# 460. *Chalcones and Related Compounds. Part V.* Addition of Nitro-compounds to Chalcones.*

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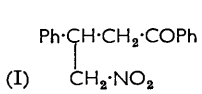
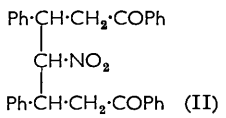
Addition of nitromethane and nitroethane to chalcones is best catalysed by sodium methoxide; diethylamine is less effective. Diethylamine is the preferred catalyst for addition of nitroacetic ester to chalcone. In some cases two isomeric adducts were formed and separated; these adducts of diaryl-pyrrolines and -pyrrolidines have been reduced and the structures of the products studied. Reduction of the adducts to yield other products was less effective.

As a result of extensive studies Kohler *et al.*[1] have recommended sodium methoxide as condensing agent for the addition of nitromethane and nitroethane to chalcones and the use of excess nitroalkane to avoid side-reaction. The primary addition product of chalcone and nitromethane is 4-nitro-1 : 3-diphenylbutan-1-one (I), further reaction yielding the bis-adduct (II). Kloetzel[2] advised the use of diethylamine as catalyst and a 10 : 1 nitromethane : chalcone ratio to avoid formation of the product (II). Rogers[3] has also added nitromethane to substituted chalcones. Sodium methoxide has been found by us to be the most effective catalyst for a number of new additions of nitromethane to chalcones and only in the case of chalcone was there any tendency for further reaction to occur. With



(I)



(II)

diethylamine as catalyst reaction was far less complete but again no tendency to form bis-adducts was observed. Previous workers[1,3] have found difficulty in obtaining these adducts crystalline; in our hands extraction of the oils with benzene and removal of the benzene by distillation has given solid adducts, probably by completely drying them. Fishman and Zuffanti[4] claimed the use of calcium hydride for such additions but this reagent gave incomplete addition of nitromethane to chalcone. Kloetzel[2a] and Kohler *et al.*,[1] on adding nitroethane to chalcone, isolated two geometrically isomeric, racemic adducts. In our work nitroethane was added to five substituted chalcones, with sodium methoxide as catalyst, and in three cases pairs of solid isomers were separated. Diethylamine or ammonia as catalyst gave incomplete reaction.

Although Dornow and Frese[5] added nitroacetic ester to benzylideneacetone in presence of diethylamine no reference to such addition to chalcone has been found. We found that sodium ethoxide or hydroxide failed to effect the addition to chalcone but use of diethylamine was effective. A crude adduct was obtained from 4 : 4′-dimethoxychalcone but in other cases no success was achieved. Alkaline hydrolysis of the adduct of nitroacetic ester and chalcone gave the ketone (I), decarboxylation occurring.

Reduction of the nitro-ketone adducts and their conversion into 2 : 4-diaryl-pyrrolines and -pyrrolidines has also been studied. Kohler and Drake[1] obtained a mixture on hydrogenation of the adduct (I), and Sonn[6] obtained pyrrolines by use of iron and acetic or

* Part IV, *J.*, 1958, 1230.

[1] Kohler, *J. Amer. Chem. Soc.*, 1916, **38**, 889; Kohler and Drake, *ibid.*, 1923, **45**, 2144; Kohler and Williams, *ibid.*, 1919, **41**, 1644; Kohler and Rao, *ibid.*, 1919, **41**, 1697; Kohler and Smith, *ibid.*, 1922, **44**, 624; Kohler, *ibid.*, 1924, **46**, 503.

[2] (*a*) Kloetzel, *J. Amer. Chem. Soc.*, 1947, **69**, 2271; (*b*) Kloetzel, Pinkus, and Washburn, *ibid.*, 1957, **79**, 4222.

[3] Rogers, *J.*, 1943, 590.

[4] Fishman and Zuffanti, *J. Amer. Chem. Soc.*, 1951, **73**, 4466.

[5] Dornow and Frese, *Annalen*, 1952, **578**, 122.

[6] Sonn, *Ber.*, 1935, **68**, 148.

hydrochloric acid. Kloetzel [2a] obtained pyrrolines by hydrogenation over Raney nickel at 25° but later, with Pinkus and Washburn,[2b] converted the adduct (I) into 2 : 4-diphenylpyrrolidine with freshly prepared Raney nickel. We reduced the adducts with zinc and acetic acid at 40—60° to the pyrrolines, but excess of zinc and careful temperature control were necessary to obtain good yields. Although Putckhin [7] claimed hydrogenation of pyrroles to pyrrolidines in presence of palladium oxide, it has been found that hydrogenation of our adduct (I) in ethanol with a palladium–charcoal catalyst gave 2 : 4-diphenylpyrroline in good yield, and this method offers advantages in ease of reaction, lack of necessity for careful control of temperature, ease of isolation, and purity of product; excess of zinc was maintained throughout in the chemical reduction and, since all the pyrrolines were difficult to crystallise, purification *via* the picrate was employed.

Reduction of the two isomeric 1 : 3-diaryl-4-nitropentan-1-ones by chemical or catalytic methods gave two isomeric pyrrolines, but there is no evidence of their configurations. Hydrogenation of ethyl 3 : 5-diphenyl-2-nitro-5-oxopentanoate in ethanol with palladium–charcoal also gave the pyrroline ester.

