

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39, MASS.]

## The Specificity of the Electron-Impact Induced Elimination of Water from Alcohols and Related Reactions in the Mass Spectrometer<sup>1</sup>

BY WOLFGANG BENZ AND K. BIEMANN

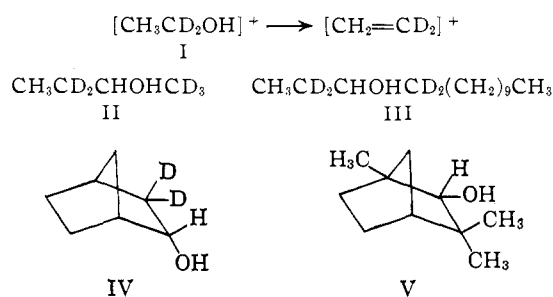
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A series of aliphatic alcohols (*n*-butyl through *n*-heptyl) with a CD<sub>2</sub> group in consecutive positions (C-1 through C-5) from the hydroxyl group has been synthesized. Their mass spectra indicate that the elimination of the elements of water which leads to the (M - 18)<sup>+</sup> ion in the undeuterated alcohols involves almost exclusively (*ca.* 90%) a hydrogen atom at C-4, the remainder coming from C-3 and C-5. The elimination of water from fragment ions of tertiary alcohols is less specific. The loss of acetic acid from *n*-alkyl acetates (to give a peak at M - 60) involves the hydrogens at C-2 and C-3 (to about 55 and 45%, respectively). The additional hydrogen required for the formation of the ion of mass 61 (CH<sub>3</sub>COOH<sub>2</sub><sup>+</sup>) seems to be abstracted rather unspecifically from all other carbons of the alkyl chain of the alcohol moiety.

The mass spectra of a large number of alcohols have been reported during the past decade, either in the form of a more or less comprehensive investigation of the spectra of this group or in connection with the discussion of the spectra of other compounds containing a hydroxyl group. In addition to an earlier paper by Collin<sup>2</sup> on the mass spectra of a few primary alcohols, Friedel, Shultz, and Sharkey have discussed<sup>3</sup> the spectra of sixty-nine aliphatic primary, secondary, and tertiary alcohols containing one to eleven carbon atoms.

One of the seemingly simplest and very characteristic fragmentation processes of alcohols is the elimination of water and formation of a C<sub>n</sub>H<sub>2n</sub>- ion, which is most prominent in primary alcohols, while in secondary and tertiary aliphatic alcohols the cleavage of the carbon-carbon bond next to oxygen is a competing reaction and the elimination of water is thus less significant. This competition is less pronounced in alicyclic alcohols, and the M - 18 peak is, therefore, easily recognized in most alicyclic hydroxyl compounds. The facile elimination of water combined with the low abundance of the molecular ion of most alcohols can even lead to misinterpretations in the determination of the molecular weight of compounds of this type, which may appear to be 18 mass units lower.

It has been generally assumed<sup>3</sup> that the elimination of water from an alcohol involves simply the formation of the corresponding olefin ion, *i.e.*, a 1,2-elimination.



This assumption was based—in addition to the obvious simplicity of such a process and its analogy to the chemical dehydration reactions—mainly on Momigny's report<sup>4</sup> that ethanol-1,1-*d*<sub>2</sub> (I) eliminates H<sub>2</sub>O rather than HDO and the observation that the olefin-type

peaks (C<sub>n</sub>H<sub>2n</sub>, C<sub>n</sub>H<sub>2n-1</sub>, C<sub>n</sub>H<sub>2n-3</sub>, etc.) in the spectra of primary unbranched alcohols, such as 1-pentanol, resemble in approximate relative intensity the corresponding peaks in 1-pentene.<sup>3</sup> These findings have, however, no bearing on the general mechanism of the elimination of water from primary alcohols as the lack of a long side chain in ethanol forces this molecule to undergo a 1,2-elimination, and the well known similarity of the mass spectra of isomeric olefins differing only in the position of the double bond makes the second argument equally uncertain.

