914. *Intramolecular Aminolysis of Amides.*

By C. J. M. Stirling.

Reactions of amino-amides have been investigated with respect to (1) $N \longrightarrow N'$ acyl migration and (2) the formation of cyclic lactams.

N-Benzoyl-*N*-phenylethylenediamine (V; R = Ph) rearranges rapidly to *N*-benzoyl-*N'*-phenylethylenediamine (VI; R = Ph); when R = *cyclo*hexyl, the conversion is very slow but irreversible. *NN*-Dibenzoylethylenediamines (XIV; R = Ph or *cyclo*hexyl) rearrange very rapidly to *NN'*-dibenzoylethylenediamines (XV), but *N*-2-aminoethylphthalimide did not rearrange: instead, ethylenediamine and an unidentified acid were obtained.

4-Alkylaminobutyranilides (XVIII; R = $Ph{\cdot}CH_2$ or *cyclo*hexyl) eliminated aniline when heated, with formation of *N*-alkylpyrrolid-2-ones (XIX), cyclisation of the benzyl compound being considerably the faster.

Reactivities of amines in the intermolecular aminolysis of amides have been measured by Smith and Adkins.[1] The observed order of reactivity was straight-chain primary > branched-chain primary $\approx$ secondary $\gg$ aromatic. Their results agree well with more recent determinations of the nucleophilic reactivities of amines in carbonyl substitution, in particular the aminolysis of esters.[2] Intramolecular aminolysis of amides must involve either (1) rearrangement, with $N \longrightarrow N'$ acyl migration, or (2) elimination of amine, as in the intermolecular reaction, with formation of a cyclic lactam.[3, 4]

Rearrangement.—This is the counterpart of the intramolecular aminolyses of carboxylic [5] and thiolcarboxylic [6, 7] esters which involve respectively, $O \longrightarrow N$ and $S \longrightarrow N$ acyl migration. These migrations occur [5] by attack of the uncharged ω-amino-group at the carbonyl group of the ester with the cyclic transition state [5, 6] (I; Y = O or S). Migration occurs most rapidly,[6] as in other intramolecular nucleophilic substitutions,[8] when $n = 2$ or 3. The only instances of $N \longrightarrow N'$ migrations (Y = NH) are those of the isomerisation of *N*-acetyl-*N*-phenylthiourea [9] and certain rearrangements which do not involve uncharged amino-groups.[10]

In the present work with *N*-benzoylethylenediamines (V; R = Ph or C_6H_{11}), it has been found, as expected, that the direction and speed of migration is determined by the relative nucleophilicities of the two nitrogen atoms concerned. *N*-Benzoylethylenediamines (V; R = Ph or C_6H_{11}) have been obtained (see scheme) as their hydrobromides by benzoylation of the urethanes (II) and subsequent removal of the benzyloxycarbonyl group with hydrogen bromide.[11] On liberation of the base (V; R = Ph) rearrangement occurred rapidly and only the secondary amide (VI; R = Ph) was isolated. The *cyclo*hexyl analogue (V; R = C_6H_{11}) was more stable and treatment of the liberated base with toluene-*p*-sulphonyl chloride gave only the primary mono- and di-toluene-*p*-sulphonamides (VII and VIII respectively) in 80% yield from the urethane (IV). The infrared spectrum of the base showed that the isomer (VI) could only be present in very small quantity if at all. Rearrangement of the base, however, occurred at 150°, 56% of the urethane (IV) being accounted for as the monosulphonamide (IX) of the secondary base and 8% as the

