uum at room temperature, the residue taken up in ether, and the solution washed with 1 *N* hydrochloric acid and water and dried. Evaporation gave 37 mg. of an oil which showed three spots on thin layer chromatography. Chromatography of the mixture on activity II neutral alumina (18 g.) using 5% benzene in hexane separated the first component (16 mg., m.p. 91.5–94°) from the other two products (8 mg.) which were eluted together as an oil. The first component, $\Delta^{17(20)}$-cholestan-16-one (XXVIIIa), was recrystallized quickly from methanol in subdued light, whereupon it melted at 97.5–98°, $\lambda_{max}^{CHCl_3}$ 5.90 and 6.21 μ; $\lambda_{max}^{cyclohexane}$ 250 mμ, ϵ 11,600.

Anal. Calcd. for $C_{27}H_{44}O$: mol. wt., 384.6. Found: mol. wt., 384 (mass spec.).

The oily mixture exhibited a very similar mass spectrum as compared to that of the crystalline isomer XXVIIIa and exhibited $\lambda_{max}^{CHCl_3}$ 5.79, 5.90, and 6.21 μ. Dehydrobromination of a mixture of XXVIIa and b gave essentially the same results. In order to obtain the other geometric isomer XXVIIIb in a pure state, 46 mg. of XXVIIIa was dissolved in 10 ml. of hexane and the solution exposed (using an aluminum foil reflector) to direct sunlight for 1 hr. The resulting mixture was chromatographed in subdued light on 20 g. of activity II neutral alumina, using 10 and 20% benzene in hexane as eluent. First there was eluted 31 mg. of recovered XXVIIIa, followed by 13 mg. of a homogeneous (thin layer chromatography) oil (XXVIIIb), which exhibited $\lambda_{max}^{CHCl_3}$ 5.90 and 6.21 μ, $\lambda_{max}^{cyclohexane}$ 248 mμ, ϵ 12,100, as well as a mass spectrometrically determined molecular ion peak at *m/e* 384.

Reduction of the Isomeric $\Delta^{17(20)}$-Cholestan-16-ones (XXVIIIa and b).—Pure $\Delta^{17(20)}$-cholestan-16-one (XXVIIIa, 50 mg.) in 15 ml. of cyclohexane was hydrogenated at 22° for 1 hr. in the presence of 25 mg. of 10% palladium-on-charcoal. The solution was filtered and evaporated, leaving a crude product, m.p. 53–56°. Recrystallization from methanol gave pure 20α-cholestan-16-one (XXIIIa), m.p. 58–59°. Sometimes another polymorphic form was obtained, m.p. 70–71°. In either case, the melting point was not depressed when mixed with the sample of XXIIIa prepared from zinc dust reduction of XXVIIa or from chromatography of the 1,4 Grignard addition reaction to XII. In each case, the R_f values (thin layer chromatography) of XXVIIa from the different sources were identical, and not as high as for XXVIIb.

An identical catalytic reduction of the oily α,β-unsaturated ketone (XXVIIIb) gave material, m.p. 89.5–92°, after recrystallization from methanol. Its m.p. was not depressed (91–94°) on admixture with XXIIIb prepared by the zinc dust reduction of XXVIIb (above), and the R_f values of XXIIIb from these sources were identical with each other, but higher than that of XXIIIa. A mixture of XXIIIa and b showed a marked melting point depression (48–63°).

A small-scale lithium in liquid ammonia reduction of XXVIIIa in tetrahydrofuran gave a mixture of XXIIIa and b (as judged by thin layer chromatography), with the 20α-isomer XXIIIb predominating; infrared spectroscopy indicated that there was no unreacted α,β-unsaturated ketone present.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY, STANFORD, CALIF.]

