TABLE I

FRAGMENTATION PATTERN OF $ClNF_2$

m/e	Relation intensity	Ion
14	3.8	N^+
19	1.6	F^+
33	37.1	NF^+
35	21.9	Cl^+
37	6.5	
49	30.1	NCl^+
51	7.2	
52	100.	NF_2^+
68	26.2	$NFCl^+$
70	22.4	
72	8.5	Cl_2^+
74	1.3	
87	46.4	NF_2Cl^+
89	14.5	

Samples giving essentially the same cracking pattern were shown to contain less than 0.5% Cl_2 by ultraviolet spectrometry.

The infrared spectrum of chlorodifluoroamine consists of very strong bands centered at 10.8 (triplet), 11.7 (doublet) and 14.4μ (triplet); a doublet of medium intensity centered at 13.4μ and weak bands at 5.4, 5.7, 5.9 and 7.3μ.

The F^{19} n.m.r. spectrum of chlorodifluoroamine consists of a single broad band centered at 8685 cycles to the low field side of trifluoroacetic acid.

Chlorine and fluorine analyses were obtained by conversion to ammonium chloride by reaction with ammonia at 150°, and by conversion to sodium chloride and fluoride by reaction with sodium in liquid ammonia at −50°. Calcd. for NF_2Cl: F, 43.45; Cl, 40.54. Found: F, 42.35; Cl, 39.92.

Chlorodifluoroamine has been kept at ambient temperatures in Pyrex vessels for extended periods without decomposition. It is reactive toward mercury at room temperature (forming N_2F_4 and Hg_2Cl_2), necessitating the use of a spoon gauge or Kel-F oil-protected manometers for pressure measurements.

Caution should be exercised in handling chlorodifluoroamine since N-halogen compounds are known to exhibit explosive properties.

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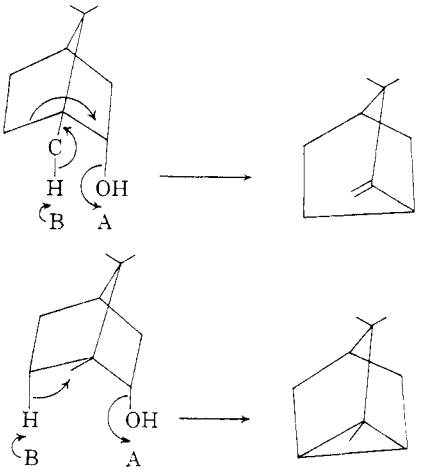
RECEIVED MARCH 18, 1960

DEHYDRATION OF ALCOHOLS OVER ALUMINA MODIFIED BY AMMONIA[1,2]

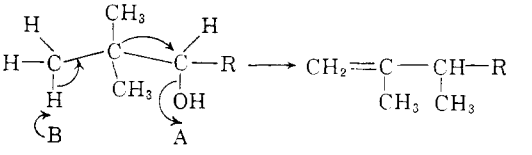
Sir:

We wish to report a new dehydration catalyst which was obtained by modifying alumina by ammonia. On the modified catalyst, *d*-borneol on dehydration forms 23% of tricyclene and 77% of *d*-camphene with 94% retention of configuration.[3] The main feature of the catalyst is the suppression of the carbonium ion character of dehydration. This is due to the preferential poisoning of the "strong acid sites" of alumina by ammonia.[4] In contrast to these results, borneol, over an unmodified alumina gave a mixture containing at least twelve hydrocarbons as shown by vapor-phase chromatography.

We suggest that the surface of the modified alumina has both acidic and basic sites and that the dehydration takes place by a concerted mechanism as shown below, A and B representing acidic and basic sites, respectively.