On the contrary, there is definite indication that the hydrogen abstracted comes from a carbon atom which is not β to the hydroxyl group. McFadden<sup>5</sup> found that 2-butanol-1,1,1,3,3-*d*<sub>5</sub> (II) does not exhibit an M - 19 peak and, therefore, does not eliminate HDO. While the peak at M - 18 is, in that case, obscured by the loss of CD<sub>3</sub> which also corresponds to eighteen mass units, the peak corresponding to M - H<sub>2</sub>O is, in fact, observed in the mass spectrum of 3-tetradecanol-2,2,4,4-*d*<sub>4</sub> (III), a molecule in which the loss of the alkyl group does not interfere.<sup>6</sup> For the case of the 1-butanols, a 1,4-elimination had been suggested,<sup>5</sup> and a very recent paper<sup>7</sup> that appeared after completion of our work presents experimental evidence in support of this suggestion. Almost identical results were reported simultaneously from another laboratory.<sup>8</sup> In both instances 1-butanol partially deuterated at C-4 was employed.

Cyclic alcohols also seem not to undergo 1,2-elimination of water as indicated by the mass spectrum of 1-norborneol-2,2-*d*<sub>2</sub> (IV), which eliminates H<sub>2</sub>O rather than D<sub>2</sub>O and the finding that fenchyl alcohol (V), while lacking any β-hydrogens, also eliminated water to a considerable extent. In a recent short communication<sup>8</sup> labeling experiments were presented in evidence of the absence of 1,2-elimination in cyclohexanols.

A detailed knowledge of the process of elimination, such as its specificity with respect to the abstraction of hydrogen from one or more carbon atoms as contrasted to a random process, is of interest not only as an extension of our understanding of the electron-impact induced fragmentation of organic molecules, but also to provide a firmer basis for certain applications of mass spectrometry. Thus, in the determination of the

(1) Paper XVIII on the Application of Mass Spectrometry to Structure Problems. Part XVII: K. Biemann, P. Bommer, A. L. Burlingame, and W. J. McMurray, *Tetrahedron Letters*, No. 28, 1969 (1963).

(2) J. Collin, *Bull. soc. chim. Belges*, 63, 500 (1954).

(3) R. A. Friedel, J. L. Shultz, and A. G. Sharkey, *Anal. Chem.*, 28, 940 (1956).

(4) J. Momigny, *Bull. soc. roy. sci. Liege*, 24, 111 (1955).

(5) W. H. McFadden, M. Lounsbury, and A. L. Wahrhaftig, *Can. J. Chem.*, 36, 990 (1958).

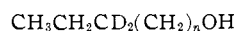
(6) See K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 110.

(7) W. H. McFadden, D. R. Black, and J. W. Corse, *J. Phys. Chem.*, 67, 1517 (1963).

(8) C. G. MacDonald, J. S. Shannon, and G. Sugowdz, *Tetrahedron Letters*, 13, 807 (1963).

amount of deuterium in a labeled alcohol, for example, one can make use of the  $M - H_2O$  peak only if the location of the abstracted hydrogen atom is known with certainty. Similarly, the presence of an  $M - 18$  peak in an alcohol does not necessarily exclude a structure in which all carbon atoms  $\beta$  to the hydroxyl group are fully substituted, as long as 1,2-elimination is not fully and generally established as the sole process leading to the  $(M - H_2O)^+$  ion.

For these reasons we have investigated the course of the elimination of water from the molecular ion of a number of aliphatic, unbranched, primary alcohols, using molecules specifically labeled with deuterium at consecutive carbon atoms. The series 1-butanol-2,2- $d_2$  (VI), 1-pentanol-3,3- $d_2$  (VII), 1-hexanol-4,4- $d_2$  (VIII), and 1-heptanol-5,5- $d_2$  (IX) were chosen for a number of reasons.



