Heterocyclic Nitrogen Compounds. Part IV. Further Condensations with Aldehydic Acids and Diamines.*

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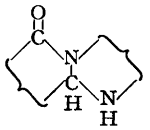
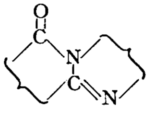
The condensation of phthalaldehydic acids and diamines reported in Part III * has been further investigated. A new preparation of 2′-formyldiphenyl-2-carboxylic acid is given and carbonyl derivatives of this compound are described.

The author (*J.*, 1952, 5024) examined the condensation of *o*-phthalaldehydic acid and 8-formyl-1-naphthoic acid with certain symmetrical diamines and showed the method to be general for the preparation of compounds containing one or other of the systems (A) or (B). This work has now been extended to include an unsymmetrical diamine and also to cover reactions of 2′-formyldiphenyl-2-carboxylic acid (I). A new preparation of (I) (previously prepared by Cook, Dickson, Jack, Louden, McKeown, MacMillan, and Williamson, *J.*, 1950, 139) is described and it has been characterised further by the preparation of several derivatives of its carbonyl group.



(A)



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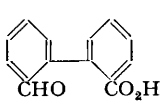
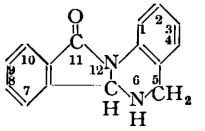
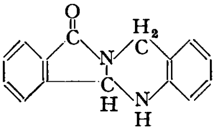


(I)

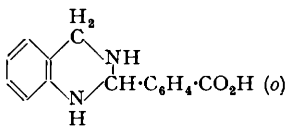


(II)

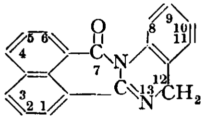
o-Phthalaldehydic acid condenses with *o*-aminobenzylamine to give a compound, m. p. 204·5—205·5°, the presence of the ·CH·NH· system rather than the C:N bond being shown by the formation of *N*-acetyl and *N*-nitroso-derivatives. The product could be (II) or (III), but provisionally has been assigned the former formula on the ground that treatment of the nitroso-derivative with alcoholic hydrogen chloride causes denitrosation (regenerating the parent compound) and not rearrangement of the NO group as would be expected if the N·NO group were attached directly to an aromatic nucleus. Gabriel (*Ber.*, 1912, **45**, 717) by distillation of 2-*o*-carboxyphenyl-1 : 2 : 3 : 4-tetrahydroquinazoline (IV) *in vacuo* obtained a compound, m p. 216—218°, which should have the structure (II) or (III). In our hands Gabriel's method gave erratic results and his product was not obtained pure. However, treatment of (IV) with concentrated sulphuric acid gave the compound, m. p. 204·5°, in small yield.



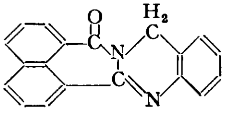
(III)



(IV)



(V)



(VI)

8-Formyl-1-naphthoic acid with *o*-aminobenzylamine gives a small yield of a product with a C:N bond which must have the structure (V) or (VI). To distinguish between these, naphthalic anhydride was condensed with *o*-aminobenzylamine. The main product, *N*-*o*-aminobenzylnaphthalimide, was cyclised in small yield at 300° to (VI), identical with the product from the " aldehydic acid " condensation. Attempts to cyclise the naphthalimide with acetic anhydride gave only a diacetyl derivative [cf. the action of acetic anhydride on *N*-2″-amino-2′-diphenylylnaphthalimide (Stephenson, *loc. cit.*)]. Condensation of 2′-formyldiphenyl-2-carboxylic acid with *o*-phenylenediamine and with 2 : 2′-diaminodiphenyl under varying conditions failed to yield pure products. The former failure may

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* Part III, *J.*, 1952, 5024.

be contrasted with the ease of formation of similar products from phthalaldehydic acid and 2 : 2′-diaminodiphenyl (Stephenson, *loc. cit.*) and from diphenic anhydride and *o*-phenylenediamine (Bistrzcyki and Fässler, *Helv. Chim. Acta*, 1923, **6**, 519).

A convenient preparation of 2 : 2′-diaminodiphenyl is described.

