fect the acetylation of the α-hydrogen of cyclohexanone or acetophenone with acetic anhydride to form the β-diketone; instead some of the ketone underwent self-condensation. Moreover, neither boron chloride nor aluminium chloride brought about acetylation of the α-hydrogen of even *p*-nitrophenylacetone, which is relatively reactive.

Similar observations were reported recently by Perfetti and Levine[5] who showed that neither aluminum chloride nor stannic chloride can effect the acetylation of acetophenone to form benzoylacetone. However, these workers did realize this acetylation with zinc chloride and ferric chloride, although the temperature employed (110°) is much higher than that (0°) known to effect the reaction with boron fluoride.

Experimental

Acetoacetylations by Boron Fluoride.—A mixture of the aromatic compound (0.20 mole) and acetic anhydride (0.80 mole) was saturated with boron trifluoride at 0–10° in two to three hours and then stirred for an additional period to make a total reaction time of four hours. A solution of 100 g. of sodium acetate in 500 ml. of water was added and the reaction mixture refluxed 15–30 minutes. The mixture was cooled and extracted two or three times with 30–60° ligroin. The combined ligroin solution was washed three times with small portions of water and once with saturated sodium bicarbonate solution. The ligroin solution was then extracted several times with cold 2% sodium hydroxide solution until the ligroin phase no longer gave a positive enol test. The combined alkaline solution was acidified at 0° and the β-diketone taken up in ether, from which it was recovered by fractionation of the dried solution (Table I). The ligroin phase was dried and fractionated, yielding the monoketone and some high-boiling residue.

Experiments with Boron Chloride and Aluminum Chloride.—A mixture of toluene (0.20 mole) and acetic anhydride (0.8 mole) was saturated with boron chloride at 10° and the reaction mixture worked up as described above for boron fluoride. There was obtained a 27% yield of *p*-methylacetophenone, b.p. 101–102° at 13 mm.

A mixture of cyclohexanone (0.15 mole) and acetic anhydride (0.30 mole) was saturated with boron chloride in 40 minutes at 10°. After stirring 30 minutes longer, the reaction mixture was decomposed with excess sodium acetate in ice-water. The mixture was extracted with ligroin and, after drying, the ligroin solution was fractionated to give 2-cyclohexylidenecyclohexanone[6] (59%), b.p. 142–143° at 17 mm.[6]; semicarbazone, m.p. 178–179°.[6]

Mixtures of acetophenone and acetic anhydride and of *p*-nitrophenylacetone and this anhydride were treated similarly with boron chloride. There were obtained some dypnone and tarry material, respectively.

A mixture of *p*-nitrophenylacetone (0.02 mole), acetic anhydride (0.06 mole), aluminum chloride (0.14 mole) and 40 ml. of carbon disulfide was stirred 12 hours at room temperature. After distilling most of the solvent, the mixture was poured onto ice and hydrochloric acid to give the original ketone (colored).

In all of these experiments, the products gave negative enol tests with ferric chloride showing the absence of β-diketones.

(5) B. M. Perfetti and R. Levine, THIS JOURNAL, **75**, 626 (1953).

(6) A. D. Petrov, *Bull. soc. chim.*, [IV] **43**, 1272 (1928).

DEPARTMENT OF CHEMISTRY
DUKE UNIVERSITY
DURHAM, N. C.

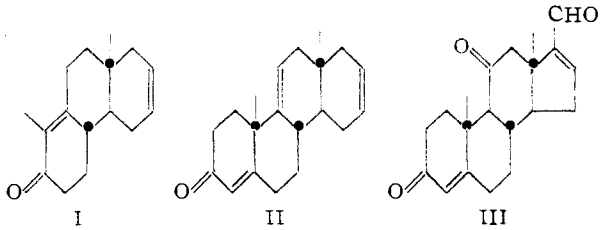
COMMUNICATIONS TO THE EDITOR

A SYNTHESIS OF *dl*-CORTISONE ACETATE

Sir:

We wish to report a direct synthesis of *dl*-cortisone acetate from the Woodward tricyclic ketone,[1] *dl*-1,14-dimethyl-2-keto-$\Delta^{1(11),6,9}$-octahydrophenanthrene. A distinguishing feature of this synthesis is that the cortical side chain and the eleven oxygen function are introduced without protecting the α,β-unsaturated ketone in ring A.

Selective hydrogenation of the Woodward tricyclic ketone with palladium on strontium carbonate gave the oily dihydrotricyclic ketone I ($\lambda_{max.}^{alc.}$ 250 mμ, ϵ15,300. Found: C, 83.5; H, 9.5). I was blocked in the 3 position by the methylanilinomethylene group[1] (m.p. 124–125°. Found: C, 82.8; H, 8.3.). The protected ketone was condensed with β-propiolactone[2] in the presence of potassium amide in ether. Removal of the blocking group yielded *dl*-1-(β-carboxyethyl)-1,14-dimethyl-2-keto-$\Delta^{6,10}$-decahydrophenanthrene as a crystalline isomer[3] (m.p. 171–173°. Found: C, 75.2; H, 8.7). This keto-acid was converted to the enol lactone (m.p. 100–102°) and thence by treatment with methylmagnesium bromide followed by cyclization[1] to the tetracyclic ketone II (m.p. 147–148°. Found: C, 84.9; H, 9.2). II was oxidized with iodine and silver acetate in wet acetic acid[4] to give a β-*cis*-glycol. Reaction with acetone gave *dl*-3-keto-16β,17β-dihydroxy-$\Delta^{4,9(11)}$-D-homoandrostadiene acetonide[5] (m.p. 174–175°). The structure of the acetonide was proved by conver-



(1) *Cf.* R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. McLamore, THIS JOURNAL, **74**, 4223 (1952).

(2) *Cf.* T. L. Gresham, J. S. Jansen, F. W. Shaver, M. R. Frederick and W. L. Beears, *ibid.*, **73**, 2345 (1951), and earlier papers.

(3) The mother liquor from the isolation of this material undoubtedly contained the epimeric compound.

(4) A reagent described in a private communication from R. B. Woodward; *cf.* S. Winstein and R. E. Buckles, THIS JOURNAL, **64**, 2787 (1942).

(5) It is to be noted that our acetonide differs from Woodward's[1] in that it was derived from a β-*cis*-glycol whereas his was from an α-*cis*-glycol, where α and β designate configuration corresponding to standard steroid convention.

sion to *dl*-$\Delta^{9(11),16}$-21-norprogesterone previously prepared by Woodward.[1]

The acetonide was converted in excellent yield to *dl* - 3 - keto - 11β,16β,17β - trihydroxy - Δ^4 - 9α-bromo-D-homoandrostene acetonide (m.p. 194–196°) with N-bromosuccinimide and sulfuric acid in aqueous acetone.[6] The crude bromohydrin was converted by alkali to *dl*-3-keto-9β,11β-oxido-16β,17β-dihydroxy-Δ^4-D-homoandrostene acetonide (m.p. 191–193°. Found: C, 74.3; H, 8.7). This crude bromohydrin was also oxidized with pyridine–chromium trioxide complex[7] to give a crude bromoketone (m.p. 195–198° dec.) which without purification was debrominated with zinc and aqueous acetic acid to give *dl*-3,11-diketo-Δ^4-16β,17β-dihydroxy-D-homoandrostene acetonide (m.p. 198–200°). Treatment with periodic acid followed by benzene and piperidine acetate[1] gave *dl*-11-keto-Δ^{16}-21-norprogesterone III (m.p. 207–209°. Found: C, 76.5; H, 7.7). Reaction with alkaline hydrogen peroxide[8] produced *dl*-11-keto-16α,17α-oxido-21-norprogesterone (m.p. 243–245°). Oxidation with silver oxide gave *dl*-3,11-diketo-16α,-17α-oxido-Δ^4-etiocholenic acid (m.p. 217–220° dec.). Reaction of the dry sodium salt with oxalyl chloride yielded an acid chloride which on treatment with diazomethane[9] gave a crystalline diazoketone (m.p. 193–195°) having strong infrared absorption at 4.75μ. Reaction of the diazoketone with hot acetic acid gave non-crystalline *dl*-16α,-17α - oxido - 3,11,20 - triketo - 21 - hydroxy - Δ^4-pregnene acetate. Opening with hydrogen bromide[8] produced *dl*-16β-bromocortisone acetate (m.p. 238–240° dec.). Debromination with Raney nickel[8] gave *dl*-cortisone acetate[10] (m.p. 240–243°) whose infrared spectrum was identical with natural cortisone acetate.

We thank Dr. R. H. Munch, Mr. G. W. Ashworth and Mr. O. E. Kinast for help with the numerous infrared and ultraviolet spectra needed in this work. In addition, we acknowledge the invaluable advice and assistance of Dr. R. B. Woodward.

(6) After the completion of our work, J. Fried and E. F. Sabo [THIS JOURNAL, **75**, 2273 (1953)] reported that they added hypobromous acid in good yield to a 3-keto-$\Delta^{4,9(11)}$ steroid. It now appears that the low yield obtained by Hicks and Wallis [*J. Biol. Chem.*, **162**, 641 (1946)] may be attributed to the fact that in their case rings A and B were *cis*.

