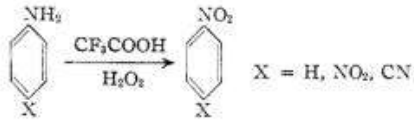
substituted anilines to nitrobenzenes in excellent yields. Aniline, *p*-nitroaniline, and *p*-aminobenzonitrile were converted to nitrobenzene, *p*-dinitrobenzene and *p*-nitrobenzonitrile in yields of 79, 86 and 98, respectively. In contrast peracetic acid oxidation of aniline yields 11% nitrobenzene and 71% azoxybenzene.[1]



It has also been demonstrated that pertrifluoroacetic acid is an extremely active reagent for the hydroxylation of olefins. Thus oleic acid was rapidly hydroxylated in quantitative yield in chloroform solution. The hydroxylation of this olefin has been reported with performic acid, but the reaction with pertrifluoroacetic acid appears to be much faster.[2] In reactions of this type the initial product is, of course, the hydroxytrifluoroacetate of the α-glycol but this is easily hydrolyzed to the glycol.

Nitrosoamines have also been oxidized to nitramines smoothly with pertrifluoroacetic acid. Di-

$$R_2N{-}NO \xrightarrow[H_2O_2]{CF_3COOH} R_2N{-}NO_2$$

ethylnitrosamine and dibutylnitrosamine were converted to the corresponding nitramines in 76 and 77% yield, respectively. The oxidation of nitrosoamines to nitramines has been reported in a few instances, but in general the reaction has been unsatisfactory as a general preparative method.[3,4]

The experimental procedures for these oxidations have in most cases been quite simple. Excess trifluoroacetic acid was normally employed as solvent and on addition of hydrogen peroxide to this reagent no evolution of heat was observed. Hydrogen peroxide was usually used as the 90% reagent although the oxidation of oleic acid was also carried out with 30% hydrogen peroxide. The equilibrium between hydrogen peroxide and trifluoroacetic acid is apparently established very rapidly and the solution of pertrifluoroacetic acid so obtained appears to be relatively stable.

In a typical experiment 5.1 ml. (0.2 mole) of 90% hydrogen peroxide was added at 20° to 40 ml. of trifluoroacetic acid. To this solution was added 5.9 g. (0.05 mole) of *p*-aminobenzonitrile in one portion. The temperature of the resulting solution was allowed to rise to 50° and kept there by intermittent cooling for one hour. The mixture was then poured into ice water and 7.2 g. (98%) of *p*-nitrobenzonitrile obtained.

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(4) R. Stoermer, *Ber.*, **31**, 2550 (1898).

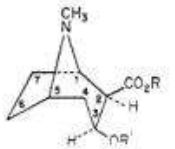
THE THREE-DIMENSIONAL STRUCTURE OF COCAINE

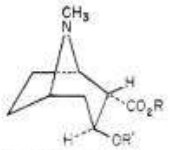
Sir:

Ecgonine is converted by the prolonged action of 33% aqueous potassium hydroxide at 100° to pseudoecgonine.[1] On the other hand, cocaine (benzoylecgonine methyl ester) has now been found to yield pseudoecgonine methyl ester by the action of as little as a tenth of a molar proportion of sodium methoxide in hot absolute methanol. The yield of pure pseudo ester is 75%: m.p. 114–116°, $[\alpha]^{20}D$ +22.8° (*c* 1.7, H_2O).

The reaction of ecgonine methyl ester with methyl iodide has been reported to yield a number of products according to the conditions employed.[2] Although somewhat different results have been obtained in attempting to reproduce this work, the rather remarkable discovery of Willstätter that both ecgonine methyl ester and the pseudo isomer react with methyl iodide to give pseudoecgonine methyl ester methiodide has been confirmed (calcd. for $C_{11}H_{20}INO_3$: C, 38.72; H, 5.91; I, 37.2. Found: C, 38.72; H, 5.88; I, 37.4). Both derivatives melted at 216–216.5° and had $[\alpha]^{20}D$ +11.3° (*c*, 2.0, methanol). The melting point of a mixture of the two products was undepressed.