Reduction of the 2 : 4-diarylpyrrolines to the pyrrolidines was effected in ethanol in presence of freshly prepared Raney nickel W.7, hydrogenation being stopped when the requisite hydrogen uptake had occurred. Further hydrogenation occurred but at about one fifth of the initial rate. Hydrogenation of the isomeric pyrrolines gave isomeric pyrrolidines; 2-ethoxy-3 : 5-diphenylpyrrolidine was obtained by hydrogenation of the pyrroline ester.

Some further reductions were carried out on the nitro-ketone adducts. Reduction of 4-nitro-1 : 3-diphenylbutan-1-one to the alcohol by aluminium *iso*propoxide or, better, sodium borohydride, gave a product, presumably a mixture of two isomers, from which one was obtained solid. Hydrogenation of the solid isomer gave a solid 4-amino-1 : 3-diphenylbutan-1-ol. Reduction of the nitro-ketone by potassium borohydride and hydrogenation of the crude product gave the same solid amino-alcohol and an oily isomer. Zinc and acetic acid yielded one isomer of 4-acetamido-1 : 3-diphenylbutan-1-ol, identical with the acetylation product of the above solid amine. Sodium borohydride reduced ethyl 2-nitro-5-oxo-3 : 5-diphenylpentanoate in aqueous ethanol to 4-nitro-1 : 3-diphenylbutan-1-ol, decarboxylation having occurred after hydrolysis during the reduction, and the product was purer than that obtained by borohydride reduction of the nitro-ketone, the ester group having perhaps made reduction more stereospecific. Reduction of the ester by aluminium *iso*propoxide and of other nitro-ketones by borohydride gave oils, or in some cases unchanged starting materials.

Some study has been made of the structures of the pyrrolines and pyrrolidines prepared in this work. Reduction of a 2-substituted pyrrole can give five possible pyrrolines. Although many pyrrolines have been reported their structures have often not been uncertain. $\Delta^3$-Pyrrolines are produced on the reduction of pyrroles with zinc and acid [8] unless aromatic substituents are present,[9] the structures having been established by ozonolysis,[10] reaction with bromine or permanganate, formation of an *N*-benzoyl derivative, an infrared absorption band at 3·02 μ (assigned to the NH group), and a study of quaternary pyrrolidinium salts.[11] For $\Delta^1$- and $\Delta^2$-pyrrolines the evidence is less reliable and some earlier references to $\Delta^1$-compounds probably refer to $\Delta^2$-isomers and *vice versa*; evidence of structure has been obtained from studies of reactivity towards ozone, bromine, permanganate, benzoyl chloride, and methylmagnesium iodide [11] and by infrared spectra. Acid

[7] Putckhin, *J. Russ. Phys. Chem. Soc.*, 1930, **62**, 2216.
[8] Anderlini, *Ber.*, 1889, **22**, 2512; Knorr and Rabe, *Ber.*, 1901, **34**, 3497; Ciamician, *ibid.*, p. 3952; Langheld, *Ber.*, 1909, **42**, 2373.
[9] Gitsels and Wibaut, *Rec. Trav. chim.*, 1941, **60**, 50; Dhent and Wibaut, *ibid.*, 1944, **63**, 81; Sonn, *Ber.*, 1935, **68**, 148; 1939, **72**, 2150.
[10] Treibe and Dinelli, *Annalen*, 1935, **517**, 170; Blaise, *Compt. rend.*, 1914, **158**, 1686; Blaise and Cornillot, *ibid.*, 1924, **178**, 1617.
[11] Lukes and Preucil, *Coll. Czech. Chem. Comm.*, 1938, **10**, 384.

reduction of arylpyrroles and cyclisation methods [12] give $\Delta^1$- or $\Delta^2$-pyrrolines. *cis*- and *trans*-Isomers of substituted pyrrolines and pyrrolidines [13] have been isolated.[11,12] For 2 : 4-diphenylpyrroline Kloetzel, Pinkus, and Washburn [2b] found no infrared band in the NH region although the general level of absorption was high in the region 2·5—3·5 μ; they pointed out the difficulties of infrared spectral studies in the NH region for pyrrolines and pyrrolidines and that the intensity of absorption depends upon the nature of substituents in the vicinity of the nitrogen atom and upon the medium. They stated however that their results are in harmony with a $\Delta^1$-structure The infrared spectra of our 2 : 4-diarylpyrrolines suggested the possibility of $\Delta^2$-structures, since a band at 3100—3400 cm.$^{-1}$ (Nujol mull) indicated a possible NH group.[14] Two aromatic bands at 1607 and 1500 cm.$^{-1}$ were also present in the 2 : 4-diphenylpyrroline spectrum. Although reduction of the 2 : 4-diarylpyrrolines could give *cis*- and *trans*-pyrrolidines, only one form was obtained in good yield The spectra of the isomers of 5-methyl-2 : 4-diphenylpyrroline contained very weak bands at about 3300 cm.$^{-1}$, suggesting possible tautomerism between $\Delta^1$- and $\Delta^2$-structures; absence of a band at 3300 cm.$^{-1}$ in the case of 5-ethoxycarbonyl-2 : 4-diphenylpyrroline suggested a $\Delta^1$-structure, an ester-carbonyl band at 1738 and aromatic bands at 1615 and 1495 cm.$^{-1}$ also being present in this spectrum. Aromatic bands at 1607 and 1497 cm.$^{-1}$ were also present in the spectra of the isomeric 5-methyl-2 : 4-diphenylpyrrolines, and the former may have masked any band due to a C=N group at 1590 cm.$^{-1}$.

