

distance and regularity in distribution of the micelles, rather than their size (which remains unchanged in most of the above experiments), determines the scattering it follows that, to a high degree, phase relationship between the micelles is involved in the scattering by these densely packed cellulose systems. Such a phase relationship will not exist in the scattering by particles in more dispersed systems. In the latter case formulas given by Guiniér and others³ are appropriate and enable the determination of the *size* of the particles; whereas the application of Bragg's law appears to be applicable in this densely packed system enabling calculation of the average *distance* between the particles.

(3) A. Guiniér, "Radiocrystallographie," Chapter XII, Dunod, Paris; *C. R. Acad. Sci. Paris*, **204**, 1115 (1937); Thesis, Paris, 1939; R. Hosemann, *Z. Physik*, **113**, 751 (1939); **114**, 133 (1939); O. Kratky, *J. Polymer Sci.*, **3**, 195 (1948).

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CLEMSON, S. C. RECEIVED JANUARY 19, 1949

Synthesis of *N*¹-*p*-Fluorophenyl-*N*⁵-isopropylidiguanide¹

BY CHARLOTTE A. HART AND CALVIN A. VANDERWERF

In connection with an investigation of the pharmaceutical properties of aromatic fluorine-containing compounds, *N*¹-*p*-fluorophenyl-*N*⁵-isopropylidiguanide, the fluoro-analog of paludrine, has been synthesized by a modification of the method described by Curd and Rose² for the preparation of disubstituted diguanides. Pharmaceutical testing of the product is in progress.

Experimental³

p-Fluorophenyldicyandiamide.—Exactly 33.0 g. (0.3 mole) of *p*-fluoroaniline⁴ was added to 150 ml. of 5 *N* hydrochloric acid and diazotized by the addition of 21 g. (0.30 mole) of sodium nitrite in a saturated water solution while the temperature was maintained at 0–5°. The diazotized solution was added quickly with stirring to a solution of 28 g. (0.33 mole) of dicyandiamide⁵ in 850 ml. of water at 20°. A total of 32 g. (0.25 mole) of sodium carbonate monohydrate was added in portions over the course of one and one-half hours, in order to maintain the alkalinity of the solution. The orange-red triazene which precipitated was separated by filtration and partially dried by means of a rubber dam.⁶ It was then added in portions during the course of one hour to a stirred solution of 45 ml. of concentrated hydrochloric acid in 200 ml. of acetone at 10–15°. The mixture was stirred for two additional hours, 600 ml. of water was added, and the resulting green precipitate of crude *p*-fluorophenyldicyandiamide (28.0 g., 52%), m. p. 178–190°, was isolated by filtration.

(1) The authors are indebted to the Office of Naval Research for a grant which made this and continuing investigations possible.

(2) Curd and Rose, *J. Chem. Soc.*, 729 (1946).

(3) All melting points are corrected; boiling points are uncorrected.

(4) Prepared by the method of Bradlow and VanderWerf, *This Journal*, **70**, 654 (1948).

(5) Obtained through the courtesy of American Cyanamid Company.

(6) A sample of the triazene which had been dried and then purified by re-precipitation from sodium hydroxide solution decomposed at 124–126° with gas evolution.

The product was purified by repeated treatment with charcoal in boiling 1 *N* sodium hydroxide solution, followed in each case by re-precipitation with hydrochloric acid, and finally by a single recrystallization from methanol. In this manner, 9.5 g. (18%) of almost colorless material melting at 204.0–205.4° was obtained.

Anal. Calcd. for C₈H₇N₄F: C, 53.9; H, 4.0; N, 31.5. Found: C, 54.0; H, 3.6; N, 31.3.

*N*¹-*p*-Fluorophenyl-*N*⁵-isopropylidiguanide Monoacetate.—A mixture of 5.5 g. (0.03 mole) of *p*-fluorophenyldicyandiamide dissolved in 50 ml. of ethanol, 6 g. (0.10 mole) of isopropylamine and 3.9 g. of copper sulfate pentahydrate dissolved in 20 ml. of water was refluxed on a steam-bath for four days, during which time a red-brown precipitate was formed. The solvent and excess isopropylamine were then removed by distillation and a solution of 15 ml. of concentrated hydrochloric acid in 150 ml. of water was added. Hydrogen sulfide was bubbled into the mixture until no further precipitation occurred, the solid material was removed by filtration, and the filtrate was poured in a thin stream into a 20% solution of sodium hydroxide. The *N*¹-*p*-fluorophenyl-*N*⁵-isopropylidiguanide separated as a gummy precipitate.

