Studies on Acid Iodides. IV. The Mechanism of Ether Cleavage

By Philip G. Stevens

Kishner[1] was the first to propose oxonium complex formation as a preliminary step in the cleavage of ethers by acid iodides. Little or no experimental evidence was advanced to support such a mechanism. A later study of this ether cleavage[2] indicated that some type of complex formation occurred, because on mixing acid iodides with ethers, appreciable amounts of heat were evolved. Further attempts to elucidate the nature of the reaction by following the conductivity of the reaction mixture, and by determining the rate of reaction, were inconclusive.[3] The rate study was complicated by side reactions; and the increase in conductivity, expected if an oxonium salt were formed, was not reproducible.

Several types of complexes could be formed. For example, there is the oxonium salt I, and its unionized counterpart II.

$$(R_2CH—O—COCH_3)^+I^-$$
I

$$R_2CH—O—COCH_3$$

(with R above and I below)

II
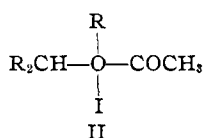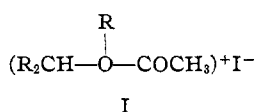
It is possible that other complexes actually may exist, which involve the carbonyl group, or hydrogen bonds, but it is difficult to see how the effective complex can be any other than I or II. No examples of either of these are known, but inasmuch as type II would be unlike known tetravalent oxygen compounds, and would require an expanded octet, the preferred complex is type I. This is supported by attempts to prepare these oxonium iodides, which lead to decomposition products exactly analogous to the cleavage products here.[4]

Increased knowledge of the mechanism of replacement reactions[5] has now made it possible to

show that the principal effective complex must be the oxonium salt I. Decomposition of this would be a case of S_N2, involving inversion. On the other hand, decomposition of complex II would be that of S_Ni, involving retention of configuration.[6] Actually cleavage of an optically active ether, d-methyl-s-hexyl ether, yielded an optically active iodide with the opposite sign of rotation, and of considerable rotatory power. This indicates that replacement has followed mainly a single course, that of inversion, and so must involve the oxonium salt. The cleavage with chloroacetyl iodide can be represented as follows.
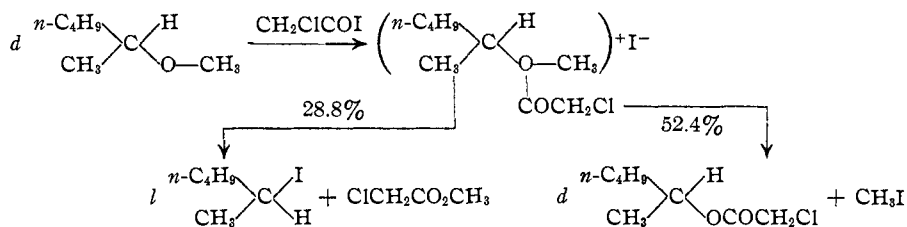
There is of course the possibility that a small part of the reaction proceeded by S_Ni via complex II. This question can best be decided by studying the cleavage of a tertiary ether with a caged structure,[7] where S_N2 cannot operate. Work in this direction is now in progress. Thanks are due to the Mallinckrodt Chemical Works for so generously donating the iodine used in this research.

Experimental Part

Cleavage of d-Methyl s-Hexyl Ether with Chloroacetyl Iodide.—12.3 grams of the ether, described elsewhere,[8] $\alpha^{23}D + 7.63°$, was treated with 23 g. of freshly distilled chloroacetyl iodide, b. p. 41–43° (10 mm.). After seventeen days at 20–25° in the dark in a sealed ampule, the reaction mixture was poured into ice water, and shaken with aqueous sodium bicarbonate containing a little bisulfite. There was very little acid present, indicating that the reaction was practically complete. After drying over anhydrous potassium carbonate, the mixture was fractionally distilled at 3 mm. through a 60-cm. reflux column packed with glass helices. The s-hexyl iodide, red with iodine, boiled

(1) Kishner, J. Russ. Phys.-Chem. Soc., 41, 651 (1909). Compare Meerwein and Maier-Hüser, J. prakt. Chem., 134, 51 (1932).

(2) Gustus and Stevens, THIS JOURNAL, 55, 378 (1933).

(3) Stevens, unpublished results.

(4) Meerwein, Hinz, Hofmann, Kroning and Pfeil, J. prakt. Chem., 147, 257 (1936).

(5) Coudrey, Hughes, Ingold, Masterman and Scott, J. Chem. Soc., 1252 (1937).