## Experimental

*Addition of Nitromethane to Chalcones.*—(*a*) *By Kohler's method.*[1] Addition of sodium (15 g.) in methanol (175 ml.) to a stirred solution of chalcone (104 g.) and nitromethane (37·5 g.) in methanol (175 ml.) at 40° gave, on cooling and acidification, a product which crystallised from ethanol in colourless needles (114 g., 85%) of 1 : 3-diphenyl-4-nitrobutan-1-one, m. p. 101—102° (Kohler gives m. p. 103°). (*b*) *Diethylamine method.* Chalcone (20·8 g., 0·1 mole), nitromethane (60 g., 1·0 mole), and diethylamine (8 g., 0·1 mole) in methanol (70 ml.) were set aside at room temperature for 7 days. Acidification with dilute acetic acid and addition of water (50 ml.) gave a viscous oil which was extracted with benzene (150 ml.). Water-washing and evaporation of the benzene layer *in vacuo*, and recrystallisation from ethanol gave 1 : 3-diphenyl-4-nitrobutan-1-one (19·4 g., 72%).

3-*p*-Methoxyphenyl-4-nitro-1-phenylbutan-1-one, prepared by method (*a*), but at 50° for 30 min., in 61% yield, had m. p. 63—65° (decomp.) (Rogers [3] gives m. p. 66°, with previous sintering and does not state a yield).

1 : 3-*Di*-p-*methoxyphenyl*-4-*nitrobutan*-1-*one* was obtained by method (*a*) as needles, m. p. 75° (70%) (Found: C, 65·1; H, 5·6; N, 4·1. $C_{18}H_{19}O_5N$ requires C, 65·6; H, 5·8; N, 4·2%) (Rogers [3] describes this as an oil).

3-p-*Methoxyphenyl*-4-*nitro*-1-p-*tolylbutan*-1-*one* was obtained by method (*a*) as an oil which on benzene-extraction, removal of the benzene *in vacuo*, and keeping the product under light petroleum (b. p. 60—80°), formed needles, m. p. 54—56° (64·1%) (Found: C, 69·3; H, 6·0; N, 4·7. $C_{18}H_{19}O_4N$ requires C, 69·0; H, 6·1; N, 4·5%).

1-m-*Hydroxyphenyl*-4-*nitro*-3-*phenylbutan*-1-*one*, obtained by method (*a*) at 50° for 1 hr., formed needles (from benzene), m. p. 98—99° (70·4%) (Found: C, 67·8; H, 5·2; N, 5·2. $C_{16}H_{15}O_4N$ requires C, 67·4; H, 5·3; N, 4·9%).

3-m-*Hydroxyphenyl*-1-p-*methoxyphenyl*-4-*nitrobutan*-1-*one*, obtained by method (*a*) but at the b. p. for 30 min., formed needles [from benzene–light petroleum (b. p. 60—80°)], m. p. 107—108° (95·5%) (Found: C, 70·1; H, 5·2; N, 4·1. $C_{17}H_{17}O_5N$ requires C, 64·8; H, 5·4; N, 4·4%).

3-o-*Chlorophenyl*-1-p-*tolyl*-4-*nitrobutan*-1-*one*, obtained by method (*a*) at 40° (addition) and then 50° (30 min.), formed needles [from light petroleum (b. p. 60—80°)], m. p. 80° (59%) (Found: C, 64·0; H, 5·1; N, 4·8. $C_{17}H_{16}O_3NCl$ requires C, 64·3; H, 5·0; N, 4·4%).

[12] Roberts and Ross, *J.*, 1952, 4288.
[13] Evans, *J. Amer. Chem. Soc.*, 1951, **73**, 5230.
[14] Bellamy, " Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 213; Barnes *et al.*, " Infra-red Spectroscopy," Rheinhold Publ. Corp., New York, p. 19.

*Additions of Nitroethane to Chalcones.*—Method (*a*) above was modified: To a stirred solution of chalcone (18·6 g., 0·09 mole) and nitroethane (8·2 g., 0·11 mole) in methanol (40 ml.) at 50° was added rapidly a solution from sodium (2·8 g.) in methanol (30 ml.). After 1 hr. at 50°, the mixture was cooled and acidified with dilute acetic acid and after 12 hr. the crude product was taken up in benzene (150 ml.), and the benzene extract dried ($Na_2SO_4$) and evaporated to give a product, m. p. 47—60° (23·9 g.). This product was dissolved in boiling ether (100 ml.) and crystals deposited after 1 hour's cooling were filtered off (10 g.; m. p. 80°). Concentration of the filtrate to 65 ml. and cooling gave a second crop, m. p. 75° (2 g.), and evaporation of the filtrate gave a product m. p. 55° (9 g.). The two high-melting fractions were combined and twice recrystallised from ether, to give needles of 4-nitro-1 : 3-diphenylpentan-1-one A, m. p. 100° (5·2 g., 20%); recrystallisation from ether of the low-melting form gave the other isomer B as needles, m. p. 67° (3·5 g., 14%) (Kohler [1] gives m. p.s 100° and 72°).