Inasmuch as the free base is difficult to recrystallize, the product was isolated as the acetate, as follows: the crude base was extracted from the mixture with ether, the ether extract dried over anhydrous sodium sulfate, and the ether removed. The residue was dissolved in dry toluene and the filtered solution treated with glacial acetic acid until a strong odor of acetic acid persisted. The precipitate was filtered, washed with toluene, and dried to yield 7.4 g. (82%) of colorless, non-hygroscopic, water-soluble crystals of *N*¹-*p*-fluorophenyl-*N*⁵-isopropylidiguanide monoacetate, melting at 169–171°. Recrystallized from 2-butanone, the pure material melted at 171.2–172.1°.

Anal. Calcd. for C₁₃H₂₀O₂N₅F: C, 52.5; H, 6.8; N, 23.6. Found: C, 52.6; H, 6.6; N, 23.4.

DEPARTMENT OF CHEMISTRY
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3,4-Dichlorotetramethylene Sulfone

BY T. EARL JORDAN AND FRANK KIPNIS¹

It has been found that following the method of Van Zuydewijn² which involved passing chlorine into a boiling solution of butadiene sulfone in benzene, 3,4-dichlorotetramethylene sulfone is obtained in approximately 50% yield. By using, instead, sulfuryl chloride in 25% excess with a little iodine, the yield is 67% and with 100% excess, the yield is 92–93%. Attempts to chlorinate further resulted in no definite compounds.

The preferred procedure is as follows: Butadiene sulfone is first prepared by the reaction of butadiene and sulfur dioxide in a bomb for several hours at about 100° and is recrystallized from alcohol. To a solution of 118 g. (1 mole) of this substance in 800 ml. of benzene containing a small crystal of iodine and maintained at 55–60° in a two-liter flask provided with a reflux condenser, stirrer and calcium chloride guard tube, 160 ml. (240 g.) of sulfuryl chloride is added with stirring during two and a half hours, after which stirring is continued for three hours at the same temperature. Excess sulfuryl chloride and the benzene are recovered by distillation at atmospheric pressure, after which the product distills at 145–150° under 5 mm. pressure; m. p. 99–100°. Recrystallization from *n*-butanol gives colorless crystals, m. p. 124°; yield 176 g. (93%). The product is soluble in acetone, cyclohexanone, hot

(1) Present address: Oxford Products, Inc., Cleveland, Ohio.

(2) Van Zuydewijn and E. de Roy, *Rec. trav. chim.*, **57**, 445 (1938).

water, hot alcohol, hot butanol, hot carbon tetrachloride, but insoluble in paraffins and xylene.

Anal. Calcd. for $C_4H_8O_2Cl_2S$: Cl, 37.10. Found: Cl, 37.15, 37.07.

Attempts to chlorinate 3,4-dichlorotetramethylene sulfone at 190–200° gave no reaction, while at 225–240° the increase in weight was 20% to give a gel-like mass, which appeared to have carbon dispersed through it. Approximately 40% distilled at 55–170° at 2–4 mm. to give portions ranging from no sulfur and 68% chlorine to 23.7% sulfur and 12.6% chlorine. No definite compound was indicated.

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Orientation in Aromatic Compounds of Phosphorus. I. Nitration of Di-*n*-butyl Benzylphosphonate

BY GENNADY M. KOSOLAPOFF

Although nitration studies have been carried out with benzylphosphonic acid,¹ dibenzylphosphinic acid and tri-benzylphosphine oxide,² the chemical literature lacks an investigation of nitration of esters of phosphonic acids having the benzyl group.

Nitration of di-*n*-butyl benzylphosphonate, with fuming nitric acid or with mixed acid, was now found to give good yields of the *p*-nitro derivative. Other isomers, of which the ortho might have been expected, were formed in such small amounts as to avoid detection. The preparation of a *p*-nitrobenzylphosphonate is of interest because of the reported failure of an attempted direct preparation from trialkyl phosphites and *p*-nitrobenzyl chloride.³

Procedure

(a) Di-*n*-butyl benzylphosphonate (28.4 g.) was added over thirty minutes to a stirred mixture of 25 ml. of concentrated sulfuric acid and 25 ml. of concentrated nitric acid at 0–2°. The mixture was stirred at this temperature for one hour and was poured into one liter of ice water. The product was isolated by extraction with benzene (300 ml.), washing with cold water and sodium carbonate solution, and distillation.

