosphoramidothioate Esters[1]

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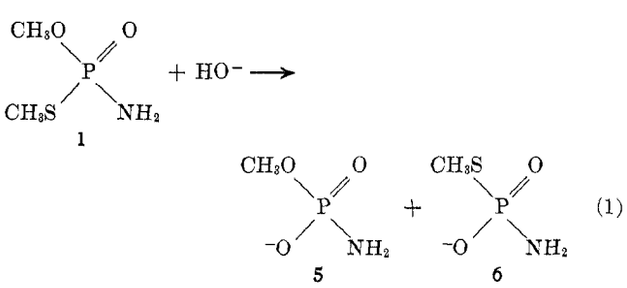
Products from the alkaline hydrolysis of *O*-methyl *S*-methyl phosphoramidothioate and its *N*-methyl and *N,N*-dimethyl derivatives were determined by analysis of pmr spectra and by glc. In aqueous potassium hydroxide *O*-methyl *S*-methyl phosphoramidothioate is hydrolyzed by P–O bond cleavage to give potassium *S*-methyl phosphoramidothioate as the major product while in the less polar solvents, methanol and acetone, P–S bond cleavage occurred to give mainly potassium *O*-methyl phosphoramidate. In ethanolic or propanolic potassium hydroxide the main products were potassium *O*-ethyl and *O*-propyl phosphoramidate, respectively, and dimethyl sulfide. Kinetic analysis showed that in water the second-order rate constants for P–O and P–S bond cleavage of *O*-methyl *S*-methyl phosphoramidothioate are 8.4 and 0.6 $M^{-1}$ $min^{-1}$, respectively. Both rate constants and the relative rates of P–O/P–S bond cleavage decreased markedly with sequential substitution of the amido protons with methyl groups, and the *N,N*-dimethyl derivative hydrolyzed virtually exclusively by P–S bond cleavage but at a rate some $10^3$ times slower than P–S cleavage in unsubstituted phosphoramidothioate. Exclusive P–S bond cleavage in the *N,N*-dimethylphosphoramidothioate evidently occurs by a normal concerted SN2 reaction in which the best leaving group departs. In phosphoramidothioates containing at least one amido proton the results are rationalized in terms of two competing processes, an addition–elimination reaction on phosphorus leading to P–O bond cleavage and an elimination reaction involving the amido proton to give P–S bond cleavage.

*O*-Methyl *S*-methyl phosphoramidothioate[2,3] (Monitor, Chevron Chemical Co.) is a relatively simple organophosphorus ester which is currently under development as a potential insecticide. Monitor or **1** is highly toxic to a variety of insects,[4] producing typical cholinergic symptoms of intoxication. In an earlier investigation[4] on the mode of action of **1** and related esters it was suggested that the alkylthiolate moiety was released when the cholinesterase enzyme was inhibited by the phosphoramidothioate ester. Subsequently, however, examination of the reaction between **1** and hydroxide ion has shown that methylthiolate ion is not always the major product but methoxide also is liberated, the relative amounts depending on the conditions of the reaction. Because of the possible connection between alkaline hydrolysis rates and anticholinesterase activity, an examination of the alkaline hydrolysis of **1** and its *N*-methyl (**2**) and *N,N*-dimethyl (**3**) analogs was initiated. Product and kinetic analyses were undertaken to sort out the various individual reactions and to assess quantitatively their relative importance in the overall hydrolysis reaction. Particular attention was given to the effect of sequential substitution of methyl groups on the nitrogen atom and of solvent on the specific rates of P–O and P–S bond cleavage.

## Results

**Products of Alkaline Hydrolysis.**—Pmr spectra of the products obtained from the hydrolysis of *O*-methyl *S*-methyl phosphoramidothioate (**1**) with equimolar amounts of potassium hydroxide in water and in 50% aqueous acetone showed that two monoanionic products were obtained, one by P–S cleavage giving *O*-methyl phosphoramidate anion (**5**) and the other by P–O cleavage giving *S*-methyl phosphoramidothioate anion (**6**). In water the major product obtained was **6**, since analysis of the pmr integrals for P–$OCH_3$ protons




(1)

(doublet centered at δ 3.7, $J$ = 11 Hz) and P–$SCH_3$ protons (doublet centered at δ 2.2, $J$ = 12 Hz) showed a ratio of **5**:**6** of 1:4.5. In 50% aqueous acetone, however, **5** was the major product, and the ratio of **5**:**6** in this case was 5.1:1. Support for the ratio of products obtained by integration of pmr spectra was provided by glc analysis after remethylation of the mixture of **5** and **6** with diazomethane. Remethylation of **5** and **6** gave dimethyl phosphoramidate (**4**), retention time 1.75 min, and **1**, retention time 3.50 min, respectively, and the ratio of these products was virtually identical with the ratio of **5**:**6** obtained by proton integration. Confirmation of product ratios by glc, therefore, allowed the use of pmr as the major means of product analysis.

Data for product analysis by pmr after alkaline hydrolysis of **1** in a variety of solvent systems are given in Table I. The results indicate that the solvent strongly influences the relative percentages of **5** and

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