4-*Nitro*-1-*phenyl*-3-p-*tolylpentan*-1-*one* was prepared as above, as needles A (from methanol), m. p. 115—116° (48%) (Found: C, 72·5; H, 6·2; N, 4·4. $C_{18}H_{19}O_3N$ requires C, 72·7; H, 6·4; N, 4·7%), and crystals B (from methanol), m. p. 93—94° (15%) (Found: C, 72·4; H, 6·5; N, 4·8%).

1 : 3-*Di*-p-*tolyl*-4-*nitropentan*-1-*one* was obtained in the one form only, plates, m. p. 75° (60%) (Found: C, 73·6; H, 7·0; N, 4·6. $C_{19}H_{21}O_3N$ requires C, 73·3; H, 6·8; N, 4·5%).

3-p-*Methoxyphenyl*-4-*nitro*-1-*phenylpentan*-1-*one* was obtained as needles A, m. p. 111—112° (32%) (Found: C, 68·7; H, 6·2; N, 4·4. $C_{18}H_{19}O_4N$ requires C, 69·0; H, 6·1; N, 4·5%), and as needles B (from ether), m. p. 84—85° (25%) (Found: C, 69·1; H, 6·2; N, 4·5%).

1 : 3-*Di*-p-*methoxyphenyl*-4-*nitropentan*-1-*one* was obtained in one form only, needles (from benzene), m. p. 95° (60%) (Found: C, 66·0; H, 6·0; N, 4·0. $C_{19}H_{21}O_5N$ requires C, 66·5; H, 6·1; N, 4·1%).

*Addition of Ethyl Nitroacetate to Chalcones.*—Ethyl nitroacetate was prepared by the following modified Bouveault and Wahl's method: Ethyl acetoacetate (5 g.), mixed with acetic anhydride (25 g.), was stirred during addition of a mixture of nitric acid (27 g.; *d* 1·52) and acetic anhydride (27 g.), the temperature being kept at 32—34°. Then the mixture was poured into water and the oil extracted with benzene (2 × 50 ml.). The benzene extract was washed with water and evaporated under reduced pressure and the oily residue distilled, to give ethyl nitroacetate (1·5 g., 27%), b. p. 93—96°/9 mm., $n_D^{20}$ 1·1992. The extraction procedure used by Bouveault *et al.*[15] was unnecessary and gave no higher yield than distillation of the product. Other methods [16] were less convenient in spite of giving higher yields.

*Ethyl* 2-*Nitro*-5-*oxo*-3 : 5-*diphenylpentanoate.*—Chalcone (8·9 g., 0·045 mole) in ethanol (50 ml.) was treated with ethyl nitroacetate (6·3 g., 0·047 mole) and diethylamine (0·3 ml.) under reflux for 15 min., cooled, acidified with 50% acetic acid (5 ml.), and diluted with water (20 ml.); the ester which separated solidified and recrystallised from ethanol as needles, m. p. 128—129° (11 g., 94%) (Found: C, 67·2; H, 5·8; N, 4·1. $C_{19}H_{19}O_5N$ requires C, 66·9; H, 5·6; N, 4·1%). Use of sodium methoxide as catalyst failed to achieve reaction, the sodium salt of ethyl nitroacetate being precipitated.

*Hydrolysis.* The nitro-ester (1 g.,) was refluxed with ethanol (5 ml.) and 2N-sodium hydroxide (3 ml.) for 1 hr., then filtered from precipitated sodium carbonate (0·25 g.) and acidified with 2N-hydrochloric acid to give an oil, which crystallised from ethanol to give colourless needles of 4-nitro-1 : 3-diphenylbutan-1-one, m. p. and mixed m. p. 98° (0·6 g., 74%) (Found: C, 71·5; H, 5·8. $C_{16}H_{15}O_3N$ requires C, 71·4; H, 5·6%).

Addition of nitroacetic ester (5·3 g., 0·04 mole) to 4 : 4′-dimethoxychalcone (10 g., 0·037 mole) in ethanol (50 ml.) and diethylamine (3 ml.) under reflux for 2 hr. gave an oil (4·9 g.). This (2 g.) in ethanol (5 ml.) with 2 : 4-dinitrophenylhydrazine (1·5 g.) in sulphuric acid (2 ml.; *d* 1·84) and ethanol (20 ml.) gave red needles of *ethyl* 3 : 5-*di*-(p-*methoxyphenyl*)-2-*nitro*-5-*oxopentanoate* 2 : 4-*dinitrophenylhydrazone*, m. p. 97—99° (0·5 g.) (Found: C, 54·4; H, 4·3; N, 12·6. $C_{27}H_{27}O_{10}N_5$ requires C, 55·7; H, 4·7; N, 12·0%).