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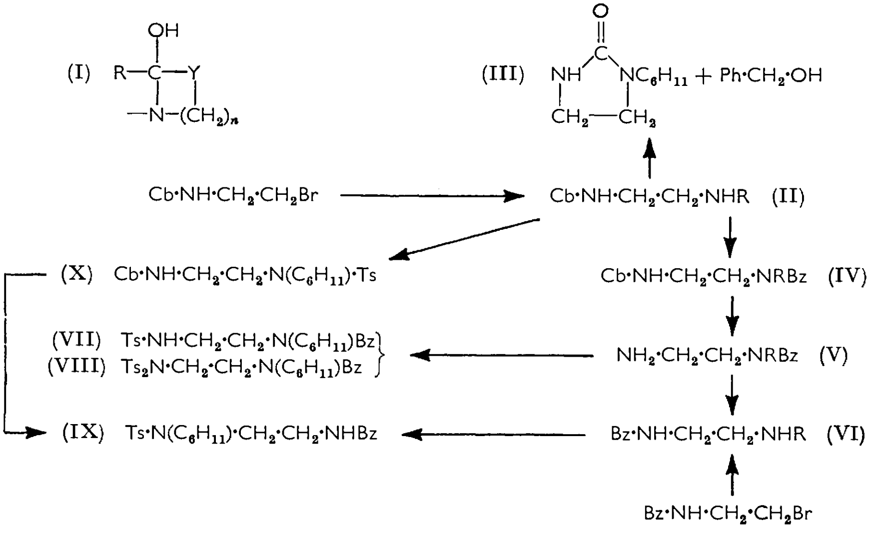
[1] Smith and Adkins, *J. Amer. Chem. Soc.*, 1938, **60**, 657.
[2] Arnett, Miller, and Day, *ibid.*, 1950, **72**, 5635.
[3] Barrass and Elmore, *J.*, 1957, 4830.
[4] Holley and Holley, *J. Amer. Chem. Soc.*, 1952, **74**, 3069.
[5] Phillips and Baltzly, *ibid.*, 1947, **69**, 200.
[6] Wieland and Hornig, *Annalen*, 1956, **600**, 12.
[7] Stirling, preceding paper.
[8] Newman, " Steric Effects in Organic Chemistry," Wiley, New York, 1956.
[9] Wheeler, *Amer. Chem. J.*, 1902, **27**, 270.
[10] Houben-Weyl, "Methoden der Organischen Chemie," Thieme, Stuttgart, 1957, Vol. XI, Part 1, p. 939.
[11] Ben-Ishai and Berger, *J. Org. Chem.*, 1952, **17**, 1564.

disulphonamide (VIII) of the primary base. The structure of the sulphonamide (VII) was confirmed by conversion into the disulphonamide, and that of the isomer (IX) by its formation from the sulphonamido-urethane (X). Isolation of both isomers under these conditions suggested that they existed in equilibrium. This possibility was tested by examination of the product of the reaction of *N*-2-bromoethylbenzamide with *cyclo*hexylamine. The infrared spectrum of the product (twice distilled at 167°) and of its toluene-*p*-sulphonamide showed that no primary amine was obtained. The isomeric benzamides (V and VI; R = C_6H_{11}) are not, therefore, in equilibrium although conversion of (V) into (VI) is extremely slow. In this connection, the urethane (II; R = C_6H_{11}) was stable, but at 180° cyclisation to the tetrahydro-oxoglyoxaline (III) occurred with elimination of benzyl alcohol.



(Cb = $Ph\cdot CH_2\cdot O\cdot CO$. Ts = p-$Me\cdot C_6H_4\cdot SO_2$.)

These results are in accord with reactivities observed in intermolecular reactions [1, 2] and the conversion of the amide (V) into its isomer (VI; R = C_6H_{11}) reflects the lowering of nucleophilic reactivity caused by α-branching.