(b) Di-*n*-butyl benzylphosphonate (20 g.) was added over thirty minutes with stirring to 100 ml. of fuming nitric acid (d. 1.5) at 0° and the solution was stirred for thirty minutes. The product was then isolated as described above.

Procedure (a) yielded 30.0 g. (91%) of the nitrated ester, while procedure (b) gave 20.0 g. (86%) of the same substance. This was a pale yellow liquid, b. p. 210–211° at 3 mm., n_D^{25} 1.5058; mol. wt. found, 326, 330; calcd., 329.

The identity of this material, as di-*n*-butyl *p*-nitrobenzylphosphonate, was shown by quantitative conversion to *p*-nitrobenzylphosphonic acid upon hydrolysis (six hours) with boiling concentrated hydrochloric acid. The resulting acid melted at 226° (recrystallized from water), which was above the previously reported figure (217°) for the acid obtained by nitration of the free phosphonic acid.¹ The equivalent weight of the acid, however, agreed well

(1) Litthauer, *Ber.*, **22**, 2145 (1859).

(2) Challenger and Peters, *J. Chem. Soc.*, 2610 (1929).

(3) Lugovkin and Arbuzov, *Doklady Akad. Nauk. S. S. S. R.*, **59**, 1801 (1948).

with the calculated value (found: 216; calcd. 217), and oxidation with alkaline permanganate gave only *p*-nitrobenzoic acid.

The distillation residues after the isolation of the nitrated ester (about 1 g. in both procedures) gave, upon hydrolysis, a further small amount of *p*-nitrobenzylphosphonic acid, while the residual mother liquors gave minute amounts of the same material, which, however, on treatment with alkaline permanganate gave *p*-nitrobenzoic acid with a somewhat low melting point (235–236°), which may indicate the presence of small amounts of isomers which were too minute for definite isolation.

Attempted reduction of di-*n*-butyl *p*-nitrobenzylphosphonate by potassium sulfide in water at 90° failed to take place and the product was recovered unchanged.

The reduction was accomplished satisfactorily, however, when ten grams of the ester was added over thirty minutes to a mixture of twenty grams of iron filings and 60 ml. of 10% acetic acid at 75–80°; the mixture was stirred for thirty minutes, cooled, mixed with 200 ml. of benzene and filtered after neutralization with sodium carbonate. The benzene extract was washed with water, dried and concentrated in vacuum (water pump). The residual di-*n*-butyl *p*-aminobenzylphosphonate was a deep yellow undistillable oil (9 g.), which could not be induced to crystallize. Its hydrochloride was similarly an uncrystallizable oil. Hydrolysis by boiling hydrochloric acid (seven hours) gave a 93% yield of the previously reported *p*-aminobenzylphosphonic acid⁴; m. p. 324–325° (with dec.).

The physiological action of these substances will be reported elsewhere.

(4) Kosolapoff, *This Journal*, **69**, 2112 (1947).

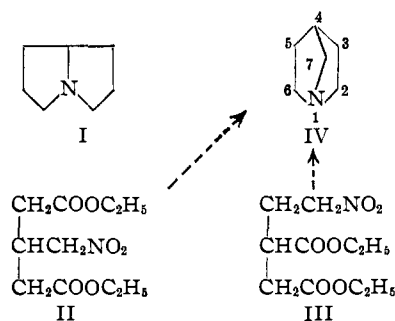
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The Addition of Nitroparaffins to Diethyl Glutaconate and Diethyl Itaconate

BY NELSON J. LEONARD AND GRADUS L. SHOEMAKER¹

The reductive cyclization of γ -nitropimelic esters has provided a convenient method for the synthesis of pyrrolizidine (I) and substituted pyrrolizidines.² In an effort to extend the reductive cyclization of nitro-diesters as a means of pro-



ducing bicyclic compounds containing a bridgehead nitrogen, the addition of nitroparaffins to glutaconic and itaconic esters was studied. The adducts of nitromethane with diethyl glutaconate (II) and with diethyl itaconate (III) should produce the same bicyclic amine, 1-azabicyclo[2.2.

(1) Present address: Department of Chemistry, Rutgers University, New Brunswick, New Jersey.

(2) Leonard, Hruda and Long, *This Journal*, **69**, 690 (1947); Leonard and Beck, *ibid.*, **70**, 2504 (1948).