4-*Nitro*-1 : 3-*diphenylbutan*-1-*ol.*—(*a*) Reduction of 4-nitro-1 : 3-diphenylbutan-1-one (8 g., 0·03 mole) by aluminium *iso*propoxide (8·1 g., 0·04 mol.) and toluene (50 ml.) under a Fenske column (3″) gave acetone (3 ml. Calc., 1·7 g.) and a product which, on acidification with 2N-sulphuric acid (60 ml.), extraction with ethyl acetate, and evaporation of the extract gave

[15] Bouveault and Wahl, *Bull. Soc. chim. France*, 1904, **31**, 847.

[16] Steinkopf, *Annalen*, 1923, **434**, 21; Fever, Weisblat, and Lyttle, *J. Amer. Chem. Soc.*, 1949, **71**, 3079.

an oil; this partly solidified after two weeks and, recrystallised from light petroleum (b. p. 40—60°), gave 4-*nitro*-1 : 3-*diphenylbutan*-1-*ol* (2·2 g.) as needles, m. p. 77—79° (Found: C, 70·5; H, 6·1; N, 5·1. $C_{16}H_{17}O_3N$ requires C, 70·8; H, 6·3; N, 5·2%).

(*b*) 4-Nitro-1 : 3-diphenylbutan-1-one (5 g., 0·019 mole) in ethanol (40 ml.) was slowly added to a solution of potassium borohydride [1·5 g. in water (2 ml.) and ethanol (50 ml.)] at room temperature with stirring and set aside for 12 hr. Removal of most of the ethanol *in vacuo* and addition of 2N-hydrochloric acid (20 ml.) gave a syrup, which was extracted with benzene. Removal of the benzene gave an oil which partially solidified after 2 weeks and on recrystallisation from light petroleum (b. p. 40—60°) gave 4-nitro-1 : 3-diphenylbutan-1-ol, needles, m. p. 77—79° (2 g., 40%) (Found: C, 70·6; H, 6·4; N, 5·2%).

4-*Amino*-1 : 3-*diphenylbutan*-1-*ol*.—(*a*) The nitro-alcohol (4 g.) in ethanol (30 ml.) was hydrogenated in presence of 5% palladium–charcoal (0·5 g.) until the requisite hydrogen uptake had taken place. Filtration, removal of ethanol *in vacuo*, and crystallisation from benzene gave 4-*amino*-1 : 3-*diphenylbutan*-1-*ol* as needles, m. p. 121—122° (2·9 g., 85%) (Found: C, 79·8; H, 7·9; N, 5·6. $C_{16}H_{19}ON$ requires C, 79·6; H, 7·9; N, 5·8%).

(*b*) The nitro-ketone (10 g., 0·037 mole) in ethanol (200 ml.) was treated with potassium borohydride solution (25 g., 0·043 mol.) in 3 : 17 aqueous ethanol (55 ml.) at 30° for 1½ hr., then evaporated *in vacuo* to a viscous syrup. Addition of 2N-hydrochloric acid (30 ml.) and benzene-extraction, followed by removal of solvent, gave an oil (8 g.). Hydrogenation of this oil in ethanol with a 70% palladium–charcoal catalyst (1·0 g.) led to absorption of 2·85 mols. Filtration and evaporation gave an oil from which 4-amino-1 : 3-diphenylbutan-1-ol was obtained as needles, m. p. 120—121° (3 g., 33%). Although no crystalline isomer could be isolated from the mother-liquors, the oil (4·2 g.) obtained after removal of solvent was treated in ether (20 ml.) with picric acid (4·2 g.) in ether (100 ml.), to give a yellow precipitate (8 g.; m. p. 165—170°) which, recrystallised from ethanol, gave a *picrate* as needles, m. p. 169—170° (6·0 g.) (Found: C, 56·3; H, 4·8; N, 11·7. $C_{22}H_{22}O_8N_4$ requires C, 56·2; H, 4·7; N, 11·9%). Treatment of this picrate (2 g.) with 2N-alkali (20 ml.), extraction with benzene (20 ml.), and removal of the benzene *in vacuo* gave the low-melting *isomer* as an oil (Found: C, 79·3; H, 7·8; N, 5·5. $C_{16}H_{19}ON$ requires C, 79·6; H, 7·9; N, 5·8%).