The ready acylation of amines by *N*-acylamides [12] suggested that intramolecular aminolysis of such compounds should be fast. The *NN*-dibenzoyl-*N*′-benzyloxycarbonylethylenediamines (XII; R = Ph or C_6H_{11}) were obtained (see scheme) by treatment of the *N*-benzoylethylenediamines with benzyl chloroformate and subsequent benzoylation of the urethanes (XI) at the amido-nitrogen atom.[13] Removal of the benzyloxycarbonyl group then gave the *NN*-dibenzoylethylenediamines as the hydrobromides (XIII). In each case, and in spite of the low nucleophilicity of the aromatic amine (R = Ph), very rapid benzoyl migration followed liberation of the base and only *NN*′-dibenzoylethylenediamines (XV) were obtained.*

These observations prompted an investigation of the stability of *N*-2-aminoethylphthalimide which could be expected to rearrange to the diamide (XVI). Spring and Woods [14] reported, without experimental details, reactions of primary amines with *N*-2-aminoethylphthalimide, and Braun and Pinkernelle [15] prepared *N*-3-aminopropylphthalimide. In neither case, however, was the stability of the aminophthalimide

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* Since this paper was submitted, Wieland and Urbach (*Annalen*, 1958, **613**, 84) have reported similar reactions of *N*-acylamides.

[12] Taschner, Kocór, and Meyer, *Roczniki Chem.*, 1952, **26**, 692.

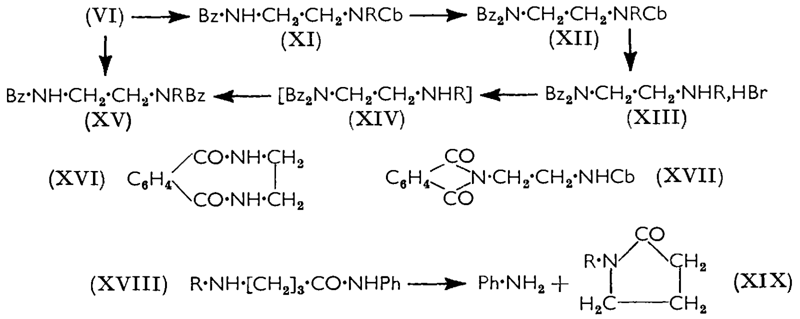
[13] Titherley, *J.*, 1904, **85**, 1673.

[14] Spring and Woods, *Nature*, 1946, **158**, 754.

[15] Braun and Pinkernelle, *Ber.*, 1934, **67**, 1056.

indicated. Treatment of the urethane (XVII) with hydrogen bromide gave *N*-2-aminoethylphthalimide hydrobromide. Liberation of the base gave only an unidentified acid without the properties of (XVI) [16] (of doubtful structure [17]), together with a small amount of ethylenediamine.

Elimination.—Elimination of amine is the result of intramolecular aminolysis when the amino-group is in the acid moiety of the amide. Instances have been given by Barrass and Elmore [3] who, while this work was in progress, reported the formation of the cyclic lactams from amides of basic amino-acids. In this work, the γ-alkylaminobutyranilides (XVIII; $R = Ph{\cdot}CH_2$ or C_6H_{11}), obtained from γ-bromobutyranilide, slowly cyclised, on being heated, to *N*-alkylpyrrolid-2-ones ($R = Ph{\cdot}CH_2$ or C_6H_{11}) with elimination of aniline. Comparison of the rates of the reactions again revealed the lowering of the nucleophilicity of the α-branched amine in spite of its greater basic strength (towards protons). Thus cyclisation of γ-benzylaminobutyranilide was complete in 1 hr. at 160° whereas that of the *cyclo*hexyl compound was incomplete after 2 hr. at 220°. Interestingly, these cyclisations are much slower than those of basic amino-acid amides.[3]



EXPERIMENTAL

The light petroleum used had b. p. 40—60°. Extracts were dried over Na_2SO_4.

N-*Benzyloxycarbonyl*-N′-*phenylethylenediamine* (II; R = Ph).—2-Benzyloxycarbonylaminoethyl bromide [18] (10 g.) was heated with aniline (25 ml.) in ethylene glycol (15 ml.) at 150° for 50 min. The mixture was poured into 10% aqueous sodium carbonate and extracted with benzene. Evaporation of the extracts and removal of excess of aniline under reduced pressure left the *amine* (6·5 g.), m. p. 50—52°, raised to 58° by crystallisation from benzene–light petroleum (Found: C, 71·5; H, 7·0; N, 10·6. $C_{16}H_{18}O_2N_2$ requires C, 71·1; H, 6·7; N, 10·4%).