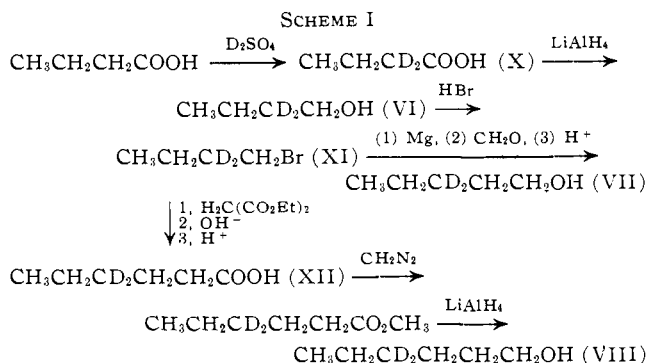
VI,  $n = 1$ ; VII,  $n = 2$ ; VIII,  $n = 3$ ; IX,  $n = 4$

First, it was considered important to have available a carbon chain which extends beyond the labeled position to avoid an apparent specificity of the hydrogen abstraction process caused by the lack of another possibility<sup>9</sup>; two additional carbon atoms were thought to be sufficient as this provides for at least one very similar group ( $CH_2$ ) beyond the labeled one ( $CD_2$ ). A methyl group alone might conceivably lead to less conclusive results if primary hydrogens were abstracted more or less easily than secondary ones.

Secondly, completely labeled methylene groups ( $CD_2$ ) were incorporated, rather than partially labeled ones ( $CHD$ ), to avoid any uncertainty in the interpretation of the results due to a possible isotope effect in the abstraction of hydrogen.<sup>10</sup>

Thirdly, the series VI through IX could be synthesized most economically from its smallest member, VI, by stepwise chain extension.

The syntheses (outlined in Scheme I) follow conventional steps which, however, are sometimes complicated by the small scale on which some of the later reactions had to be carried out. Gas chromatography was used to purify the final products and some of the intermediates. Because of the many steps involved, a sizable amount of starting material, *n*-butyric acid-2,2- $d_2$  (X),



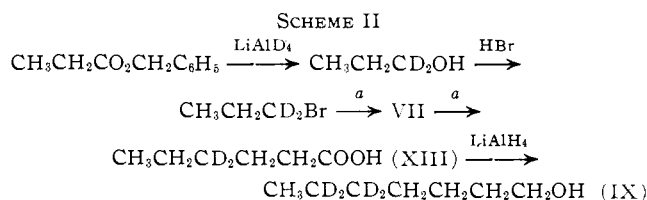
(9) The experiments published in the meantime<sup>11</sup> using 1-butanol incompletely labeled at C-4 are valid, *a priori*, only for butanol and do not exclude the abstraction of hydrogen from a carbon atom beyond C-4 in higher aliphatic alcohols.

(10) The differences in the ratios of 1,3-elimination *vs.* 1,4-elimination (20:80) reported in the case of butanol<sup>11</sup> and those of our work (6:90) may be due to this effect, in addition to errors involved in subtracting the contributions due to less highly labeled material ( $\geq 83\% d_1$ ,  $\leq 17\% d_0$ , and  $56\% d_3$ ,  $17\% d_2$ ,  $5\% d_1$ ,  $21\% d_0$ ,<sup>8</sup> respectively, at C-4; the values for ref. 7 are taken from the n.m.r. data in Table I therein).

had to be used. It was prepared by acid-catalyzed exchange of the  $\alpha$ -hydrogens with  $D_2SO_4$ <sup>11</sup> employing eight consecutive equilibrations.

From the mass spectrum of the resulting butyric acid it could be concluded<sup>12</sup> that it consisted of 95.5%  $d_2$ , 4%  $d_1$ , and 0.5%  $d_0$  species. Thus, all the alcohols synthesized from this precursor, namely, VI, VII, and VIII, have the same label distribution at the appropriate carbon atom. The mass spectra taken of some of the intermediates in the syntheses confirmed the expected retention of deuterium.

The amounts of VIII obtained proved insufficient for the preparation of even a small quantity of pure IX, which thus had to be prepared from new starting material. This time the route depicted in Scheme II was chosen.<sup>14</sup> The first step there appears to be more expensive but is much less time consuming than the repeated equilibration of butyric acid employed in the sequence described first.



