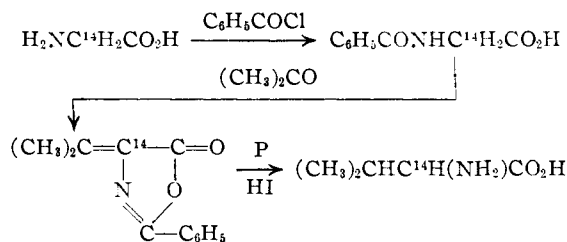


exchange resins) for the purification of products, a particularly important point in many small scale radiochemical syntheses.

In the preparation described in this paper, glycine-2-C¹⁴ was used as the starting material, so that labeled valine was obtained.



Experimental

2-Phenyl-4-isopropylidene-(oxalalone-4-C¹⁴)-5.—Glycine-2-C¹⁴ (120 μc ., 0.76 g., 10.1 millimoles) was converted to hippuric-2-C¹⁴ acid by reaction with benzoyl chloride.⁷ The product was ground to a fine powder with 0.6 g. of freshly fused sodium acetate and dissolved in 35 ml. of dry acetone. Acetic anhydride (5 ml.) was added dropwise and the mixture heated under reflux for 15 hours.⁸ The hot solution was poured onto crushed ice and diluted to 250 ml. with water. The precipitate was collected by filtration and dried *in vacuo*. The oxalalone (m.p. 98–100°) weighed 1.16 g. (5.77 millimoles, 57% yield from glycine) and contained 71 μc . or 59% of the initial radioactivity. Thus, the specific activity was correct within the limits of accuracy of the activity determinations ($\pm 5\%$). The filtrate contained 36 μc . (30% of the glycine activity), of which 28 μc . (23%) was recovered as 0.27 g. (2.42 millimoles, 23.9%) of glycine hydrochloride.

Valine-2-C¹⁴.—The oxalalone was mixed with 2.0 g. of red phosphorus and 12.5 ml. of acetic anhydride. Hydroiodic acid (12.5 ml., specific gravity 1.7) was added and the solution was heated under reflux for 20 hours. The reaction mixture was filtered and the filtrate evaporated to dryness *in vacuo*. The residue, dissolved in 100 ml. of 70% ethanol, was poured through a glass column containing 60 ml. of Dowex-50 cation exchange resin (50–100 mesh) in the acid form. The amino acid remained quantitatively on the resin, while all anions were removed by rinsing with 100 ml. of 70% ethanol followed by 250 ml. of water.

The amino acid was eluted from the resin with 250 ml. of 2 *N* ammonium hydroxide followed by 250 ml. of water. The eluate was evaporated to dryness on a steam-bath *in vacuo*. The resulting valine-2-C¹⁴ (50 μc ., 0.504 g., 4.3 millimoles) was shown to be free from radioactive or amino acid contaminants by two-dimensional paper chromatography and radioautography.⁸ The yield was 74.5% by weight from the oxalalone (70.5% radioactivity recovery), or 56% by weight (54% of the radioactivity) from unrecovered glycine-2-C¹⁴.

Acknowledgment.—The authors wish to thank Prof. M. Calvin for his interest and assistance in this work.

(7) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 328.

(8) A. A. Bensod, *et al.*, *THIS JOURNAL*, **72**, 1710 (1950).

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The Reduction of Picryl Chloride to 1,3,5-Trinitrobenzene¹

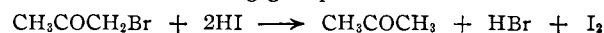
By A. H. BLATT AND E. W. TRISTRAM

RECEIVED JULY 18, 1952

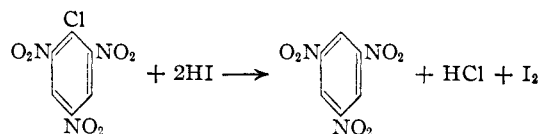
As part of a study that will be reported at an-

(1) This note is based on work done under Contract DA-19-020-ORD-12 with the Office of the Chief of Ordnance and has been approved for publication by the Public Information Division, National Military Establishment.

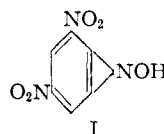
other time it was necessary to replace the halogen atom in a heterocyclic nitro aryl halide by hydrogen. The usual methods of replacing halogen by hydrogen could not be used because they would also reduce the nitro groups. It occurred to us that the reduction of α -halo ketones by acidified potassium iodide, the second step in the Kurt Meyer indirect titration of enols, might be suitable provided the reaction did not involve the carbonyl group as such but depended rather upon the proper location of the halogen atom with respect to electron-attracting groups.



