consisting of 96 cc. of acetone and 38 cc. of water[22] to yield 53% of (*a*), m.p. 180–181°, 81% of (*b*), m.p. 225–226° and 59% of (*c*), m.p. 201.5–202.5°. The acids were recrystallized from acetone-water.

Anal. Calcd. for $C_{12}H_{10}NO_3F_3$: C, 52.75; H, 3.69. Found: *ortho-* compound: C, 53.24; H, 4.02; *meta-* compound: C, 52.51; H, 3.76; *para-* compound: C, 52.83; H, 3.56.

(a) *N-Acetyl-o-trifluoromethylphenylalanine;* (b) *N-acetyl-m-trifluoromethylphenylalanine;* (c) *N-acetyl-p-trifluoromethylphenylalanine;* (d) *N-benzoyl-o-trifluoromethylphenylalanine and* (e) *N-benzoyl-m-trifluoromethylphenylalanine.* In a typical reaction, 10 g. of the substituted acrylic acid was dissolved in 95% ethanol to which was added 1 g. of 5% palladium on charcoal. The mixture was shaken for 3 hr. in the presence of 40 lb. pressure of hydrogen. After filtering the mixture, the colorless filtrate was concentrated *in vacuo* and the solid residue recrystallized from acetone-water to yield 8 g. of product: (*a*) m.p. 179–180°, (*b*) m.p. 132–133°, (*c*) m.p. 178–178.5°, (*d*) m.p. 172–173°, and (*e*) m.p. 167–168°.

Anal. Calcd. for $C_{12}H_{12}NO_3F_3$: C, 52.36; H, 4.40. Found, compound (*b*): C, 52.49; H, 4.42.

Anal. Calcd. for $C_{17}H_{14}NO_3F_3$: C, 60.53; H, 4.18. Found, compound (*e*): C, 60.59; H, 4.05.

(a) *o-Trifluoromethylphenylalanine hydrochloride;* (b) *m-trifluoromethylphenylalanine hydrochloride;* (c) *p-trifluoromethylphenylalanine hydrochloride.* In a typical reaction, 5 g. of the *N*-acetylphenylalanine was hydrolyzed with 100 cc. of concd. hydrochloric acid under reflux for 10 hr. After concentrating the aqueous mixture, a white crystalline solid separated. The pure amino acid hydrochloride was dried *in vacuo.* A second crop of less pure product was obtained on further concentration. The total yield was 2.5 g. (51%). The *N*-benzoyl analogs were much more resistant to hydrolysis under a variety of conditions and no amino acids could be isolated. The decomposition points of the *o*-, *m*-, and *p*-trifluoromethyl amino acid hydrochlorides were 190–195°, 199–202°, and 196–203°, respectively.

Anal. Calcd. for $C_{10}H_{11}NO_2F_3Cl$: C, 44.54; H, 4.11; N, 5.19. Found: *o*-amino acid: C, 44.32; H, 4.15; N, 5.05; *m*-amino acid: C, 44.56; H, 4.23; N, 5.03; *p*-amino acid: C, 44.76; H, 3.92; N, 4.65.

(a) *o-Trifluoromethylphenylalanine;* (b) *m-trifluoromethylphenylalanine;* (c) *p-trifluoromethylphenylalanine.* In a typical conversion, 1 g. of the amino acid hydrochloride was dissolved in 50 cc. of hot water and the resulting solution passed through a column of Dowex-3 (a weakly basic ion-exchange resin). Hot water was then passed through the column until amino acid could no longer be detected in the eluate (ninhydrin test). The eluate gave a negative test for chloride ion. The solution was distilled *in vacuo* on a steam bath and the resulting solid collected and dried.

CHICAGO 16, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WEST VIRGINIA UNIVERSITY]

Condensation Reactions of a Nitro Group. II.[1] Preparation of Phenanthridine-5-oxides and Benzo(c)cinnoline-1-oxide[2]

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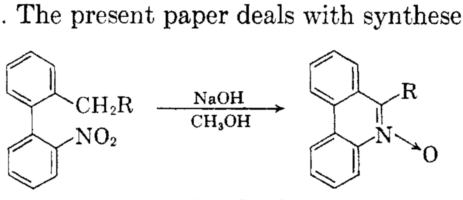
Additional examples in the biphenyl series of the condensation of a nitro group in the 2-position with an activated methylene group in the 2′-position in the presence of methanolic sodium hydroxide have been found. The additional activating groups are benzoyl and benzenesulfonyl; the phenyl group did not serve as an activator. Apparently, the benzoyl and benzenesulfonyl compounds underwent ring closure followed by nucleophilic displacement reactions by hydroxide ion to produce benzoate and benzenesulfinate ions, respectively. 2-Amino-2′-nitrobiphenyl reacted with both sodium hydroxide and sodium methoxide in methanol to yield benzo(c)cinnoline-1- oxide. The intramolecular reaction of a nitro group was not observed in appropriate test compounds outside the biphenyl series.