N-*Benzoyl*-N′-*benzyloxycarbonyl*-N-*phenylethylenediamine* (IV; R = Ph).—Benzoylation (Schotten–Baumann) of the preceding amine gave the *amide*, m. p. 108—109° (needles from benzene–light petroleum) (Found: C, 74·0; H, 5·7. $C_{23}H_{22}O_3N_2$ requires C, 73·8; H, 5·9%).

Rearrangement of N-*Benzoyl*-N-*phenylethylenediamine* (V; R = Ph).—Treatment of the amide (IV; R = Ph) with 50% hydrogen bromide in acetic acid and addition of anhydrous ether after reaction was complete, yielded a hygroscopic hydrobromide which gave no picrate and a hygroscopic perchlorate. An aqueous solution of the hydrobromide [from 2 g. of (IV)] was basified with sodium hydroxide and extracted with chloroform. Evaporation of the extracts at room temperature and treatment of the residue with light petroleum gave *N*-benzoyl-*N′*-phenylethylenediamine (1·1 g.), m. p. 120°. Crystallisation from methanol raised the m. p. to 127°, alone or mixed with an authentic specimen.[19]

N-*Benzyloxycarbonyl*-N′-cyclo*hexylethylenediamine* (II; $R = C_6H_{11}$).—2-Benzyloxycarbonylaminoethyl bromide (13 g.) was heated with *cyclo*hexylamine (35 ml.) at 95° for 30 min. The mixture was added to an excess of aqueous potassium hydroxide, and the suspension was

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[16] Anderlini, *Gazzetta*, 1894, **24**, 401.

[17] Beilstein's "Handbuch der Organischen Chemie," Springer, Berlin, 1933, Vol. XVII, p. 480.

[18] Katchalski and Ben-Ishai, *J. Org. Chem.*, 1950, **15**, 1067.

[19] Gabriel and Stelzner, *Ber.*, 1895, **28**, 2929.

extracted with benzene. The extracts, on being shaken with 20% hydrochloric acid (100 ml.), gave a precipitate of N-*benzyloxycarbonyl*-N′-cyclo*hexylethylenediamine hydrochloride* (14·5 g.), m. p. 179°, raised to 182° by crystallisation from ethanol (Found: C, 61·4; H, 7·9; N, 8·7. $C_{16}H_{25}O_2N_2Cl$ requires C, 61·5; H, 7·7; N, 9·0%). The *base*, liberated from the hydrochloride with aqueous sodium carbonate, had m. p. 70° (from ether) (Found: N, 10·0. $C_{16}H_{24}O_2N_2$ requires N, 10·2%).

N-*Benzoyl*-N′-*benzyloxycarbonyl*-N-cyclo*hexylethylenediamine* (IV; $R = C_6H_{11}$).—Treatment of the base with benzoyl chloride in pyridine gave the *amide*, m. p. 114° (from benzene–light petroleum) (Found: C, 73·2; H, 7·6. $C_{23}H_{28}O_3N_2$ requires C, 72·6; H, 7·4%).