(6) The only essential difference between this case and those advanced by Ingold and co-workers (loc. cit.) is that in the former the entering atom is once removed from the receiving carbon atom, and in the latter twice removed.

(7) Bartlett and Knox, THIS JOURNAL, 61, 1630 (1939).

(8) Stevens and Deans, Can. J. Research, 17, 290 (1939).

at 22–27°, weight 6.5 g. This was shaken with mercury until colorless, and then redistilled, taking the fraction b. p. 45.0–45.6° (9 mm.), 3.8 g., α^{23}D −19.42°, n^{25}D 1.4878. The s-hexyl chloroacetate, crude yield 9.9 g., boiled at 80.0–80.3° (9 mm.), α^{23}D +8.06°, n^{25}D 1.4235, d^{25}_4 1.0212. The lower boiling products were collected in appropriately cooled traps and identified as methyl iodide, b. p. 42–43°, and methyl chloroacetate, b. p. 129–130°, contaminated with a little olefin. The yields of s-hexyl iodide and chloroacetate, 28.8 and 52.4%, indicated that the cleavage proceeded approximately one-third to the hexyl iodide, and two-thirds to the hexyl chloroacetate. The activity of the hexyl iodide, had optically pure carbinol been used to prepare the ether, would have been α^{23}D −26.6°, $(M)^{23}$D −39.6°. This value is about 50% of that reported by

Pickard and Kenyon,[9] using the optically pure carbinol and hydrogen iodide. The lower activity found here may be due to racemization by the iodide ion, and/or to decomposition of complex II by S_Ni.

Summary

1. Cleavage of d-methyl s-hexyl ether with chloroacetyl iodide yields l-s-hexyl iodide.

2. The mechanism of ether cleavage has thus been shown to proceed mainly through an ionized oxonium salt.

(9) Pickard and Kenyon, J. Chem. Soc., **99**, 45 (1911).

Semiquinones of Oxazines, Thiazines and Selenazines

By S. Granick, L. Michaelis and Maxwell P. Schubert

1. After it had been shown[1] that thionine and methylene blue yield free semiquinone radicals on partial reduction, a more systematic study of the dyestuffs of this class was suggestive. It will be shown in this paper that its various representatives vary greatly with respect to the magnitude of the formation constant and the optical properties of the semiquinone. The investigations were extended over suitable representatives not only of thiazines, but also oxazines and selenazines. The better known dyestuffs with two auxochromic amino groups such as methylene blue were compared with those containing only one, either an amino or a hydroxy group. The experiments will show that all of these compounds easily form semiquinones under similar conditions as does thionine, namely, in sufficiently acid solution. In part the separation of the two steps of oxidation is very distinct even in weakly acid solutions, especially for 3-hydroxythiazine and 3-hydroxyoxazine. In these two compounds, on increasing the acidity, it is easy to reach the value 10^{+6} for the semiquinone formation constant, by far the largest constant of this type encountered as yet. All these semiquinones show a characteristic absorption spectrum in the visible range of wave lengths. There are two types of absorption spectra: either there is one rather intense and sharp band; or there is such a complicated series of bands as recently described for thionine and

methylene blue. It is not yet possible to correlate the chemical structure with the type of absorption spectrum. In every case the spectrum of the semiquinone is quite different from that of the quinonoid form of the dye. The high stability of those radicals, often largely exceeding that of the thionine radical under comparable conditions, was rather unexpected from the theoretical point of view as tentatively adopted in the previous paper, and will be commented on in the discussion.

2. **Material.**—The nomenclature of these dyestuffs is rather cumbersome. Bernthsen's nomenclature as applied in his classical papers is not systematic enough to cover derivatives in addition to those investigated by him. The nomenclature of the leuco compounds is always quite easy, so we recommend using always the name of the leuco dye. The prefix "pheno" in phenothiazine, phenoxazine or phenoselenazine may be omitted. Whenever it is necessary to distinguish the leuco compounds from their oxidation products, we add the prefix r-, s- or t-, to distinguish the reduced form, the semi-oxidized or semiquinone form, and the totally oxidized or quinonoid form. For instance, thionine then is t-3,9-diaminothiazine, and when no misunderstanding arises the t- is omitted. The numbering of the skeleton as shown is the customary one. "X" stands for O in oxazine, for S in thiazine, and for Se in selenazine

(1) L. Michaelis, M. P. Schubert and S. Granick, This Journal, **62**, 204 (1940).