These two isomerizations indicate that the ecgonine-pseudoecgonine transformation involves epimerization at the α-carbon atom (C_2, structure I). It is well known that the α-hydrogen of carboxylate ions is less labile than that of esters thereof,[3] and the lability of hydrogen in analogous quaternary ammonium compounds has also been established.[3,4] It is difficult to account for these two reactions by means of Willstätter's opinion that this transformation involves the epimerization of the β-carbon atom (C_3, structure I),[2,5] and it appears that he did not consider the possibility of epimerization at C_2.





I, R = R′ = H
II, R = CH_3, R′ = H
III, R = CH_3, R′ = COC_6H_5
IV, R = R′ = H
V, R = CH_3, R′ = H
VI, R = CH_3, R′ = COC_6H_5

That the transformation does not affect both the α- and β-carbon atoms is evident from G. Fodor's demonstration that the carboxyl and hydroxyl groups are *cis* to one another in ecgonine but *trans* in pseudoecgonine.[6] Fodor has found also that the ease of isomerization of N-acetylnorpseudoecgonine ethyl ester (to the O-acetyl isomer) is comparable to that of N-benzoyl- and N-acetylnorpseudotropine.[6,7] It is therefore concluded that

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(2) R. Willstätter, O. Wolfes and R. Mader, *Ann.*, **434**, 111 (1923).
(3) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Company, New York, N. Y., 1940, pp. 243–244.
(4) E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 523 (1933).
(5) (a) R. Willstätter and A. Bode, *Ann.*, **326**, 42 (1903); (b) R. Willstätter and M. Bommer, *ibid.*, **422**, 15 (1921).
(6) G. Fodor, *Nature*, **170**, 278 (1952).
(7) G. Fodor and K. Nádor, *ibid.*, **169**, 462 (1952); see also, A. Nickon and L. Fieser, THIS JOURNAL, **74**, 5588 (1952).

in pseudoecgonine the hydroxyl is *cis* to the nitrogen, as in pseudotropine, and that the carboxyl is *trans* to both the nitrogen and the hydroxyl group (IV).[8] Therefore also, the carboxyl group of ecgonine itself is *cis* to these two functions. Ecgonine may accordingly be called, the nitrogen atom being used as the point of reference, 2-*cis*-carboxy-3-*cis*-hydroxytropane (I).

The failure of N-acetylnorecgonine ethyl ester to rearrange to the O-acetyl isomer was considered by Fodor to favor Willstätter's opinion. This failure is, however, negative evidence, and it has been found here that O-benzoylnorecgonine [*Anal.* Calcd. for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.24; N, 5.09. Found: C, 65.30; H, 6.24; N, 5.20], m.p. 250° (hydrochloride, m.p. 219–221°[8]) rearranges in dilute aqueous potassium carbonate to N-benzoylnorecgonine [*Anal.* Calcd. for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.24; N, 5.09. Found: C, 65.67; H, 6.19; N, 4.87], m.p. 163.5°. The neutral O-benzoyl isomer (Nujol mull) has broad weak absorption from *ca.* 3.65 to 5.5 μ attributable to NH_2^+ of a zwitterion[9] and maxima at 5.80 μ and 6.45 μ ascribable to benzoate and carboxylate ion,[9] respectively. The acidic N-benzoyl isomer (Nujol mull) has absorption maxima at 3.12 and 5.76 μ assignable to bonded hydroxyl and the carboxyl group, respectively, and a double maximum at 6.21 and 6.26 μ attributable to the disubstituted amide linkage.

Ecgonine methyl ester, cocaine, pseudoecgonine methyl ester, and pseudococaine are, in view of the foregoing considerations, to be represented by II, III, V and VI. I shall present a more detailed account of this investigation in the near future.

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(9) L. Larsson, *Acta Chem. Scand.*, **4**, 27 (1950).

