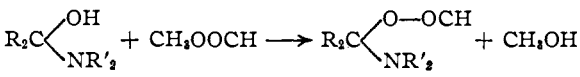
presumably involve a transesterification step to form carbinolamine formates



Experimental

All of the Leuckart reactions were run essentially as described below for the example of cyclohexanone.

N-Cyclohexylpiperidine.—Piperidine (43 g., 0.5 mole) was added to 98% formic acid (23 g., 0.5 mole) rapidly with cooling by tap water, and cyclohexanone (25 g., 0.25 mole) was added to the hot mixture which was then refluxed for five and one-half hours; the addition of a boiling chip was imperative to prevent evolution of the generated carbon dioxide in violent bumps. The cooled solution was poured into several volumes of water, acidified with 50 cc. of concd. hydrochloric acid, and extracted with three portions of benzene. Distillation of the dried extracts yielded 1.3 g. (5%) of recovered cyclohexanone.

To the aqueous solution, digested for six hours to hydrolyze N-formylpiperidine, which is otherwise difficult to fractionate from N-cyclohexylpiperidine, was added 30 g. of sodium hydroxide in concentrated aqueous solution. About 400 cc. of steam distillate was then condensed, from which the product was collected by separation of the layers and extraction of the aqueous phase with petroleum ether (b. p. 60–75°). The combined dried extracts were distilled *in vacuo;* yield 25.4 g. (61%) of N-cyclohexylpiperidine, b. p. 114–118° (25 mm.),[7] $n^{20}D$ 1.4862. From the hold-up in the distilling apparatus was obtained an additional quantity of amine as its hydrochloride; wt. 0.66 g. (1.3%), m. p. 291–293° (cor.).

(7) Previous b. p.'s reported for N-cyclohexylpiperidine are 106–107° (16 mm.) (C. Mannich and H. Davidsen, *Ber.*, **69**, 2106 (1936)), 122–123° (22 mm.) (ref. 6), and 98–100° (100 mm.) (French Patent 751,206, Goodyear Tire and Rubber Co., *C. A.*, **28**, 1049[4] (1934)). We assume the last value to be a typographical error for 98–100° (10 mm.).

DEPARTMENT OF CHEMISTRY
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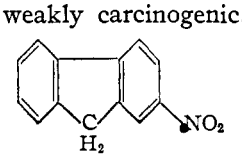
RECEIVED JULY 9, 1949

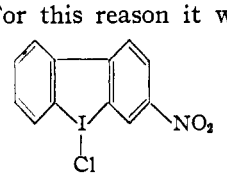
Preparation of 4-Nitrodiphenyleneiodonium Chloride

BY ALEX WASYLEWSKY,[1] ROBERT K. BROWN AND REUBEN B. SANDIN

Recent work[2] has shown that 2-nitrofluorene (I) is weakly carcinogenic. For this reason it was

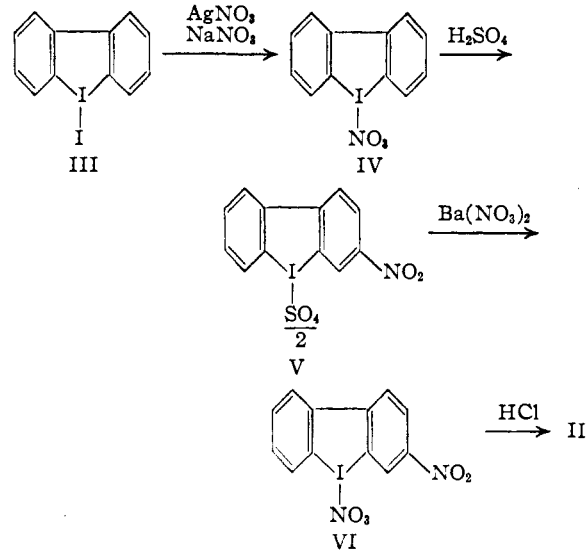


I



II

considered possible that 4-nitrodiphenyleneiodonium chloride (II) might show similar activity. Although II is a salt, there is a superficial structural resemblance between II and I. Moreover, iodonium compounds have been shown to have a certain chemotherapeutic action.[3] Iodonium compounds have also been shown to react with thiol compounds.[4] In this communication is described the preparation of 4-nitrodiphenyleneiodonium chloride and some of its derivatives. The reactions are



Experimental[5]