(7) A reagent first announced at the Gordon Research Conferences, A.A.A.S., New Hampton, N. H., August 4–8, 1952; *cf.* G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, THIS JOURNAL, **75**, 422 (1953).

(8) *Cf.* P. L. Julian, E. W. Meyer, W. J. Karpel and I. R. Waller, *ibid.*, **72**, 5145 (1950).

(9) *Cf.* A. L. Wilds and C. H. Shunk, *ibid.*, **70**, 2427 (1948).

(10) L. H. Sarett, G. E. Arth, R. M. Lukes, R. E. Beyler, G. I. Poos, W. F. Johns and J. M. Constantin, *ibid.*, **74**, 4974 (1952).

ORGANIC CHEMICALS DIVISION
ST. LOUIS RESEARCH DEPARTMENT
MONSANTO CHEMICAL COMPANY
ST. LOUIS, MISSOURI

LLOYD B. BARKLEY
MARTIN W. FARRAR
WILLIAM S. KNOWLES
HAROLD RAFFELSON

RECEIVED JULY 7, 1953

THE RECONSTRUCTION OF THE FATTY ACID OXIDIZING SYSTEM OF ANIMAL TISSUES

Sir:

A system including seven enzymes has been shown to catalyze the following sequence

$$\text{Butyrate} \xrightarrow[\text{(I)}]{\text{ATP, CoA}^1} \text{BuCoA} \xrightarrow[\text{(II)}]{-2\text{E}} \text{Crotonyl CoA} \xrightarrow[\text{(III)}]{\text{H}_2\text{O}} \beta\text{-Hydroxy}$$

$$\text{BuCoA} \xrightarrow[\text{(IV)}]{\text{DPN}} \text{AcAcCoA} \xrightarrow[\text{(V)}]{\text{CoA}}$$

$$2\,\text{AcCoA} \xrightarrow[\text{(VI, VII)}]{\text{2 Malate, DPN}} 2\,\text{Citrate}$$

where (I) represents the fatty acid activating enzyme,[2,3] (II) fatty acyl CoA dehydrogenase, (III) unsaturated acyl CoA hydrase, (IV) β-hydroxyacyl CoA dehydrogenase,[4] (V) AcAcCoA cleavage enzyme,[4,5,6] (VI) malic dehydrogenase[7] and (VII) AcCoA-oxalacetate condensing enzyme.[8] Enzymes (I–V) have been isolated from beef liver mitochondria. Tz is the final electron acceptor with pyocyanine as intermediary carrier. Diaphorase[9] (VIII) catalyzes the oxidation of DPNH. The over-all balanced reaction is

$$\text{BuO}^- + 4\text{Tz} + 2\,\text{Malate} + \text{ATP} \longrightarrow 2\,\text{Citrate} + 4\text{Fz} + \text{AMP} + \text{PP}_\text{I} \quad (1)$$

The observed citrate:Fz ratio of 1:2.2 is in good agreement with the 1:2 ratio of equation (1).

Preparations of (I) at the highest purity level are homogeneous in the ultracentrifuge. At *p*H 10 with heptanoate as substrate, 1 mg. of (I) catalyzes the formation of 3.8 μ mole of acyl CoA per min. at 38°. (I) activates a wide variety of odd or even, straight (C_4–C_{12}), branched chain, or substituted fatty acids as well as α,β- and β,γ-unsaturated acids. (I) has proved invaluable for preparation of all acyl CoA derivatives required as substrates for (II–IV). The mechanism of activation by ATP is the same as for the acetate activation enzyme system.[10]

(IIg) a green copper flavoprotein[11] has been isolated in a form which is homogeneous in both the ultracentrifuge and Tiselius apparatus. The riboflavin content of the homogeneous enzyme is 1.2%. The prosthetic flavin has the same absorption spectrum and enzymatic activity as FAD.[12,13] (IIg) can be converted into an apoenzyme at *p*H 3.7

(1) The following abbreviations will be used: adenosinetriphosphate (ATP); adenosine-5'-phosphate (AMP); coenzyme A (CoA); di- and triphosphopyridine nucleotide (DPN, DPNH and TPN, TPNH); flavin adenine dinucleotide (FAD); acetyl (Ac); acetoacetyl (AcAc); butyryl (Bu); triphenyltetrazolium (Tz); formazan (Fz); and inorganic pyrophosphate (PP_I).

(2) H. R. Mahler, "Phosphorus Metabolism," Vol. 2, 286, Johns Hopkins Press, Baltimore, 1953; H. R. Mahler, S. J. Wakil and R. M. Bock, *J. Biol. Chem.*, in press.

(3) G. Drysdale and H. A. Lardy, "Phosphorus Metabolism," Vol. 2, p. 281, Johns Hopkins Press, Baltimore, Md., 1953.

(4) F. Lynen, L. Wessely, O. Wieland and L. Rueff, *Angew. Chem.*, **64**, 687 (1952).

(5) J. R. Stern, M. J. Coon and A. del Campillo, *Nature*, **171**, 28 (1953).

(6) D. E. Green, D. S. Goldman, S. Mii and H. Beinert, *J. Biol. Chem.*, **202**, 137 (1953).

(7) F. B. Straub, *Z. physiol. Chem.*, **275**, 63 (1942).

(8) S. Ochoa, J. R. Stern and M. C. Schneider, *J. Biol. Chem.*, **193**, 691 (1951).

(9) J. G. Dewan and D. E. Green, *Biochem. J.*, **32**, 626 (1938).

(10) H. Beinert, D. E. Green, P. Hele, H. Hift, R. W. Von Korff and C. V. Ramakrishnan, *J. Biol. Chem.*, **203**, 35 (1953).

(11) H. R. Mahler, THIS JOURNAL, **75**, 3288 (1953).

(12) E. Negelein and H. Brömel, *Biochem. Z.*, **300**, 225 (1939).

(13) O. Warburg and W. Christian, *Biochem. Z.*, **298**, 150 (1938).

whose activity can be restored by addition of either FAD or the prosthetic flavin. (IIg) catalyzes the oxidation of acyl CoA's from C_3 to C_8. Setting the rate with BuCoA as 100 the respective rates for C_3, C_5, C_6, C_7, C_8, and C_{10} acyl CoA are 25, 55, 45, 35, 10 and 0. At the highest purity level (IIg) catalyzes the reduction of 200 μmoles of indophenol/min./μmole of bound flavin at 22°. The product of the oxidation of BuCoA by indophenol in presence of (IIg) has been identified as butenoyl CoA since it is not acted upon by (IV) (specific for β-hydroxyacyl CoA's) except in presence of the hydrase (III). Solutions of (IIg) are bleached within three seconds by BuCoA or instantaneously by dithionite. The leuco enzyme can be reoxidized by crotonyl CoA. The E_0' of the system Bu-CoA $\overset{-2E}{\rightleftharpoons}$ crotonyl CoA lies in the range of indophenol (*ca.* + 0.2 v. at *p*H 7.0).

A flavoprotein (IIf), different and readily separable from (IIg) has been isolated from beef liver mitochondria and shown to catalyze only the oxidation of acyl CoA's with chain length > C_6.

Purified preparations of (III) have been obtained free of (I, II, IV and V) which catalyze the reactions

$$\text{RCH=CHCH}_2\text{COSCoA} \overset{\text{H}_2\text{O}}{\rightleftharpoons} \textit{d}\text{-RCH}_2\text{CHOHCH}_2\text{COSCoA} \overset{\text{H}_2\text{O}}{\rightleftharpoons} \text{RCH}_2\text{CH=CHCOSCoA} \quad (2)$$

(III) acts upon all unsaturated acyl CoA's tested from C_4 to C_{12}. At the highest purity level, 1 mg. catalyzes the hydration of 500 μmoles of crotonyl CoA to *d*-β-hydroxybutyryl CoA per min. at 22°. At *p*H 9.0 the equilibrium ratio unsaturated:β-hydroxyacyl CoA lies between 0.5 and 1. (III) is not active on *cis*-crotonyl CoA. The isomerization of the *cis*- and *trans*-forms appears to be catalyzed by a separate enzyme. (III) is inhibited by sulfhydryl reagents.

The oxidizing enzyme[4] (IV) has been isolated without contamination by (I–III, V). It catalyzes the reaction

$$\textit{d}\text{-RCHOHCH}_2\text{COSCoA} + \text{DPN}^+ \rightleftharpoons \text{RCOCH}_2\text{COSCoA} + \text{DPNH} + \text{H}^+ \quad (3)$$

All hydroxyacyl CoA's from C_4 to C_{12} which have been tested are oxidized at approximately the same rate. At the highest purity level 1 mg. catalyzes the oxidation of 200 μmoles of β-hydroxyhexanoyl CoA per min. at 22° and at *p*H 9. DPN can be replaced by coenzyme III[14] but not by TPN. The enzyme is optically specific for the product of the hydrase reaction, *i.e.*, *d*-β-hydroxyacyl CoA.[15] The E_0' for the reaction has been found to be −0.224 v.[16] The products of oxidation of the C_4, C_6 and C_8 β-hydroxyacyl derivatives of CoA were isolated and identified as the β-ketoacyl derivatives by chemical, enzymatic and optical methods.[17]

(14) T. P. Singer and E. B. Kearney, *Biochim. et Biophys. Acta*, **8**, 700 (1952).