EXPERIMENTAL

Microanalyses were made by the C.S.I.R.O. Micro-analytical Service.

o-*Nitrobenzylamine*.—Powdered sodium azide (6·5 g.) was added (7—8 min.) with stirring to a mixture of *o*-nitrophenylacetic acid (7·24 g.), chloroform (40 ml.), and concentrated sulphuric acid (10 ml.), the temperature rising to 30—35°. The mixture was then heated first at 47—48° and then at 43—46° for 3 hr. (stirring), and the chloroform layer decanted and extracted with sodium carbonate solution to remove a little *o*-nitrophenylacetic acid. The sulphuric acid layer was decomposed with crushed ice and, after removal of unchanged *o*-nitrophenylacetic acid (total recovery 3·1—3·3 g.), the *o*-nitrobenzylamine was recovered by making the filtrate strongly alkaline and extracting the product with benzene in a continuous extractor for 9 hr. After removal of the benzene the base was dissolved in ethanol (10 ml.) and addition of concentrated hydrochloric acid (5 ml.) gave *o*-nitrobenzylamine hydrochloride (2·2—2·4 g.), m. p. 248—250° (decomp.). The *benzenesulphonyl* derivative, prepared under Schotten–Baumann conditions, separated from aqueous alcohol (charcoal) in prisms, m. p. 92—93° (Found : C, 53·6; H, 4·1; N, 9·5; S, 11·0. $C_{13}H_{12}O_4N_2S$ requires C, 53·4; H, 4·1; N, 9·6; S, 11·0%). *N*-*o*-Nitrobenzylphthalimide was obtained in $\nless$90% yield by refluxing equimolar amounts of phthalic anhydride and *o*-nitrobenzylamine hydrochloride in glacial acetic acid with excess of anhydrous sodium acetate for 3 hr.; precipitation with water and recrystallisation from acetic acid gave pale cream crystals, m. p. 219—221° [Gabriel (*Ber.*, 1887, **20**, 2227; 1903, **36**, 807) gives m. p. 217·5—219°].

o-*Aminobenzylamine*.—Gabriel and Colman's method (*Ber.*, 1904, **37**, 3644) for the reduction of *o*-nitrobenzylamine proved wasteful. An aqueous solution of *o*-nitrobenzylamine hydrochloride containing 10% excess of sodium acetate was shaken with Raney nickel and hydrogen (at approx. 1 atm.) until the theoretical amount of hydrogen had been absorbed. After removal of the catalyst, the base, m. p. 60—62° ($\nless$85%), was obtained by basifying the mixture and continuously extracting it with benzene (9 hr.). It is best converted into its dihydrochloride, m. p. 215—218° (decomp.). Its dibenzoyl derivative (Schotten–Baumann) formed needles [from alcohol (charcoal)], m. p. 195—196° (Found : C, 76·7; H, 5·7. Calc. for $C_{21}H_{18}O_2N_2$: C, 76·3; H, 5·5%).

5 : 6 : 11 : 6a-*Tetrahydro*-11-*oxo*isoindolo[2 : 1-a]*quinazoline* (Ring Index No. 2416) (II).—(i) *o*-Phthalaldehydic acid (0·75 g.), *o*-aminobenzylamine dihydrochloride (0·98 g.), hydrated sodium acetate (1·5 g.), water (22·5 ml.), and acetic acid (12·5 ml.) were refluxed for 8 hr., and, after cooling, the yellow solution was partially neutralised with sodium hydroxide. After 12 hr. the precipitate (1·1 g.) was collected and chromatographed in benzene on alumina (B.D.H.; 2·3 × 10 cm.). The *compound* (II) (0·44 g.) was eluted first as a colourless solution in benzene. Crystallisation from ethanol gave prisms, m. p. 204·5—205·5° (Found : C, 76·4; H, 5·1; N, 12·1. $C_{15}H_{12}ON_2$ requires C, 76·2; H, 5·1; N, 11·9%). The *acetyl* derivative, prepared in boiling acetic anhydride, formed stout prisms, m. p. 163—164·5° (Found : C, 73·5; H, 5·0; N, 10·1. $C_{17}H_{14}O_2N_2$ requires C, 73·4; H, 5·1; N, 10·1%). The *nitroso*-derivative was obtained when (II) (0·24 g.), in acetic acid (9 ml.) and water (2 ml.) and cooled to 8°, was treated with sodium nitrite (75 mg.) in water (2 ml.). The product (0·26 g.) was precipitated with water and crystallised from ethanol as pale cream, hair-like prisms, m. p. 212·5—213·5° (decomp.) (Found : C, 68·1; H, 4·1; N, 15·8. $C_{15}H_{11}O_2N_3$ requires C, 67·9; H, 4·2; N, 15·8%). It gave a positive Liebermann's nitroso-reaction, and was decomposed by alcoholic hydrogen chloride with regeneration of (II) (m. p. and mixed m. p.) in nearly quantitative yield.

