grams and electrophoresis strips coincided exactly with the NAN positive spots.

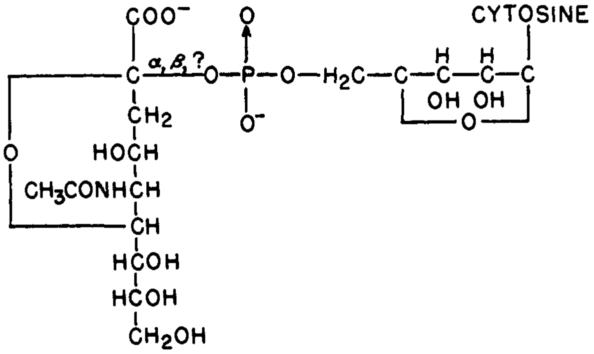
C5P-NAN is labile to acid; *e.g.*, 0.01 *N* HCl at 23° for 5 min. yielded 83% hydrolysis. After hydrolysis, the fragments were characterized as follows:

C5P by its absorption spectra, paper chromatography in three solvent systems,[8] stability of the phosphate ester to acid hydrolysis, rate of liberation of inorganic phosphate and cytidine on treatment with the 5′-nucleotidase, and resistance to purified phosphodiesterase.[9]

NAN was identified by paper chromatography and electrophoresis, its conversion to pyruvate and N-acetyl-D-mannosamine on incubation with purified NANaldolase, and the characteristic sialic acid color reactions with the resorcinol, direct Ehrlich, and thiobarbituric acid reagents.

The available data suggest that the carbonyl group of NAN is bound to the 5′-phosphate group of cytidine by a glycosidic bond. Treatment of C5P-NAN with hydroxylamine[10] yielded no hydroxamate. Further, the keto function was resistant to reduction with sodium borohydride and to oxidation with hypoiodite which was not the case in a mixture of NAN and CMP.

The data summarized above suggest a tentative structure for C5P-NAN (Fig. 1).



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[8] Two of the solvent systems easily separated deoxycytidine-5′-monophosphate from C5P; in addition, the unknown CMP spots yielded positive reactions to the periodate spray reagent.

[9] The crude rattlesnake venom used for the 5′-nucleotidase showed no activity at comparable concentrations against the 2′- and 3′-nucleoside monophosphates. The phosphodiesterase had been purified free of 5′-nucleotidase and was a gift of Mr. Ronald Somerville, Department of Biological Chemistry, The University of Michigan.

[10] M. E. Jones, S. Black, R. M. Flynn and F. Lipmann, *Biochim. et Biophys. Acta*, **12**, 141 (1953).

[11] U. S. Public Health Service Medical Student Trainee at the Rackham Arthritis Research Unit (U.S.P.H.S. 2A-5026; training grant).

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RECEIVED SEPTEMBER 11, 1959

ACTIVATION BY ELECTRON TRANSFER—INDUCED CIS–TRANS ISOMERISM[1]

Sir:

In an earlier note[2] evidence was presented for the activation of a bridging group for ester hydrolysis by electron transfer. In a similar series of experiments in which the reactants were methylmaleatopentamminocobaltic ion and Cr^{++} or V^{++}, we find that not only does ester hydrolysis occur during electron transfer in the presence of H^+, but there is also activation of the ligand for isomerization to the fumarate.

On the basis of the following observations we feel justified in concluding that this activation of the ligand resulting in isomerization occurs only as a result of electron transfer.

The importance of H^+ is shown by a series of experiments using Cr^{++} as reductant.[3] The resulting solutions were passed through a cation exchange resin, eluted first with 0.15 *M* $HClO_4$ to remove monopositive ions, then with 1 *M* to remove dipositive ions. The relative proportions of the two ions are shown in the table: the ratio (+2 ion/+1 ion) varies linearly with the H^+ concentration. After the reaction, the organic ligand is complexed with Cr(III). The maleate is present as a monopositive ion, while any fumarate will be present in solution as a dipositive ion, since the fumarate cannot chelate. In solutions of lower acidity, the fumarate complex does lose a proton and can be eluted as a monopositive ion.