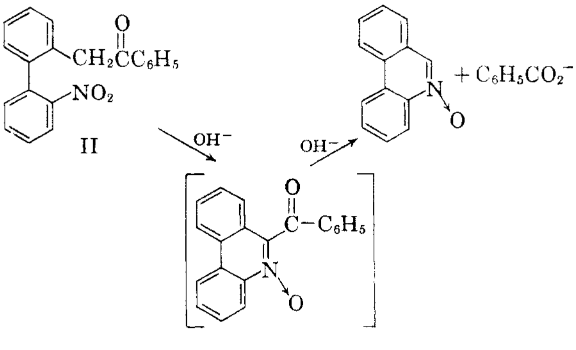
DISCUSSION

Recently it was reported[1] that certain biphenyls of the following type react with methanolic sodium hydroxide to form 6-substituted phenanthridine-5-oxides. The present paper deals with syntheses and testing of additional compounds to determine more about the generality of the foregoing ring closure reaction.



Type I R = CN, CO_2CH_3, $CONH_2$

Three more type I compounds have been treated with methanolic sodium hydroxide. First, with R as benzoyl in 2-(benzoyl)methyl-2′-nitrobiphenyl (II) ring closure occurred to produce phenanthridine-5-



II

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[1] Paper I, C. W. Muth, J. C. Ellers, and O. F. Folmer, *J. Am. Chem. Soc.*, **79**, 6500 (1957).

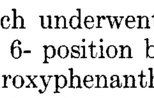
[2] Supported by the National Science Foundation Research Grant G-4236, whose help we wish to gratefully acknowledge. In part from the master's thesis of R. B. Wotring, 1958, and N. Abraham, 1960, both from West Virginia University.

oxide and sodium benzoate in nearly quantitative yields. Although it could not be isolated, apparently 6-benzoylphenanthridine-5-oxide formed as an intermediate and underwent a nucleophilic displacement reaction on the carbonyl carbon by the hydroxide ion. The foregoing cleavage reaction may be considered as analogous to those undergone by *beta*-keto esters and *beta*-diketones.[3] Efforts to oxidize 6-benzoylphenanthridine[4] with peracetic acid to 6-benzoylphenanthridine-5-oxide were unsuccessful.

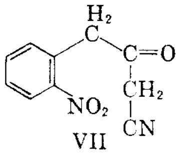
Second, with R as benzenesulfonyl in 2-(2′-nitrophenyl)benzyl phenyl sulfone (III), a ring closure occurred and the products isolated were 6-hydroxyphenanthridine-5-oxide and/or its tautomer, *N*-hydroxyphenanthridone, and benzenesulfinic acid as 2,4-dinitrodiphenyl sulfone.[5] In this case 6-benzenesulfonylphenanthridine-5-oxide was probably an intermediate which underwent a nucleophilic displacement at the 6- position by the hydroxide ion to produce 6-hydroxyphenanthridine-5-oxide or its tautomer[6] and the benzenesulfinate ion. This postulate is different from the one made for the benzoyl compound where the attack was considered to occur on the carbonyl carbon.

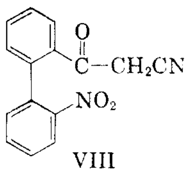
Third, with R as phenyl in 2-benzyl-2′-nitrobiphenyl (IV) no ring closure occurred with sodium hydroxide or sodium methoxide in methanol. This was not surprising because the phenyl group is not as strong an electron-attracting group[7] as the carbonyl and sulfonyl groups. Only the stronger electron-attracting groups have been found to be activators for the ring closure.[1]

When 2-amino-2′-nitrobiphenyl (V) [CH_2R of type I replaced by NH_2] was treated with either sodium hydroxide or sodium methoxide in methanol a ring closure occurred to produce benzo(c)cinnoline-1-oxide (VI). This condensation reaction between the nitro and amino groups required about two hours, which is much longer than the time required for the condensation reaction between the nitro and methylene groups. The foregoing was not unexpected because benzo(c)cinnoline-1-oxide (VI) has been prepared[8] by the chemical reduction of 2,2′-dinitrobiphenyl in the presence of sodium hydroxide.


VI

The intramolecular reaction of a nitro group with a methylene group in the presence of methanolic sodium hydroxide *did not* occur with 4-(2′-nitrophenyl)-3-butanonitrile (VII) or [2-(2′-nitrophenyl)] benzoylacetonitrile (VIII). Likewise, in contrast to the behavior of 4-chloro-2-nitrophenylurea,[9] *o*-nitrophenylacetamide did not react intramolecularly with 30% sodium hydroxide.