Picryl chloride was an ideal model compound for testing this possibility; not only because of its ready availability and structural similarity to the heterocyclic compound in which we were interested, but also because the reduction of picryl chloride to trinitrobenzene has been the object of so much study. A review of the literature² did not reveal any attempts to carry out the reduction in the way we had in mind, so we undertook the necessary experiments and found that picryl chloride can be readily reduced to trinitrobenzene by sodium iodide in formic acid at the temperature of the steam-bath, or in acetic acid at the temperature of the steam-bath or at the boiling point, or in acetone containing some acetic acid at room temperature. The yield of crude trinitrobenzene varies between 70 and 100% depending on the experimental conditions; the yield of pure product averages 55–60%. Since the method of purification permits a maximum recovery of 80% of the trinitrobenzene present in the crude product, the yield of pure product corresponds to a yield of about 70% in the reaction.



After these experiments had been completed we reviewed the relevant literature again and found that the reaction had been done before, but the results were incorrectly interpreted, the product was listed as a substance of unknown structure, and the reaction had accordingly been overlooked for nearly 60 years. Willgerodt³ had reported that a solution of picryl chloride and potassium iodide in acetic acid or formic acid or ethanol gave on boiling under reflux a product which he formulated originally as a dinitrophenol of unspecified orientation and later as the dinitro-*o*-phenylenehydroxylamine (I). The properties reported by Willgerodt for his product, including even the formation of addition products with



(2) L. Desvergnès, *Chimie & Industrie*, **25**, 291 (1931); Roger Adams and C. S. Marvel, OSRD-312, December, 1941. A later reference is W. T. Smith, Jr., *THIS JOURNAL*, **71**, 2855 (1949).

(3) C. Willgerodt, *Ber.*, **24**, 592 (1891); *J. prakt. Chem.*, [2] **45**, 145 (1892).

naphthalene and other aromatic hydrocarbons, are those of trinitrobenzene. Willgerodt's analyses of his product, however, were in error by several per cent.; this error led to the formulas which he proposed.

Our results confirm those reported by Willgerodt when he ran the reaction in boiling acetic acid. The product we obtained was identical with an authentic specimen of trinitrobenzene by analysis, melting point and mixed melting point, and infrared absorption. We were unable to duplicate the results Willgerodt obtained when he ran the reaction in boiling formic acid; under these conditions we obtained a high melting product of undetermined structure. We did not attempt to repeat Willgerodt's experiment with potassium iodide and picryl chloride in ethanol for this experiment has been reported by others⁴ to yield picryl iodide as one would expect.

The reduction of picryl chloride with hydriodic acid is of particular interest because it is in such striking contrast with the usual reactions of that chloride in which the halogen is displaced by nucleophilic reagents.⁵ We have not made a study of the mechanism of the reaction but it seems reasonable at present to interpret the process as involving, after the initial conversion of picryl chloride to the iodide, the removal of the iodine atom as iodine as a result of attack by iodide ion, followed by the pick up of a proton. The usual nucleophilic displacement does take place to an appreciable extent for some picric acid is produced.³

We are presenting our results both to correct the earlier reports about the reaction and to call the attention of other chemists to a reaction which should have considerable usefulness. We have, for example, been able by means of this reaction to replace the iodine in 2-iodo-3,5-dinitrothiophene by hydrogen and thus relate this compound and the 2,4-dinitrothiophene obtained by the direct nitration of thiophene. Similarly, Dr. Ellis V. Brown and Mr. Raymond P. Kurkijy have converted 2-bromo-5-nitrothiazole to the hitherto unknown 5-nitrothiazole.

Experimental

In order to be able to handle picryl chloride and trinitrobenzene efficiently in the laboratory, preliminary experiments were run on the crystallization of these two substances from various solvents. Picryl chloride can be crystallized with an 80% recovery by solution in hot formic acid (2 ml. per gram) and chilling. Trinitrobenzene can be crystallized with an 80% recovery by solution in hot toluene (2 ml. per gram), addition of an equal volume of ethanol, and chilling.