Rearrangement of N-*Benzoyl*-N-cyclo*hexylethylenediamine* (V; $R = C_6H_{11}$).—The amide (IV; $R = C_6H_{11}$) (10 g.) was treated with a 50% solution of hydrogen bromide in acetic acid (25 ml.). When reaction was complete, water (100 ml.) and ether (200 ml.) were added. The aqueous layer was separated and divided into two equal parts: part (i) was basified with sodium hydroxide, and toluene-*p*-sulphonyl chloride (10 g.) in acetone (20 ml.) was added. When reaction was complete, the suspension was acidified and extracted with chloroform. Evaporation of the extracts gave a residue (5·9 g.), m. p. 143—150°, which was boiled with ethanol (25 ml.). Filtration of the cold mixture gave N-*benzoyl*-N-cyclo*hexyl*-N′N′-*ditoluene*-p-*sulphonylethylenediamine* (VIII) (3·6 g.), m. p. 175—176° (Found: C, 63·0; H, 6·2. $C_{29}H_{34}O_5N_2S_2$ requires C, 62·9; H, 6·1%). Concentration of the mother-liquors gave N-*benzoyl*-N-cyclo*hexyl*-N′-*toluene*-p-*sulphonylethylenediamine* (VII) (1·2 g.), m. p. 117—119° raised to 121—122° (from benzene–light petroleum) (Found: C, 66·0; H, 6·6. $C_{22}H_{28}O_3N_2S$ requires C, 66·0; H, 7·0%). The residual solution was evaporated to dryness. The residue (0·7 g.) had m. p. 105—106° alone or mixed with the monosulphonamide (VII) but depressed the m. p. of the sulphonamide (IX) (below). Treatment of the monosulphonamide (VII) with toluene-*p*-sulphonyl chloride gave the disulphonamide (VIII), m. p. and mixed m. p. 176°.

Part (ii) was basified similarly and extracted with benzene. The extracts were evaporated and the residue (3·4 g.) was heated at 150° for 1 hr. Subsequent treatment with toluene-*p*-sulphonyl chloride (10 g.) gave an oil (4·8 g.) which, with ethanol (10 ml.), gave the disulphonamide (VIII) (0·6 g.), m. p. and mixed m. p. 165—168°. The mother-liquors, in benzene (24 ml.), were poured on an alumina column (25 × 2 cm.). Elution with 1 : 1 benzene–chloroform gave N′-*benzoyl*-N-cyclo*hexyl*-N-*toluene*-p-*sulphonylethylenediamine* (IX) (2·9 g.), m. p. 94—97°, raised to 113—114° (from ethanol) (Found: C, 66·4; H, 7·1%). Further elution gave only yellow gums.

N′-*Benzyloxycarbonyl*-N-cyclo*hexyl*-N-*toluene*-p-*sulphonylethylenediamine* (X).—The urethane (II; $R = C_6H_{11}$) with toluene-*p*-sulphonyl chloride and aqueous sodium hydroxide gave the *sulphonamide*, m. p. 94° (from ethanol) (Found: C, 64·6; H, 7·1. $C_{23}H_{30}O_4N_2S$ requires C, 64·3; H, 7·0%). Removal of the benzyloxycarbonyl group (hydrogen bromide in acetic acid) and subsequent benzoylation of the base (Schotten–Baumann) gave the sulphonamide (IX), m. p. and mixed m. p. 113—114°.

N-*Benzoyl*-N′-cyclo*hexylethylenediamine* (VI; $R = C_6H_{11}$).—*N*-2-Bromoethylbenzamide [19] and *cyclo*hexylamine (40 ml.) were kept at 100° for 50 min. The mixture was poured into dilute hydrochloric acid and extracted with benzene. The aqueous layer was basified with sodium hydroxide and re-extracted with benzene. Distillation of the residue after evaporation of the extracts gave (i) 2-phenyloxazoline (6 g.), b. p. 80°/0·1 mm. (picrate, m. p. 183°; lit.,[20] m. p. 186°), and (ii) the *amino-amide* (5 g.), b. p. 167°/0·01 mm. (Found: N, 11·4. $C_{15}H_{22}ON_2$ requires N, 11·4%). In contact with air the latter compound gave a carbonate, m. p. 58—62°, but of variable composition (Found: N, 10·6, 9·8, 9·4. Calc. for $C_{15}H_{22}ON_2,\frac{1}{2}H_2CO_3$: N, 10·1%). Treatment with toluene-*p*-sulphonyl chloride gave the sulphonamide (IX), m. p. and mixed m. p. 113—114°.