4-*Acetamido*-1 : 3-*diphenylbutan*-1-*ol*.—4-Nitro-1 : 3-diphenylbutan-1-one (9·3 g., 0·034 mole) in ethanol (100 ml.) was added slowly with stirring to potassium borohydride (4·7 g., 0·087 mole) in 95% ethanol (250 ml.) and kept at room temperature for 12 hr., then most of the ethanol was removed *in vacuo*. Acidification with 2N-hydrochloric acid gave a viscous oil which was extracted with benzene. From the benzene extract an oil (9 g.) was isolated which was dissolved in glacial acetic acid (30 ml.) at 50°, stirred, and reduced at 50° with zinc dust (15 g.). The mixture was kept at 50° for a further 15 min., cooled, and filtered, the residue being washed with a little acetic acid. The filtrates were basified with 5N-sodium hydroxide and extracted with benzene (2 × 100 ml.). After washing and removal of the benzene *in vacuo* the resulting syrup (7 g.) was dissolved in benzene (25 ml.) and set aside; crystals (4 g.) were obtained. Recrystallisation from ethanol gave the *acetamide* as needles, m. p. 185° (3 g., 35%) (Found: C, 76·4; H, 7·6; N, 4·6. $C_{18}H_{21}O_2N$ requires C, 76·3; H, 7·5; N, 4·9%). The isomeric reduction product could not be isolated. Acetylation of the form, m. p. 121—122°, of the amine with boiling acetic acid for 1 hr. gave a product, which on purification *via* solution in benzene and recrystallisation from ethanol, furnished needles of the acetamide, m. p. and mixed m. p. 185°.

*Reduction of Ethyl* 2-*Nitro*-5-*oxo*-3 : 5-*diphenylpentanoate*.—A solution of the ester (5 g.) in ethanol (100 ml.) was added rapidly to one of sodium borohydride (2·5 g.) in 85% ethanol (150 ml.) and kept for 12 hr. at room temperature. Evaporation *in vacuo*, acidification with 2N-acid (20 ml.), and benzene-extraction, yielded a syrup on removal of the benzene. This crystallised slowly on treatment with ethanol (10 ml.) and recrystallisation from light petroleum (b. p. 40—60°) gave needles of 4-nitro-1 : 3-diphenylbutan-1-ol (3 g., 75%), m. p. and mixed m. p. 79—80° (Found: C, 70·6; H, 6·4; N, 5·0. Calc. for $C_{16}H_{17}O_3N$: C, 70·8; H, 6·3; N, 5·2%). Attempts to reduce the ester with sodium borohydride at pH *ca.* 5·0, to avoid hydrolysis of the ester, or with aluminium *iso*propoxide in toluene, gave only the starting ester.

*Preparation of* 2 : 4-*Diarylpyrrolines*.—(a) *By catalytic hydrogenation*. 4-Nitro-1 : 3-diphenylbutan-1-one (21·5 g., 0·056 mole) was hydrogenated in methanol (70 ml.) in presence of 10% palladium–charcoal (0·3 g.) in 30 min.; absorption then ceased, 0·17 mol. of hydrogen having been absorbed. Filtration and evaporation *in vacuo* to dryness gave a product (11·5 g.)

which was fractionated under reduced pressure to give an oil (b. p. 138—140°/0·5 mm.) which crystallised from light petroleum in needles (9·2 g., 75%), m. p. 49—50° (Rupe and Gisiger [17] give m. p. 50°).

(b) *With zinc dust and acetic acid.* 4-Nitro-1 : 3-diphenylbutan-1-one (15 g.) in glacial acetic acid (150 ml.) was reduced at 50—60° by the addition of zinc dust (50 g.) in 30 min. After a further 15 min. at 60°, the product was cooled and filtered, the residue being washed with acetic acid (2 × 20 ml.), poured into water (500 ml.) and basified with 5N-sodium hydroxide. The separated oil was extracted with benzene and recovered (10·2 g.). One half was distilled and recrystallised from light petroleum (b. p. 40—60°), to yield needles of 2 : 4-diphenylpyrroline, m. p. 48—50° (3·9 g., 58%). To the other portion, dissolved in ether (20 ml.), picric acid (4·2 g.) in ether (30 ml.) was added. The precipitate was filtered off and recrystallised from benzene to give 2 : 4-diphenylpyrroline picrate as yellow needles, m. p. 155—156° (Rupe and Gisiger [17] give m. p. 156°) (6·0 g.). The picrate was shaken with benzene (20 ml.), and 2N-sodium hydroxide (20 ml.) added; the organic layer was separated, washed with water, dried ($Na_2SO_4$), and evaporated *in vacuo*. Recrystallisation from light petroleum (b. p. 40—60°) gave needles of 2 : 4-diphenylpyrroline (2 g., 28%), m. p. 48—50° (total yield, 82%).

(c) *With zinc dust, acetic acid, and acetic anhydride.* 4-Nitro-1 : 3-diphenylbutan-1-one (10 g.) in acetic acid (50 ml.) and acetic anhydride (25 ml.) was reduced at 30—40° by zinc dust (40 g. in small portions) in 30 min. After a further hour at this temperature, the mixture was cooled and filtered, and the residue washed with acetic acid (2 × 10 ml.). The filtrate was poured into water (200 ml.) and made alkaline with 5N-sodium hydroxide. The separated oil (9·2 g.) was refluxed for 1½ hr. with 5N-hydrochloric acid (37 ml.) and ethanol (50 ml.). Evaporation gave an oil which yielded 2 : 4-diphenylpyrroline picrate (1·7 g.), m. p. 154—156°.

The following pyrrolines were obtained by method (b):

4-*p*-Methoxyphenyl-2-phenylpyrroline, needles [from light petroleum (b. p. 40—60°)], m. p. 26° (62%) (Rogers [3] gives m. p. 27°).