Mass Spectrometry in Structural and Stereochemical Problems. XLI.[1] Isotope Effect in Hydrogen Rearrangement Processes: The Mass Spectra of Methyl Butyrate and Its γ-Mono-, Di-, and Trideuterio Analogs

BY D. H. WILLIAMS, H. BUDZIKIEWICZ, AND CARL DJERASSI

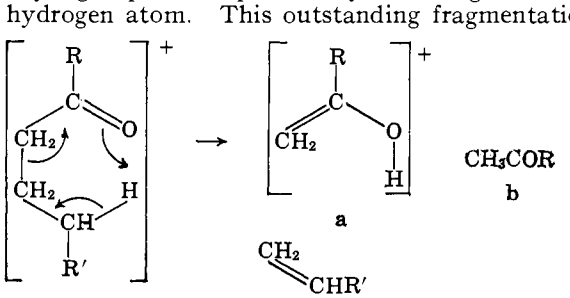
RECEIVED AUGUST 5, 1963

The mass spectra of methyl butyrate and its γ-mono-, di-, and trideuterio analogs have been measured and an isotope effect corresponding to a transfer of 0.88 atom of deuterium per atom of hydrogen in a specific rearrangement process has been observed. This effect is probably also operative in many related γ-hydrogen rearrangements observed in mass spectrometry.

The usefulness of deuterium-labeling of organic molecules for gaining insight into fragmentation and specially rearrangement processes under electron impact has been demonstrated frequently, some recent examples being provided by fatty acids[2] and steroids.[3] In some cases, hydrogen transfer reactions are straightforward and involve the shift of only one specific hydrogen atom, whereupon they can be followed easily in the deuterated analogs. In other instances, one specific fragmentation process involves a complex series of different hydrogen rearrangements (*e.g.*, 11-keto steroids[4]), and for the elucidation of such fragmentations, quantitative measurements of deuterium transferred from different positions is necessary.

It has been shown that deuterium is less easily split off from hydrocarbons than is hydrogen,[5] and that in the loss of water from cyclic ketones[6] or cyclohexanol[1] discrimination against deuterium takes place. No isotope effect is usually taken into consideration for cyclic transition states,[3] mainly because no relevant data are available. It seemed of importance, therefore, to investigate this problem in a specific, well-defined mechanism, which would allow, if possible, wide generalization.

One of the most important fragmentation processes of aliphatic carbonyl compounds (ketones,[7] aldehydes,[8] esters[9]) is cleavage of the carbon–carbon bond β to the carbonyl group accompanied by rearrangement of one hydrogen atom. This outstanding fragmentation



process was soon subject to many investigations. Thus Beynon[10] pointed out that this rearrangement must be energetically very favorable since it can be observed at low energies where hydrogen rearrangement processes are usually not observed. By labeling the carboxyl group of butyric acid with ^{13}C it could be demonstrated[11] that the fragment in question definitely retains this carbon atom. McLafferty[12] was the first to suggest that the genesis of this cleavage product involves a six-membered transition state in which a γ-hydrogen atom is transferred to oxygen. Appearance potential measurements of the rearrangement ion are in agree-

(1) Paper XL: H. Budzikiewicz, Z. Pelah, and C. Djerassi, *Monatsh.*, in press.

(2) N. Dinh-Nguyen, R. Ryhage, S. Ställberg-Stenhagen, and E. Stenhagen, *Arkiv Kemi*, **18**, 393 (1961).

(3) C. Beard, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 269 (1964), and references cited therein.

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(5) F. H. Field and J. L. Franklin, "Electron Impact Phenomena," Academic Press, Inc., New York, N. Y., 1957, Chapter 5.

(6) E. Lund, H. Budzikiewicz, J. M. Wilson, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 941 (1963).

(7) A. G. Sharkey, J. L. Shultz, and R. A. Friedel, *Anal. Chem.*, **28**, 934 (1956).

(8) J. A. Gilpin and F. W. McLafferty, *ibid.*, **29**, 990 (1957).

(9) R. Ryhage and E. Stenhagen, *Arkiv Kemi*, **13**, 513 (1959).

(10) J. H. Beynon, "Mass Spectrometry and its Application to Organic Chemistry," Elsevier Publishing Co., New York, N. Y., 1960, p. 356.

(11) G. P. Hap and D. W. Stewart, *J. Am. Chem. Soc.*, **74**, 4404 (1952).

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

ment with the formation of a positively charged enol (a) rather than the isomeric oxo structure (b).[13] The final proof for this mechanism was given by measuring the mass spectra of fatty acid esters deuterated in all possible positions (long chain acid methyl esters[2,14] and ethyl butyrate[15]), which indicated that only one γ-hydrogen is transferred in this fragmentation process, and that the hydrogens bound to the α- and β-carbon atoms are completely retained. Since the same explanation has been offered for analogous cleavage processes in olefins,[16] alkylbenzenes,[17] phenyl ethanols,[18] aryl ethers,[12] amides,[19] nitriles,[20] and isothiocyanates,[21] it seems to be a rather common process and thus the two conditions stated above—namely well-defined mechanism and possible generalization—are met by this hydrogen rearrangement.