VII


VIII

The new compounds prepared and characterized in this work are: 2-(benzoyl)methyl-2′-nitrobiphenyl (II); 2-(2′-nitrophenyl)benzyl phenyl sulfide (X); 2-(2′-nitrophenyl)benzyl phenyl sulfone (III); 2-nitro-2′-benzylbiphenyl (IV); ethyl 4-(2′-nitrophenyl)-3-keto-2-cyanobutanoate (IX); 4-(2′-nitrophenyl)-3-ketobutanonitrile (VII); ethyl [2-(2′-nitrophenyl)]benzoylcyanoacetate (XI); [2-(2′-nitrophenyl)]benzoylacetonitrile (VIII); 2-nitro-2′-acetylbiphenyl (XII); 2,4-dinitrophenylhydrazone and semicarbazone of XII.

EXPERIMENTAL[10]

2-(Benzoyl)methyl-2′-nitrobiphenyl (II). When 2-nitro-2′-biphenylacetyl chloride[11] prepared from 3.00 g. (0.0117 mole) of 2-nitro-2′-biphenylacetic acid and thionyl chloride was mixed with 18 ml. of carbon disulfide and 3.0 g. (0.0224 mole) of aluminum chloride a red oil separated. Five minutes later 8 ml. of benzene and 8 ml. of carbon disulfide were added. After 20 min. the mixture was boiled for 2 min. and then poured onto ice and conc. hydrochloric acid. The resulting mixture was extracted with ether. The ether extract was washed with cold 10% hydrochloric acid, 5% sodium bicarbonate, water, and saturated sodium chloride solution. After filtering through Drierite the solution was concentrated by distillation. The residue crystallized to a yellow solid (3 g.) after most of the benzene had been removed.

The bicarbonate solution was acidified to yield 0.20 g. of starting acid, m.p. 113–120°.

The yellow solid was dissolved in hot benzene and treated with decolorizing charcoal. To this filtrate was added 95% ethanol. After the mixture was cooled 1.24 g. (36%) of II as nearly white crystals, m.p. 98–100°, separated. After

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(3) Jack Hine, *Physical Organic Chemistry*, McGraw-Hill Book Co., Inc., New York, N. Y., 1956, pp. 292–295.

(4) H. Gilman and J. Eisch, *J. Am. Chem. Soc.*, **79**, 4425 (1957).

(5) J. D. Loudon, *J. Chem. Soc.*, **537** (1935).

(6) This material (calcd. for $C_{13}H_9NO_2$: C, 73.92%: H, 4.30%: N, 6.63%. Found: C, 74.06%; H, 4.44%; N, 6.69%), was the same, as described by mixed melting point and infrared spectrum, as that obtained and characterized by Shih-Tsung Chiang, master's thesis, West Virginia University, 1959, in an independent study. This work will be reported later.

(7) G. E. K. Branch and M. Calvin, *The Theory of Organic Chemistry*, Prentice Hall, Inc., New York, N. Y., 1941, Chap. VI.

(8) F. E. King and T. J. King, *J. Chem. Soc.*, 824 (1945).

(9) F. J. Wolf, R. M. Wilson, Jr., K. Pfister III, and M. Tischler, *J. Am. Chem. Soc.*, **76**, 4611 (1954).

(10) All melting points are uncorrected unless otherwise stated. All microanalyses by Galbraith Microanalytical Laboratories, Knoxville, Tenn. All infrared absorption values are in μ. We wish to thank Miss Patricia Estep for the infrared data taken in potassium bromide wafers.

(11) C. W. Muth, W. L. Sung, and Z. B. Papanastassiou, *J. Am. Chem. Soc.*, **77**, 3393 (1955).

three crystallizations from methanol pale yellow crystals were obtained, m.p. 98–100°, infrared absorption at 5.95 C=O, 6.65 and 7.45 μ NO_2 (chloroform).

Anal. Calcd. for $C_{20}H_{15}NO_3$; C, 75.68; H, 4.76; N, 4.41. Found: C, 75.68; H, 4.74; N, 4.45.

When the foregoing reaction was conducted at reflux temperature for 5 hr., none of II was isolated.