(15) A. L. Lehninger and G. D. Greville, THIS JOURNAL, **75**, 1515 (1953).

(16) 0.320 v. was used as the E_0' for the DPN couple; K. Burton and T. H. Wilson, *Biochem. J.*, **54**, 93 (1953).

(17) H. Beinert, *J. Biol. Chem.*, in press.

(V)[4,5,6] which has been separated from the other enzymatic components catalyzes the reaction

$$\text{RCOCH}_2\text{COSCoA} + \text{CoA} \rightleftharpoons \text{RCOSCoA} + \text{AcCoA} \quad (4)$$

The same enzyme appears to be active on all β-ketoacyl CoA derivatives regardless of chain length, at least from C_4 to C_{12}. At the highest purity level 1 mg. of (V) catalyzes the cleavage of 10 μmoles of β-ketohexanoyl CoA per min. at 30° and *p*H 7.7. The products of the cleavage of β-ketohexanoyl CoA have been identified as BuCoA and AcCoA.

All the enzymatic steps of fatty acid oxidation have been shown to be reversible. The enzymatic synthesis of BuCoA in high yield from AcCoA has now been demonstrated. For this synthesis IIg and reduced DPN and benzyl viologen are necessary. BuCoA was identified as Bu hydroxamic acid after chromatographic separation from other acyl derivatives.[18]

INSTITUTE FOR ENZYME RESEARCH
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN

HELMUT BEINERT
R. M. BOCK
DEXTER S. GOLDMAN
D. E. GREEN[19]
H. R. MAHLER[20]
SANAE MII
P. G. STANSLY
S. J. WAKIL

RECEIVED MAY 15, 1953

(18) Since this manuscript was first submitted for review on April 8, 1953, communications have appeared in THIS JOURNAL by Stern and del Campillo (**75**, 2277 (1953)), and by Seubert and Lynen (**75**, 2787 (1953)) on aspects of fatty acid oxidation.

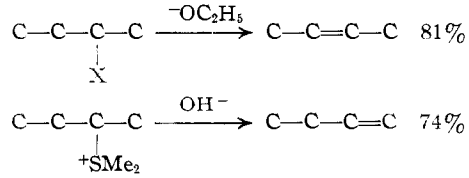
(19) Supported by a grant from the National Heart Institute of the National Institutes of Health.

(20) Supported by a grant-in-aid of the American Cancer Society (on recommendation by the committee on Growth, National Research Council).

A NEW TECHNIQUE FOR CONTROLLING THE DIRECTION OF ELIMINATION REACTIONS

Sir:

It has been maintained by Ingold and his coworkers [Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapter VIII] that bimolecular eliminations from alkyl halides result in the predominant formation of the most highly branched olefin (Saytzeff rule), whereas onium salts give the least branched olefins (Hofmann rule).



They have attributed the change in direction of elimination to the inductive effect of the positive pole in the onium salt. Schramm [C. H. Schramm, *Science*, **112**, 367 (1950)] suggested that the effect might be due not to the charge, but to the large steric requirements of the dimethylsulfonium or trimethylammonium group which would favor attack by the base on a terminal hydrogen atom.

We had previously observed that the unimolecular elimination of diisobutylene hydrochloride proceeds to give predominantly the 1-olefin

and attributed this result to steric effects [H. C. Brown and H. L. Berneis, THIS JOURNAL, **75**, 10 (1953)]. We were therefore led to consider the possibility that steric effects might be made to control the direction of elimination and that such steric effects might be the structural basis for eliminations according to the Hofmann rule.

We have now found it possible to control the direction of elimination in alkyl halides by varying the steric requirements of the attacking base. The use of potassium *t*-butoxide gives predominantly the 1-olefin in cases where the ethoxide results in the 2-derivative.

Alkyl halide	% 1-Olefin EtO⁻	% 1-Olefin *t*-BuO⁻
$C_2H_5CHBrCH_3$	19 (ref. 1)	53.4
$C_3H_7CHBrCH_3$	29 (ref. 1)	66
$C_2H_5CBr(CH_3)_2$	29 (ref. 1)	72
$(CH_3)_2CHCBr(CH_3)_2$		87
$(CH_3)_3CCH_2CBr(CH_3)_2$	85	99

Bases with larger steric requirements result in a further increase of the 1-olefin. This may be illustrated by the increasing yields of 3-methyl-1-butene which are obtained from *t*-amyl bromide in bimolecular eliminations utilizing a series of alkoxides of increasing steric requirements.

Potassium salt of	% 1-Olefin
Ethyl alcohol	29
t-Butyl alcohol	72
t-Amyl alcohol	78
Triethylcarbinol	89

Sufficient potassium metal was dissolved in 200 ml. of the alcohol to give a solution approximately 1.5 *M* in the alcoholate. The *t*-halide was then dissolved in the solution, maintaining a 50% molar excess of base. The solution was heated at 75° for two hours to ensure completion of the reaction. The temperature was then raised and the olefin distilled out of the reaction mixture through an efficient micro column. Olefin yields (based on *t*-halide) of 93–99% were obtained. The products were analyzed by refractive index and checked in selected test cases by infrared analysis.

The use of potassium *t*-butoxide and other even more hindered bases should be a valuable synthetic tool in controlling the direction of elimination and should do away with the need to synthesize quaternary ammonium compounds in order to obtain high yields of terminal olefins.

We have now been able to demonstrate a general trend from elimination according to the Saytzeff rule toward elimination according to the Hofmann rule by (1) increasing the steric requirements of the alkyl groups on the incipient double bond (Me_2< Me, Et<Me_3<Me_4<Me_2, *t*-Bu), (2) increasing the steric requirements of the group undergoing elimination (Br^-<$^-OSO_2R$<SMe_2<NMe_3), and (3) increasing the steric requirements of the attacking base (EtO^-<*t*-BuO^-).

These results leave little doubt that steric effect must be the basis of eliminations according to the Hofmann rule.

DEPARTMENT OF CHEMISTRY
PURDUE UNIVERSITY HERBERT C. BROWN
LAFAYETTE, INDIANA ICHIRO MORITANI

RECEIVED JULY 20, 1953

NUCLEOTIDE SYNTHESIS BY MALT AND PROSTATE PHOSPHATASES

Sir:

In an extension of previous work[1] on the phosphorylation of nucleosides by phosphate transfer we have made a search for other transfer systems. As regards the malt enzyme used in the previous experiments, the mononucleotides themselves have been found to be much more efficient donors, as judged by the transfer ratio,[2] than sodium phenylphosphate employed previously.[1] Deoxy- and ribonucleotides, but only the 5′-isomers, were equally effective as donors.

It has, in addition, been found that human prostate phosphatase also is able to catalyze the phosphorylation of nucleosides and that in this case, in contrast to the malt enzyme, which produces only the 5′-nucleotides, all possible nucleotide isomers are formed. In the prostate enzyme system, phenylphosphate served as a donor, but mononucleotides did not. These differences in specificity are summarized below.

Enzyme	Donor	Nucleotides synthesized: 5′-ribo	3′-ribo	2′-ribo	5′-deoxy	3′-deoxy
Malt	Phenylphosphate	+	−	−	+	−
	Mononucleotide	+	−	−	+	−
Prostate	Phenylphosphate	+	+	+	+	+
	Mononucleotide	−	−	−	−	−

With the use of the prostate enzyme and of phenylphosphate as donor, the three isomers of ribocytidylic acid and the two isomers of thymidylic acid have been synthesized and isolated by ion exchange chromatography.

This work was supported by research grants from the National Institutes of Health, U. S. Public Health Service, and the Rockefeller Foundation. One of us (G. B.) was aided by a Predoctoral Research Fellowship from the U. S. Public Health Service.

(1) G. Brawerman and E. Chargaff, THIS JOURNAL, **75**, 2020 (1953).

(2) B. Axelrod, *J. Biol. Chem.*, **172**, 1 (1948).

DEPARTMENT OF BIOCHEMISTRY GEORGE BRAWERMAN
COLLEGE OF PHYSICIANS AND SURGEONS
COLUMBIA UNIVERSITY ERWIN CHARGAFF
NEW YORK 32, N. Y.

RECEIVED JULY 6, 1953

THE INFRARED SPECTRUM OF THE OXONIUM ION

Sir:

The infrared absorption spectra of films of oxonium chloride and oxonium bromide have been observed at −195° and spectra which are typical of those obtained are reproduced in Fig. 1. The films were prepared by condensing an equimolar mixture of gaseous H_2O and HX on a previously cooled KBr plate. The OH_3^+ must be the source of the four absorption bands at 1050 cm.$^{-1}$, 1700 cm.$^{-1}$, 2100 cm.$^{-1}$ and 2570 cm.$^{-1}$ in OH_3Cl (similarly, at 1100 cm.$^{-1}$, 1700 cm.$^{-1}$, 2100 cm.$^{-1}$ and 2610 cm.$^{-1}$ in OH_3Br). In addition, some films of

both salts show an absorption maximum near 3200 cm.$^{-1}$ as part of the broad absorption region which extends to frequencies above 3500 cm.$^{-1}$. Very little of the observed spectrum can be attributed to ice, whose intense bands[1] at 812 cm.$^{-1}$ and 3150 cm.$^{-1}$,[2] do not appear. Except for the peaks at 2770 cm.$^{-1}$ in OH_3Cl and 2410 cm.$^{-1}$ in OH_3Br, the halides cannot be responsible either since the same bands occur in both salts.