Formation of N-cyclo*Hexyltetrahydro*-2-*oxoglyoxaline* (III).—The base (II; $R = C_6H_{11}$) (1 g.) was heated at 180°/20 mm. Benzyl alcohol (0·4 g.) slowly distilled (b. p. *ca.* 90°; *p*-nitrobenzoate, m. p. and mixed m. p. 83—84°). The residual glyoxaline derivative (0·6 g.) had m. p. 170·5° (from benzene–light petroleum) (Found: N, 16·3. Calc. for $C_9H_{16}ON_2$: N, 16·7%). Abramovitch [21] gives m. p. 166—168°.

N′-*Benzoyl*-N-*benzyloxycarbonyl*-N-cyclo*hexylethylenediamine* (XI; $R = C_6H_{11}$).—*N*-Benzoyl-*N*′-*cyclo*hexylethylenediamine (3·8 g.) and benzyl chloroformate (3·8 ml.) were shaken with 10%

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[20] Goldberg and Kelly, *J.*, 1948, 1919.

[21] Abramovitch, U.S.P. 2,518,264.

aqueous sodium carbonate. Excess of the chloroformate was destroyed by addition of ethereal pyridine. Evaporation of the ethereal extract and distillation of the residue gave the *amido-urethane* (5·7 g.), b. p. 230°/0·02 mm. (Found: C, 72·1; H, 7·3. $C_{23}H_{28}O_3N_2$ requires C, 72·6; H, 7·4%).

NN-*Dibenzoyl*-N′-cyclo*hexylethylenediamine Hydrobromide* (XIII; R = C_6H_{11}).—The amido-urethane (4 g.) in pyridine (10 ml.) was heated with benzoyl chloride (3 ml.) at 100° for 30 min. The mixture was poured into water and extracted with benzene. The extracts were washed successively with 10% aqueous sodium carbonate, dilute hydrochloric acid, and water. Evaporation of the extracts gave a red oil which was treated directly with a 50% solution of hydrogen bromide in acetic acid (15 ml.). When reaction was complete, addition of ether precipitated the *hydrobromide* (4·5 g.), m. p. 190—192° raised, on crystallisation from methanol, to 201—202° (Found: C, 61·2; H, 6·2. $C_{22}H_{27}O_2N_2Br$ requires C, 61·2; H, 6·3%).

Rearrangement of the Base.—The hydrobromide (2·4 g.), suspended in ethanol (5 ml.), was added to 10% aqueous sodium carbonate (20 ml.). The mixture was diluted with water and filtered. The residue, NN′-*dibenzoyl*-N-cyclo*hexylethylenediamine* (1·8 g.), had m. p. 203° raised to 205—206° (from ethanol) (Found: C, 75·0; H, 7·4. $C_{22}H_{26}O_2N_2$ requires C, 75·4; H, 7·4%). The m. p. was undepressed on admixture with the compound, m. p. 205—206°, obtained by benzoylation of *N*-benzoyl-*N′*-*cyclo*hexylethylenediamine (VI).

N′-*Benzoyl*-N-*benzyloxycarbonyl*-N-*phenylethylenediamine* (XI; R = Ph).—Treatment of *N*-benzoyl-*N′*-phenylethylenediamine with benzyl chloroformate as for the *cyclo*hexyl compound gave the *amido-urethane*, m. p. 80° (from benzene–light petroleum) (Found: C, 73·5; H, 6·1; N, 7·3. $C_{23}H_{22}O_3N_2$ requires C, 73·8; H, 5·9; N, 7·5%).