(ii) 2-*o*-Carboxyphenyl-1 : 2 : 3 : 4-tetrahydroquinazoline (IV) (0·2 g.) and concentrated sulphuric acid (1 ml.) were heated in a boiling-water bath for 7 min., and the clear solution was poured on crushed ice. After basification with ammonia and storage for 12 hr., the product (90 mg.) was collected and chromatographed on alumina (B.D.H.; 1·5 × 5 cm.), being eluted (35 mg.) as a colourless solution by benzene. After crystallisation from ethanol it was identified as (II) by m. p. and mixed m. p.

Condensation of 8-*Formyl*-1-*naphthoic Acid and* o-*Aminobenzylamine*.—8-Formyl-1-naphthoic acid (1 g.), *o*-aminobenzylamine dihydrochloride (1 g.), hydrated sodium acetate (1·5 g.), acetic acid (40 ml.), and water (10 ml.) were refluxed for 7 hr. After partial neutralisation with sodium hydroxide the mixture was kept for 20 hr. The yellow precipitate (1·6 g.) was collected and chromatographed in benzene on alumina (B.D.H.; 2·5 × 35 cm.), dark by-products being more strongly adsorbed and the product (140 mg.) eluted as a bright yellow solution in benzene. Repeated crystallisation from ethanol gave long, thin, yellow-orange prisms, m. p. 211—212° (Found: C, 80·4; H, 4·2; N, 10·1. $C_{19}H_{12}ON_2$ requires C, 80·3; H, 4·3; N, 9·9%). This compound (VI), 7-*oxo*-7H : 9H-8 : 14-*diazabenz*[d,e]*naphthacene*, is unaffected by boiling acetic anhydride or hot 10% aqueous sodium hydroxide. The presence of a C:N bond rather than a •CH•NH• system is indicated by analysis and by stability to boiling acetic anhydride.

N-o-*Aminobenzylnaphthalimide*.—*o*-Aminobenzylamine dihydrochloride (2 g.), naphthalic anhydride (2 g.), anhydrous sodium acetate (1·8 g.), and glacial acetic acid (100 ml.) were refluxed for 4 hr. Treatment with water (50 ml.) and 30% sodium hydroxide solution (80 ml.) (cooling) gave an emulsion. After 60 hr. the mustard-coloured precipitate (1·5 g.) (A) was collected and digested with aqueous sodium carbonate on the water-bath to remove unchanged naphthalic anhydride (260 mg.). No pure reaction product was isolated from the carbonate-insoluble precipitate. The acid filtrate from (A) was basified with sodium hydroxide, and a yellow precipitate of N-o-*aminobenzylnaphthalimide* (1·2 g.) separated. After crystallisation from butanol it gave shiny, pale yellow prisms, m. p. 233·5—235° (Found: C, 75·8; H, 4·8; N, 9·1. $C_{19}H_{14}O_2N_2$ requires C, 75·5; H, 4·7; N, 9·3%); it is easily diazotised, and coupled with β-naphthol to give a bright red azo-dye. In boiling acetic anhydride it formed a *diacetyl* derivative, pale cream, shiny plates (from ethanol), m. p. 190—191·5° (Found: C, 71·7; H, 4·9; N, 7·6. $C_{23}H_{18}O_4N_2$ requires C, 71·5; H, 4·7; N, 7·3%). The naphthalimide showed considerable resistance to cyclisation, being recovered largely unchanged after being heated to 250°. At 300° it was converted into a dark tar which on chromatography in benzene on alumina gave a complex series of bands from which (VI) separated first and was eluted as a bright yellow solution in benzene. Crystallisation from ethanol gave long, thin, yellow-orange prisms (50 mg. from 250 mg. of the naphthalimide), identified as (VI) by m. p. and mixed m. p.