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RECEIVED JULY 13, 1953

OXIDATION-REDUCTION POTENTIALS OF HORSERADISH PEROXIDASE

Sir:

A systematic, potentiometric study of horseradish peroxidase (HRP), organized as a joint project of the Department of Biochemistry, Medical Nobel Institute, and the Department of Physiological Chemistry, The Johns Hopkins University School of Medicine, has now been carried to a first point of general interest.

Our studies to date indicate that the oxidation-reduction potentials of the ferri HRP/ferro HRP system are much more negative than the corresponding potentials that have been determined for other hemoproteins. Detailed data over a large range of *p*H are not yet available, but measurements made between *p*H 6 and 8 indicate that here the values of E_0' are more negative even than those reported for free iron protoporphyrin IX. The contrasts are shown in the table.

System	Temp., °C.	*p*H	E_0', volt	Ref.
ferri HRP/ferro HRP	30	6.1	−0.21	
		7.3	−0.27	
ferri protoporphyrin IX/ ferro protoporphyrin IX	30	7.0	−0.14[a]	1
metmyoglobin/myoglobin	30	7.0	+0.05	2
methemoglobin/hemoglobin	30	7.0	+0.14	3
ferri cytochrome c/ ferro cytochrome c	30	7.0	+0.25	4, 5

[a] Value found by extrapolation of experimental data on the basis of an estimated pK_a' value.

It would appear that the different ferri hemoprotein/ferro hemoprotein systems range from among the most positive biological oxidation–reduction systems known to among the most negative systems known. It seems reasonable to ask now whether the well-known resistance to reduction displayed by free catalase might not be at least in part the result of a very negative oxidation–reduction potential for the ferri catalase/ferro catalase system.

The author wishes to acknowledge the great aid of Dr. Hugo Theorell and Dr. Karl-Gustav Paul, who directed the preparation of HRP in crystalline form. Dr. W. Mansfield Clark has lent invaluable advice, and has supplied the equipment for the potentiometric measurements.

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RECEIVED AUGUST 7, 1953

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(2) J. F. Taylor and V. J. Morgan, *ibid.*, **144**, 15 (1942).
(3) J. F. Taylor and A. B. Hastings, *ibid.*, **131**, 649 (1939).
(4) F. L. Rodkey and E. G. Ball, *ibid.*, **182**, 17 (1950).
(5) K. G. Paul, *Arch. Biochem.*, **13**, 441 (1947).
(6) Public Health Service Research Fellow of the National Institutes of Health, 1951–1953. These studies supported in part by a grant from Eli Lilly and Company.

MAGNAMYCIN.[1] II. MYCAROSE, AN UNUSUAL BRANCHED-CHAIN DESOXYSUGAR FROM MAGNAMYCIN

Sir:

Methanolysis of the antibiotic Magnamycin[2,3] by 1 *N* methanolic hydrochloric acid yields a crystalline *base* of the formula $C_{29-30}H_{47-49}NO_{12}$ and an oily *neutral substance*, $C_{13}H_{24}O_5$ [b.p. 116° (1.1 mm.), $n^{25}D$ 1.4493, $[\alpha]^{25}D$ − 10.7° (*c* 9, $CHCl_3$), *Anal.* Calcd. for $C_{13}H_{24}O_5$: C, 59.98; H, 9.29; OCH_3, 11.90; mol. wt., 260. Found: C, 60.04; H, 9.40; OCH_3, 11.70; sap. eq., 263]. We wish to record evidence which proves that the neutral substance is the 4-isovaleryl methyl glycoside (I)[4] of a new sugar, *mycarose*, of the structure (II).[4]

(1) Magnamycin is the registered trade name of Chas. Pfizer and Company for the antibiotic carbomycin.
(2) F. W. Tanner, A. R. English, T. M. Lees and J. B. Routien, *Antibiotics and Chemotherapy*, **2**, 441 (1952).
(3) R. L. Wagner, F. A. Hochstein, K. Murai, H. Messina and P. P. Regna, THIS JOURNAL, in press.
(4) These formulas should be regarded as devoid of configurational implications. The stereochemistry of mycarose is now under investigation.