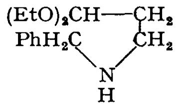
55. *The 2-Phenylpyrrolines: A Redetermination of the Structures of the Supposed 2-Phenyl-Δ^3- and -Δ^4-pyrrolines.*

By F. E. King, J. R. Marshall, and P. Smith.

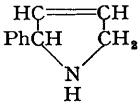
As already briefly reported (King, *J.*, 1949, 1318), the crystalline product resulting from the action of hydrochloric acid on ethyl 3-benzylaminopropionacetal (3-benzylamino-1 : 1-diethoxypropane) is a salt of 2 : 4 : 6-tri-(2-benzylaminoethyl)trioxan, the aldehyde trimer, and not 2-phenyl-Δ^3-pyrroline hydrochloride (Wohl, *Ber.*, 1901, **34**, 1914). On the other hand, cyclisation to a pyrroline does apparently occur with the homologous butyracetal since its acid-hydrolysis product can be reduced to 1-benzylpyrrolidine.

The 2-phenylpyrroline prepared by Gitsels and Wibaut and believed by them to be the Δ^4-pyrroline (*Rec. Trav. chim.*, 1941, **60**, 50), has been shown by oxidation to *N*-α-carboxybenzylglycine to be the Δ^3-isomer. By analogy the dihydronicotyrine of Wibaut and Hackmann (*ibid.*, 1932, **51**, 1157), regarded by Späth, Wibaut, and Kesztler (*Ber.*, 1938, **71**, 100) as a Δ^2-pyrroline, is very probably 2-3′-pyridyl-Δ^3-pyrroline, a conclusion independently reached by Haines and Eisner (*J. Amer. Chem. Soc.*, 1950, **72**, 1719).

Wohl (*Ber.*, 1901, **34**, 1914; 1905, **38**, 4154) has shown that the action of acids on 3-amino-1 : 1-diethoxypropane and 1 : 1-diethoxy-3-ethylaminopropane (ethyl 3-amino- and 3-ethylaminopropionacetal) leads to the formation of salts of the aldehyde polymers, and analogous compounds were similarly obtained by Voet (*Bull. Soc. chim.*, 1929, **45**, 61) from other secondary amino- and from tertiary amino-propionacetals. The pure products possess only weak aldehydic properties, and from a cryoscopic determination of the molecular weight of the 3-ethylamino-base were believed to be three-fold polymers. The 3-benzylamino-acetal (I), however, appeared to be exceptional in giving with cold concentrated hydrochloric acid a salt which Wohl (*loc. cit.*, 1901) described as the hydrochloride of 2-phenyl-Δ^3-pyrroline (II). Neither the free base nor any other derivative was prepared, and although the constitution of the compound has hitherto been accepted without comment (see Gitsels and Wibaut, *Rec. Trav. chim.*, 1941, **60**, 50; Murray and Cloke, *J. Amer. Chem. Soc.*, 1946, **68**, 126), the evidence for this unique synthesis of a Δ^3-pyrroline seemed unconvincing, and the reaction has therefore been re-investigated.



(I.)



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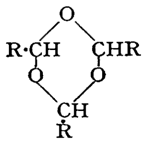


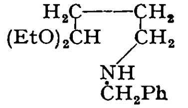
(III.)

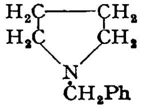
The required acetal (I) was prepared both by Wohl's method, *i.e.*, reduction of the benzylideneamino-acetal, and also from the 3-chloro-acetal by heating it with benzylamine. The identity of the products, which are liquid, was shown by their common crystalline picrolonate. On treatment with the appropriate reagents, the benzylamino-acetal rapidly formed the 2 : 4-dinitrophenylhydrazone hydrochloride and sulphate.