<sup>a</sup> Malonic ester condensation involving steps analogous to those outlined for the conversion of XI  $\rightarrow$  VIII (Scheme I).

Having thus available the specifically deuterated alcohols VI-IX, their mass spectra were determined along with those of the unlabeled analogs. As we are mainly concerned with the fragment formed on elimination of water, only the regions between  $M - 15$  and  $M - 20$  of these spectra are shown in Table I. It clearly can

TABLE I  
PARTIAL MASS SPECTRA OF ALCOHOLS

	<i>m/e</i>	54	55	56	57	58	59	60
1-Butanol		0.9	16.2	100	9.6	0.4		
1-Butanol-2,2- $d_2$ (VI)				3.5	20.0	100	6.5	1.0
	<i>m/e</i>	68	69	70	71	72	73	74
1-Pentanol		0.1	13.5	100	6.9	0.1		
1-Pentanol-3,3- $d_2$ (VII)				6.8	11.3	100	7.0	1.0
	<i>m/e</i>	82	83	84	85	86	87	88
1-Hexanol		2.8	23.8	100	31.3	2.4	1.3	
1-Hexanol-4,4- $d_2$ (VIII)		2.2	4.8	17.2	100	18.2	25.2	2.0
	<i>m/e</i>	96	97	98	99	100	101	102
1-Heptanol		3.0	21.8	100	9.5	2.2	2.0	
1-Heptanol-5,5- $d_2$ (IX)				11	26	100	14	4

be seen that the masses of these fragments are increased by two mass units in the case of VI, VII, and IX, indicating retention of the deuterium in these species; on the other hand, in the deuterated hexanol VIII the peaks are displaced mainly one mass unit, indicating 1,4-elimination. Careful comparison of the spectra of the two pentanols and of the two heptanols reveals a small amount of HDO elimination in both cases. From the intensities of all these peaks, one can conclude (see Table II) that the hydrogens at C-3 are involved to 6%; those at C-4 to 90%; and those at C-5 to 5% in the elimination of water from the molecular ion. Thus,

(11) V. N. Setkina and E. V. Bykova, *Dokl. Akad. Nauk SSSR*, **92**, 341 (1953); *cf. Chem. Abstr.*, **49**, 164c (1955).

(12) Determined from the rearrangement peak (at  $m/e = 60$  in nondeuterated butyric acid) due to the elimination of  $C_2H_4$  (C-3 and C-4). The validity of this approach is supported by earlier experiments in our laboratory<sup>12</sup> using specifically deuterated butyric acids.

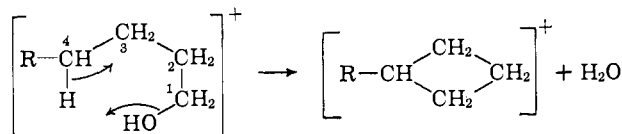
(13) Reference 6, pp. 120-121 and 190.

(14) The deuterium content of the propanol and the products derived therefrom was  $>99\% d_2$  as determined on the intermediate bromopentane-1.

TABLE II  
ELIMINATION OF HDO FROM DEUTERATED ALCOHOLS

	1,2-	1,3-	1,4-	1,5- Elimination
1-Butanol-2,2- $d_2$ (VI), %	<1			
1-Pentanol-3,3- $d_2$ (VII), %		6( $\pm$ 2)		
1-Hexanol-4,4- $d_2$ (VIII), %			90( $\pm$ 1)	
1-Heptanol-5,5- $d_2$ (IX), %				5( $\pm$ 2)

it seems that the most favorable path for this elimination involves an arrangement of the chain in such a manner that the hydroxyl oxygen and one hydrogen at C-4 achieve the geometry of a six-membered ring, as suggested previously.<sup>5</sup>