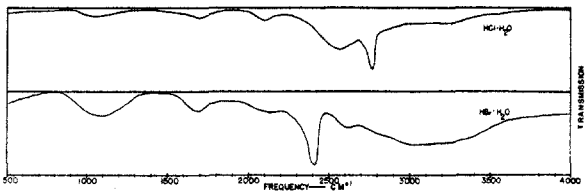


Fig. 1.—The infrared absorption spectrum of oxonium chloride and oxonium bromide at −195°.

To confirm these conclusions we have, in addition to the equimolar compounds, condensed five gas mixtures with composition ranging from 90% HCl–10% H_2O to 20% HCl–80% H_2O, and these showed the expected HCl or ice spectrum superimposed on that of the OH_3^+ ions. The compositions containing excess HCl showed two peaks very close to those reported for pure crystalline HCl at 2704 cm.$^{-1}$ and 2746 cm.$^{-1}$.[3,4] Therefore the HCl responsible for the 2770 cm.$^{-1}$ peak in the OH_3Cl sample must be in a different environment, *e.g.*, as HCl molecules in the OH_3Cl lattice. In this case they may be produced by the equilibrium

$$OH_3Cl \rightleftharpoons H_2O + HCl$$

but we have not yet investigated this possibility. Altogether, the general outlines of the experimental situation seem clear, but some details still need clarification. A number of films have been prepared and the spectra were not completely reproducible, differing chiefly in two respects: (a) the shape of the diffuse absorption region between 2350 cm.$^{-1}$ and 3500 cm.$^{-1}$ and (b) the height of the peak we have ascribed to free HX molecules. Further studies are continuing.

Whereas the observed spectrum is different from either ice or the hydrogen halides, it is closely parallel to that of ammonia. The hydrogen stretching frequencies are lower and the bands broader but both of these features may be attributed to strong hydrogen bonds. It may therefore be concluded that the OH_3^+ ion which is isoelectronic with NH_3, also exists in a symmetrical pyramidal configuration. This conclusion agrees with that derived from proton resonance measurements.[5-6]

METCALF CHEMICAL LABORATORIES
BROWN UNIVERSITY C. C. FERRISO
PROVIDENCE 12, RHODE ISLAND D. F. HORNING

RECEIVED JULY 27, 1953

(1) F. P. Reding, Thesis, Brown University, 1951.
(2) J. J. Fox and A. E. Martin, *Proc. Roy. Soc.* (*London*), **A174**, 234 (1940).
(3) G. Hettner, *Z. Physik*, **78**, 141 (1932).
(4) Lee, Sutherland and Wu, *Proc. Roy. Soc.* (*London*), **A176**, 493 (1940).
(5) Y. Kakiuchi, *et al.*, *J. Chem. Phys.*, **19**, 1069 (1951).
(6) R. E. Richards and J. A. S. Smith, *Trans. Far. Soc.*, **47**, 1261 (1951).

A METHOD FOR STUDYING THE MOBILITY OF CHEMISORBED FILMS: OXYGEN ON TUNGSTEN[1]

Sir:

Field emission microscopy has been applied to the above named problem as follows: A small sealed-off field emission tube is immersed in liquid helium kept in an unsilvered Dewar vessel.[2] The tip is cleaned off by electric heating. The resultant clean single crystal emission pattern is stable indefinitely if the tube contains no helium. It is now possible to liberate gas from an auxiliary filament (also heated electrically). If the gas emitter is so placed that it is seen by only a part of the field emitter tip, only that region of the latter will become contaminated with gas. This results from the sufficiently high accommodation coefficient of the internal surface of the tube at 4°K. It is then possible to heat the field emitter electrically and thus to determine how and at what temperature mobility sets in. Field emitter temperature is determinable from its electrical resistance.

Experiments with oxygen on tungsten were carried out with three oxygen sources: A CuO, covered Pt wire, a BaO_2 covered Pt wire, and a rope consisting of ~20 strands of 0.00045 mil W wire on which oxygen condensed on cooling to helium temperatures if the tube contained oxygen at a pressure of 10 mm. The results agree for these sources and are as follows. If small amounts of oxygen are evaporated onto the tip, mobility does not become appreciable below 350°K., and increases with increasing temperature. The phenomenon is definitely not a two-dimensional melting but a gradual, activation-energy-limited diffusion process. Certain regions of the crystal, particularly those in the zone connecting (211) with (211) via (110) hold oxygen most tenaciously. On these regions (the first to show oxygen contamination in this experiment) the oxygen is bound so firmly that desorption seems to precede mobility, setting in at about 1800°K. On other planes mobility seems quite fast at temperatures where these regions cannot retain oxygen for periods of time longer than those required for diffusion to the firmly bonding regions. This is shown by the fact that it is impossible to contaminate regions other than those mentioned above if oxygen is evaporated onto a clean tip kept at 1000°K. or higher. If a previously contaminated tip is heated to these temperatures, however, very complicated patterns result, indicating that desorption is slow and may proceed via the formation of metastable surface oxides.

If oxygen is evaporated in larger amounts onto a tip kept at 4°K. totally different behavior occurs. Under these conditions spreading sets in at 70°K. It is possible to watch the film cover the tip like the unrolling of a carpet. However, the layer thus formed is not itself mobile; if the amount of oxygen initially evaporated is only enough to "unroll the carpet" part way, the sharp boundary thus formed will not change until the tip temperature is 300°K. unless more oxygen is evaporated onto the tip.

(1) Work supported in part by Contract AF 33(038)-0534 with the U. S. Air Force.
(2) Apparatus very similar to that used is described by R. Gomer and J. K. Hulm, *J. Chem. Phys.*, **20**, 1500 (1952).

This shows that oxygen is mobile on an oxygenated tungsten surface at 70°K. The low temperature spreading thus consists of diffusion on top of the already covered regions of the surface, oxygen presumably becoming adsorbed on the clean tungsten at the edge of the layer, making it possible for other molecules to diffuse over the newly covered region.[3] The layer formed at 70°K. seems to have the high work function of a layer produced at ordinary temperatures and does not undergo detectable changes below 500°K. It would therefore seem that no appreciable activation is necessary even at 70°K. for the formation of a chemisorbed layer of oxygen on tungsten. Since the gas adsorbed directly on the tip comes from a source of at least 70°K. or higher, it is impossible at present to decide whether activation is necessary at 4°K.

We hope to obtain quantitative information on these phenomena by measurements on other gases and substrates.

(3) Diffusion with a sharp boundary is known to occur in cases where the diffusant is removed by reaction with the xarrier matrix (see H. Fujita, *J. Chem. Phys.*, **21**, 700 (1953)).

INSTITUTE FOR THE STUDY OF METALS
THE UNIVERSITY OF CHICAGO
CHICAGO 37, ILL.
ROBERT GOMER
JOHN K. HULM

RECEIVED JUNE 25, 1953

EVIDENCE FOR THE EXISTENCE OF RADICALS IN THE PRESENCE OF LEWIS ACIDS[1]

Sir:

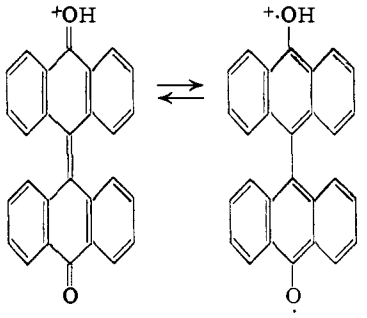
Paramagnetic resonance absorption spectroscopy has been used to detect radicals formed by several organic compounds in the presence of Lewis acids and, in some cases, the concentration of the paramagnetic species has been estimated.

Solutions of the following compounds in concentrated sulfuric acid, 96–98%, are deeply colored and were found to show paramagnetic resonance absorptions: (1) bianthrone, (2) fluorenone, (3) anthraquinone, (4) triphenylmethyl peroxide, (5) thiophenol, (6) *p*-thiocresol, (7) thio-β-naphthol), (8) diphenyl disulfide, (9) thianthrene (diphenylene disulfide).

The same compounds, when heated with anhydrous aluminum chloride to temperatures ranging from 60 to 180° and cooled to room temperature, yielded deeply colored solids which showed no paramagnetic absorptions. Bianthrone and fluorenone were also dissolved in anhydrous ether to which was added an ether solution of aluminum chloride. Both solutions were deep red and paramagnetic.

Neither the pure compounds nor their solutions in inert solvents (*e.g.*, ethanol, benzene, carbon disulfide, decalin) at room temperature showed any detectable paramagnetism. Rough preliminary estimates of the fraction of the dissolved material which exists in the radical form are: less than 5% for compounds (2), (3), and (4); 10% or more for the other compounds.