For the present experiment methyl butyrate was chosen, since butyric acid and its esters are the simplest, and at the same time, best investigated[11,15] representatives of this group of compounds. The methyl ester has been selected since the possibility of catalytic decomposition in the inlet system of the mass spectrometer is much lower than for the free acid, and the peak in the spectrum (Fig. 1) in question (m/e 74, a, R = OMe) has no appreciable neighbor (in contrast to the ethyl ester[15]) which might complicate calculations. For these reasons the γ-d_1 (II), γ-d_2 (III), and γ-d_3 analogs of methyl butyrate (I, Fig. 1) were prepared (see Experimental section) and their mass spectra measured. The values used below for the calculations are the mean of at least five independent measurements.

The fragmentation pattern of I (Fig. 1) corresponds to the earlier findings[9,15] and the fragment ions are indicated in the spectrum. It can be seen that in the critical region (around m/e 74) no other peaks occur which might cause complications in the interpretation of the observed shifts. One difficulty, however, had to be overcome. The ill-defined molecular ion does not allow a check of the isotopic purity of the labeled compounds, which from the method of preparation should be about 98%. Therefore, the fragment m/e 71 (c), formed by the loss of the methoxyl group, and retaining all deuterium had to serve for this purpose.

In order to describe the isotope effect (I.E.) we chose the following definition: I.E. = atoms of deuterium per atom of hydrogen transferred for the hypothetical case in which equal numbers of deuterium and hydrogen atoms are available for transfer. This gives values I.E. < 1 if there is discrimination against deuterium and I.E. > 1 if deuterium is transferred preferentially. This seems a more concise way of presentation than expressions derived from deviations from the statistical value (in our case 33.3 or 66.7%).

Table I gives relative intensities of fragment c (m/e 71 in Fig. 1) and its surrounding peaks, which were used for the determination of the isotopic purity of the samples. Tables II and III contain the detailed calculations of the isotope effect.

(13) A. G. Sharkey and W. M. Hickam, ASTM E-14 Conference, New York, N. Y., 1957, quoted by K. Biemann in "Mass Spectrometry," McGraw-Hill Book Co., New York, N. Y., 1962, p. 120.

(14) E. Stenhagen, *Z. anal. Chem.*, **181**, 462 (1961).

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(18) J. A. Gilpin, *J. Chem. Phys.*, **28**, 521 (1958).

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(20) F. W. McLafferty, *Anal. Chem.*, **34**, 26 (1962).

(21) A. Kjaer, M. Ohashi, J. M. Wilson, and C. Djerassi, *Acta Chem. Scand.*, in press.

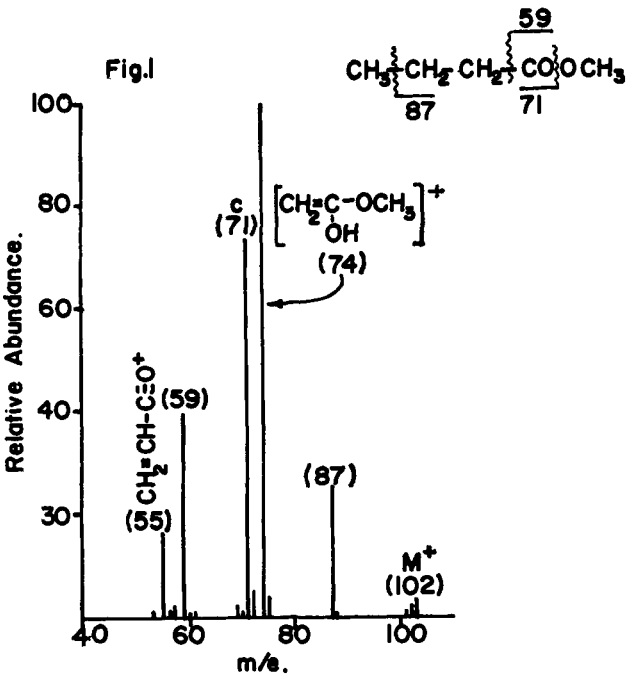


Fig. 1.—Mass spectrum of methyl butyrate.