2-(Benzoyl)methyl-2'-nitrobiphenyl (II) *and Sodium Hydroxide.* As 0.27 g. (0.0068 mole) of sodium hydroxide in 6 ml. of methanol was added to a slurry of 2-(benzoyl)methyl-2'-nitrobiphenyl (II) in 6 ml. of methanol the solution color changed from yellow to orange-yellow. In 4 min. the temperature rose from 29 to 33°. The mixture was shaken intermittently. After 10 min. of reaction time the solid had dissolved; after 13 min. of reaction time the solution was cooled with ice water; and after 20 min. of reaction time 0.50 g. (25%) of light pink phenanthridine-5-oxide, m.p. 223–226° (lit.,[1] m.p. 226–228°), m.m.p. 223–226°, was filtered.

The filtrate was concentrated by warming under reduced pressure to yield a purple solid which became tan after washing with water. The tan phenanthridine-5-oxide weighed 0.115 g. (57%), m.p. 220–224°, m.m.p. 222–225°, and its infrared spectrum was the same as the spectrum of phenanthridine-5-oxide. The picrate of this product melted at 193–198° (lit.,[1] m.p., 198–200°).

The filtrate from the tan material was extracted with chloroform, acidified and extracted with ether. The ether solution was dried and concentrated by distillation to a residue which was sublimed to yield 0.80 g. (63%) of benzoic acid, m.p. 117–120°, m.m.p. with authentic benzoic acid showed no depression of the former. An additional 0.023 g. (17%) of slightly less pure benzoic acid was also obtained.

The chloroform extract yielded 0.03 g. of buff solid, m.p. 205–217°, m.m.p. with first crop 215–224°.

In a similar experiment with the initial temperature at 32° the yield of phenanthridine-5-oxide obtained by filtering the reaction mixture after 8 min. was 40%. The total yield of oxide after completing the isolation process was 96%.

From another experiment in which the reactants were refluxed for 1 hr., phenanthridine-5-oxide, m.p. 219–227° (88%) and benzoic acid, m.p. 115–120° (91%) were obtained.

2-(2'-Nitrophenyl)benzyl phenyl sulfide (X). In duplicate experiments adapted from the procedure of Bost *et al.*,[12] 4.00 g. (0.100 mole) of sodium hydroxide was added to 11.5 g. (0.104 mole) of benzenethiol in 300 ml. of absolute ethanol. This mixture was added to 14.6 g. (0.05 mole) of 2-(2'-nitrophenyl)phenylbromomethane dissolved in 50 ml. of absolute ethanol. Mild refluxing and stirring were used for 1 hr. Then the solution was filtered and concentrated to dryness under reduced pressure. The residue was leached with ether and the ether was washed with sodium hydroxide solution, water, and saturated sodium chloride solution and filtered through Drierite. Evaporation of the ether yielded 15.8 g. (99%) of X as a yellow, waxy solid, m.p. 48–55°.

The analytical sample, prepared by several crystallizations from 70% ethanol, consisted of yellow crystals, m.p. 54–55°, infrared absorption at 3.2, 6.4 NO_2 and 7.4 μ NO_2 (carbon tetrachloride).

Anal. Calcd. for $C_{19}H_{15}NO_2S$: C, 70.90; H, 4.70; N, 4.35; S, 9.97. Found: C, 70.66; H, 4.79; N, 4.47; S, 10.00.

2-(2'-Nitrophenyl)benzyl phenyl sulfone (III). The following procedure is modeled after a procedure of Truce and Knospe.[13] To 12.0 g. (0.038 mole) of X dissolved in 54 ml. of 1:1 glacial acetic acid-acetic anhydride was added 22 ml. (0.214 mole) of 30% hydrogen peroxide. The mixture stood at room temperature for 4 days and then was heated for 1.5 hr. on a steam bath. After cooling, manganese dioxide was added and the solvent was removed under reduced pressure to yield a brown oil. The oil was extracted with 400 ml. of absolute ether and the mixture was filtered to remove some brown solid. The filtrate was chromatographed on a 3 × 20 cm. column of Aluminum Oxide Merck using 200 ml. of absolute ether as the developer. The eluate was concentrated to yield 12.5 g. (93%) of greenish yellow oil. The oil partially decomposed when it was vacuum distilled. The analytical sample was chromatographed three times; infrared absorption at 6.6 and 7.4 NO_2, 7.5, 8.7, and 8.8 SO_2 and 9.3 μ (carbon tetrachloride).

Anal. Calcd. for $C_{19}H_{15}NO_4S$: C, 64.54; H, 4.27; N, 3.96; S, 9.07. Found: C, 64.38; H, 4.43; N, 4.07; S, 9.03.