It is well known that bianthrone is thermochromic[2] and, when the deep red sulfuric acid solution is added to ice water, the bianthrone that precipitates is, for a short period of time, a dark green solid which is similar in color to the heated substance.[3] The thermally excited species is paramagnetic[4] and thus there may be a similarity in the paramagnetism of the thermally excited and the acid induced forms. Since thermochromism has been explained by assuming an equilibrium between a singlet molecule and a thermally excited triplet modification,[1,2] it is proposed that in acid solutions there may exist an equilibrium of the following type with either one or two protons attaching to a molecule of bianthrone



Herbert, Goren and Vernon[5] were unable to determine, by cryoscopic methods, whether one or two protons were taken up.

The intensity of the paramagnetic resonance spectrum of the sulfuric acid solution of bianthrone shows that about 10% of the dissolved material is in the paramagnetic form at room temperature. This is about ten times as large a fraction of excited molecules as that estimated to exist in inert solvents at room temperature.[2b] The triplet modification is thus a stronger base than the singlet form, and the acid lowers the difference in stability between the singlet and triplet species. Measurements are being made to determine accurately the equilibrium constant and the heat of reaction for this system.

Certain similarities in the colors and the paramagnetic spectra of all the thio compounds (5–9) indicate that similar species may be contributing to the paramagnetism in all these compounds. Fries and Volk[6] have reported that thiophenol in the presence of sulfuric acid, aluminum chloride, or stannic chloride yields thianthrene as a product. They also report analogous behaviors for thio-*p*-cresol and thio-α-naphthol. Stenhouse[7] reported that thiophenol is easily oxidized to diphenyl disulfide in sulfuric acid.

We are attempting to ascertain what molecular species are responsible for the unusual paramagnetic resonance spectra that are observed in the thio compounds.

DEPARTMENT OF CHEMISTRY
COLUMBIA UNIVERSITY
NEW YORK 27, N. Y.
JACK M. HIRSHON
DONALD M. GARDNER
GEORGE K. FRAENKEL

RECEIVED JULY 13, 1953

(1) Supported in part by the Squier Signal Laboratory, U. S. Army Signal Corps.

(2) (a) W. T. Grubb and G. B. Kistiakowsky, THIS JOURNAL, **72**, 419 (1950); (b) W. Theilacker, G. Kortüm, G. Friedheim, *Ber.*, **83**, 508 (1950).

(3) G. Kortüm, W. Theilacker, H. Zeininger and H. Elliehausen, *ibid.*, **86**, 294 (1953).

(4) W. G. Nilsen and G. K. Fraenkel, submitted for publication.

(5) R. A. Herbert, M. B. Goren and A. A. Vernon, THIS JOURNAL, **74**, 5779 (1952).

(6) K. Fries and W. Volk, *Ber.*, **42**, 1170 (1909).

(7) J. Stenhouse, *Ann.*, **149**, 247 (1869).

ON THE STRUCTURE OF TETRABORANE

Sir:

We have reinvestigated gaseous tetraborane by electron diffraction. The butane-like model with tetrahedral bond angles as reported by Bauer[1] is incompatible with our data; values of ∠B–B–B = 90° and ∠B–B–H = 133.5° do bring it into agreement, but the latter angle is out of the question, especially for the "methylenic" hydrogen atoms. No exhaustive investigation of the butane-like structure was attempted, however, because a structure (Fig. 1) plausibly related to the known boron hydride structures[2] was discovered and shown

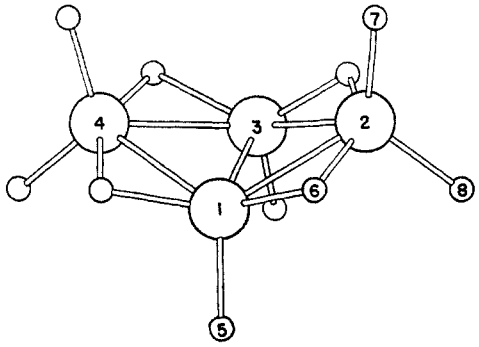


Fig. 1.—The B_4H_{10} structure.

to be in excellent agreement with the diffraction pattern early in our work,[3,4] and has since been established by Nordman and Lipscomb by the crystal structure investigation reported in the following Communication. The atomic arrangement is closely similar to that of the apical groups in decaborane and is comparable to the arrangements in diborane and stable pentaborane.

Approximate values for the numerous parameters of the C_{2v} model are

B_1–B_2 = 1.85 Å., B_1–B_3 = 1.76 Å.

$B_2 \cdots B_3$ = 2.88 Å. (Dihedral ∠$B_1B_3B_4$–$B_1B_3B_2$ = 124°32′)

B_1–H_5 = B_2–H_7 = B_2H_8 = 1.19 Å.

B_2–H_6 = 1.33 Å., B_1–H_6 = 1.43 Å., H_6 in plane of $B_1B_2B_3$

∠B_3–B_1–H_5 = 118°20′ and ∠$B_{1,3}$–B_2–$H_{7,8}$ = 117°6′

These values were obtained primarily from the radial distribution curve (Fig. 2); they were refined by a (necessarily incomplete) correlation treatment. The H_6 parameters are highly uncertain, but the B–H distance 1.19 Å. and the B–B bond distances warrant comparison with the crystal values.

We are indebted to Professor A. B. Burg and Mr. E. S. Kuljian for the samples of tetraborane and to the Office of Naval Research (Contract N6onr 24423) for support during this investigation.

CONTRIBUTION NO. 1828
GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA 4, CALIFORNIA
MORTON E. JONES
KENNETH HEDBERG
VERNER SCHOMAKER

RECEIVED JUNE 30, 1953

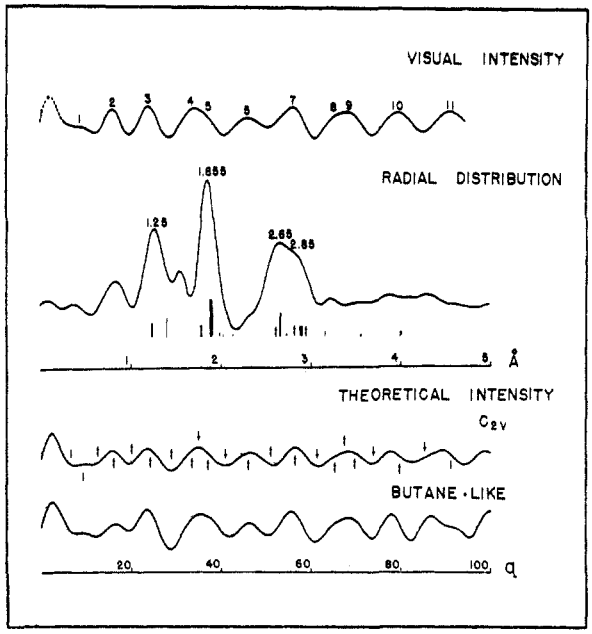


Fig. 2.—Visual, radial distribution and theoretical intensity curves. The theoretical intensity curves are for the butane-like model with ∠ B–B–B = 90° and ∠ B–B–H = 133.5° and for the C_{2v} model described in the text.

(1) S. H. Bauer, THIS JOURNAL, **60**, 805 (1938).

(2) For references and discussion see K. Hedberg, M. E. Jones, and V. Schomaker, *Proc. Nat. Acad. Sci. U. S.*, **38**, 679 (1952).

(3) K. Hedberg, V. Schomaker and M. E. Jones, Paper E.D. 17, Second International Congress of Crystallography, Stockholm, June 27–July 5, 1951. The structure, although not mentioned in the Abstract, was presented at the meeting.

(4) Quarterly Progress Report, October 23, 1951, Contract N6onr 24423.

THE MOLECULAR STRUCTURE OF B_4H_{10}

Sir:

As a result of a complete analysis of 616 observed reflections from a single crystal of B_4H_{10}, we have determined the molecular structure. There are four molecules in a monoclinic unit cell having parameters a = 8.68, b = 10.14, c = 5.78Å. and β = 105.9°. The space group $P2_1/n$ is unambiguous, and the twelve independent positional parameters of the boron atoms were determined from three-dimensional Fourier analysis. The hydrogen atoms were readily observable, and were also located more precisely from a three-dimensional Fourier series from which the boron atoms had been subtracted.

The molecular structure of B_4H_{10} is shown in Fig. 1. No molecular symmetry elements are required by the space group of the crystal, but the molecular dimensions indicate that the symmetry of the isolated molecule is C_{2v}. For brevity, we

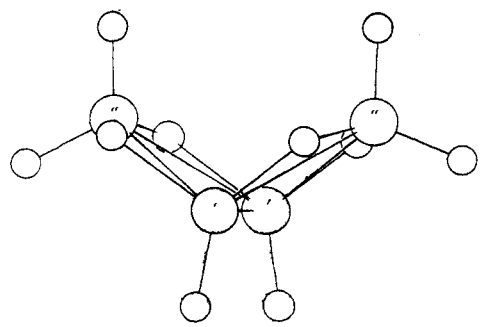


Fig. 1.—The molecular structure of B_4H_{10}.

record average bond distances with their average deviations on the assumptions that the molecular symmetry is C_{2v} and that the two B′–H and the four B″–H distances are all equal. Molecular parameters[1] are four B′–B″ = 1.845 ± 0.002Å., B′–B′ = 1.750Å., B″–B″ = 2.786Å., six B–H = 1.11 ± 0.04, four B′–H_b (bridge) = 1.21 ± 0.03Å. and four B″–H_b = 1.37 ± 0.10Å. Assuming a boron radius of 0.75Å., and therefore single bond distances of 1.50Å. for B–B and 1.10Å. for B–H, bond orders are 0.27 for B′–B″, 0.38 for B′–B′, 0.01 for B″–B″, 0.96 for B–H, 0.65 for B′–H_b and 0.35 for B″–H_b. The total bond order for the molecule is thus 11.2, close to the expected value of 11. The assumed boron radius is smaller than that calculated for B_2H_6 (0.79Å.), B_5H_9 (0.78Å.) and $B_{10}H_{14}$ (0.81), and as in B_5H_9 the over-all size of the molecule is smaller than that reported in the preceding electron diffraction study by Jones, Hedberg and Schomaker. A similar effect has been observed in B_5H_9 and in hexamethylenetetramine.