The values calculated for the isotope effect from the d_1- (II) (Table II) and the d_2- (III) (Table III) species agree well and give a mean of 0.88, which expresses a serious discrimination against the transfer of deuterium compared to hydrogen. This isotope effect must be taken into consideration if quantitative evaluations of complicated rearrangement processes are undertaken from a study of deuterated analogs.

It only remains to rationalize the origin of this isotope effect. In the case under consideration, fission of a carbon–hydrogen bond competes with that of a carbon–

TABLE I
CALCULATION OF ISOTOPIC PURITY OF DEUTERATED METHYL BUTYRATES

Methyl ester	m/e 69	70	71	72	73	74	Isotopic purity, %
	Relative abundance, %						
Butyrate (I)	3.5	1.5	100	5.0	1	...	100.0
γ-d_1-Butyrate (II)	...	3.5	4.0	100	5.0	...	97.6 (2.4% d_0)
γ-d_2-Butyrate (III)	...	...	3.5	4.2	100	(5.0)	97.3 (2.7% d_1)

TABLE II
ISOTOPE EFFECT IN METHYL γ-d_1-BUTYRATE (II)

	a[a]	b[a]	c[a]	d[a]	I.E.
m/e 74	100	100	96.6	69.6	$\frac{30.4}{34.8} = 0.875$
m/e 75	46.2	42.3	42.3	30.4	

[a] a, observed values; b, m/e 75 corrected for natural ^{13}C contribution (3.3%) of m/e 74 and for finite value (0.6%) of intrinsic m/e 75 in 1 (total of 3.9%, deduced from the nondeuterated specimen 1); c, correction for nondeuterated material (see Table I; 2.4% of 142.3 = 3.4%); d, corrected values standardized.

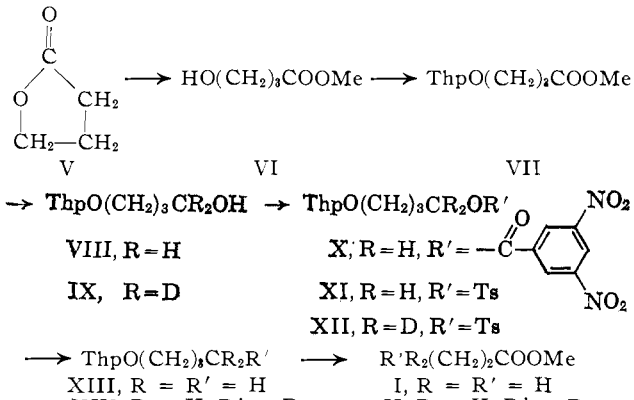
TABLE III
ISOTOPE EFFECT IN METHYL γ-d_2-BUTYRATE (III)

	a[a]	b[a]	c[a]	d[a]	e[a]	I.E.
m/e 74	67.0	57.4	57.4	54.6	36.1	$\frac{31.95}{36.1} = 0.886$
m/e 75	100	100	97.8	96.4	63.9	

[a] a, as in Table II; b, correction for ^{13}C contribution (4.4%) of m/e 73 and for finite value (0.6%) for m/e 72 and m/e 73 in the spectra of I and II, respectively (total of 5.0%, see Table I); this 5% is then adjusted (9.6%) for the ratio m/e 73:m/e 74 = 100:52; c, same as (b) in Table II; d, correction for d_1-material (see Table I) (2.7% of 155.2 = 4.2%; $^2/_3$ of the d_1-material will contribute to m/e 74 and $^1/_3$ to m/e 75; e, corrected values standardized.

hydrogen linkage. In general, the former process is favored.[22] In addition, the smaller van der Waals radius for deuterium, makes the transition state less likely for deuterium than for hydrogen. This is in agreement with a recent observation of Mislow and co-workers[23] that a trideuteriomethyl blocking group is smaller than a methyl group, since racemization of an optically active bridged biphenyl proceeded more rapidly on replacing CH_3 by CD_3.