TABLE I

$[H^+]$, *M*	+1 ion	+2 ion	Ratio +2 ion/+1 ion
0.5	16	84	5.25
0.2	35	65	1.85
0.045	90	10	0.11

Using V^{++} as reductant, similar proportions of fumaric and maleic acids are obtained: these proportions were determined by extraction of the reaction mixture with ether and infrared examination of the organic material. The amount of fumaric acid produced increases with increasing H^+ concentration (in 0.5 *M* $HClO_4$, 85% of the total organic acid was extracted in the first three hours and was found to be almost pure fumaric acid: the rest was maleic).

In an experiment with V^{++} repeated in 99.5% D_2O containing 0.6 *M* $HClO_4$, the fumaric acid was separated from the maleic by selective extraction. Infrared examination of the two acids showed the presence of C-D bonds at 2200, 2090 and 940 $cm.^{-1}$ in the fumaric but not in the maleic acid; this we believe indicates that there cannot be exchange between D^+ (or H^+) and maleato complex. It is known from the preparative method that the maleato complex does not isomerize in acid solution in the absence of reductant. Furthermore, a similar experiment with fumaratopentamminocobaltic ion with V^{++} in D_2O produced fumaric acid containing no C–D bonds.[4] Thus we conclude that the ligand is activated for isomerization during the electron transfer process in the presence of H^+. As a minimum, the exchange results show that in the reaction path which leads to fumaric acid, a new C–H bond is formed when maleate absorbs the electron—a proton is necessarily lost again when the electron passes to the Co(III).

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[1] This work is supported by the Atomic Energy Commission under Contract AT(11-1)-378.

[2] R. T. M. Fraser, D. K. Sebera and H. Taube, THIS JOURNAL, **81**, 2906 (1959).

[3] In all experiments, Co(III) and reductant were 0.010 *M*.

[4] D. K. Sebera, Ph.D. Dissertation, University of Chicago.

In the reaction of maleatopentamminocobaltic ion with Cr^{++}, fumaric acid is again produced during the electron transfer. The ratio fumaric/maleic acid increases linearly from zero with H^+ concentration, but at 0.5 M $HClO_4$, only 32% fumaric acid is formed.

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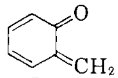
RECEIVED JULY 20, 1959

o-QUINONONE METHIDE[1]

Sir:

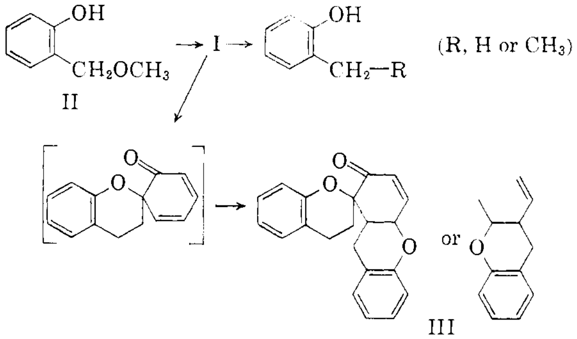
A multitude of reactions of substituted *o*-hydroxybenzyl alcohols give products which have been rationalized in terms of an *o*-quinone methide intermediate (I).[2] These could have been formed by other reaction paths, however, and the evidence for the actual existence of I, even as a transient species,[3] is therefore lacking.



I

We wish to report the preparation of I in an impure state by the pyrolysis of *o*-methoxymethylphenol (II). Passage of II in the gaseous state through an open (unpacked) quartz tube in a state of high dilution (nitrogen) at a total pressure of 1–5 mm. and a temperature of 500–650° afforded a light yellow pyrolysate. This material, trapped at liquid nitrogen temperature, remained solid up to about −50° where it became liquid and appeared to be quite stable. As the temperature was allowed to rise to 0° colorless solid began to form and the mixture became a "slush" at 25°. The solid was shown from chemical and spectral data to be a trimer of I having structure III (m.p. 191–192°) and was obtained in yields of 15–20%. Treatment of the liquid pyrolysate at −50° with cold ethereal $LiAlH_4$ gave *o*-cresol in about the same yield as that obtained of trimer in a "warming" experiment (isolated as the phenylurethane, m.p. and m.m.p. 139–140°). Similarly, treatment with cold ethereal CH_3MgI afforded *o*-ethylphenol (phenylurethan, m.p. and m.m.p. 140°) in about the same yield. The starting ether was shown not to react with these reagents under the conditions used. A heptane solution of pyrolysate (*ca.* 10^{-5} M), allowed to warm while being studied in a spectrophotometer, showed profound spectral changes in the ultraviolet during the first five minutes and was still changing after 24 hr. at room temperature. Absorption by other components in the mixture precluded specific spectral assignments although it is clear that III had started to form before the first reading was made and its concentration increased steadily with time.