It is of interest that the B″B′B″ bond angle is 98° which is a value about midway between the corresponding angle of 90° in the octahedron and 108° in the icosahedron. Thus the boron arrangement may be regarded as a fragment from either the octahedron or the icosahedron. The relatively open structure of this, the first member of the B_nH_{n+6} series compared with the relatively compact higher B_nH_{n+4} structures, probably is a factor relating to the comparatively greater reactivity.

Support of this research by the Office of Naval Research is gratefully acknowledged. All of the three-dimensional Fourier syntheses were carried out on the X-Ray Analogue Computer at Pennsylvania State College through the courtesy of Professor R. Pepinsky. We are also indebted to Dr. L. V. McCarty of the General Electric Company for supplying us with a sample of pure B_4H_{10}.

Details of this investigation will be submitted elsewhere.

(1) Where the distance is observed more than once we record average deviations, which are comparable with estimated probable errors, except for B′–B″ for which a probable error of ±0.01 Å. is estimated.

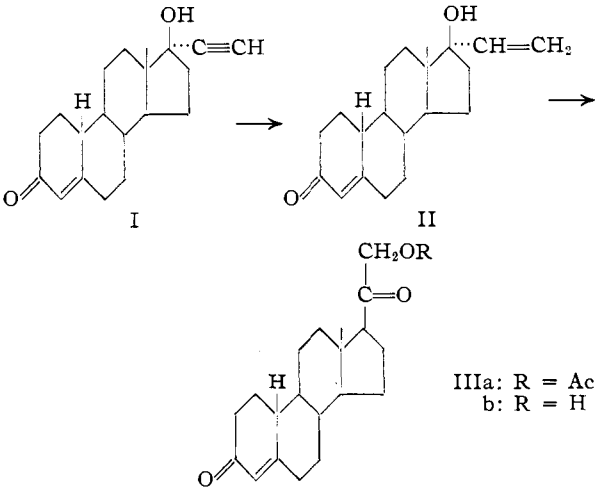
SCHOOL OF CHEMISTRY
UNIVERSITY OF MINNESOTA CHRISTER E. NORDMAN
MINNEAPOLIS 14, MINNESOTA WILLIAM N. LIPSCOMB

RECEIVED JUNE 30, 1953

STEROIDS. XLIX.[1] 19-NOR-DESOXYCORTICOSTERONE, A POTENT MINERALOCORTICOID HORMONE

Sir:

19-Nor-progesterone,[1,2] 19-nor-17-methyltestosterone,[3] and 19-nor-17-ethinyltestosterone (I)[3] have all been shown to possess biological activity of a higher order than the parent hormones. It was therefore of considerable interest to make available for biological testing the 19-nor analogs of adrenal cortical hormones, especially in view of the report by Ehrenstein[4] that an amorphous product, believed to be a 19-nor-desoxycorticosterone isomer and obtained by a lengthy degradation from strophanthidin, was devoid of biological activity. In this communication we record the synthesis and physiological activity of 19-nor-desoxycorticosterone (IIIb), which possesses the same configuration at all asymmetric centers as does desoxycorticosterone.



Chromic acid oxidation of 19-nor-testosterone[5] yielded 19-nor-Δ^4-androstene-3,17-dione [m.p. 171–172°, $[\alpha]^{20}D$ +139° ($CHCl_3$), $\lambda_{max.}^{EtOH}$ 240 mμ, log ε 4.24. Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.39; H, 8.99] which upon conversion to 19-nor-3-ethoxy-$\Delta^{3,5}$-androstadien-17-one [m.p. 141–143°, $[\alpha]^{20}D$ −87° (pyridine), $\lambda_{max.}^{EtOH}$ 242 mμ, log ε 4.26. Calcd. for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39. Found: C, 79.80; H, 9.15], ethinylation with potassium in *t*-amyl alcohol and acid hydrolysis furnished 19-nor-17-ethinyltestosterone (I) [m.p. 203–204°, $[\alpha]^{20}D$ −25° ($CHCl_3$), $\lambda_{max.}^{EtOH}$ 240 mμ, log ε 4.24. Calcd. for $C_{20}H_{26}O_2$: C, 80.49; H, 8.78. Found: C, 80.83; H, 8.80]. Partial hydrogenation in pyridine solution over a 5% palladium–calcium carbonate catalyst[6] led to the corresponding vinyl carbinol II [m.p. 169–170°, $[\alpha]^{20}D$ +25° ($CHCl_3$), $\lambda_{max.}^{EtOH}$ 240 mμ, log ε 4.25. Calcd. for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39. Found: C, 79.64; H, 9.27]. This latter compound was hydroxylated with osmium tetroxide,[7] and the product without purification was acetylated and subjected to a Serini reaction in toluene solution.[8] The resulting 19-nor-desoxycorticosterone acetate (IIIa) [m.p. 169–171°, $[\alpha]^{20}D$ +153° ($CHCl_3$), $\lambda_{max.}^{EtOH}$ 240 mμ, log ε 4.26, infrared bands (chloroform) at 1744 and 1718 cm.$^{-1}$ (21-acetoxy-20-ketone) and 1668 cm.$^{-1}$ (Δ^4-3-ketone). Calcd. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44. Found: C, 73.88; H, 8.23] was saponified with sodium bicarbonate in aqueous methanol

(1) Steroids. XLVIII, C. Djerassi, L. Miramontes and G. Rosenkranz, THIS JOURNAL, **75**, November (1953).

(2) L. Miramontes, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 3540 (1951).

(3) C. Djerassi, L. Miramontes and G. Rosenkranz, Abstracts, 121st Meeting of the Am. Chem. Soc., Milwaukee, 1952.

(4) M. Ehrenstein, *J. Org. Chem.*, **9**, 435 (1944).

(5) A. J. Birch, *J. Chem. Soc.*, 367 (1950); A. L. Wilds and N. A. Nelson, THIS JOURNAL, in press.

(6) *Cf.* L. Ruzicka and P. Müller, *Helv. Chim. Acta*, **22**, 755 (1939).

(7) *Cf.* A. Serini and W. Logemann, *Ber.*, **72**, 1862 (1938).

(8) *Inter al.* A. Serini, W. Logemann and W. Hildebrand, *ibid.*, **72**, 391 (1939); C. Djerassi and C. R. Scholz, THIS JOURNAL, **71**, 3962 (1949).

at room temperature,[9] and yielded 19-nor-desoxycorticosterone (IIIb) (m.p. 131–132°, $\lambda_{max.}^{EtOH}$ 240 mμ, log ε 4.24).

19-Nor-desoxycorticosterone was tested for its mineralocorticoid activity by the assay method of Simpson and Tait[10] and found to be *ca.* twice as active as desoxycorticosterone.

JOINT CONTRIBUTION FROM THE
INSTITUTO DE QUÍMICA
UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO
TACUBA, MÉXICO D. F., AND
RESEARCH LABORATORIES OF SYNTEX, S.A.
LAGUNA MAYRAN 413
MEXICO CITY 17, D. F.

A. SANDOVAL
L. MIRAMONTES
G. ROSENKRANZ
CARL DJERASSI[11]
FRANZ SONDHEIMER

RECEIVED JUNE 25, 1953

(9) We are indebted to Dr. A. Zaffaroni and Mr. J. Iriarte for carrying out this step.

(10) S. A. Simpson and J. F. Tait, *Endocrinology*, **50**, 150 (1952). We would like to thank Drs. Simpson and Tait for carrying out this assay.

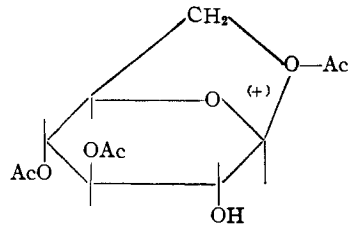
(11) Department of Chemistry, Wayne University, Detroit, Mich.