Synthesis of Deuterated Methyl Butyrates.—Treatment of γ-butyrolactone (V) with sodium methoxide in anhydrous methanol gave a mixture which contained predominantly methyl γ-hydroxy butyrate (VI) along with unchanged lactone V, as determined by infrared spectroscopy. On reaction of this mixture with dihydropyran, there was obtained the pyranyl ether VII, the lactone V being conveniently separated at this stage by washing with aqueous sodium carbonate. Reduction of VII with lithium aluminum hydride gave the alcohol VIII, which was characterized by esterification with 3,5-dinitrobenzoyl chloride (see X), followed by mild acid hydrolysis, yielding crystalline tetramethylene glycol mono-3,5-dinitrobenzoate. The alcohol VIII was converted to the tosylate XI on relatively brief treatment (1.5 hr.) with tosyl chloride in pyridine at room temperature; reaction for longer periods led to heterogeneous products. The tosylate XI decomposed on standing; therefore, to procure optimum yields, it was reduced immediately to the pyranyl ether XIII, which was identical with an authentic sample prepared from 1-butanol. Alternatively, reduction of the ester VII with lithium aluminum deuteride gave d_2-IX, which was converted to 4,4-d_2-



butan-1-ol pyranyl ether (XV) *via* reduction of the tosylate XII with hydride; when the removal of the tosylate group was accomplished with deuteride, 4,4,4-d_3-butan-1-ol pyranyl ether (XVI) was obtained. Finally, reduction of the tosylate XI with lithium aluminum deuteride gave 4-d_1-butan-1-ol-pyranyl ether (XIV). The mono-, di-, tri-, and nondeuterated butanol pyranyl ethers were converted to the corresponding butyric acids by oxidation with chromium trioxide and then to methyl-4-d_1-butyrate (II), methyl-4,4-d_2-butyrate (III), methyl-4,4,4-d_3-butyrate (IV), and methyl butyrate (I), respectively, by esterification with diazomethane. All the esters were isolated in a pure state by preparative gas-phase chromatography.

Experimental[24]

Methyl γ-Hydroxybutyrate Tetrahydropyranyl Ether (VII).—γ-Butyrolactone (10 g.) and anhydrous methanol (40 cc.) containing dissolved sodium (300 mg.) were heated under reflux for 1 hr. The solution was then poured into water (40 cc.) containing concentrated hydrochloric acid (3 cc.) and 10% sodium carbonate solution then added until the solution had pH 8. Continuous ether extraction of the aqueous solution overnight and evaporation of the extract gave a colorless oil (10.5 g.), which showed λ_{max}^{film} 2.9 (OH), 5.75 (COOMe), and 5.65 μ (γ-lactone). A portion of this product (4.8 g.) and dihydropyran (4 cc.) were mixed and 1 drop of concentrated hydrochloric acid was added. The solution was kept overnight at room temperature, diluted with ether (100 cc.), and then poured into a 10% solution of sodium carbonate (50 cc.). The ether phase was washed three times with water, dried, and evaporated giving crude methyl γ-hydroxybutyrate tetrahydropyranyl ether (VII) (6.0 g., approximately 95% pure from gas-phase chromatography) which exhibited λ_{max}^{film} 5.73 μ and no hydroxyl absorption. Distillation gave pure material (4.2 g.), b.p. 90–92° (1.0 mm.).

Anal. Calcd. for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 59.17; H, 8.95.

Tetramethylene-1,4-diol Monotetrahydropyranyl Ether (VIII).—A solution of VII (8.23 g.) in ether (100 cc.) was added dropwise to a suspension of lithium aluminum hydride (4.4 g.) in ether (40 cc.). After stirring the mixture for 3 hr. at room temperature, the excess of hydride was destroyed by the dropwise addition of a saturated solution of ammonium chloride. After separation of the ether phase, the aqueous phase was washed once with ether and the combined extracts dried and evaporated giving VIII (6.97 g.), λ_{max}^{film} 2.95 μ (OH) and no carbonyl absorption. On thin layer chromatography (plate developed by benzene–ether, 1:2) only one spot (R_f 0.5) was obtained.