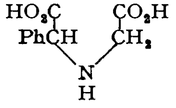
The composition attributed by Wohl to the product obtained from the acetal and hydrochloric acid rests on analyses of nitrogen and chlorine, but from more complete determinations which have now been made it is evident that the empirical formula of the salt is $C_{10}H_{13}ON,HCl$, and not $C_{10}H_{11}N,HCl$ as stated by Wohl. Intensive desiccation does not eliminate the additional elements H_2O, and analyses of the oxalate, sulphate, and picrolonate which were then prepared confirm that the elementary composition of the base is $C_{10}H_{13}ON$. The latter is, of course, the molecular formula of 3-benzylaminopropaldehyde but, although the free amine—a syrupy liquid obtained by shaking an aqueous solution of the hydrochloride with magnesium oxide under ether—resinified on attempted distillation, even under very low pressure, from its lack of reducing properties it was clearly not the simple aldehyde. However, when the amine hydrochloride was heated with the necessary reagent, 3-benzylaminopropaldehyde 2 : 4-dinitrophenylhydrazone hydrochloride was slowly formed, thus demonstrating Wohl's compound to be merely a polymer of the aldehyde. The degree of polymerisation was indicated by a determination of the molecular weight of the base in benzene. The first values obtained corresponded to rather more than two units per molecule, but after the compound had been kept in a vacuum over phosphoric oxide for several days a steady figure indicative of the trimer, 2 : 4 : 6-tri-(2-benzylaminoethyl)trioxan (III; R = $Ph\cdot CH_2\cdot NH\cdot CH_2\cdot CH_2\cdot$), was attained. The rising value of the molecular weight is thought to be caused by the slow removal of a small amount of water originally present; there is no evidence that when first liberated from its hydrochloride the product contains unassociated amino-aldehyde.

The formation of cyclic amines through intramolecular condensation of aldehyde and active methylene groups, though later successfully used by Wohl in the well-known synthesis of cincholoiponic acid (Wohl, *Ber.*, 1907, **40**, 4679; Wohl and Losanitsch, *ibid.*, p. 4698), therefore does not occur in the extreme case of benzylaminopropaldehyde, in which the activating effect of the phenyl group, already feeble, is probably opposed, even in acid solution, by the adjacent nitrogen atom. However, at an early stage in the investigation the presence of oxygen in the formula was tentatively attributed to a ring-closure of the type postulated by Wohl but without dehydration, thus giving 3-hydroxy-2-phenylpyrrolidine. In order to detect the possible hydroxyl group the amine hydrochloride was heated with acetic anhydride, whereupon hydrogen chloride was evolved and a high-boiling liquid, $C_{16}H_{21}O_5N$, isolated, which from its ready formation of a 2 : 4-dinitrophenylhydrazone was later recognised as 1 : 1-diacetoxy-3-*N*-benzylacetamidopropane (IV). The original 3-benzylamino-acetal, on the other hand, was converted under these conditions into 3-*N*-benzylacetamidoprop-1-enyl ethyl ether (V), which, of course, gave the same 2 : 4-dinitrophenylhydrazone.

(IV.) $PhCH_2\cdot NAc\cdot CH_2\cdot CH_2\cdot CH(OAc)_2$ $PhCH_2\cdot NAc\cdot CH_2\cdot CH\colon CH\cdot OEt$ (V.)


(VI.)


(VII.)


(VIII.)

As was to be expected, the effect of hydrochloric acid on the higher homologue, 4-benzylamino-1 : 1-diethoxybutane (ethyl 4-benzylaminobutyracetal) (VI), leads to intramolecular condensation of the liberated aldehyde group with the basic atom. The acid-cyclised base could not be isolated in a pure condition, although a picrolonate was obtained which may have been that of the pyrroline, but when the hydrochloric acid solution was heated with tin the nature of the initial reaction was apparent from the formation of 1-benzylpyrrolidine (VII) characterised by its picrate (Schlinck, *Ber.*, 1899, **32**, 953) and picrolonate. The benzylaminobutyracetal (VI) was synthesised by reduction of the benzylideneamino-compound. In connexion with intended synthetical experiments, the *N*-cyanomethyl compounds of both the 4-aminobutyracetal and (I) were prepared by the Strecker method.

