vanadium(III) ions. The possibility of rapid separation-induced exchange brought about when the reaction mixture is added to alcoholic α,α'-dipyridyl is not excluded by these observations. Dodson's work with the iron(II)–iron(III) exchange showed exchange half-times of the order of 15–50 seconds with the reactant species at *ca.* 0.001 *f* each. Reduction of the concentrations of the vanadium reactants may slow the observed rapid exchange rate to a point where kinetic studies could be undertaken, but the techniques used so far have not permitted this because of difficulties with oxidation of both vanadium species in solutions at high dilution by traces of oxygen present.

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RECEIVED JUNE 6, 1952

SYNTHESIS OF DEGRADATION PRODUCTS OF AUREOMYCIN

Sir:

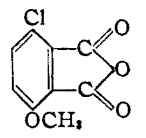
The synthesis of several degradation products[1] of Aureomycin by unequivocal methods has been accomplished. In each case these synthetic products were compared with the degradation products by means of m.p., mixed m.p., ultraviolet and infrared absorption spectra, and other properties to prove their identity.

TABLE I

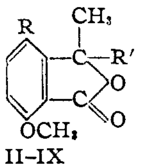
No.	R	R'	M.p., °C.	Theory C	Theory H	Theory OCH_3	Theory Cl	Found C	Found H	Found OCH_3	Found Cl
II	H	—H	73–75	67.4	5.6			66.9	6.0		
III	Cl	—H	113–14	56.5	4.2		16.7	57.0	4.6		16.3
IV	H	—OH	164–65	61.8	5.2	16.0		62.1	5.9	16.4	
V	Cl	—OH	204–206	52.4	3.9		15.5	52.3	3.9		15.4
VI	H	—COOH	168–70	59.5	4.5			59.8	5.2		
VII	Cl	—COOH	199–200	51.5	3.5		13.8	51.7	3.9		13.8
VIII	H	—CH_2COOH | —CH_2COOH	207–209.5	57.1	4.8	10.5		57.3	5.2	9.7	
IX	Cl	CH_2COOH | CH_2COOH	209–210.5	51.1	4.0		10.8	51.4	4.4		10.9

The first of these products is 6-chloro-3-methoxyphthalic anhydride (I) which definitely places the position of the methoxyl and chloro groups in relation to the other 2 substituents on the benzene ring. This compound was prepared from 3-methoxy-6-chloroanthranilic acid[2] by replacement of the amino group by a cyano group through a Sandmeyer reaction and hydrolysis to the phthalic acid derivative, m.p. 187–188°. *Anal.* Calcd. for $C_9H_5O_4Cl$: C, 50.8; H, 2.4; Cl, 16.7. Found: C, 51.5; H, 2.7; Cl, 16.7.

The remaining compounds are phthalides of the following general formula in which R = chlorine and R' = groups as shown in Table I. These phthalides can be degraded to phthalic or benzoic acid derivatives to prove the position of the chlorine atom as indicated in the previous paper.[1]



I



II–IX

4-Chloro-7-methoxy-3-methyl-phthalide (III) was prepared from 2-amino-3-methoxyacetophenone[3] by reducing the ketone to the alcohol and replacing the amino by a cyano group. On hydrolysis, II was formed which was chlorinated to III with chlorine in acetic acid or with sodium hypochlorite and hydrochloric acid.

4-Chloro-3-hydroxy-7-methoxy-3-methylphthalide (V) was prepared by replacement of the amino by cyano in 2-amino-3-methoxyacetophenone, hydrolysis to IV and chlorination to V. Both IV and V probably exist in equilibrium with the corresponding *o*-carboxyacetophenone structure and both will form "normal" esters with diazomethane and "pseudo" esters with acid–methanol or acid chloride–methanol procedures.

4-Chloro-7-methoxy-3-methyl-3-phthalidecarboxylic acid (VII) was prepared by adding hydrogen cyanide to 2-cyano-3-methoxyacetophenone, hydrolysis of the product to VI and chlorination to VII. The compound was resolved by crystallizing the brucine salt from water; $[\alpha]^{28}\text{D}$ +25° (1.2% in ethanol).

3-(4-Chloro-7-methoxy-3-methylphthalidyl)-succinic acid (IX) was prepared by treating IV with phosphorus pentachloride to form the "pseudo" acid chloride which reacted with sodio diethyl carbethoxysuccinate. Hydrolysis and decarboxylation yielded VIII which was chlorinated to IX. Two racemates resulted and the higher melting one, m.p. 228–229° with gas, was resolved by crystallizing the brucine salt from ethanol; m.p. 209–210.5° with gas; $[\alpha]^{25}\text{D}$ −20.4° (5% in alcohol).

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[1] B. L. Hutchings, *et al.*, THIS JOURNAL, **74**, 3710 (1952).

[2] B. R. Baker, *et al.*, *J. Org. Chem.*, **17**, 160 (1952).

[3] J. C. E. Simpson, *et al.*, *J. Chem. Soc.*, 646 (1945).

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DEGRADATION OF AUREOMYCIN

Sir:

In a preliminary report[1] certain of the physical and chemical properties of aureomycin were out-

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[1] R. W. Broschard, A. C. Dornbush, S. Gordon, B. L. Hutchings, A. R. Kohler, G. Krupka, S. Kushner, D. V. Lefemine and C. Pidacks, *Science*, **109**, 199 (1949).