On the modified alumina catalyst, neopentyl alcohol yielded on dehydration 70% of 2-methyl-1-butene (I) and 30% of 2-methyl-2-butene, while pinacolyl alcohol formed 73% of 3,3-dimethyl-1-butene and 25% of 2,3-dimethyl-1-butene (II). On the unmodified alumina a complex mixture of olefinic hydrocarbons is obtained. The formation of I and II is in accordance with the postulated mechanism in which the participation of the γ-carbon atom occurs



Menthol was dehydrated over the modified alumina to form 2-menthene of 91% purity, while neomenthol gave a mixture of 2- and 3-menthene, the latter forming 75% of the total. These experiments demonstrate that when dehydration proceeds by a 1,2-elimination, the *trans* elimination is the preferred one. On the unmodified alumina dehydration is not selective.

The experimental technique involves passing a stream of ammonia along with the alcohol over the heated catalyst. Pure alumina, prepared by the hydrolysis of aluminum isopropoxide and modified by ammonia in this manner gave the best selectivity with the highest dehydration activity. The reactions were carried out in the temperature range of 240–340°.

The synthetic uses of the new catalyst are evident. 3,3-Dimethyl-1-butene could be prepared

(1) Part V of the series, "Alumina: Catalyst and Support"; for paper IV, see H. Pines and C. T. Chen, THIS JOURNAL, in press.

(2) This work was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is made to the donors of this fund.

(3) The camphene and tricyclene could be separated from each other by chromatography over silica gel.

(4) H. Pines and W. Haag, THIS JOURNAL, **82**, May 20 (1960).

in better than 98% purity by the dehydration of 3,3-dimethyl-1-butanol over this catalyst. Previous methods of dehydrating this alcohol were accompanied by appreciable rearrangement.[5]

The mechanism suggested here seems to be the most reasonable. However, one involving participation by a neighboring group is not excluded.[6]

Further work with these and other alcohols and with bases other than ammonia and the study of the details of the mechanism are currently being carried out.

(5) V. N. Ipatieff, W. W. Thompson and H. Pines, THIS JOURNAL, **73**, 553 (1951).

(6) S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, *ibid.*, **74**, 1113 (1952), and other papers in that series.

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RECEIVED MARCH 14, 1960

THE BIOSYNTHESIS OF TETRACYCLINE ANTIBIOTICS

Sir:

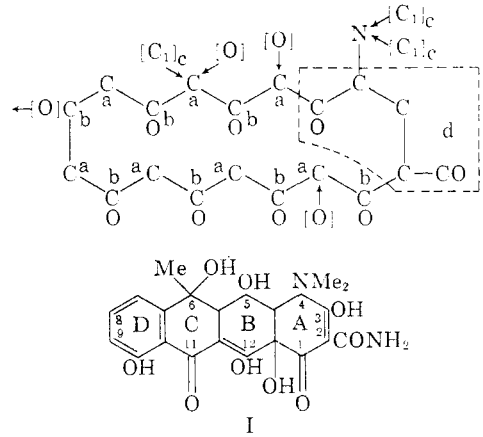
Inspection of the formulas of tetracycline antibiotics, *e.g.*, oxytetracycline, I, suggests that a considerable part of the molecule may arise biosynthetically by the acetic acid route,[1,2,3] with the probable introduction of one methyl group bonded to carbon and two methyl groups bonded to the amino nitrogen group.

The first experimental support for this idea was provided by Snell, *et al.*,[2] who showed that sodium acetate-2-C^{14} was a fermentation precursor (incorporation 5–10%) by a fairly direct route, since the specific activity of the product was directly proportional to the quantity of tracer added. Degradation[2] showed less activity in ring A than in rings B, C and D. Glutamate has been found to be a unique amino-acid source of oxytetracycline in a semi-synthetic medium, and addition to a fermentation of (±)glutamic acid-2-C^{14} gave an active oxytetracycline. Degradation of the product showed that terracinoic acid (from rings B, C, D) contained only 5% of the activity, suggesting that glutamate may be a fairly direct precursor of part at least of ring A.[3]