The revision of the formula assigned by Wohl to the acid-hydrolysis product of (I) affects the argument used by Gitsels and Wibaut (*loc. cit.*) when proposing a structure for the 2-phenylpyrroline they obtained by zinc–acid reduction of 2-phenylpyrrole. The dihydro-base is readily methylated, from which these authors concluded that it was not a Δ^1- or a Δ^5-pyrroline; its stability to acid is, in any case, sufficient for us to reject these two structures. In view of the existence of the 2-phenyl-Δ^2-pyrroline (Gabriel and Colman, *Ber.*, 1908, **41**, 513), and also, apparently, of the Δ^3-isomer, Gitsels and Wibaut therefore considered their dihydropyrrole to be the Δ^4-compound.

With the elimination of Wohl's Δ^3-pyrroline other evidence is necessary to establish the constitution of the isomer prepared by Gitsels and Wibaut. The synthesis of the supposed Δ^4-pyrroline has accordingly been repeated; by reversing the published procedure, and slowly treating an ethanolic solution of 2-phenylpyrrole and zinc dust with acid, thus avoiding undue contact of the latter with the pyrrole, the yield of pyrroline has been considerably increased. The constitution of Δ^3-pyrroline, also obtained by zinc–acid reduction from pyrrole, was determined by ozonolysis (Treibs and Dinelli, *Annalen*, 1935, **517**, 170), the oxidation ultimately giving iminodiacetic acid, but Gitsels and Wibaut report that a similar attempt to oxidise their phenyldihydropyrrole was unsuccessful owing to extensive decomposition. The passage of ozone into an aqueous acid solution of the 2-phenylpyrroline, although at first causing the deposition of dark amorphous material, ultimately gave a nearly colourless solution. After further oxidation with hydrogen peroxide, and treatment with ethanolic hydrogen chloride, a liquid base was isolated which was identified by means of its hydrochloride, picrolonate, and the crystalline acid obtained on hydrolysis (all of which were indistinguishable from specimens previously synthesised), as the diethyl ester of *N*-α-carboxybenzylglycine (VIII). The synthesis of *N*-α-carboxybenzylglycine was accomplished by the Strecker reaction from benzaldehyde, ethyl aminoacetate, and hydrogen cyanide (Stadnikoff, *Ber.*, 1908, **41**, 4364; Scheibler and Baumgarten, *ibid.*, 1922, **55**, 1358), the intermediate cyano-ester being hydrolysed with boiling hydrochloric acid. The ethyl ester was obtained from a previously heated solution of α-phenylglycine ethyl ester and chloroacetic acid by refluxing with hydrogen chloride, and, in addition to the derivatives mentioned above, the toluene-*p*-sulphonyl derivative was prepared.

In view of the evidence now available that 2-phenylpyrrole undergoes 1 : 4-hydrogenation on zinc–acid reduction, it is difficult to accept the conclusion that the 2-3′-pyridylpyrroline of Wibaut and Hackmann (*Rec. Trav. chim.*, 1932, **51**, 1157), which is formed from nicotyrine under similar conditions, is as Späth, Wibaut, and Kesztler claim (*Ber.*, 1938, **71**, 100), the Δ^2-derivative. Instances of 1 : 2(or 3 : 4)-addition in the reduction of pyrroles have been reported (Sonn, *Ber.*, 1935, **68**, 148; 1939, **72**, 2150), but they refer to compounds having substituents on the 3- or the 4-position of the pyrrole ring. Haines and Eisner (*J. Amer. Chem. Soc.*, 1950, **72**, 1719) have recently proved that the dihydronicotyrine is not, as Späth, Wibaut, and Kesztler supposed, identical with *N*-methylmyosmine, the Δ^2-pyrroline, and taking into account the acid stability of the dihydronicotyrine have decided that it is, in fact, the Δ^3-pyrroline, in agreement with our view.

EXPERIMENTAL.