NN-*Dibenzoyl*-N′-*benzyloxycarbonyl*-N′-*phenylethylenediamine* (XII; R = Ph).—Treatment of the previous compound with benzoyl chloride in pyridine at 100° gav ethe NN-*dibenzoyl-amide* (70%), m. p. 133—134° (from ethanol) (Found: C, 75·6; H, 5·4. $C_{30}H_{26}O_4N_2$ requires C, 75·2; H, 5·4%). Treatment of this compound with hydrogen bromide–acetic acid gave NN-*dibenzoyl*-N′-*phenylethylenediamine hydrobromide* (XIII; R = Ph) (80%), m. p. 143° (from ethanol–ether) (Found: C, 62·3; H, 5·3. $C_{22}H_{21}O_2N_2Br$ requires C, 62·1; H, 4·9%).

Rearrangement of the Base.—20% Aqueous sodium hydroxide (5 ml.) was added to the preceding hydrobromide (2 g.) in ethanol (10 ml.), and the mixture was immediately poured into water (400 ml.). Part of the oil which separated was removed and it subsequently solidified (m. p. 143—147°). The remainder was extracted with chloroform. Evaporation of the extracts gave *NN′*-dibenzoyl-*N*-phenylethylenediamine (1·5 g.), m. p. 150° alone or mixed either with an authentic specimen, m. p. 151° (lit.,[19] 147·5°), or with the material of m. p. 143—147°.

N-2-*Benzyloxycarbonylaminoethylphthalimide* (XVII).—Potassium phthalimide (13 g.) and *N*-2-benzyloxycarbonylaminoethyl bromide (21 g.) were heated in xylene (50 ml.) for 5 hr. at 170°. Light petroleum (250 ml.) was added and the suspension was filtered. The residue was washed with water and crystallisation from ethanol gave the *urethane* (6·9 g.), m. p. 166—167° (Found: C, 67·2; H, 4·8. $C_{18}H_{16}O_4N_2$ requires C, 66·7; H, 4·9%).

N-2-*Aminoethylphthalimide.*—Treatment of the urethane with hydrogen bromide gave N-2-*aminoethylphthalimide hydrobromide*, m. p. 272° (from ethanol–ether) (Found: C, 44·5; H, 4·1. $C_{10}H_{11}O_2N_2Br$ requires C, 44·4; H, 3·9%). The hydrobromide (1·3 g.) in water (20 ml.) was treated with 10% aqueous sodium carbonate (10 ml.). The mixture was set aside for 24 hr., then filtration gave a trace of residue which sintered at 275°. The filtrate was treated with an excess of benzoyl chloride, and the product was extracted with chloroform. Evaporation of the extracts gave *NN′*-dibenzoylethylenediamine (0·1 g.), m. p. and mixed m. p. 243—247°. The aqueous solution, acidified and extraction with ether, yielded only benzoic acid, m. p. and mixed m. p. 120°. The residual aqueous solution was basified with sodium carbonate and evaporated to dryness. The residue was extracted with boiling absolute ethanol (50 ml.). Evaporation of the extracts gave a hygroscopic residue (1·3 g.) which gave an *S*-benzylthiuronium salt, m. p. 152° (from ethanol–ether) (Found: C, 60·7; H, 5·0; N, 11·4; S, 6·5. Calc. for $C_{25}H_{24}O_5N_4S$: C, 60·9; H, 4·9; N, 11·4; S, 6·5%).

γ-*Bromobutyranilide.*—γ-Bromobutyric acid, obtained by hydrolysis of γ-butyrolactone with 60% hydrobromic acid,[22] had b. p. 142°/25 mm. (lit.,[23] b. p. 126—129°/7 mm.). γ-Bromobutyryl chloride (from 31·5 g. of acid) in benzene was treated with aniline (38 g.). When reaction was complete, the mixture was washed with hydrochloric acid, and evaporation of the benzene

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[22] Henry, *Compt. rend.*, 1886, **102**, 368.