Tetramethylene-1,4-diol Mono-3,5-dinitrobenzoate.—3,5-Dinitrobenzoyl chloride (200 mg.) was added to a solution of VIII (114 mg.) in pyridine (1.0 cc.) and the solution kept overnight at room temperature. The product (254 mg., isolated in the usual manner, except that acid washings were avoided) in hexane (3 cc.) was placed on a column of alumina (30 g., Grade III, Merck, neutral) and the pure ester X (210 mg.) eluted by benzene (50 cc.) after first eluting traces of other substances with 20% benzene in hexane (50 cc.). This product could not be induced to crystallize and was therefore taken up in methanol (4 cc.) and treated with 10% sulfuric acid (0.5 cc.). Hydrolysis was complete in 5 min. at 35°. Addition of more water caused crystallization of tetramethylene-1,4-diol mono-3,5-dinitrobenzoate (125 mg.), m.p. 97–98°. Recrystallization from acetone–hexane gave an analytical sample (90 mg.), m.p. 98–98.5°; $\lambda_{max}^{CHCl_3}$ 2.78 and 2.91 (–OH), 5.78 (ester), and 6.47 μ (C–NO_2).

Anal. Calcd. for $C_{11}H_{12}N_2O_7$: C, 46.48; H, 4.26; N, 9.86. Found: C, 46.7; H, 4.35; N, 9.87.

Tetramethylene-1,4-diol 4-Tetrahydropyranyl Ether 1-Tosylate (XI).—Tosyl chloride (1.8 g.) was added to a solution of VIII (867 mg.) in pyridine (6 cc.). After 1.5 hr. at room temperature, water (1 cc.) was added, the temperature being maintained below 30°. The solvents were then removed under high vacuum at room temperature and the semisolid residue taken up in ether (50 cc.). The ether solution was washed once with saturated sodium bicarbonate solution, dried, and evaporated giving the crude tosylate XI (1.64 g.) as a colorless oil, λ_{max}^{film} 6.25 (m), 7.36 (s), and 8.48 μ (s) (all characteristic of tosylates); thin layer chromatography (plate developed by benzene containing 10% ether) indicated that this product was essentially homogeneous.

1-Butanol Pyranyl Ether (XIII).—The crude tosylate (1.64 g.) from above, in ether (50 cc.), was added during 2 min. to a magnetically stirred suspension of lithium aluminum hydride (800 mg.) in ether (200 cc.). After 30 min., the excess of hydride was destroyed by the addition of saturated ammonium chloride solution. After separation of the ether phase, the aqueous phase was washed once with ether and the combined ether extracts dried and evaporated, giving a pale yellow, mobile oil (650 mg.). The product was distilled at approximately 120° (25 mm.) giving 1-butanol tetrahydropyranyl ether (XIII, 500 mg.), identical with an authentic sample by thin layer and gas-phase chromatography, as well as infrared and n.m.r. spectroscopy.

Methyl Butyrate (I).—A 6 *N* solution of chromium trioxide in 15% sulfuric acid (5 cc.) was added rapidly to the tetrahydropyranyl ether (200 mg.). A condenser was *immediately* put into place to prevent any loss of the relatively volatile butyraldehyde during the vigorous exothermic reaction which ensued. After 5 min., acetone (2 cc.) was added and the solution then heated under reflux for 4 hr. Volatile substances were then removed by distillation to dryness and the distillate treated with an excess of ethereal diazomethane. The ether phase was separated and

(22) L. Melander, "Isotope Effects on Reaction Rates," Ronald Press, New York, N. Y., 1960, *e.g.*, p. 66.

(23) K. Mislow, R. Graeve, A. J. Gordon, and G. H. Wahl, *J. Am. Chem. Soc.*, **85**, 1199 (1963).

(24) Analyses were performed by Messrs. E. Meier and J. Consul, Microanalytical Laboratory, Department of Chemistry, Stanford University. Melting points are determined in capillaries and are corrected. Mass spectra were obtained with a Consolidated Electrodynamics Corporation mass spectrometer Model No. 21-103C using an all-glass inlet system heated to 200°. The ionizing energy was kept at 70 e.v. and the ionizing current at 50 μa.

ether and acetone then removed by fractional distillation until a residue of approximately 0.2 cc. remained. Analytical gas-phase chromatography showed that this residue contained approximately 50% of methyl butyrate, the remainder being acetone and ether and only traces of substances having considerably longer retention times. Pure methyl butyrate was isolated from this mixture by preparative gas-phase chromatography (Wilkens Aerograph Instrument, Walnut Creek, Calif.) on a 20% silicone rubber column operating at 60°, the retention time of the ester being approximately 10 min. The absolute purity of the ester obtained in this manner was confirmed on an analytical instrument (Wilkens, Hy-F1 instrument).