3-*Benzylamino*-1 : 1-*diethoxypropane* (*Ethyl* 3-*Benzylaminopropionacetal*) (I).—The reaction between 3-chloro-1 : 1-diethoxypropane (*Org. Synth.*, Vol. XI, p. 26) (19 g., 1 mol.) and benzylamine (25 g., *ca.* 2 mols.) was slow at 100° and the mixture was therefore heated at 120—130° for 4 hours. When cold, the brown semi-solid mass was treated with 10% aqueous sodium hydroxide (60 c.c.), and the resulting oil extracted with ether and distilled. The fraction of b. p. 110—130°/3 mm. (14 g.) gave on redistillation ethyl 3-benzylamino-1 : 1-diethoxypropane as a colourless liquid, b. p. 140—144°/4 mm., which readily formed a *picrolonate*, crystallising from alcohol as stout yellow prisms, m. p. 178°, identical with that obtained from a specimen of the acetal prepared as by Wohl (*loc. cit.*) through reduction of 3-benzylideneamino-1 : 1-diethoxypropane (Found : C, 57·9; H, 6·2; N, 14·4. $C_{14}H_{23}O_2N,C_{10}H_8O_5N_4$ requires C, 57·5; H, 6·2; N, 14·0%).

When the acetal was added to an equivalent of 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid, precipitation of a solid quickly occurred. Crystallised from acetic acid, this *dinitrophenylhydrazone hydrochloride* formed glistening plates, m. p. 185° (decomp.) (Found : C, 50·5; H, 4·7. $C_{16}H_{17}O_4N_5,HCl$ requires C, 50·5; H, 4·7%). The corresponding *sulphate* was thrown down by the addition of water to a warm solution of the reagents in alcohol containing a few drops of sulphuric acid, and crystallised from acetic acid in small rectangular plates, m. p. 171° (Found : C, 43·4; H, 4·3; S, 6·8. $C_{16}H_{17}O_4N_5,H_2SO_4$ requires C, 43·5; H, 4·3; S, 7·2%).

2 : 4 : 6-*Tri*-(2-*benzylaminoethyl*)*trioxan* (III; $R = PhCH_2{\cdot}NH{\cdot}CH_2{\cdot}CH_2{\cdot}$).—The above benzylaminoacetal (14 g.) was slowly dropped into concentrated hydrochloric acid (60 c.c.), stirred, and kept at 0°. The colourless solution was left at room temperature for 4 hours and then evaporated to dryness at 50° under reduced pressure. The residue was powdered under alcohol, thus giving a white solid (7 g., 62%) which was collected and dissolved in boiling alcohol with the addition of a small quantity of water. The 2 : 4 : 6-*tri*-(2-*benzylaminoethyl*)*trioxan hydrochloride* separated on cooling as a voluminous mass of colourless fine needles, m. p. 244° (decomp.) (Found, after drying at 157°/15 mm. for 2 hours : C, 60·4; H, 7·0; N, 6·8; Cl, 17·4. $C_{10}H_{13}ON,HCl$ requires C, 60·2; H, 7·0; N, 7·0; Cl, 17·8%). The salt does not reduce ammoniacal silver nitrate or hot Fehling's solution and forms benzylaminopropaldehyde 2 : 4-dinitrophenylhydrazone hydrochloride only slowly when heated or after a very prolonged time at room temperature. The action of boiling hydrochloric acid (50 c.c. of 10%) on the trioxan hydrochloride (5 g.) for 6 hours was to produce benzylamine, isolated as the hydrochloride, m. p. 256°, by evaporating the solution to dryness and stirring the residue with chloroform; the insoluble residue was then crystallised from alcohol–ethyl acetate. The well-washed pasty precipitate obtained from an acid solution of the trioxan hydrochloride and sodium nitrite gave Liebermann's nitroso-reaction.

The free trioxan *base* was obtained by shaking a cold aqueous solution of the hydrochloride with ether and magnesium oxide for 2 hours. The ether was evaporated under reduced pressure, a white solid appearing, but at room temperature the residue was a very pale straw-coloured oil which decomposed when heated at 0·05 mm. [Found : *M* (cryoscopically in 3% solution in benzene), after 1 day, 388; 2 days, 400; 4 days, 409; 5 days, 434; 8 days, 469; 14 days, 508; 60 days, 509. $(C_{10}H_{13}ON)_2$ requires *M*, 326; $(C_{10}H_{13}ON)_3$ requires *M*, 489].