2-(2'-Nitrophenyl)benzyl phenyl sulfone (III) *and Sodium Hydroxide.* After 2.01 g. (0.0063 mole) of III and 30 ml. of methanol containing 1.43 g. (0.036 mole) of sodium hydroxide had been heated for 1.5 hr. on a steam bath a white flocculent solid separated and the mixture was concentrated using reduced pressure to yield a solid residue which had pink, white, and yellow colors. The residue was made acidic by adding 3.2 ml. of conc. hydrochloric acid and the resulting mixture was extracted with ether, filtered, and washed with hot water to yield 1.07 g. (80%) of 6-hydroxyphenanthridine-5-oxide or its tautomer[6] as a buff-colored solid, m.p. 250–255°. The ether extracts were extracted three times with 5% sodium hydroxide with a total volume of 15 ml. A considerable amount of glistening white solid (A) was removed by filtration after the first sodium hydroxide extraction was made. The sodium hydroxide solution was concentrated to about 7 ml. volume, acidified with hydrochloric acid, and made slightly basic with sodium hydroxide. A gray solid (B) was removed by filtration.

The filtrate was heated for 1/2 hr. with 0.40 g. (0.0013 mole) of 2,4-dinitrochlorobenzene and about 10 ml. of 95% ethanol to yield after filtering and washing with 95% ethanol, 0.26 g. of pale yellow solid and filtrate A. The pale yellow solid was leached with 2 ml. of boiling acetic acid and the mixture was filtered to remove a white solid. On cooling, the filtrate yielded 0.11 g. of 2,4-dinitrodiphenyl sulfone, m.p. 154–156° (lit.,[5] m.p. 159–160°).

Filtrate A, solids A and B, and 0.2 g. (0.00065 mole) of 2,4-dinitrochlorobenzene were refluxed for 1/2 hr. to yield 0.50 g. of 2,4-dinitrodiphenyl sulfone (31% combined yields based on III) as nearly white crystals, m.p. 155–158°. The foregoing yielded 0.33 g. of nearly white crystals, m.p. 156–158°, after crystallization from acetic acid. In other experiments the yields of 6-hydroxyphenanthridine or its tautomer and 2,4-dinitrodiphenyl sulfone were as high as 90% and 38%, respectively.

2-Benzyl-2'-nitrobiphenyl (IV). As 6.1 g. (0.0021 mole) of 2-(2'-nitrophenyl)benzyl bromide was added with stirring to 125 ml. of benzene and 0.4 g. (0.003 mole) aluminum chloride an orange mixture resulted. The mixture was stirred for 1 day and allowed to stand 3 days before being poured into cold dilute hydrochloric acid. Benzene was added and the organic layer was separated, washed with dilute hydrochloric acid, 5% sodium carbonate, and water before being concentrated by distillation to yield a brown solid. The solid was recrystallized from ethanol to yield 4.79 g. (80%) of IV as nearly white crystals, m.p. 98–101°.

Anal. Calcd. for $C_{19}H_{15}NO_2$: C, 78.9; H, 5.23; N, 4.84. Found: C, 78.6; H, 4.95; N, 5.08.

2-Amino-2'-nitrobiphenyl (V). The methods of Purdie[14] and Badger and Sasse[15] involving the reduction of 2,2'-dinitrobiphenyl yielded orange and red oils, respectively. In both cases, for purification, the oil was dissolved in a minimum amount of ether and treated with a slight excess of 6*N* hydrochloric acid. After cooling, 2-nitro-2'-aminobiphenyl hydrochloride separated. Recrystallization from ethanol gave a light yellow product, m.p. 225–227° (lit.,[16]

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(12) R. W. Bost, J. O. Turner, and R. D. Norton, *J. Am. Chem. Soc.*, **54**, 1985 (1932).

(13) W. E. Truce and R. H. Knospe, *J. Am. Chem. Soc.*, **77**, 5063 (1955).

(14) D. J. Purdie, *J. Am. Chem. Soc.*, **63**, 2276 (1941).

(15) G. M. Badger and W. F. H. Sasse, *J. Chem. Soc.*, 4 (1957).

(16) A. E. S. Fairful, D. A. Peak, W. F. Short, and T. I. Watkins, *J. Chem. Soc.*, 4709 (1952).

m.p. 228–229°). The yellow product was mixed with ammonium hydroxide and the mixture was extracted with ether which after evaporation yielded a red oil. After several conversions from the hydrochloride to the amine a solid product was obtained. After three crystallizations from ethanol and two from benzene-petroleum ether orange crystals, m.p. 62–64° (lit.,[15,16] 64–65°, lit.,[14] m.p. 94–94.5°), of 2-nitro-2′-aminobiphenyl were obtained.