Methyl 4-d_1-Butyrate (III).—A solution of the tosylate XI (1.58 g.) in ether (50 cc.) was added to a magnetically stirred suspension of lithium aluminum deuteride (420 mg.) in ether (150 cc.). After 30 min. the product (728 mg.) was isolated in the usual manner and gave, after distillation, 4-d_1-butanol 1-tetrahydropyranyl ether (II, 564 mg.). A portion of this material (250 mg.) was oxidized (using 7 cc. of 6 *N* Jones reagent[25]) and methylated as described above and pure methyl 4-d_1-butyrate (II) isolated by preparative gas-phase chromatography.

Methyl 4,4-d_2-Butyrate (III).—A solution of the ester VII (800 mg.) in ether (40 cc.) was added to a magnetically stirred suspension of lithium aluminum deuteride (400 mg.) in ether (150 cc.). After 1 hr., the product was isolated in the usual manner giving 1,1-d_2-tetramethylene-1,4-diol 4-tetrahydropyranyl ether (IX, 700 mg.). On treatment of this material with tosyl chloride (1.5 g.) in pyridine (5 cc.) for 1.5 hr., there was obtained, after the usual work-up, 1,1-d_2-tetramethylene-1,4-diol 4-tetrahydropyranyl ether 1-tosylate (XII, 1.3 g.). A solution of this tosylate in ether (25 cc.) was added to a magnetically stirred suspension of lithium aluminum hydride (300 mg.) in ether (150 cc.). After 15 min., the usual isolation procedure gave a colorless oil (560 mg.), which was purified by distillation giving 4,4-d_2-butanol tetrahydropyranyl ether (XV) (480 mg.). A portion of this material (280 mg.) was oxidized (using 8 cc. of Jones reagent[24]) and methylated as previously described and pure methyl 4,4-d_2-butyrate (III) isolated in the above described manner.

Methyl 4,4,4-d_3-Butyrate (IV).—A solution of XII (1.4 g.) in ether (40 cc.) was reduced with lithium aluminum deuteride (300 mg.) in ether (180 cc.) in the usual manner. The resulting 4,4,4-d_3-butanol tetrahydropyranyl ether (XVI, 520 mg.) was oxidized and the derived butyric acid esterified with ethereal diazomethane to give methyl 4,4,4-d_3-butyrate (IV).

Acknowledgment.—Financial support was provided by the National Institutes of Health (Grant No. 5T4-CA5061 and AM-04257) of the U. S. Public Health Service.

(25) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

COMMUNICATIONS TO THE EDITOR

The Existence of Sulfenes

Sir:

The intermediacy of a sulfene ($RR'C{=}SO_2$) has been proposed to rationalize the course of three general reactions: (1) the reaction of sulfonyl halides of the type $RR'CHSO_2Cl$ with tertiary amines,[1] (2) the reaction of diazoalkanes with sulfur dioxide,[2] and (3) the photolysis of unsaturated sultones.[3] Although the formation of sulfenes in these transformations is currently regarded[3,3a,4] as highly probable, in no case has it been proved. We wish to describe our experiments which show that sulfenes are produced in reaction 1, above.