A mixture of the base and aqueous oxalic acid gave a microcrystalline hydrated *hydrogen oxalate*, m. p. 234° (decomp.), which was recrystallised from water (Found, after drying at 100° under reduced pressure : C, 54·8, 54·9; H, 5·9, 6·4. $C_{10}H_{13}ON,C_2H_2O_4,\frac{1}{2}H_2O$ requires C, 55·0; H, 6·1%). The sparingly soluble *picrolonate*, m. p. 226° (decomp.), was prepared from the hydrochloride and potassium picrolonate in aqueous alcohol as a yellow powder, and could be recrystallised from nitrobenzene or *cyclo*hexanone (Found : C, 56·0; H, 4·8; N, 16·3. $C_{10}H_{13}ON,C_{10}H_8O_5N_4$ requires C, 56·1; H, 4·9; N, 16·4%). An alcoholic solution of the base mixed with the calculated quantity of dilute sulphuric acid and evaporated under reduced pressure gave the hydrated *hydrogen sulphate*, crystallising from alcohol in short, fine needles, m. p. 141° (Found, after drying at 100° under reduced pressure : C, 44·4; H, 6·1; S, 11·8. $C_{10}H_{13}ON,H_2SO_4,\frac{1}{2}H_2O$ requires C, 44·4; H, 5·9; S, 11·8%).

1 : 1-*Diacetoxy*-3-N-*benzylacetamidopropane*.—The trioxan hydrochloride (2 g.) was heated at 140°

with acetic anhydride (10 c.c.) until hydrogen chloride ceased to be evolved. The remaining anhydride was then evaporated under reduced pressure and the thin syrupy residue distilled. 1 : 1-*Diacetoxy*-3-N-*benzylacetamidopropane* was thus obtained as a colourless liquid, b. p. 170°/0·1 mm. (Found : C, 62·5; H, 6·9; N, 4·4; MeCO, 43·6. $C_{16}H_{21}O_5N$ requires C, 62·5; H, 6·8; N, 4·6; 3MeCO, 42·0%). When this was treated with a cold 2N-hydrochloric acid solution of 2 : 4-dinitrophenylhydrazine, 3-N-*benzylacetamidopropaldehyde dinitrophenylhydrazone* gradually formed, which crystallised from alcohol as a yellow powder, m. p. 133° (Found : C, 56·1; H, 5·0; N, 17·8. $C_{18}H_{19}O_5N_5$ requires C, 56·1; H, 4·9; N, 18·2%).

3-N-*Benzylacetamidoprop*-1-*enyl Ethyl Ether* (V).—3-Benzylamino-1 : 1-diethoxypropane (4·2 g.) was heated with acetic anhydride (20 c.c.) at 140—150° for 1 hour and the solution then distilled. The fraction of b. p. *ca.* 140°/0·4 mm. (3·9 g., 80%) was a colourless liquid which gave 3-*N*-benzylacetamidopropaldehyde 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 133°, and consisted of 3-N-*benzylacetamidoprop*-1-*enyl ethyl ether* (Found : C, 72·2; H, 8·2; N, 5·5; EtO, 18·3. $C_{14}H_{19}O_2N$ requires C, 72·1; H, 8·2; N, 6·0; EtO, 19·3%).