The reduction in acetone was effected by adding a solution of 10 g. (0.04 mole) of picryl chloride in 25 ml. of acetone to a solution of 15 g. (0.10 mole) of sodium iodide in 50 ml. of acetone and 5 ml. of acetic acid. An intense brown color developed as soon as the solutions were mixed. After it had stood for 24 hours at room temperature, the reaction mixture was poured into a solution of 5 g. of sodium bisulfite in 320 ml. of water. The dried crude product (quantitative yield) was crystallized from toluene and ethanol and furnished 5.2 g. (60%) of trinitrobenzene, m.p. 115–117°; mixed with pure trinitrobenzene (m.p. 120–121°) the product melted at 117–119°. In a parallel experiment that was allowed to run for 48 hours, the yield of recrystallized trinitrobenzene was 58%.

For reduction in acetic acid, a hot solution (steam-bath)

of 10 g. (0.04 mole) of picryl chloride in 20 ml. of acetic acid was added to a similarly heated solution of 15 g. (0.10 mole) of sodium iodide in 50 ml. of acetic acid. The reaction mixture was heated on the steam-bath for 6 hours, then poured into a solution of 5 g. of sodium bisulfite in 280 ml. of water. The crude product was crystallized from a mixture of toluene and ethanol to furnish 3.7 g. (43%) of trinitrobenzene, m.p. 115–117°; mixed with pure trinitrobenzene (m.p. 120–121°) the product melted at 117–119°. In a parallel experiment that was allowed to run for 18 hours, the yield was 47%. In another experiment, run for 6 hours at the boiling point of the reaction mixture, the yield was 55%.

For reduction in formic acid, a hot solution (steam-bath) of 10 g. (0.04 mole) of picryl chloride in 20 ml. of formic acid was added to a similarly heated solution of 15 g. (0.10 mole) of sodium iodide in 50 ml. of formic acid. The reaction mixture was heated on the steam-bath for 6 hours, then worked up as in the experiments with acetic acid. The yield of crude trinitrobenzene was 6.1 g. (70%); this furnished 4.7 g. (55%) of recrystallized product. A parallel reaction in formic acid at the boiling point yielded no trinitrobenzene. The product was an orange solid that melts above 275° and whose structure has not been determined. *Anal.* Found: C, 46.10; H, 3.24.

The trinitrobenzene obtained in these reductions had a faint yellow color that was difficult to remove by crystallization. An analytical sample was prepared by crystallization from toluene-ethanol followed by crystallization from ethanol. This material melted at 120–121° and the melting point was not lowered by admixture with an authentic sample of trinitrobenzene (Eastman Kodak Co.). *Anal.* Calcd. for C₆H₃N₃O₆: C, 33.80; H, 1.41. Found: C, 34.09; H, 1.68. The infrared absorption spectrum of our material was identical with that of trinitrobenzene obtained from the Eastman Kodak Co.

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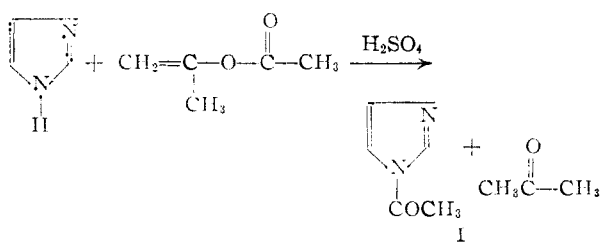
The Acetylation of Imidazole

By J. H. BOYER

RECEIVED AUGUST 1, 1952

Oddo and Ingraffia¹ in 1931 reported their unsuccessful attempts to produce N-acetylimidazole (I). They were, however, able to isolate a C-acetylimidazole (II), m.p. 80°, from the magnesium salt of imidazole heated with acetyl chloride in a sealed tube. Recently the acetylation of 2-benzoyl-4(or 5)-phenylimidazole by isopropenyl acetate was reported to produce 1-acetyl-2-benzoyl-4-phenylimidazole.²

The reaction between imidazole and isopropenyl acetate has now been shown to produce a different acetyl derivative which is assigned the structure of I.



As predicted by Oddo and Ingraffia¹ I is extremely sensitive to hydrolysis. The most successful method for purification was recrystallization from isopropenyl acetate. A moist ether solution of I

(4) P. Hepp, *Ann.*, **215**, 361 (1882).

(5) J. P. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 272 (1951).

(1) B. Oddo and F. Ingraffia, *Gazz. chim. ital.*, **61**, 446 (1931).

(2) J. H. Boyer and D. Straw, *This Journal*, **74**, 4506 (1952).