Diphenyleneiodonium iodide (III) was prepared according to Mascarelli and Benati.[6] To a vigorously stirred suspension of III (29 g.) in 1000 ml. of boiling water was added a saturated solution of 25 g. of silver nitrate in boiling water. The reaction mixture was then treated with 200 ml. of a hot saturated solution of sodium nitrate. Stirring was continued for one-half hour and after cooling in an ice–water-bath, the combined diphenyleneiodonium nitrate (IV) and silver iodide was collected. The iodonium salt was extracted with boiling water (4 l.) and precipitated by the addition of sodium nitrate. The yield of crude iodonium nitrate, decomposing at 226–228°, was 70%. Several recrystallizations from water raised the decomposition temperature to 240°.

Anal. Calcd. for $C_{12}H_8O_3NI$: I, 37.32. Found: I, 37.39, 37.41.

The mononitration of the iodonium nitrate was readily accomplished by the use of concentrated sulfuric acid. The nitrate (10 g.) was slowly added with stirring to 30 ml. of concentrated sulfuric acid, cooled in an ice–water-bath. After standing at room temperature for one-half hour, the reaction mixture was poured into 400 ml. of a mixture of ice and water. The 4-nitrodiphenyleneiodonium sulfate (V) precipitated immediately as an orange cream colored solid which was very insoluble in water and alcohol. For purification the salt was extracted several times with boiling water and alcohol. The residue was the pure iodonium compound, decomposing at 268–271°.

Anal. Calcd. for $C_{24}H_{14}O_8N_2SI_2$: S, 4.30. Found: S, 4.38, 4.50.

4-Nitrodiphenyleneiodonium nitrate (VI) was obtained when a hot water suspension of the above sulfate was treated with an excess of hot saturated barium nitrate

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(2) Morris, Dubnik, Dunn and Johnson, *Cancer Research*, **I**, 730 (1947).

(3) Freedlander and French, *Proc. Soc. Expll. Biol. Med.*, **63**, 319 (1946): *C. A.*, **41**, 2115 (1947).

(4) Sandin, Christiansen, Brown and Kirkwood, THIS JOURNAL, **69**, 1550 (1947).

(5) All temperatures are uncorrected.

(6) Mascarelli and Benati, *Gazz. chim. ital.*, **38**, II, 624 (1908); *C. A.*, **3**, 781 (1909). See also Searle and Adams [THIS JOURNAL, **55**, 1649 (1933)], who have applied this method successfully to the preparation of 4,4′-dicarboethoxydiphenyleneiodonium iodide.

solution. The combined barium sulfate and compound VI was collected and extracted with hot water. Addition of sodium nitrate to the filtrate afforded the crude iodonium nitrate VI, decomposing at 233°; yield 77%. Recrystallization from water raised the decomposition temperature to 236°.

Anal. Calcd. for $C_{12}H_7O_5N_2I$: I, 32.79. Found: I, 32.91, 32.78.

VI was characterized by reducing it to the known 2-iodo-4'-nitrobiphenyl. A suspension of VI in alcohol was treated with just *enough* sodium to bring about complete solution. Addition of water afforded 2-iodo-4'-nitrobiphenyl, m. p. 98–99°, which when mixed with an authentic sample showed no depression of the melting point.

VI was converted into the iodonium chloride (II) by treating its aqueous solution with dilute hydrochloric acid. The chloride was very insoluble in water and alcohol. It decomposed at 279–282°; yield almost quantitative.

Anal. Calcd. for $C_{12}H_7O_2NICl$: Cl and I, 45.16. Found: Cl and I, 45.28, 45.16.

The dinitration[7] of IV afforded 4,4'-dinitrodiphenyleneiodonium sulfate. It was very insoluble in water and alcohol. For purification it was extracted repeatedly with hot alcohol. The yield was 95%; decomposition temperature 281–283°.

Anal. Calcd. for $C_{24}H_{12}O_{12}N_4SI_2$: I, 30.35; S, 3.83. Found: I, 30.75, 30.66; S, 3.89, 3.79.

Acknowledgment.—The authors express their appreciation to the Canadian Cancer Society for financial help in connection with this work. We are also grateful to Drs. J. A. Miller and E. C. Miller of the McArdle Memorial Laboratory, Madison, Wisconsin, for determining the carcinogenic properties of 4-nitrodiphenyleneiodonium chloride. Their results will be published elsewhere.