2-Amino-2′-nitrobiphenyl (V) *and sodium hydroxide or sodium methoxide.* In a three necked flask equipped with a reflux condenser was placed 2.00 g. (0.0105 mole) of 2-nitro-2′-aminobiphenyl, m.p. 62–64°. One hundred milliliters of boiling 1*N* methanolic sodium hydroxide was added and as refluxing was continued 25-ml. portions of the deep orange solution were withdrawn after 15 min., 30 min., 1 hr. and 2 hr. Each of the 25 ml. portions was immediately put in an ice bath, diluted with 50 ml. of water, and allowed to stand for approximately 1 hr.

Each portion was treated as follows: The solid material and/or oil was removed by filtration or decantation and the filtrate (A) was saved. The solid and/or oil was leached with 70 ml. of 3*N* hydrochloric acid to remove starting material. The greenish yellow crystalline benzo(c)-cinnoline-1-oxide (VI) which remained was filtered, washed with water, and twice crystallized from aqueous ethanol. Filtrate (A) was concentrated by distillation and the residue was treated as in the foregoing.

The yields of (VI), m.p. 137–138° or 138–139° (lit.,[8] m.p. 138°) for reaction times of 15 min., 30 min., 1 hr., and 2 hr. were 17%, 33%, 61%, and 92%, respectively.

In one experiment similar to the foregoing except that sodium methoxide was used instead of sodium hydroxide the results were the same after 2 hr. reaction time, but the yields of VI were considerably lower at the other times.

o-Nitrophenylacetyl Chloride. In a system protected from moisture 96 g. (0.54 mole) of *o*-nitrophenylacetic acid (Eastman Kodak Co.) was mixed with 250 ml. of anhydrous ether and to this was added 213 g. of redistilled thionyl chloride. The mixture was refluxed for 5 min. and the resulting dark red solution was allowed to stand overnight. The solution was concentrated by distillation at atmospheric pressure at first and then under reduced pressure with a bath temperature which did not exceed 65°. (*In another attempt when this acid chloride was heated at 83°/1–3 mm. it decomposed violently.*) The yield of red oil was 105.5 g. The red oil was shaken with 35–37° petroleum ether and separated. It reacted with ammonium hydroxide to produce 2-nitrophenylacetamide, m.p. 160–161° (lit.,[17] 160–161°).

Ethyl 4-(2-nitrophenyl)-3-keto-2-cyanobutanoate (IX). The procedure was adapted from the method of Dornow and Fust.[18] In a three necked flask were placed 56.5 g. (0.50 mole) of ethyl cyanoacetate and 375 ml. of ether, and 10 g. (0.43 gram atom) of sodium shot was added. Vigorous stirring was used for 2.5 hr. during which time a white suspension developed. Then 50.4 g. (0.254 mole) of 2-nitrophenylacetyl chloride in 50 ml. of ether was added during 15 min. and the mixture was refluxed for 6 hr. Fifty milliliters of ether was added during the reflux period to thin the slurry which was present.

Fifty milliliters of ethanol was added and the reaction mixture was allowed to stand overnight after which time a red oil had separated. The mixture was extracted three times with a total volume of 800 ml. of ice cold 5% sodium hydroxide. Some unchanged sodium was destroyed during the first extraction. The combined red aqueous layers were extracted with ether and then acidified with cold dilute sulfuric acid. This mixture was extracted with benzene. About 1 g. of brown solid was insoluble in both layers. The red benzene solution was dried and concentrated by distillation to yield 46 g. of red oil which solidified after cooling. Two recrystallizations of the crude product from ethanol yielded 31.0 g. (45%) of IX as straw colored needles, m.p. 104.5–106.5°, infrared absorptions at 4.50 CN, 6.06 C═O, 6.55 and 7.45 μ NO_2 (potassium bromide wafer).

This compound did not react with 2,4-dinitrophenylhydrazine.

Anal. Calcd. for $C_{13}H_{12}N_2O_5$: C, 56.52; H, 4.38; N, 10.14; neut. equiv., 276.2. Found: C, 56.30; H, 4 17; N, 9.92; neut. equiv., 276.8, 279.3, 277.7.

4-(2′-Nitrophenyl)-3-ketobutanonitrile (VII). Two grams of IX was refluxed with 60 ml. of 3*N* hydrochloric acid for 5 hr. As the mixture cooled white needle crystals separated as well as a small amount of brown solid, both of which were crystallized from ethanol. The yield of VII was 1.33 g. (90%), m.p. 139–140°, m.m.p. with 2-nitrophenylacetic acid (m.p. 140°) 115–120°, infrared absorptions at 4.41 (weak) CN, 5.80 C═O, 6.58 and 7.42 μ NO_2 (potassium bromide wafer).

Anal. Calcd. for $C_{10}H_8N_2O_3$: C, 58.82; H, 3.95; N, 13.72; neut. equiv., 204.2. Found: C, 58.85; H, 3.82; N, 13.59; neut. equiv., 205, 206, 207.