Trimer III may be obtained directly in yields as high as 70% by increasing the concentration of pyrolysis substrate. In these experiments, the trimer appears to be formed in the gaseous state and solidifies on the walls of the tube immediately below the heated zone.



III

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RECEIVED SEPTEMBER 3, 1959

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[1] The authors are indebted to the Robert A. Welch Foundation for the financial support of this study.

[2] *Cf.* N. J. L. Megson, "Phenolic Resin Chemistry," Academic Press, Inc., New York, N. Y., 1958.

[3] P. D. Gardner, H. Sarrafizadeh R. and L. Rand, THIS JOURNAL, **81**, 3364 (1959).

STEROIDS. CXXXV.[1] 10β-FLUORO STEROIDS; A NOVEL REACTION OF PERCHLORYL FLUORIDE.

Sir:

Treatment of estradiol (I) in dimethylformamide with perchloryl fluoride (ClO_3F)[2] for twenty hours at room temperature afforded a compound (60–70%), m.p. 152–154°, $[\alpha]_D - 27°$,[3] γ_{max}^{EtOH} 240 mμ, log ϵ 4.06 infrared ν_{max}^{KBr} at 2.9, 6.0, 6.12 and 6.21 μ, which we formulate as 10β-fluoro-Δ^1-dehydro-19-nortestosterone (II) on the basis of the spectral characteristics and analysis (found for $C_{18}H_{23}O_2F$: C, 74.20; H, 7.60; F, 6.20) and the reactions. Reduction of II with sodium borohydride in methanol or with Raney nickel in refluxing methanol gave back estradiol (I). Catalytic hydrogenation of II in pyridine, dioxane or ethanol solution over 10% palladium–barium sulfate catalyst afforded, in addition to some estradiol, a saturated ketone (III), m.p. 181–182.5°, $[\alpha]_D + 14°$, infrared ν_{max}^{KBr} at 2.8 and 5.86 μ (found for $C_{18}H_{27}O_2F$: C, 73.78; H, 9.16; F, 6.17). The rotatory dispersion curve of II was very similar to that of 1,4-cholestadiene-3-one[4] from which the 10-fluorine atom is presumed to be in the β configuration, while the rotatory dispersion curve of the saturated ketone (III) was of the type characteristic for rings A/B *cis*-fused steroids[5] and the compound is therefore formulated as 10β-fluoro-19-nor-5β-androstan-17β-ol-3-one.

The above reaction with perchloryl fluoride has been applied to a large number of other steroidal phenols with analogous results. For example 3-hydroxy-17β-acetyl-1,3,5(10)-estratriene ("aromatic progesterone")[6a,b,c] (IV) yielded 10β-fluoro-Δ^1-dehydro-19-norprogesterone (V), m.p. 108–109.5°, $[\alpha]_D + 62°$, γ_{max}^{EtOH} 241 mμ, log ϵ

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[1] Paper CXXXIV, L. Knox, J. Zderic, J. Pérez Ruelas, C. Djerassi and H. J. Ringold, THIS JOURNAL, **81**, in press (1959).

[2] Pennsylvania Salt Manufacturing Co., Philadelphia 2, Pa.

[3] Melting points are uncorrected. Rotations were determined in chloroform.

[4] C. Djerassi, R. Riniker and B. Riniker, THIS JOURNAL, **78**, 6362 (1956).

[5] C. Djerassi and W. Closson, *ibid.*, **78**, 3761 (1956).

[6] (a) L. Velluz and G. Muller, *Bull. soc. chim. France*, 166 (1950); (b) C. Djerassi, G. Rosenkranz, J. Iriarte, J. Romo and J. Berlin, THIS JOURNAL, **73**, 1523 (1951); (c) J. S. Mills, H. J. Ringold and C. Djerassi, *ibid.*, **80**, 6118 (1958).