2 : 4-*Di*-p-*methoxyphenylpyrroline*, needles, m. p. 102° (70%) (Found: C, 76·4; H, 6·7; N, 4·7. $C_{18}H_{19}O_2N$ requires C, 76·8; H, 6·8; N, 5·0%); *picrate*, needles (from ethanol), m. p. 158—159° (Found: C, 56·2; H, 4·2; N, 10·7. $C_{24}H_{22}O_9N_4$ requires C, 56·3; H, 4·3; N, 11·0%).

2-m-*Hydroxyphenyl*-4-*phenylpyrroline*, plates, m. p. 118—120° (64%) (Found: C, 80·7; H, 6·8; N, 6·1. $C_{16}H_{15}ON$ requires C, 81·0; H, 6·3; N, 5·9%).

4-*m*-Hydroxyphenyl-2-*p*-methoxyphenylpyrroline (75%), b. p. 225—228°/0·6 mm.; *picrate*, needles (from ethanol), m. p. 145—146° (Found: C, 55·5; H, 4·3; N, 11·2. $C_{23}H_{20}O_9N_4$ requires C, 55·6; H, 4·0; N, 11·3%).

4-o-*Chlorophenyl*-2-p-*tolylpyrroline*, needles [from benzene–light petroleum (b. p. 60—80°)], m. p. 61—62° (76%) (Found: C, 75·4; H, 6·1; N, 5·5. $C_{17}H_{16}NCl$ requires C, 75·7; H, 5·9; N, 5·2%).

4-p-*Methoxyphenyl*-2-p-*tolylpyrroline*, b. p. 230—234°/0·5 mm. (85%) (Found: C, 81·2; H, 7·1; N, 5·6. $C_{18}H_{19}ON$ requires C, 81·5; H, 7·2; N, 5·3%); *picrate*, needles (from ethanol), m. p. 188—189° (Found: C, 58·2; H, 4·7; N, 11·1. $C_{24}H_{22}O_8N_4$ requires C, 58·3; H, 4·5; N, 11·3%).

2 : 4-*Diphenylpyrrolidine*.—2 : 4-Diphenylpyrroline (5 g.) in ethanol (20 ml.) was hydrogenated in presence of Raney nickel W.7 (1 g.). After filtration and removal of ethanol *in vacuo*, the oily residue (5 g.) was converted into its picrate (m. p. 132—138°), and the base regenerated. The hydrochloride of the base gave needles (from methanol), m. p. 170—171° (Kohler and Drake [1] give m. p. 171—172°). Similarly hydrogenation of 2 : 4-di-*p*-methoxyphenylpyrroline gave the pyrrolidine as an oil, which yielded a *picrate* as yellow needles (from ethanol), m. p. 181—182° (Found: C, 56·2; H, 4·9; N, 10·6. $C_{24}H_{24}O_9N_4$ requires C, 56·3; H, 4·7; N, 10·9%).

*Preparation of* 3 : 5-*Diaryl*-2-*methylpyrrolines*.—Reduction of the isomeric nitroethane–chalcone adducts was effected by method (a) or (b) above, see Table.

*Preparation of* 3 : 5-*Diaryl*-2-*methylpyrrolidines*.—3-*p*-Methoxyphenyl-2-methyl-5-phenylpyrroline A (5 g.) in ethanol (30 ml.) was hydrogenated in presence of Raney nickel W.7. (1 g.), 1 mol. of hydrogen being taken up. The product was filtered and evaporated *in vacuo*. The resulting oil (4·3 g., 86%) was converted into a *picrate*, which crystallised from benzene in needles, m. p. 205—206° (Found: C, 57·8; H, 4·5; N, 11·0. $C_{24}H_{24}O_8N_4$ requires C, 58·1; H, 4·9; N, 11·3%). The *base* was obtained from the picrate as above, as an oil, $n_D^{20}$ 1·5610

[17] Rupe and Gisiger, *Helv. Chim. Acta*, 1925, 8, 338.

(Found: C, 81·2; H, 8·1; N, 4·9. $C_{18}H_{21}ON$ requires C, 80·9; H, 7·9; N, 5·2%). Isomer B gave an isomeric 3-p-*methoxyphenyl*-2-*methyl*-5-*phenylpyrrolidine*, $n_D^{20}$ 1·5480 (Found: C, 81·3; H, 8·2; N, 5·1%), which yielded a *picrate*, needles (from benzene), m. p. 264—265° (Found: C, 58·2; H, 5·1; N, 11·6%).