(7) Sandin, McClure and Irwin, THIS JOURNAL, **61**, 3061 (1939).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF ALBERTA
EDMONTON, CANADA

RECEIVED OCTOBER 3, 1949

NEW COMPOUNDS

Tetrabenzoyl-α-D-glucopyranosyl Bromide–Carbon Tetrachloride Addition Compound[1]

Ten grams of pentabenzoyl-α-D-glucopyranose was dissolved in 50 ml. of hot glacial acetic acid and cooled to room temperature. To this was added 40 ml. of hydrobromic acid–acetic acid solution (30–32% hydrobromic acid). After two hours at room temperature the clear yellow solution was poured into 1 liter of ice-water and the product separated by filtration. This solid was dissolved in 500 ml. of carbon tetrachloride and the solution washed once with distilled water, twice with saturated sodium bicarbonate solution, once more with water, filtered through glass wool, and dried over calcium chloride. After filtration, the product crystallized on addition of low boiling petroleum ether to the carbon tetrachloride solution. Three recrystallizations from carbon tetrachloride and petroleum ether mixtures yielded colorless needles; m. p. 103–105° (uncor.), $[\alpha]^{22}D$ + 120° (*c*, 2.26, toluene), $[\alpha]^{25}D$ + 99° (*c*, 3.95, chloroform).

Anal. Calcd. for $C_{34}H_{27}O_9Br \cdot CCl_4$: C, 51.68; H, 3.35; halogen, 39.83. Found: C, 51.83; H, 3.49; halogen, 38.59 (gravimetric).

Recrystallization of the addition compound from ether and petroleum ether mixtures yielded the known tetrabenzoyl-α-D-glucopyranosyl bromide without the molecule of carbon tetrachloride of crystallization; m. p. 127–128°, $[\alpha]^{25}D$ + 146° (*c*, 2.05, toluene); + 119° (*c*, 3.62, chloroform).

The author is indebted to Lawrence E. Brown and Julian F. Jurgens for the analytical data presented.

SOUTHERN REGIONAL RESEARCH LABORATORY
NEW ORLEANS, LOUISIANA LAURENCE W. MAZZENO, JR.

RECEIVED SEPTEMBER 26, 1949

2-Chloromethyl-5-hydroxy-6-chloro-4-pyrone

2-Chloromethyl-5-hydroxy-4-pyrone (2-chlorokojic acid) was prepared from kojic acid[1] essentially as described by Kipnis, *et al.*[2]

Seven grams of 2-chlorokojic acid was shaken with 0.5 g. of anhydrous aluminum chloride in a 250-ml. flask and fitted with a reflux condenser (all-glass standard-taper connections). The mixture was then treated with 11.4 g. of sulfuryl chloride introduced through the top of the condenser. When the reaction had subsided the mass was carefully heated at 70° by a hemispherical mantle, and maintained at that temperature for about twenty minutes. The resulting material was a yellow solid which was then mixed with 50 ml. of water and filtered.

The substance was recrystallized from alcohol and then from chloroform. Finally, because of the reoccurrence of a faint red coloration, the crystals were washed with distilled water and then air-dried.

The compound consisted of white needles which became yellow upon storage. Yield 4.4 g. (51%) m. p. 139–141°. *Anal.*[3] Calcd for $C_6H_4Cl_2O_3$: Cl, 36.33. Found: Cl, 36.30.

The compound when treated with a dilute solution of ferric chloride gave a red coloration. The substance is assigned the probable structure of 2-chloromethyl-5-hydroxy-6-chloro-4-pyrone since it has been shown[4] that several 4-pyrones are most vulnerable to attack by a halogen at position 6.

TEXAS STATE UNIVERSITY FOR NEGROES
HOUSTON, TEXAS L. L. WOODS

RECEIVED AUGUST 25, 1949

(1) Contribution from the Southern Regional Research Laboratory, one of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture. Not copyrighted.

(1) The kojic acid used in this experiment was furnished by the Northern Regional Laboratory of the United States Department of Agriculture, Peoria, Ill.

(2) Kipnis, Soloway and Ornfelt, THIS JOURNAL, **70**, 4264 (1948).

(3) Analysis by Dr. Carl Tiedcke, Teaneck, New Jersey.

(4) See references to the formation of 2-hydroxymethyl-5-hydroxy-6-bromo-γ-pyrone and 2-methyl-5-hydroxy-6-bromo-γ-pyrone by Barham and Smits, *Transactions of Kansas Academy of Science*, **37**, 91–113 (1934).