This product reacted with 2,4-dinitrophenylhydrazine to form fine yellow crystals, m.p. 184–186°, after recrystallization from dimethylformamide.

(2-Nitrophenyl)acetone. After 2.0 g. of VII had been refluxed with 44 ml. of 6*N* hydrochloric acid for 3.5 hr. the mixture was made basic with potassium hydroxide and was extracted with ether. The ether extract was dried and concentrated to yield 1.22 g. (70%) of brown solid which gradually melted as the temperature rose to 29° (lit.,[19] m.p. 29°). The basic solution yielded 0.34 g. of VII, m.p. 135–140°, when it was acidified with hydrochloric acid. Semicarbazone, m.p. 212–214° (lit.,[19] m.p. 213–214°).

Ethyl [2-(2′-nitrophenyl)] benzoylcyanoacetate (XI). In a three necked flask equipped with an additional funnel, stirrer, and condenser with a soda lime tube were placed 2.54 g. (0.11 gram atom) of sodium and 100 ml. of absolute ether. To this was added 16.4 g. (0.145 mole) of ethyl cyanoacetate. After 2.5 hr. of refluxing and stirring all the sodium had been consumed and a white paste had formed. Then 2-(2′-nitrophenyl)benzoyl chloride[11] from 27.0 g. (0.11 mole) of 2-nitro-2′-carboxybiphenyl in 75 ml. of ether was added with stirring during 1/2 hr. The color of the solution changed to pale orange as refluxing and stirring were continued for 2 hr. After cooling, 30 ml. of ethanol was added and the mixture was refluxed for 30 min. before standing overnight. The mixture was extracted with one 150-ml. and three 100-ml. portions of 10% sodium carbonate. The basic extracts were acidified with dilute sulfuric acid to give a tan solid which was filtered, washed repeatedly with water and recrystallized from ethanol to yield 14.0 g. (40%) of XI as fine white crystals, m.p. 135–136°, infrared absorption at 4.4 CN, 5.98 C═O, 6.3, 6.58 and 7.40 NO_2, 7.8 μ (chloroform).

Anal. Calcd. for $C_{18}H_{14}N_2O_5$: C, 63.91; H, 4.17; N, 8.28. Found: C, 63.72; H, 4.23; N, 8.32.

[2-(2′-Nitrophenyl)]benzoylacetonitrile (VIII). With vigorous stirring 3.79 g. (0.011 mole) of XI was refluxed for 23 hr. with 100 ml. of 6*N* hydrochloric acid. Stirring without heat was continued for an additional 3 hr. and the mixture was allowed to stand for 2 days. Initially there was a white suspension and after 10 hr. a yellow-brown oil.

The aqueous layer was decanted from the oil and extracted with ether. When the oil was triturated with ether, 0.6 g. of white solid, m.p. 125–145°, separated. After two recrystallizations from ethanol the melting point was 142–145°.

The ether extract was extracted with 10% sodium hydroxide and then the sodium hydroxide solution was acidified with hydrochloric acid to yield 0.69 g. of white solid, m.p. 125–135°. After two recrystallizations from ethanol the melting point of VIII was 142–145°. The ether layer was dried and concentrated to yield 1.3 g. of 2-nitro-2′ acetylbiphenyl as a light brown solid.

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[17] A. Reissert, *Ber.*, **41**, 3814 (1908).

[18] A. Dornow and K. Fust, *Ber.*, **87**, 985 (1954).

[19] F. Arndt, B. Eistert, and W. Partale, *Ber.*, **61**, 1117 (1928).

In another experiment like the foregoing except that the acidic material was extracted with sodium bicarbonate, the acidic material (VIII) which was only soluble in sodium hydroxide was a tan solid, m.p. 135–143°, weight 0.455 g. (14%). The yield of 2-nitro-2′-acetylbiphenyl, m.p. 58–61°, was 1.47 g. (51%).

Repeated recrystallizations of VIII from ethanol yielded cream-colored crystals, m.p. 144–145.5°; infrared absorption 4.4 CN, 5.98 C=O, 6.3, 6.58 NO_2, 7.40 NO_2, 7.8 μ (chloroform).

Anal. Calcd. for $C_{15}H_{10}N_2O_3$: C, 67.66; H, 3.79; N, 10.52. Found: C, 67.72; H, 3.59; N, 10.68.

2-Acetyl-2′-nitrobiphenyl (XII). The light brown solid, m.p. 58–61°, obtained during the preparation of VIII was recrystallized three times from ethanol to yield nearly white crystals of XII, m.p. 60–61°.

Anal. Calcd. for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81. Found: C, 69.60, 69.83; H, 4.57, 4.62; N, 5.83, 5.90.