The data presented are compatible with the assumption that in 6% of the molecular ions the transfer involves specifically a hydrogen directly from C-3, and in 5% of the cases the hydrogen from C-5. However, the possibility has to be considered that, in about 10% of all molecular ions, migration of hydrogen to neighboring carbon atoms may take place before fragmentation. Thus the apparent 1,3-elimination observed in the spectrum of VII could conceivably be due to the abstraction of deuterium from C-4 where it has migrated from C-3. At least one rearrangement involving the abstraction of hydrogen from an alkyl chain has been investigated by extensive labeling experiments,<sup>15</sup> namely, the rearrangement in esters, and this process was shown to be highly specific, in that case ruling out the rearrangement of hydrogen atoms along an alkyl chain before that particular fragmentation process takes place. Any such analogy is somewhat weak as the energy requirements and rate constants of the two processes compared might be quite different. The possibility of such hydrogen migration must, nevertheless, always be considered when relative ratios of competing processes are estimated on the basis of the mass spectra of deuterium-labeled substances. Nevertheless, we believe that it is least probable to occur prior to the fragmentation of molecular ions of saturated molecules, but may be much more prevalent for molecular ions of unsaturated substances, or for fragment ions as hydrogen migration to carbon is facilitated if that carbon atom is part of a double bond or bears a positive charge.

This leads us to another problem, namely, the course of the elimination of water from *fragment ions* of alcohols still containing the hydroxyl group, as such ions are also capable of elimination of water in a second step. Preliminary experiments, using tertiary alcohols such as 2-methyl-2-hexanol-4,4- $d_2$  (XI) and 2-methyl-2-heptanol-5,5- $d_2$  (XII), have shown that the elimination of water from the  $(M - CH_3)^+$  ion is much less specific (about 30% each 1,3- and 1,4-elimination). This is in contrast with the high specificity (1,4-elimination) in the case of the molecular ion of the primary alcohols described earlier in this paper and points out that the mechanism of a seemingly identical process (*i.e.*, the

(15) Ng, Dinh-Hguyen, R. Ryhage, S. Stållberg-Stenhagen, and E. Stenhagen, *Arkiv Kemi*, **18**, 393 (1961); see also ref. 6, pp. 120 and 121.

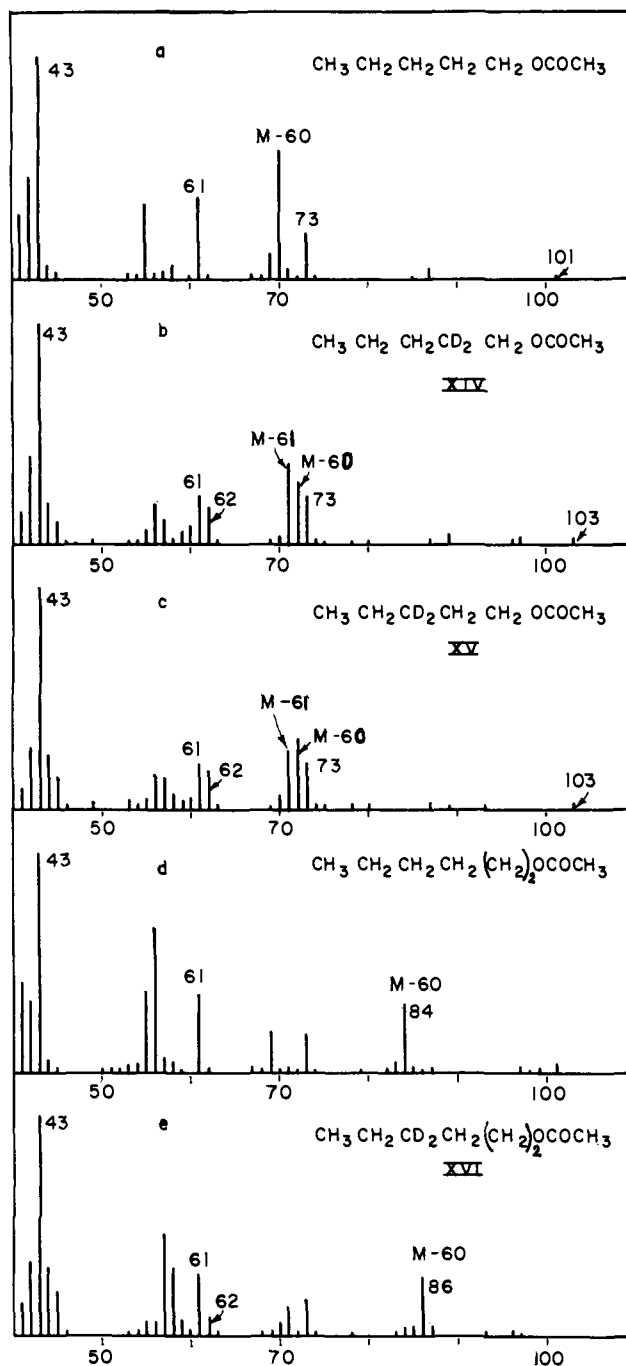
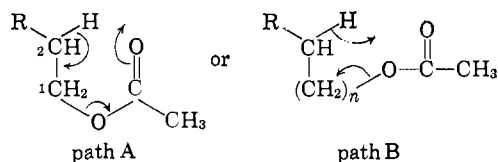