A CHEMICAL SYNTHESIS OF SUCROSE

Sir:

Tri-*O*-acetyl-D-glucosan<1,5>α<1,2>,[1] 4 mM., and sirupy 1,3,4,6-tetra-*O*-acetyl-D-fructofuranose,[2] 4 mM., dried by azeotropic distillation with benzene, were heated together in a sealed tube at 100° for 104 hours. The product was deacetylated and the sugars were fractionated by preparative paper chromatography[3] using butanol–ethanol–water (5:1:4)[4] on Whatman 3 MM paper. The fraction expected to contain sucrose was acetylated and the product was chromatographed on Magnesol–Celite (5:1) according to the general procedure developed by McNeely, Binkley and Wolfrom.[5] A zone was detected at the position on the column expected for sucrose octaacetate. Elution with acetone and crystallization from ethanol gave 147 mg., 5.5% yield, of a substance with melting point 81–86°. After three crystallizations from ethanol, the substance possessed the physical constants expected for sucrose octaacetate,[6] m.p. 89–90°, $[\alpha]^{25}D$ +60° (*c*, 1 in chloroform). The melting point was unchanged on admixture with authentic sucrose octaacetate. The substance pressed with potassium bromide into a window[7] possessed an infrared absorption spectrum identical to that measured for sucrose octaacetate under the same conditions. Deacetylation yielded a substance, m.p. 187°, $[\alpha]D$ +66.7° (water), which gave a positive Raybin test.[8] The mixed melting point with sucrose, m.p. 187°, $[\alpha]D$ +66.5° (water), was 187°.

This appears to be the first purely chemical synthesis of sucrose. Levi and Purves[9] have reviewed the numerous unsuccessful attempts. Our present success is believed due to the formation of the ion I as an intermediate in reactions of the Brigl anhydride with alcohols at elevated temperature.[10,11,12] β-Maltose octaacetate was prepared[13] through reaction of the anhydride with 1,2,3,6-tetra-*O*-acetyl-β-D-glucopyranose.



I

(1) P. Brigl, *Z. physiol. Chem.*, **122**, 245 (1922).

(2) W. W. Binkley and M. L. Wolfrom, THIS JOURNAL, **68**, 2171 (1946).

(3) C. Yanofsky, E. Wasserman and D. M. Bonner, *Science*, **111**, 61 (1950).

(4) E. L. Hirst and J. K. N. Jones, *Discuss. Faraday Soc.*, **7**, 271 (1949).

(5) W. H. McNeely, W. W. Binkley and M. L. Wolfrom, THIS JOURNAL, **67**, 527 (1945).

(6) R. P. Linstead, A. Rutenberg, W. G. Dauben and W. L. Evans, THIS JOURNAL, **62**, 3260 (1940).

(7) M. M. Stimson and M. J. O'Donnell, *ibid.*, **74**, 1805 (1952).

(8) H. W. Raybin, *ibid.*, **56**, 2603 (1933).

(9) I. Levi and C. B. Purves, *Advances in Carbohydrate Chemistry*, **4**, 27 (1949).

(10) W. J. Hickinbottom, *J. Chem. Soc.*, 3140 (1928).

(11) W. N. Haworth and W. J. Hickinbottom, *ibid.*, 2847 (1931).

(12) E. Hardegger and J. de Pascual, *Helv. Chim. Acta*, **31**, 281 (1948).

(13) R. U. Lemieux, *Can. J. Chem.*, in press.

PRAIRIE REGIONAL LABORATORY
NATIONAL RESEARCH COUNCIL
SASKATOON, SASKATCHEWAN, CANADA

R. U. LEMIEUX
G. HUBER

RECEIVED JULY 13, 1953

OBSERVATIONS ON THE MECHANISM OF ELECTRON TRANSFER IN SOLUTION[1]

Sir:

An important problem in the field of mechanisms of "electron transfer" reactions is concerned with the changes taking place in the coördination spheres of the oxidant and the reductant on electron transfer. This problem has been but little elucidated for reaction of cations, as for example $Ti^{+++} + Fe^{+++} = Ti(IV) + Fe^{++}$ (net change) or $Fe^{*++} + Fe^{+++} = Fe^{*+++} + Fe^{++}$ (virtual change). Thus it is not known whether electron transfer takes place by an electron jump through several layers of solvent, or whether it accompanies the transfer of a group such as OH from oxidant to reductant; or H from reductant to oxidant.[2] Similarly the particular role played by negative ions such as Cl^- or F^- in catalyzing[3,4,5] the reaction of cations is not understood. The principal reason for the lack of a detailed understanding is that the systems are generally very labile with respect to changes in the coördination sphere so that intermediate stages which would supply evidence about the nature of the activated complexes change to final products too rapidly for convenient observation. One method of attack on these problems is to alter conditions so as to slow up the changes; another is to exploit the ions which are less labile with respect to substitution under ordinary conditions.

We have followed the latter line of attack, choosing the reductant $Cr^{++} \rightarrow Cr(III)$. This system

(1) This work was supported by the Office of Naval Research under Contract N6-Ori-02026.

(2) See W. F. Libby, "Symposium on Electron Transfer and Isotopic Reactions," *J. Phys. Chem.*, **56**, 863 (1952); discussion by R. W. Dodson, N. Davidson, O. L. Forchheimer, pp. 866, *et seq.*

(3) J. Silverman and R. W. Dodson, *J. Phys. Chem.*, **56**, 846 (1952).

(4) D. J. Meier and C. S. Garner, *ibid.*, **56**, 853 (1952).

(5) H. C. Hornig and W. F. Libby, *ibid.*, **56**, 869 (1952).

has the virtue that any group found in the coördination sphere of Cr(III) when it is formed from Cr^{++} must have been present in the activated complex. Substitution reactions on Cr(III) are sufficiently slow so that entry of groups after completion of the oxidation can be ruled out at least for some systems. (For Cr(II), however, substitutions are rapid[6].)

A significant result is that when Cr^{++} is oxidized by Fe^{+++} in perchloric acid medium (1 *M*) in a solution containing Cl^- (0.05 *M*), chloride ion is found attached to the product Cr(III) (0.5 mole/mole Cr(III) for these conditions). Hence, we can conclude that Cl–Cr bonds must have been established in the activated complex. The experiments, however, do not distinguish the activated complexes $[Cr\text{–}Cl\text{–}Fe]^{+4}$ (implying Cl atom transfer as the act producing electron transfer) or $[ClCr^{+}\cdot water\cdot Fe^{+++}]$ (implying electron transfer through the solvent facilitated by Cl^- attached to Cr^{++}). A decision in favor of the former type of explanation is reached on the basis of experiments we have done using as oxidizing agents complex ions which are slow with respect to substitution. We find that when $Co(NH_3)_5Cl^{++}$ is reduced by Cr^{++} in 1 *M* $HClO_4$, one Cl^- appears attached to chromium for each Cr(III) which is formed or Co(III) reduced. Furthermore, when the reaction is carried out in a medium containing radioactive chloride, the mixing of the Cl^- attached to Cr(III) with that in solution is found to be less than 0.5%. The experiment with radioactive chloride shows that transfer of chlorine from the oxidizing agent to the reducing agent is direct, rather than by release and reëntry of Cl^-, and leads to the formulation of the activated complex as $[(NH_3)_5Co\text{–}\overset{\frown}{Cl}\text{–}Cr]^{+4}$ (apart from the participation by solvent and its ions). Transfer from $Co(NH_3)_5Br^{++}$ to Cr(III) is also found to be complete. In both cases the net changes are to form $Cr(H_2O)_6^{+++}$ and X^- as final products, with, however, CrX^{++} as a recognizable intermediate stage.

The observations on relative rates are also significant. Rates of reduction increase in the order: $Co(NH_3)_6^{+++}$, $Co(NH_3)_5H_2O^{+++}$, $Co(NH_3)_5Cl^{++}$, $Co(NH_3)_5Br^{++}$. The groups H_2O, Cl^- and Br^- have available pairs of unshared electrons as points of attack, the polarizability of the groups increasing in the order named. With $Co(NH_3)_6^{+++}$, a proton must be removed to provide a pair of electrons as point of attack for Cr^{++}, or the electron must be transferred through the proton coördination shell.

We propose an activated complex of the type $[(NH_3)Co\text{–}X\text{–}Cr]^{+4}$ as a model for processes in which negative ions catalyze electron exchange between cations. Experiments are in progress to determine whether oxygen atom transfer occurs in the reaction of Cr^{++} with $Co(NH_3)_5H_2O^{+++}$. These have significance in their relation to processes involving activated complexes such as $[Ti^{+++}\cdot Fe^{+++}]aq.$, $[Fe^{++}\cdot Fe^{+++}]aq.$, etc. We recognize that an activated complex of the type we have formulated is not always readily accessible, as for example, when both partners are inert to substitution changes. When at least one partner is labile, the direct bridge complex seems a likely path.

(6) H. Taube, *Chem. Reviews*, **50**, 99–101 (1952).