Detailed degradations have now been carried out on oxytetracycline derived from (i) $C^{14}H_3$-methionine and (ii) 2-$C^{14}H_3CO_2H$. (i) Oxytetracycline (r.m.a.[4] 50.9 × 10^3) gave by Kuhn–Roth oxidation CH_3CO_2H (r.m.a. of $BaCO_3$ from the CH_3 group, 17.3 × 10^3; r.m.a. of $BaCO_3$ from the CO_2H, 0) and by standard degradation[5] to tetramethylammonium iodide (r.m.a. 34.8 × 10^3). All the activity, as expected, is in the C_6-CH_3 and the $N(CH_3)_2$, the activity of all CH_3 groups being the same. (ii) Oxytetracycline (r.m.a. 42.2 × 10^3) from $C^{14}H_3CO_2H$ after degradations[5] gave products with these r.m.a. × 10^{-3}: terracinoic acid, 27.1; 7-acetoxy-3-methylphthalide 18.7; decarboxyterracinoic acid 26.4; $BaCO_3$ from C_{11}, 0.3; $BaCO_3$ from C_6, 4.0; $BaCO_3$ from C_6-CH_3, 0.3; $BaCO_3$ from C_2-$CONH_2$, 0.6; tetramethylammonium iodide, 0.5.

These results are quantitatively in accord with the production of the molecule by the head to tail linkage of acetic acid units at least from C_5-C_{12} (except C_6-CH_3). It is necessary to assume that the incorporated unit from $C^{14}H_3CO_2H$ has its activity randomized to the extent of 5% and that the methyl-pool has become slightly labelled from this source. It is likely that the glutamate portion extends from the C_2-$CONH_2$, which is differently labelled to an acetate carboxyl, through C_2 to C_{4a}. Degradations to deal with this part of the molecule are inefficient.

The results are in accord with the distributions of label shown in I: (i) r.m.a. contributions of a, b, d = 0, c = 17.3 × 10^3; (ii) r.m.a. contributions of a = 4 × 10^3; b = 0.3 × 10^3; c = 0.25 × 10^3; with glutamic acid-2-C^{14} as source the r.m.a. contribution of d is much greater than a, b and c.



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We are indebted to Dr. Herchel Smith for assistance with some of the tracer measurements; financial aid from the Rockefeller Foundation and Chas. Pfizer & Co., Inc., supported parts of the work.

(1) A. J. Birch, Fortschr. Chem. Org. Naturstoffe, Springer, Vienna, **14**, 186 (1957); R. Robinson, "Structural Relations of Natural Products," Oxford Press, New York, N. Y., 1955.

(2) J. F. Snell, R. L. Wagner and F. A. Hochstein, "Internat. Conf. on Peaceful Uses of Atomic Energy," **12**, 431 (1956).

(3) J. F. Snell, in "Radioactivity for Pharmaceutical and Allied Research Laboratories," Academic Press, Inc., New York, N. Y., in press.

(4) Relative molar activity, proportional to molar activity *cf.*[6]

(5) F. A. Hochstein, C. R. Stephens, L. H. Conover, P. P. Regna, R. Pasternak, P. N. Gordon, F. J. Pilgrim, K. J. Brunings and R. B. Woodward, THIS JOURNAL, **75**, 5455 (1953), and references cited therein.

(6) A. J. Birch, R. A. Massy-Westropp, R. W. Rickards and H. Smith, *J. Chem. Soc. (London)*, 360 (1958).

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RECEIVED MARCH 21, 1960

A NEW CLASS OF ACTIVE STEROIDS: THE 19-NOR-$\Delta^{4,9}$-3-KETOSTEROIDS

Sir:

Since the initial demonstration that Δ^1-unsaturation of the corticoids results in enhanced biological and therapeutic activity,[1] numerous investigations have been made of other conjugated systems. The $\Delta^{4,6}$-unsaturated derivatives of the

(1) H. L. Herzog, A. Nobile, S. Tolksdorf, W. Charney, E. B. Hershberg, P. L. Perlman and M. M. Pechet, *Science*, **121**, 176 (1955).