2′-*Formyldiphenyl*-2-*carboxylic Acid* (I).—The conversion of acid hydrazides into aldehydes by use of potassium ferricyanide and ammonia was studied by Kalb and Gross (*Ber.*, 1926, **59**, 727). Wingfield, Harlan, and Hanmer (*J. Amer. Chem. Soc.*, 1952, **74**, 5796) have shown that, for nicotin hydrazide, at least, sodium metaperiodate is a superior oxidising agent and it is now used for the oxidation of diphenic acid monohydrazide. To a cooled solution of periodic acid (as H_5IO_6; 6 g.) in water (230 ml.) and 8% aqueous ammonia (90 ml.), diphenic acid monohydrazide (6·4 g.) in 8% ammonium hydroxide (40 ml.) was added with vigorous stirring, the temperature being kept at 5—10° (6—8 min.). Stirring was continued for 5 min. longer, gas evolution then having practically ceased. After 15 min. at room temperature the crude product was precipitated (usually as a gum) by acidification with sulphuric acid, and was best purified through the acetyl derivative. After dissolution of the product in acetic anhydride (20 ml.) and concentrated sulphuric acid (10 drops) and 48 hours' standing, the acetyl derivative was separated by stirring the mixture with water (100 ml.), saturated sodium hydrogen carbonate solution (55 ml.), and ethanol (16 ml.) for 3 hr. The product (usually obtained as a gum) was washed well with water, and stirred with ethanol (9 ml.), filtered off, and washed with ethanol (4 ml.) to remove sticky by-products. The white product was crystallised from aqueous ethanol, giving 2·2—2·5 g. of prisms, m. p. 137—138° (lit., 125°) (Found: C, 71·8; H, 4·7. Calc. for $C_{16}H_{12}O_4$: C, 71·6; H, 4·5%). The acetyl derivative (6·7 g.) was hydrolysed by refluxing acetic acid (50 ml.) and 6N-sulphuric acid (50 ml.) for 90 min. After cooling and seeding, the product (5·1 g.) was precipitated with water (120 ml.). Crystallisation from aqueous acetic acid gave small, stout, rectangular prisms, m. p. 135—136° (lit., 132°) (Found: C, 74·2; H, 4·5. Calc. for $C_{14}H_{10}O_3$: C, 74·3; H, 4·5%). Simple derivatives of the carbonyl group of (I) do not appear to have been described. The *phenylhydrazone* separated when (I) (56 mg.), phenylhydrazine (3 drops), and 40% acetic acid (2 ml.) were warmed for 10 min. (water-bath). The product (72 mg.) gave, on crystallisation from aqueous ethanol, cream-coloured prisms, m. p. 194—195° (decomp.) (Found: C, 76·2; H, 5·1; N, 9·0. $C_{20}H_{16}O_2N_2$ requires C, 75·9; H, 5·1; N, 8·9%). The *oxime* was formed by refluxing (I) (113 mg.), hydroxylamine hydrochloride (106 mg.), ethanol (10 ml.), and pyridine (2 ml.) for 4 hr., then evaporating the ethanol and adding crushed ice. The product (112 mg.) was precipitated (first as a gum which soon solidified) by just acidifying the solution to Congo-red with dilute hydrochloric acid. Crystallisation from aqueous ethanol gave colourless platelets, m. p. 173·5—174·5° (Found: C, 70·1; H, 4·7; N, 6·1. $C_{14}H_{11}O_3N$ requires C, 69·7; H, 4·6; N, 5·8%). This product dissolves in aqueous sodium hydrogen carbonate solution with effervescence. Under similar conditions *o*-phthalaldehydic acid is converted into hydroxyiminophthalimide (Hatt and Stephenson, *J.*, 1952, 205). (I) readily gives a positive test with Brady's reagent, and a positive reaction with benzenesulphohydroxamic acid (cf. Feigl, " Qualitative Analysis by Spot Tests," 3rd English edn., transl. by R. Oesper; Elsevier Publ. Co., 1947, p. 346). It does not reduce Fehling's solution.

2 : 2'-Diaminodiphenyl is conveniently prepared from the readily available diphenic acid by a Schmidt reaction (cf. Stephenson, *J.*, 1949, 2620). Sodium azide (11·7 g.) was added portionwise to diphenic acid (9·7 g.) in sulphuric acid (*d* 1·84; 75 ml.) so that the temperature was kept at 30—40° with intermittent cooling (15 min.), and the mixture was then heated at 30—40° (water-bath) for 70 min. It was poured on crushed ice (700 ml.), phenanthridone (1 g.) removed by filtration, and the diamine obtained by basification of the filtrate with sodium hydroxide (120 g.) in water (380 ml.). The crude product was taken up in benzene and chromatographed on a short column of alumina, the diamine being easily eluted with benzene. Crystallisation from aqueous alcohol gave white crystals (4·9 g.), m. p. 81—82°.

When in the above preparation the volume of sulphuric acid was reduced to 20 ml., and 40 ml. of pure chloroform were added, the yield of purified diamine was 1·1 g., and 6·1 g. of phenanthridone was recovered.

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