[23] Marvel and Birkhimer, *J. Amer. Chem. Soc.*, 1929, **51**, 260.

solution under reduced pressure gave the *anilide* (34 g.), m. p. 65—67°, raised to 73—74° (from benzene–light petroleum) (Found: C, 49·8; H, 4·9. $C_{10}H_{12}ONBr$ requires C, 49·6; H, 5·0%).

γ-cyclo*Hexylaminobutyranilide* (XVIII; R = C_6H_{11}).—γ-Bromobutyranilide (34 g.) and *cyclo*hexylamine (60 ml.) were kept at 100° for 50 min. In a preliminary experiment, addition of ether to the mixture gave a precipitate which was washed with water and crystallised from ethanol, to give γ-cyclo*hexylaminobutyranilide hydrobromide*, m. p. 194—195° (Found: C, 56·5; H, 7·3; N, 8·3. $C_{16}H_{25}ON_2Br$ requires C, 56·4; H, 7·1; N, 8·2%). In subsequent experiments, the mixture was poured into 10% aqueous potassium hydroxide (200 ml.), and the suspension was extracted with benzene. The benzene extracts, on being shaken with concentrated hydrochloric acid (75 ml.), gave a precipitate of the *hydrochloride* (17·5 g.), m. p. 226° (from ethanol) (Found: Cl, 12·3. $C_{16}H_{25}ON_2Cl$ requires Cl, 12·0%). Treatment of the hydrochloride with saturated aqueous potassium bromide gave the hydrobromide, m. p. and mixed m. p. 194—195°. The *base*, liberated with aqueous sodium carbonate, had m. p. 83—84° (Found: C, 73·8; H, 8·9; N, 11·1. $C_{16}H_{24}ON_2$ requires C, 73·9; H, 9·3; N, 10·8%).

Formation of N-cyclo*Hexylpyrrolid-2-one*.—*γ-cyclo*Hexylaminobutyranilide (4 g.) was heated at 220°/20 mm. After 2 hr. the distillate was redistilled to give (i) aniline (0·7 g.), b. p. 78°/7 mm., n_D^{15} 1·5860 (benzanilide, m. p. and mixed m. p. 166°), and (ii) N-cyclo*hexylpyrrolid-2-one* (1·4 g.), b. p. 154°/7 mm., n_D^{15} 1·5043 (Found: C, 71·9; H, 10·3; N, 8·2. $C_{10}H_{17}ON$ requires C, 71·9; H, 10·2; N, 8·4%).

Cyclisation of γ-Benzylaminobutyranilide.—γ-Bromobutyranilide (19 g.) and benzylamine (35 ml.) were kept at 100° for 30 min. The mixture was treated as for the *cyclo*hexyl compound; the acid extracts were basified and extracted with benzene. The benzene extracts were evaporated and the residue, after removal of excess of benzylamine under reduced pressure, was dissolved in ether. Saturation of the solution with hydrogen chloride gave a precipitate which was filtered off and washed sparingly with water. The residue, *γ-benzylaminobutyranilide hydrochloride* (3·4 g.), had m. p. 212—213° (from ethanol–ethyl acetate) (Found: C, 66·8; H, 7·1; Cl, 12·2. $C_{17}H_{21}ON_2Cl$ requires C, 67·0; H, 6·9; Cl, 11·7%). The base (2·6 g.), extracted from a basified aqueous solution of the hydrochloride with chloroform, was heated at 160°/7 mm. During 1 hr., aniline (0·8 g.), b. p. 88°/7 mm., n_D^{18} 1·5827, distilled (benzanilide, m. p. and mixed m. p. 166°). The residue (1·8 g.) was distilled to give *N*-benzylpyrrolid-2-one (1·7 g.), b. p. 180°/10 mm., n_D^{22} 1·5490 (Found: N, 7·8. Calc. for $C_{11}H_{13}ON$: N, 8·0%). Hanford and Adams [24] give b. p. 122°/2 mm., n_D^{20} 1·5570.

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[24] Hanford and Adams, *J. Amer. Chem. Soc.*, 1935, **57**, 921.