3-N-*Benzyl*-N-*cyanomethylamino*-1 : 1-*diethoxypropane*.—The acetal (I) (2·1 g.) was mixed with a saturated aqueous solution of sodium hydroxymethylenesulphonate (1·2 g.) and sufficient alcohol added to give a clear liquid. A solution of potassium cyanide (0·74 g.) in water (2—3 c.c.) was then introduced, which resulted in the appearance of an oil. After removal of the alcohol by aspiration of the hot mixture, this oil was extracted with ether and distilled. 3-N-*Benzyl*-N-*cyanomethylamino*-1 : 1-*diethoxypropane* (2 g.) was thereby obtained as a colourless liquid, b. p. 125°/0·05 mm. (Found : C, 69·4; H, 8·7; N, 9·8. $C_{16}H_{24}O_2N_2$ requires C, 69·5; H, 8·7; N, 10·1%). The 2 : 4-*dinitrophenylhydrazone sulphate* of the derived aldehyde separated on treatment of the acetal with a warm alcoholic sulphuric acid solution of the reagent, and was with some difficulty recrystallised from nitrobenzene–ethanol as an orange-brown powder, m. p. 165° (decomp.) (Found : C, 44·7; H, 3·8. $C_{18}H_{18}O_4N_6,H_2SO_4$ requires C, 44·8; H, 4·1%).

4-N-*Cyanomethylamino*-1 : 1-*diethoxypropane*.—4-Amino-1 : 1-diethoxybutane (2 g.) was dissolved in a saturated aqueous solution of sodium hydroxymethylenesulphonate (1·7 g.) and treated with a concentrated aqueous solution of potassium cyanide (0·8 g.). The oily layer which separated was removed by ether and distilled, giving the *cyanomethylamino-acetal* as a colourless liquid (2 g.), b. p. 90°/0·1 mm. (Found : C, 60·0; H, 10·0. $C_{10}H_{20}O_2N_2$ requires C, 60·0; H, 10·0%). The 2 : 4-*dinitrophenylhydrazone hydrochloride* of the derived aldehyde crystallised from nitromethane as a yellow microcrystalline powder, m. p. 160° (decomp.) (Found : C, 42·0; H, 4·6; N, 23·7; Cl, 9·6. $C_{12}H_{14}O_4N_6,HCl$ requires C, 42·1; H, 4·4; N, 24·5; Cl, 10·4%).

4-*Benzylideneamino*-1 : 1-*diethoxybutane*.—On the addition of benzaldehyde (5·3 g.) to 4-amino-1 : 1-diethoxybutane (8 g.) (Wohl, *Ber.*, 1906, **39**, 1952), heat was evolved and the mixture became turbid. The product was directly distilled, and the *benzylideneamino-acetal* (11·1 g.) obtained as a colourless and faintly odoriferous oil, b. p. 135°/0·04 mm. (Found : C, 72·1; H, 9·5; N, 5·6. $C_{15}H_{23}O_2N$ requires C, 72·3; H, 9·2; N, 5·6%).

4-*Benzylamino*-1 : 1-*diethoxybutane* (VI).—The above benzylidene compound (11 g.), dissolved in absolute ethanol (120 c.c.), was reduced by sodium (6 g.) added in ten portions to the solution boiling under reflux. Water (60 c.c.) was then introduced and the alcohol removed by drawing air through the solution heated on a steam-bath. Extraction of the cooled aqueous residue yielded the 3-*benzylamino-acetal* (9·8 g.) as a colourless mobile liquid, b. p. 133°/0·03 mm. (Found : C, 71·3; H, 9·9. $C_{15}H_{25}O_2N$ requires C, 71·7; H, 10·0%). The *picrolonate* crystallised from alcohol in yellow long rectangular plates, m. p. 146—147° (effervescence) (Found : C, 58·6; H, 6·6. $C_{25}H_{33}O_7N_5$ requires C, 58·3; H, 6·4%).

1-*Benzylpyrrolidine* (VII).—Distillation of the base liberated from a solution of the foregoing acetal which had been left in concentrated hydrochloric acid for several hours caused polymerisation. From the undistilled liquid a crystalline *picrolonate*, m. p. 140° (decomp.), sparingly soluble in ethanol, was obtained (Found, in a specimen dried at 70° : C, 58·6; H, 5·2; N, 15·7. $C_{11}H_{13}N,C_{10}H_8O_5N_4,\frac{1}{2}H_2O$ requires C, 58·4; H, 5·1; N, 16·1%).