Fig. 1.—Partial mass spectra of (a) 1-pentyl acetate, (b) 1-pentyl-2,2- $d_2$  acetate (XIV), (c) 1-pentyl-3,3- $d_2$  acetate (XV), (d) 1-hexyl acetate, and (e) 1-hexyl-4,4- $d_2$  acetate (XVI).

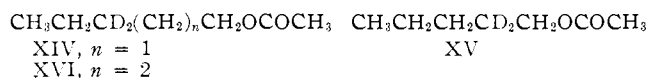
elimination of  $H_2O$  from hydroxyl-containing compounds) might be quite different if it occurs in a fragment ion. Whether the elimination follows here, in fact, more than one path or whether it is preceded by hydrogen migration, is presently difficult to decide.

Another apparent analogy to the elimination of water from primary alcohols is the elimination of acetic acid from 1-alkyl acetates. The availability of the deuterated primary alcohols mentioned above prompted us to determine the spectra of some of the corresponding esters. Complications are to be expected in such cases, as the elimination can involve either abstraction of a hydrogen atom from C-2 by the carbonyl oxygen of the ester grouping (path A) in addition to abstraction

of hydrogen from the alkyl chain by the ether oxygen (path B)



*n*-Pentyl-2,2-*d*<sub>2</sub> acetate (XV), *n*-pentyl-3,3-*d*<sub>2</sub> acetate (XIV), and *n*-hexyl-4,4-*d*<sub>2</sub> acetate (XVI) were prepared by acetylation of the corresponding alcohols and their mass spectra determined (Fig. 1).



The results (Table III) indicate loss of hydrogen from C-2 to be 55% while hydrogen at C-3 is involved to 45%. In agreement with this, the spectrum of XVI indicates that the hydrogens at C-4 are not involved in the elimination of acetic acid. While the "1,2"-elimination would be predicted in analogy to the high specificity of this type of reaction and has been suggested previously,<sup>16</sup> the extent of 1,3-elimination and the complete retention of hydrogen at C-4 (in contrast to the alcohols themselves) is surprising. Path B must thus involve the formation—at least formally—of an alkylcyclopropane, *i.e.*,  $n = 2$ .

TABLE III  
ELIMINATION OF CH<sub>3</sub>COOD FROM DEUTERATED ALKYL  
ACETATES

Acetate	1,2-	1,3-	1,4-Elimination
<i>n</i> -Pentyl-2,2- <i>d</i> <sub>2</sub> (XIV), %	55(±3)		
<i>n</i> -Pentyl-3,3- <i>d</i> <sub>2</sub> (XV), %		45(±3)	
<i>n</i> -Hexyl-4,4- <i>d</i> <sub>2</sub> (XVI), %			0

The elimination of acetic acid from acetates leads always to an  $(M - 60)^+$  ion rather than  $(\text{CH}_3\text{COOH})^+$  and a peak at  $m/e$  60 is thus not observed. Only if the acetic acid moiety abstracts in addition another hy-