Benzylsulfonyl chloride, when treated with an alcohol in the presence of triethylamine, is quantitatively converted in less than 1 min. at room temperature into the corresponding ester. Two possible mechanisms for this reaction are: (a) a bimolecular nucleophilic substitution at the sulfur atom by the alcohol[5] (or its conjugate base) or (b) initial formation of phenylsulfene by an elimination reaction, followed by addition of the alcohol. In an experiment to distinguish these possibilities, benzylsulfonyl chloride (1.9 mmoles) was treated with triethylamine in isopropyl alcohol-*d* (~13 mmoles, estimated deuterium content: 92 ± 2% of the active hydrogen). The following data show the constitution of the ester so obtained. (1) The melting point of a mixture with natural abundance isopropyl benzylsulfonate is undepressed. (2) *Anal.* Calcd. for a mixture of 91% $PhCHDSO_3CH(CH_3)_2$ and 9% $PhCH_2SO_3CH(CH_3)_2$: 6.49 atom % excess D. Found: 6.48 atom % excess D. (3) The intensity of the band at 4.15 δ in the deuterated ester corresponded to the presence of ~90% $PhCHDSO_3CH(CH_3)_2$; the other bands in the spectrum were identical with those of the natural abundance ester. (4) The infrared spectrum of the deuterated material (0.6 *M* in CCl_4) was virtually identical with that of the natural abundance compound above 1450 cm.$^{-1}$; below that the spectra were basically similar[6] but the deuterated sample showed additional bands at 1223 (m), 1188 (s), 1154 (s), and 940 cm.$^{-1}$ (s), and lacked the bands at 1410 (w), 1268 (m), 1204 (s), 1158 (w), and 1137 cm.$^{-1}$ (m) present in the natural abundance ester. (5) The peaks in the mass spectrum[7] of the natural abundance ester at *m/e* 91 (61.2% of Σ_{38}) and *m/e* 107 (1.8% of Σ_{38}) were largely shifted in the spectrum of the deuterated material to *m/e* 92 and 108, the relative intensities in the latter spectrum corresponding well with the content of monodeuterated ester as estimated by the above methods. The intensities of the bands at *m/e* 93 and 109 in the mass spectrum of the deuterated material were such as to exclude the possibility of >2% $PhCD_2SO_3CH(CH_3)_2$.

It is concluded from the above data that with the quantities and reactants given, the ester formed contains about 90% of the monodeuterated ester, $PhCHDSO_3CH(CH_3)_2$, the remainder being the nondeuterated ester with very little or none of the dideuterated compound, $PhCD_2SO_3CH(CH_3)_2$. The formation of such a product requires that the deuterium be incorporated in an irreversible step (and clearly excludes any significant incorporation of deuterium either by the sulfonyl chloride prior to reaction with the alcohol, or by the ester). We feel that mechanism b uniquely ful-

(1) E. Wedekind and D. Schenk, *Ber.*, **44**, 198 (1911).

(2) H. Staudinger and F. Pfenninger, *ibid.*, **49**, 1941 (1916).

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(3a) Like results and conclusions to those reported herein have been obtained by W. E. Truce, *et al.*, *J. Am. Chem. Soc.*, **86**, 288 (1964), as regards the system

$$CH_3SO_2Cl + ROD + Et_3N \longrightarrow CH_2DSO_3R + Et_3NH^+Cl^-$$

(4) (a) G. Stork and I. J. Borowitz, *J. Am. Chem. Soc.*, **84**, 313 (1962); (b) G. Opitz and H. Adolph, *Angew. Chem.*, **74**, 77 (1962); (c) W. E. Truce, J. J. Breiter, D. J. Abraham, and J. R. Norell, *J. Am. Chem. Soc.*, **84**, 3030 (1962); W. E. Truce, and J. R. Norell, *ibid.*, **85**, 3231 (1963); (d) J. F. King and T. Durst, *Tetrahedron Letters*, 585 (1963); (e) R. H. Hasek, P. G. Gott, R. H. Meen, and J. C. Martin, *J. Org. Chem.*, **28**, 2496 (1963).

(5) Such a mechanism has been proposed for the uncatalyzed alcoholyses of aryl- and alkylsulfonyl chlorides: E. Tommila and P. Hirsjärvi, *Acta Chem. Scand.*, **5**, 659 (1951); P. Hirsjärvi and E. Tommila, *ibid.*, **5**, 1097 (1951); R. B. Scott, Jr., and R. E. Lutz, *J. Org. Chem.*, **19**, 830 (1954).

(6) The other significant peaks below 1450 cm.$^{-1}$ for the deuterated material are at 1388 (m), 1365 (vs), 1345 (vs), 1175 (s), 1096 (s), 1077 (w), 1030 (w), 920 (vs), 883 (vs), 825 (w), 695 cm.$^{-1}$ (s), and for the natural abundance ester are at 1387 (m), 1365 (vs), 1345 (vs), 1173 (vs), 1095 (s), 1073 (w), 1030 (w), 920 (vs), 887 (vs), 825 (w), 697 cm.$^{-1}$ (s).

(7) We wish to express our thanks to Dr. W. A. Ayer (University of Alberta), through whose courtesy this mass spectrum was obtained.