The clear solution obtained by adding the 4-benzylamino-acetal (5 g.) to ice-cold concentrated hydrochloric acid (45 c.c.) was left for 4 hours at room temperature and then heated on a steam-bath with granulated tin (14 g.) for 1½ hours. The liquid was cooled, treated with excess of concentrated aqueous sodium hydroxide, and steam-distilled. Extraction of the distillate with ether isolated a colourless liquid (2·4 g.) which on fractionation gave 1-benzylpyrrolidine (1·9 g.), b. p. 245°, identified as the picrate, long hexagonal plates, m. p. 128°, first described by Schlinck (*Ber.*, 1899, **32**, 953) (Found : N, 14·4. Calc. for $C_{11}H_{15}N,C_6H_3N_3O_7$: N, 14·4%), and as the *picrolonate*, m. p. 137° (Found : C, 59·1; H, 5·7. $C_{11}H_{15}N,C_{10}H_8O_5N_4$ requires C, 59·3; H, 5·4%).

Ethyl N-α-*Cyanobenzylaminoacetate*.—Literature directions were followed for this preparation, the cyano-ester being isolated as hydrochloride. Stadnikoff (*loc. cit.*) found m. p. 82° (decomp.) and Scheibler and Baumgarten (*loc. cit.*) 83·5°; no analyses have been recorded. The unpurified product had m. p. 85—87° and, after it had been dried in a vacuum over calcium chloride, m. p. 95—97°. Crystallisation from ethanol–light petroleum gave the *cyano-ester hydrochloride* as colourless needles, m. p. 102° (decomp.) (Found : C, 56·9; H, 6·4; N, 11·0; Cl, 13·9. $C_{12}H_{14}O_2N_2,HCl$ requires C, 56·6; H, 6·0; N, 11·0; Cl, 13·5%).

N-α-*Carboxybenzylglycine* (VIII).—(i) The α-cyanobenzylaminoacetate hydrochloride (9 g.) was heated under reflux with hydrochloric acid (50 c.c. of 20%) for 90 minutes. The solution was evaporated to dryness on a steam-bath, and the solid residue dissolved, together with sodium acetate (5 g.), in water (50 c.c.). The amino-acid (1·8 g.) which separated during 2 days had m. p. varying with the preparation and with rate of heating, from *ca.* 202° to 218—220° (decomp.). Stadnikoff (*loc. cit.*) found m. p. 220° (decomp.), but samples prepared as above on recrystallisation from water showed m. p. 206—207° (decomp.) on rapid heating (Found : C, 57·6; H, 5·4; N, 6·7. $C_{10}H_{11}O_4N$ requires C, 57·4; H, 5·3; N, 6·7%).

(ii) The diethyl ester of this acid (2 g.) was heated under reflux with aqueous sodium hydroxide (20 c.c. of 2N.) for 90 minutes. The solution was then neutralised with 2N-hydrochloric acid, and on concentration and setting aside in the cold, the acid (VIII) crystallised, having m. p. after recrystallisation, 206—207° (decomp.) (Found : C, 57·5; H, 5·5; N, 6·6%).