(16) F. W. McLafferty, *Anal. Chem.*, **31**, 82 (1959).

drogen (*i.e.*, transfer of a total of 2H to the CH<sub>3</sub>COO-group) is a species with a sufficiently stabilized positive charge obtained, namely an acetyloxonium ion, CH<sub>3</sub>CO<sub>2</sub>H<sub>2</sub><sup>+</sup> of mass 61. From the distribution of the peaks at  $m/e$  61 and 62, one can conclude that the abstraction of the first hydrogen follows the same path as the elimination of acetic acid when leading to the  $(M - 60)^+$  ion. The second hydrogen required for the formation of  $m/e$  61 is neither removed from the same carbon atom as the first one (no significant peak at  $m/e$  63) nor is it derived exclusively from C-4. Random abstraction is in best agreement with the mass spectrum of XV (Fig. 1).

This result is in qualitative agreement with earlier conclusions<sup>17</sup> concerning the elimination of CH<sub>3</sub>CO-OH<sub>2</sub><sup>+</sup> from *sec*-butyl-3,3-*d*<sub>2</sub> acetate. More recently, however, a selective transfer of one hydrogen at C-3, followed by a randomly selected hydrogen had been suggested.<sup>18</sup> These conclusions were based on the mass spectrum of *n*-butyl-3-*d*<sub>1</sub> acetate alone and without having available the derivative deuterated at C-2, which renders such an interpretation less reliable.

### Experimental

All mass spectra were determined with a CEC 21-103C mass spectrometer, equipped with a heated inlet system (170°). Ionizing voltage 70 e.v. Gas chromatographic separations were performed with either SE 30 or Apiezon L as a liquid phase.

The syntheses of the deuterated compounds is mentioned in principle in the theoretical part of this paper and follows conventional steps except that specifically deuterated reagents were used. Their more detailed description was omitted on suggestion of the referee. All products were identified by comparison of gas chromatographic retention times with that of authentic samples. Specimens for mass spectra were purified by gas chromatography.

**Acknowledgment.**—We are indebted to the Petroleum Research Fund of the American Chemical Society for financial support (Grant No. 625).

(17) F. W. McLafferty and M. C. Hamming, *Chem. Ind. (London)*, 1366 (1958).

(18) D. R. Black, W. H. McFadden, and J. W. Corse, Symposium on Mass Spectrometry, 11th Annual Conference on Mass Spectrometry and Allied Topics, San Francisco, Calif., May, 1963.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENTS OF THE UNIVERSITIES OF KANSAS, LAWRENCE, KAN., AND MASSACHUSETTS, AMHERST, MASS.]

## Mechanisms of Substitution Reactions at Phosphorus. X. The Wittig Reaction and the Decomposition of Quaternary Phosphonium Hydroxides

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An optically active, noncyclic quaternary phosphonium salt in which the phosphorus atom is the sole center of asymmetry has been prepared. This compound, methylethylphenylbenzylphosphonium iodide (I), undergoes a stereospecific reaction with sodium hydroxide to produce toluene and methylethylphenylphosphine oxide (VII). Arguments and experimental data are presented to show that the phosphorus atom undergoes inversion of configuration in this reaction. Also, the choice of possible mechanisms is reduced to a small number by the stereochemical and kinetic data. The Wittig reaction, with benzaldehyde, of the ylid derived from optically active I has also been found to be stereospecific, and arguments are advanced as to why this reaction should take place with retention of configuration of the phosphorus atom.

In previous communications we have reported: (1) the successful resolution of methylethylphenyl-

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benzylphosphonium iodide (I),<sup>3</sup> (2) the stereospecific reaction of this salt with sodium hydroxide to give methylethylphenylphosphine oxide (VII) and toluene,<sup>4</sup>

(3) K. F. Kumli, C. A. VanderWerf, and W. E. McEwen, *J. Am. Chem. Soc.*, **81**, 248 (1959).