(I^{131}) in day-old white leghorn chicks[6] fed a low-iodine starter mash,[7] a modification of that described by Shellabarger.[8] The minimally effective dose of the U.S.P. standard by this method is 10 milliunits. Assays were carried out using 2 dose levels of unknowns with 2 or 3 dose levels of the U.S.P. standard, 5 to 8 chicks per group.

Once purified, TSH can be readsorbed providing the excess cations are removed by dialysis, and by this means the specific activity of the final preparation can be further enhanced. The system also has been found to operate in batch preparation and is capable of removing TSH activity from other purified anterior pituitary hormone preparations. The finer mesh carboxylic cation exchange resin XE-64 also has been used but found to possess no apparent advantages over IRC-50 with respect to capacity for TSH activity.

Other investigators[9] working independently have recently reported to us that they have obtained similar reversible adsorption of TSH activity with IRC-50.

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(6) White leghorn chicks were obtained from the Hall Bros. Hatchery Inc., of Wallingford, Conn.

(7) Low-iodine starter mash was furnished by the Wirthmore Feeds through the courtesy of Dr. W. A. Glista.

(8) C. J. Shellabarger, *J. Applied Physiol.*, **6**, 721 (1954).

(9) R. W. Bates and P. G. Condliffe, personal communication.

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The Mode of Hydrolysis of Tetraalkyl Titanates

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It was of interest to determine the mode of hydrolysis of the tetraalkyl titanates. The hydrolysis may occur either by cleavage of the C–O– bond by SN1 or SN2 attack or by cleavage of the Ti–O– bond by attack of water along the coördinate axis of titanium.

That SN1 attack does not occur has been shown by Cullinane and co-workers[1] who obtained isobutyl alcohol on hydrolysis of tetraisobutyl titanate. If SN1 attack has occurred, isomerization of the primary carbonium ion would have led to the isolation of *sec*-butyl alcohol.

Due to the nature of the neopentyl system[2] it was felt that investigation of hydrolysis of tetraneopentyl titanate would distinguish between cleavage of the C–O– bond and cleavage of the Ti–O– bond by attack along the coördinate axis of titanium. If the attack of water is along the coördinate axis of titanium, with subsequent breaking of the Ti–O– bond, then the alcohol produced will be neopentyl alcohol. However, if the C–O– bond is broken, then a rearrangement of the carbon skeleton will occur with the formation of isoamyl alcohol.

Accordingly, tetraneopentyl titanate was triturated with water and the alcohol produced separated from the resulting titanium dioxide. The solid alcohol gave an infrared curve identical with that of an authentic sample of neopentyl alcohol. Thus the attack of hydrolytic reagents on titanium alkylates must proceed along the coördinate axis of titanium with subsequent cleavage of the titanium–oxygen bond.

Experimental

Materials.—The trimethylacetic acid was obtained from Eastman Kodak Co. and the tetraisopropyl titanate from E. I. du Pont Co.

Neopentyl Alcohol.—Trimethylacetic acid was reduced to neopentyl alcohol with $LiAlH_4$,[3] m.p. 51–53°, in 85% yield.

Tetraneopentyl Titanate.—Neopentyl alcohol (88.15 g., 1.0 mole) and titanium tetraisopropylate (71.0 g., 0.25 mole) were mixed together and allowed to stand overnight.

The mixture was fractionally distilled and a fraction boiling at 130–132° at 1 mm. was collected. This material solidified immediately in the collecting flask. It weighed 62 g. and melted at 58–60°.

Anal. Calcd. for $C_{20}H_{44}O_4Ti$: Ti, 12.1. Found: Ti, 12.7.

Hydrolysis of Tetraneopentyl Titanate.—Tetraneopentyl titanate (7.93 g., 0.02 mole) was triturated with 25 ml. of water for one hour. The mixture was extracted with ether and the ether layer dried over anhydrous sodium sulfate.

After filtering from the sodium sulfate the ether solution was fractionally distilled. On removal of the ether and cooling of the residue, a solid weighing 5.2 g. and melting at 51–53° precipitated out.

Comparison of the infrared curve of this material with the infrared curve of an authentic sample of neopentyl alcohol showed that the two are identical.

Acknowledgment.—The authors are indebted to Mrs. Celia M. Jorgensen for the infrared spectra and Drs. Jason Salsbury and John T. Shaw for their interest in this problem.

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(1) N. Cullinane, *et al.*, *J. Soc. Chem. Ind.*, **69**, S 38–40 (1950).

(2) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 317–318.

(3) R. Nystrom and W. G. Brown, THIS JOURNAL, **69**, 2548 (1947).

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Nature of the Organic Base in Reissert Compounds[1]

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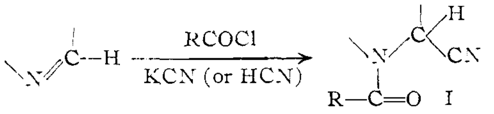
Reissert compounds (I) result from the addition of an acyl and a cyano group to the azomethine linkage of certain N-heterocyclics.[2] However, Gassman and Rupe[3] found that among a variety of



I

quinoline derivatives there was no easily discernible relation between the electronic nature of the substituent and the ability to form a Reissert compound. The series of quinoline bases studied by Rupe is more noteworthy for the examples of failure than success.[4] In addition to quinoline itself, 6-methoxyquinoline[3] and 7-methoxyquinoline[5] have been

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(1) Supported in part by a Cottrell grant from the Research Corporation.

(2) (a) A. Reissert, *Ber.*, **38**, 1603; 3415 (1905); (b) for a complete discussion of "Reissert Compounds" see W. E. McEwen and R. L. Cobb, *Chem. Rev.*, in press.

(3) A. Gassman and H. Rupe, *Helv. Chim. Acta*, **22**, 1241 (1939).

(4) Quinolines with the following substituents did not give the Reissert compound by the method of Rupe: 2-methyl-, 5-nitro-, 5-amino-, 6-dimethylamino-, 7-nitro-, 8-hydroxy-, 8-methoxy-, 8-benzoyloxy- and 8-acetoxy-.

(5) E. Späth and O. Brunner, *Ber.*, **57**, 1234 (1924).