Ethyl N-*α-Carbethoxybenzylglycine*.—To a solution of α-phenylglycine ethyl ester (65 g.) in ethanol (100 c.c.), chloroacetic acid (17 g.) in ethanol (50 c.c.) was slowly added, and after 3 hours' heating under reflux the solution was saturated with hydrogen chloride. After further heating for 3 hours the solvent was evaporated and the residue carefully shaken with benzene and aqueous sodium hydrogen carbonate. The dried benzene solution gave on distillation an oil (16 g.), b. p. 140—154°/1 mm., which was further purified by dilution with an equal volume of anhydrous ether, thereby next day causing the separation of a small quantity of solid. Redistillation of the filtered liquid gave ethyl *N*-α-carbethoxybenzylglycine (13·2 g.), b. p. 134°/0·5 mm., characterised by the following crystalline derivatives : (a) *Hydrochloride*, prepared in anhydrous ether, and crystallising from chloroform–light petroleum in needles, m. p. 114—115° (Found : C, 55·9; H, 6·6. $C_{14}H_{19}O_4N,HCl$ requires C, 55·7; H, 6·7%). (b) *Picrolonate*, crystallising from ethanol in clusters of prisms, m. p. 145—146° (Found : C, 54·8; H, 5·1. $C_{14}H_{19}O_4N,C_{10}H_8O_5N_4$ requires C, 54·45; H, 5·15%). (c) *Toluene*-p-*sulphonyl* derivative, obtained from a mixture of toluene-*p*-sulphonyl chloride (2·3 g.), ester (3·2 g.), and pyridine (6 c.c.), which after 2 days at room temperature was poured into water, washed in ethereal solution with acid, and crystallised from light petroleum containing a little benzene; it formed prisms, m. p. 64—65° (Found : C, 60·6; H, 6·2; N, 3·7. $C_{28}H_{25}O_6NS$ requires C, 60·1; H, 6·0; N, 3·35%).

2-*Phenyl*-Δ^3-*pyrroline* (cf. Gitsels and Wibaut, *Rec. Trav. chim.*, 1940, **59**, 1102) (II).—A solution of 2-phenylpyrrole (4·8 g.) in ethanol (15 c.c.) containing zinc dust (15 g.) was stirred and heated under reflux for 2 hours during the gradual addition of hydrochloric acid (30 c.c. of 20%, followed by 20 c.c. of 30%). After refluxing for a further hour, the liquid was cooled, decanted from residual zinc, and made strongly alkaline with aqueous sodium hydroxide. The mixture was then steam-distilled and the distillate acidified with concentrated hydrochloric acid. When non-basic material had been removed by ether the solution was again basified, and further ether-extraction gave 2-phenyl-Δ^3-pyrroline as a colourless oil (4 g.), b. p. 112—113°/11 mm., which was identified by the picrate, m. p. 139—140° (140—141°, Gitsels and Wibaut, *loc. cit.*) (Found : C, 51·3; H, 4·0. Calc. for $C_{10}H_{11}N,C_6H_3O_7N_3$: C, 51·35; H, 3·8). The *toluene*-p-*sulphonyl* derivative (0·5 g.), prepared by shaking the pyrroline (0·35 g.) and toluene-*p*-sulphonyl chloride (0·7 g.) in aqueous sodium hydroxide (5 c.c.; 2N.) containing acetone (1 c.c.), crystallised from aqueous alcohol in long needles, m. p. 124—125° (Found : C, 68·1; H, 5·9. $C_{17}H_{17}O_2NS$ requires C, 68·2; H, 5·7%).

Oxidation of 2-*Phenyl*-Δ^3-*pyrroline*.—Ozonised oxygen was passed for 2 hours into a solution of 2-phenyl-Δ^3-pyrroline (2 g.) in 2N-hydrochloric acid (20 c.c.) at 0°. Hydrogen peroxide (5 c.c.; 40-vol.) was then added to the clear pale yellow solution, and 2 hours later the excess was destroyed by warming in presence of platinum wire to 60°. The solution was concentrated to small bulk at 40° under low pressure and treated with sodium acetate (1 g.) but, since after the mixture had been kept at 0° only a little tarry material separated, the remaining water was removed, an operation which led to further decomposition, the dark residue smelling of benzaldehyde. The dried product was heated under reflux with alcoholic hydrogen chloride, and the resulting ester (1 g.) isolated in the usual manner. It gave with picrolonic acid (1 g.) a product (1·6 g.), m. p. 142—146°, which after recrystallisation from acetone–ether and finally ethanol had m. p. 145—146° alone or mixed with the picrolonate of ethyl *N*-α-carbethoxybenzylglycine. The ester which was recovered from the dried chloroform layer after shaking a chloroform solution of the crystallised picrolonate with aqueous lithium hydroxide, gave the hydrochloride, m. p. and mixed m. p. 114—115°, and was hydrolysed to give *N*-α-carboxybenzylglycine, m. p. 206—207 (decomp.).

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