The 2,4-dinitrophenylhydrazone of XII after two recrystallizations from ethanol–ethyl acetate consisted of orange crystals, m.p. 191–192.5°.

Anal. Calcd. for $C_{20}H_{15}N_5O_6$: N, 16.62. Found: N, 16.88, 16.78.

The semicarbazone of XII after three crystallizations from aqueous ethanol was a white powder, m.p. 214–216° dec.

Anal. Calcd. for $C_{15}H_{14}N_4O_3$: N, 18.78. Found: N, 18.78, 18.97.

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[CONTRIBUTION FROM THE CHEMISTRY RESEARCH LABORATORY OF THE DEPARTMENT OF SURGERY, UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE]

Derivatives of Fluorene. VII. New Mono and Dinitro Compounds and Some of Their Reactions[1]

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New mono and dinitro derivatives of substituted fluorenes are reported with some improved routes to known compounds. Usefulness of the trifluoroacetyl radical on the amino group is noted both with regard to its strong directing influence and the great ease with which it is removed. The first triamino- and tetraminofluorene are described.

In studying various series of fluorene compounds, especially ring-fluorinated *N*-2-fluorenylacetamides, we have found that hitherto unreported nitrations of some derivatives of 2-fluorenamine are extremely useful in giving substances with certain desired positions substituted or blocked. Reduction of this nitro group and further nitration, followed by a deamination at the first position of nitration, has given us high over-all yields of some disubstituted fluorenes by the best route available.

Like *N*-2-fluorenylperfluorobutyramide,[3] *N*-2-fluorenyltrifluoroacetamide can be nitrated in the 7- position. The yields approach 90%. *N*-2-Fluorenylacetamide on the other hand gives a mixture of the 3- and 7-nitro derivatives.[3–5] The 7-nitro derivative is obtained from the latter reaction in low yield following a time-consuming separation.[3,4] The trifluoroacetyl group is additionally useful because of ready cleavage. A few minutes in hot dilute alkali leads to almost quantitative recovery of high quality 7-nitro-2-fluorenamine. Anyone who has tried the customary dinitration of fluorene, separation of isomers, and monoreduction of 2,7-dinitrofluorene, will appreciate over-all yields of 75 to 80% from 2-fluorenamine in three easy steps, all conveniently carried out in a beaker or Erlenmeyer flask (one-mole level customarily). *N*-2-(7-nitrofluorenyl)trifluoroacetamide can be reduced with Raney nickel and hydrazine hydrate[6] (0.05 mole, 90%), and the resulting amine acetylated and hydrolyzed in hot alkali to give the known 2-acetamido-7-aminofluorene. The latter is also equally conveniently obtained from 2-amino-7-nitrofluorene by acetylation and reduction[6] (0.05 mole, 90%).

Nitration of *N*-2-(7-nitrofluorenyl)trifluoroacetamide, of *N*-2-(3-nitrofluorenyl)trifluoroacetamide and dinitration of *N*-2-(fluorenyl)trifluoroacetamide all gave 80 to 90% yields of *N*-2-(3,7-dinitrofluorenyl)trifluoroacetamide which was readily hydrolyzed to the known 2-amino-3,7-dinitrofluorene, identical with the hydrolysis product of *N*-2-(3,7-dinitrofluorenyl)acetamide.[7]

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[2] To whom communications regarding this manuscript should be addressed.

[3] E. Sawicki, B. Chastain, and H. Bryant, *J. Org. Chem.*, 21, 754 (1958).

[4] *N*-2-(9-Oxofluorenyl)acetamide gives a 90% yield of the 3-nitro derivative [N. Ishikawa and M. Hayashi, *Yûki Gôsei Kagaku Kyôkai Shi*, **15**, 405 (1957)]. For certain 2,3- or 3-substituted fluorenones (*e.g.* 2,3-diamino- or 3-amino-) which can be reduced to fluorenes in high yield, nitration of *N*-2-(9-oxofluorenyl)acetamide is to be preferred as an approach.

[5] *N*-2-Fluorenyl-*p*-toluenesulfonamide gives high yields of the 3-nitro isomer but hydrolysis of the tosyl group is troublesome [N. Ishikawa and M. Hayashi, *Yûki Gôsei Kagaku Kyôkai Shi*, **15**, 202 (1957)].

[6] T. L. Fletcher and M. J. Namkung, *J. Org. Chem.*, **23**, 680 (1958). Footnote[d] in the table of this reference erroneously gives the melting point of the analytical sample of *N*-2-(7-nitrofluorenyl)trifluoroacetamide as 201–201.5°; this should read 248.5–249.5°.