*3-Aryl-2-methyl-5-phenylpyrrolines.*

| No. | 3-Aryl | Starting ketone | Method | Yield (%) | B. p./mm. | $n_D^{20}$ | Found (%) C | H | N | Formula | Required (%) C | H | N |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Ph | A | b; 70° | 85 | 150—154°/ 0·9 | 1·5110 | 86·5 | 7·2 | 6·1 | $C_{17}H_{17}N$ | 86·8 | 7·3 | 6·0 |
| 2 | ,, | B | ,, | — | — | 1·5100 | 86·2 | 7·4 | 5·8 | ,, | ,, | ,, | ,, |
| 3 | *p*-MeO·$C_6H_4$ | A | b; 50° | 88 | 172—174°/ 0·1 | 1·5000 | 81·2 | 7·1 | 5·1 | $C_{18}H_{19}ON$ | 81·5 | 7·2 | 5·3 |
| 4 | ,, | B | ,, | — | 180—183°/ 1·5 | — | 81·6 | 6·9 | 5·5 | ,, | ,, | ,, | ,, |
| 5 | *p*-Tolyl | A | a | 80 | 190—195°/ 0·8 | — | 86·5 | 7·4 | 5·3 | $C_{18}H_{19}N$ | 86·7 | 7·7 | 5·6 |
| 6 | ,, | B | a | — | 200—205°/1 | — | 86·4 | 7·4 | 5·7 | ,, | ,, | ,, | ,, |

*Picrates*

| No. | Form | M. p. | Found (%) C | H | N | Formula | Required (%) C | H | N |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Plates [a] | 149—150° | 59·1 | 4·6 | 12·0 | $C_{23}H_{20}O_7N_4$ | 59·5 | 4·3 | 12·1 |
| 2 | ,, | 145—146 [b] | 59·2 | 4·9 | 12·2 | ,, | ,, | ,, | ,, |
| 3 | ,, | 168—169 | 58·2 | 4·7 | 11·5 | $C_{24}H_{22}O_8N_4$ | 58·3 | 4·5 | 11·3 |
| 4 | ,, | 171—172 [c] | 57·9 | 4·5 | 11·1 | ,, | ,, | ,, | ,, |
| 5 | Needles | 200—201 | 60·5 | 4·2 | 11·5 | $C_{24}H_{22}O_7N_4$ | 60·2 | 4·6 | 11·7 |
| 6 | Plates | 190—191 | 59·9 | 4·3 | 11·4 | ,, | ,, | ,, | ,, |

[a] From $C_6H_6$. [b] Mixed with no. 1, 120—130°. [c] Mixed with no. 3, 150—155°.

Similarly catalytic hydrogenation of isomer A of 2-methyl-5-phenyl-3-*p*-tolylpyrroline gave a 2-*methyl*-5-*phenyl*-3-p-*tolylpyrrolidine* (91%), $n_D^{20}$ 1·5100 (Found: C, 86·4; H, 7·9; N, 5·8. $C_{18}H_{19}N$ requires C, 86·7; H, 7·7; N, 5·6%), which gave a *picrate*, needles (from benzene), m. p. 145—146° (Found: C, 60·5; H, 4·9; N, 11·8. $C_{24}H_{22}O_7N_4$ requires C, 60·2; H, 4·6; N, 11·7%). The isomeric *base* had $n_D^{20}$ 1·5670 (Found: C, 86·4; H, 7·4; N, 5·3%) and gave a *picrate*, needles (from ethanol), m. p. 118—119° (Found: C, 60·5; H, 4·5; N, 11·9%).

5-*Ethoxycarbonyl*-2 : 4-*diphenylpyrroline* was obtained by hydrogenation of the nitro-ketone ester by method (a) above as a syrup (86% yield) (Found: C, 78·1; H, 6·6; N, 4·7. $C_{19}H_{19}O_2N$ requires C, 77·8; H, 6·5; N, 4·8%) and gave a *picrate*, needles, m. p. 155—156° (Found: C, 57·6; H, 4·1; N, 10·7. $C_{25}H_{22}O_9N_4$ requires C, 57·3; H, 4·2; N, 10·7%).

Hydrogenation of the pyrroline ester in ethanol with Raney nickel W.7 gave the *pyrrolidine*, $n_D^{20}$ 1·5520 (Found: C, 77·7; H, 7·4; N, 4·4. $C_{19}H_{21}O_2N$ requires C, 77·3; H, 7·2; N, 4·7%) [*picrate*, needles, m. p. 128—129° (Found; C, 57·1; H, 4·5; N, 10·8. $C_{25}H_{24}O_9N_4$ requires C, 57·3; H, 4·6; N, 10·7%)].

The ester (1 g.) was refluxed with 2N-hydrochloric acid (6 ml.) for 2 hr. The solution was concentrated under reduced pressure to 2 ml. Aqueous ammonia was added and the product extracted with benzene. Water-washing and removal of the benzene gave the *pyrrolidine-acid* as a gum (0·7 g., 78%) (Found: C, 74·9; H, 5·4; N, 5·5. $C_{17}H_{15}O_2N$ requires C, 77·0; H, 5·6; N, 5·2%), whose *picrate* formed needles (from ethanol), m. p. 184—185° (Found: C, 55·7; H, 3·8; N, 11·4. $C_{23}H_{18}O_9N_4$ requires C, 55·8; H, 3·7; N, 11·3%).

We are grateful to Miss E. M. Tanner, Parke Davis & Co., Hounslow, Middlesex, for determining the infrared spectra and for suggestions on their interpretation.

THE POLYTECHNIC, 309, REGENT ST., LONDON, W.1. [*Received, November 25th,* 1957.]