GEORGE HERBERT JONES LABORATORIES
UNIVERSITY OF CHICAGO
CHICAGO 37, ILLINOIS
HENRY TAUBE
HOWARD MYERS
RONALD L. RICH

RECEIVED JULY 6, 1953

THE STEREOCHEMISTRY OF THE SN2′ REACTION

Sir:

During the last few years considerable evidence has accumulated that bimolecular displacement with rearrangement (SN2′ displacement) is possible with certain allylic halides.[1]

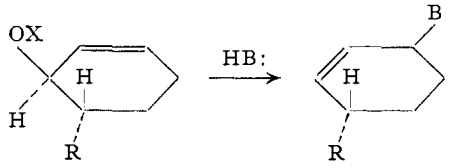
We are now presenting evidence which demonstrates that in SN2′ reactions the entering group comes in *cis* to the departing group: 6-alkyl-2-cyclohexenones (alkyl group = methyl, isopropyl and *t*-butyl) prepared by modified Birch reduction of suitable derivatives of anisole and aniline, were purified by conversion to 6-alkyl-3-(1-piperidyl)-cyclohexanones and regeneration *via* the crystalline methiodides. The cyclohexenones were reduced with lithium aluminum hydride to the corresponding 6-alkyl-2-cyclohexenols which were obtained pure by hydrolysis of their crystalline 3,5-dinitrobenzoates (methyl, m.p. 117.9–118.6°; isopropyl, m.p. 79.7–80.7°; *t*-butyl, m.p. 105.7–106.4°). The stereochemistry of these cyclic allylic alcohols was proved to be *trans* by catalytic hydrogenation and comparison of the 3,5-dinitrobenzoates of the saturated compounds with the corresponding authentic *trans* 2-alkylcyclohexanol 3,5-dinitrobenzoates (methyl, m.p. 113.8–114.7°; isopropyl, m.p. 132.2–133.2°; *t*-butyl, m.p. 122.2–123.0°). Attempts to convert the cyclohexenols to *p*-toluenesulfonates were totally unsuccessful, even *via* oxidation of the easily accessible *p*-toluenesulfinates[2] which were themselves unreactive toward piperidine. A solution to the problem was eventually found in the use of the 2,6-dichlorobenzoates of the 6-alkyl-2-cyclohexenols (methyl, m.p. 56.8–57.6°; isopropyl, m.p. 66.5–67.2°; *t*-butyl, m.p. 71.2–71.9°). Displacement with piperidine[3] could be effected by heating, without solvent or in xylene solution, at 130° for twen-

(1) Credit for the postulation and demonstration of this reaction is difficult to assign. The Ingold school has laid claim to the reaction as its appanage (see C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 584–594), a claim all the more striking as it had been most active in adducing theoretical arguments against the possibility of SN2′ displacements. In any event, the first clear-cut demonstration of the reaction, Ingold's captious comments notwithstanding, is due to R. E. Kepner, S. Winstein and W. G. Young, THIS JOURNAL, **71**, 115 (1949), and particularly clear examples were later published by W. G. Young, I. D. Webb and H. L. Goering, *ibid.*, **73**, 1076 (1951), see also W. G. Young and R. Clement, *Science*, **115**, 488 (1952). It may not be out of place to point out that the reactions of the halocodides offer much earlier instances of the phenomenon, although the reactions were only recently recognized as SN2′ displacements (G. Stork in R. H. F. Manske and H. Holmes, "The Alkaloids," Vol. II, Academic Press, New York, 1952, p. 185, and G. Stork and F. H. Clarke, THIS JOURNAL, **75**, in preparation.

(2) H. Phillips, *J. Chem. Soc.*, **127**, 2552 (1925); R. M. Hann, THIS JOURNAL, **57**, 2166 (1935).

(3) Displacement reactions have been carried out on esters previously; see L. P. Hammett and H. L. Pfluger, THIS JOURNAL, **55**, 4079 (1933); J. F. Bunnett, M. M. Robison and F. C. Pennington, *ibid.*, **72**, 2378 (1950).

ty-four to seventy-two hours. The unsaturated amines which were formed in good yield were reduced catalytically to the corresponding cyclohexyl compounds. Conversion in high yields to pure picrates, picrolonates and methiodides demonstrated that in each instance a *single isomer had been formed in the displacement reaction.* This single isomer was shown in each of the three cases studied to be a *trans*-4-(1-piperidyl)-alkylcyclohexane by infrared evidence as well as by direct comparison with the proper derivatives of the authentic reference compound (methyl: picrate, m.p. 153.3–154.3°; picrolonate, m.p. 188.5–188.9°; methiodide, m.p. 239.4–239.7°; isopropyl: picrate, m.p. 123.5–124.2°; picrolonate, m.p. 174.7–175.1°; methiodide, m.p. 250.2–250.4°; *t*-butyl: picrate, m.p. 166.5–167.5°; picrolonate, m.p. 199.4–199.9°; methiodide, m.p. 253.0–253.2°). *The reaction followed bimolecular kinetics in each case* as demonstrated by the use of the van't Hoff differential method.[4] *The cis relationship of the entering and departing groups is thus demonstrated in the SN2′ reaction.*[5,6]



(4) K. J. Laidler, "Chemical Kinetics," McGraw-Hill Book Co., Inc., New York, N. Y., 1950, pp. 14–15.

(5) The possibility that the ester might rearrange before displacement was ruled out by isolation of the original ester in a state of purity from incomplete reactions.

(6) The steric results are in agreement with the ideas of Winstein and of Young: see W. G. Young, I. D. Webb and H. L. Goering, reference 1.

CHEMICAL LABORATORIES
HARVARD UNIVERSITY
CAMBRIDGE 38, MASSACHUSETTS

CHANDLER LABORATORY
COLUMBIA UNIVERSITY
NEW YORK 27, NEW YORK

GILBERT STORK
WILLIAM N. WHITE

RECEIVED JULY 15, 1953

BOOK REVIEWS

Polysaccharide Chemistry. By ROY LESTER WHISTLER, Professor of Biochemistry and Assistant Head, Department of Agricultural Chemistry, Purdue University, Lafayette, Indiana, and CHARLES LOUIS SMART, Purdue University, Lafayette, Indiana. Academic Press, Inc., 125 East 23rd Street, New York 10, N. Y. 1953. xv + 493 pp. 16 × 23.5 cm. Price $10.80.

Polysaccharide chemistry stands as an interesting record of man's inquisitiveness. It reveals that in this area his unquenchable and inexhaustible curiosity runs the gamut from the albumin glands of the vineyard snail (*Helix pomatia*) to the antigens which enable human beings to be separated into blood groups. Along the way, to select but a few examples, he has asked searching questions about red and brown algae, timothy pollen, gastric mucosa, slippery elm mucilage, lobster shells, wing remains of *Coleoptera* from the middle Eocene Period, chondromalacia, and type-specificity and virulence of pneumococci. Huge industries, based on starch and cellulose, prove once again that academic thirst for knowledge can lead to the market place.

There has long been a need to have the entire field of polysaccharides presented as a unified division of carbohydrate chemistry, and the authors merit praise and thanks for their achievement. This compilation of information will enable workers in apparently unrelated spheres of work to see their common ground and techniques, and it will save much time and effort for those who desire a compact presentation of subject matter as well as a guide to significant publications. The authors have made judicious selections from the extensive literature of cellulose, starch and pectic substances.

The first chapter, consisting of twenty-six pages, deals with the occurrence, nomenclature and classification of polysaccharides. Detailed tables summarize the classes of substances which are to be treated in later chapters. The second chapter condenses a vast amount of information regarding methods of analysis and proofs of structure. In the next thirty-three chapters each family of polysaccharides is systematically developed under the subdivisions of Occurrence, Preparation, Composition and Structure, Properties, Derivatives and Uses.

Abridgment and terseness are functional necessities in a book of this size, but condensation is carried to such an extent in the description of laboratory methods that the uninitiated reader may be beguiled into thinking that a procedure which in reality is difficult or which has pitfalls, is easy to carry out. The authors obviously and for good reason decided mainly to give the reader reassurance that methods are available, and where to find them. For useful information and critical evaluations, however, the original literature will have to be consulted. An example of this is the statement: "Xylose may be quantitatively and selectively fermented in the presence of other sugars." At times the authors are disarmingly uninformative, and the reader will, to use a theatrical term, do a "double-take." This is illustrated by the following: "Analysis of agar containing plants are sometimes in error because the raw material may not be uniform." The reviewer's favorite is found on page 334. "The acid pulp from the (Tamarind) seeds has been used for many years in the making of preserves and in the preparation of a cooling laxative drink."

There are evidences in the book that a balanced picture of the average reader was a matter of editorial concern because tritylation is explained parenthetically "with triphenylchloromethane." On the other hand, on page 105 the chemical formula of *bis*-chloromethylsulfone is uniquely presented in place of the name of the compound. However, on page 425 it is assumed that the word *bleb* is part of the vocabulary of that average reader. The most mysterious editorial decision is to list Anonymous in the author index.

These are minor criticisms of an excellent book. The important thing to bear in mind is that the authors have eminently succeeded in their objectives, and that there is now a book on polysaccharides which should be widely read and used.

DEPARTMENT OF CHEMISTRY
BROOKLYN COLLEGE
BROOKLYN 10, NEW YORK

LOUIS SATTLER

Structure of Metals—Crystallographic Methods, Principles, and Data. Second Edition. By CHARLES S. BARRETT, Ph.D., Professor, Institute for the Study of Metals, University of Chicago. McGraw-Hill Book Company, Inc., 330 West 42nd Street, New York 36, N. Y. 1952. xvi + 661 pp. 16.5 × 23.5 cm. Price, $10.00.

The laudable plan of Dr. Barrett's book consists of background chapters on crystallography, X-ray diffraction, re-