TABLE I

1,1′-(R)-BIS-(2,5-DIMETHYLPYRROLES)

Where (R) is:	M. p., °C.	B. p. °C.	B. p. Mm.	Crystallizing solvent	Color	Empirical formula	Nitrogen, % Found	Nitrogen, % Found	Nitrogen, % Calcd.
m-Phenylene[1a]	264			Benzene	v.l.tan	$C_{18}H_{20}N_2$	10.49	10.71	10.61
Ethylene[1b]	136.5			Alcohol	v.l.tan	$C_{14}H_{20}N_2$	12.60	12.79	12.95
Hexamethylene	105.5–106.0			Alcohol	v.l.tan	$C_{18}H_{28}N_2$	10.09	10.46	10.29
Nonamethylene		211	2		Colorless	$C_{21}H_{34}N_2$	8.83	8.92	8.92
Decamethylene	68.5– 69.5			Alcohol	v.l.tan	$C_{22}H_{36}N_2$	8.20	8.44	8.55
(1,3-Butylene)		195	23		Yellow	$C_{16}H_{24}N_2$	11.36	11.39	11.48
Propylene	67.5– 68.0	160	8	Alcohol	l.yellow	$C_{15}H_{22}N_2$	12.18	12.21	12.17
(4,4′-Phenoxyphenyl)	178			Me cyclohexane	Brown	$C_{24}H_{24}ON_2$	7.61	7.64	7.65
β,β′-Diethyleneimine	80.0– 80.2			Alcohol	Yellow	$C_{16}H_{25}N_3$	15.99	16.03	16.16

TABLE II

MONO PYRROLES

1-R-2,5-Dimethylpyrroles

Where (R) is:	Empirical formula	M. p., °C.	B. p. °C.	B. p. Mm.	Crystallizing solvent	Color	Nitrogen, % Found	Nitrogen, % Found	Nitrogen, % Calcd.
(*o*-Aminophenyl)[1a]	$C_{12}H_{14}N_2$	77.0			Alcohol	L.brown	14.75	14.96	15.05
(*p*-Aminophenyl)[1a]	$C_{12}H_{14}N_2$	97.5–98.0			Alcohol	L.brown	14.93	14.93	15.05
(*o*-Tolyl)[1b]	$C_{13}H_{15}N$		105	7.5		Colorless	7.55	7.69	7.57
Butyl	$C_{10}H_{17}N$		69	4		Colorless	9.01	9.46	9.28
Amyl	$C_{11}H_{19}N$		80	4		Colorless	8.15	8.15	8.49
Octyl	$C_{14}H_{25}N$		118	4		Colorless	6.63	6.65	6.79
(3-Diethylaminopropyl)	$C_{13}H_{24}N_2$		113	3		Colorless	13.09	13.45	13.46
(β-Hydroxyethyl)[4]	$C_6H_{13}ON$	52.0	106	4	Cyclohexane	Colorless			
(β-Phenylethyl)	$C_{14}H_{17}N$		142	7		Colorless	6.81	6.92	7.04
(3-Phenyl-*n*-propyl)	$C_{15}H_{19}N$		175	14		Colorless	6.43	6.56	6.58
(*p*-Ethylphenyl)	$C_{14}H_{17}N$	57.5–58.0			Alcohol	Colorless	6.90	7.07	7.04
(*p*-Isopropylphenyl)	$C_{15}H_{19}N$		109–110	4		Colorless	6.54	6.60	6.58
(*p*-Cyanomethylphenyl)	$C_{14}H_{14}N_2$	102–103			Alcohol	Gray	13.06	13.49	13.33
(4-Morpholylethyl[2])	$C_{12}H_{20}ON_2$		149	8		Colorless	13.21	13.23	13.46
(*p*-Acetylphenyl)	$C_{14}H_{15}ON$	110–110.5			Alcohol	L.brown	6.53	6.66	6.57
(*p*-Carboxyphenyl)[5]	$C_{13}H_{13}O_2N$	208–209			Cyclohexane	Green-gray	6.38	6.57	6.52
(2,5-Dichlorphenyl)[1b]	$C_{12}H_{11}NCl_2$		139	9		Colorless	5.70	5.88	5.84
Anilino[6]	$C_{12}H_{14}N_2$	115–115.5			Alcohol	Yellow			
(*p*-Phenylazophenyl)	$C_{18}H_{17}N_3$	76.0			Alcohol	Orange-red	15.01	15.05	15.27
(2-Benzothiazolyl)	$C_{13}H_{12}N_2S$	79.0–79.5			Hexane	L.brown	11.99	12.02	12.28

Raney nickel, but with considerable difficulty, several hours at 200° being required. After filtering off the catalyst, the alcohol is evaporated and 1,1′-ethylene-bis-2,5-dimethylpyrrolidine fractionated; $C_{14}H_{28}N_2$, colorless, b. p. 120° at 13 mm. Nitrogen content found was 12.10 and 12.24%; calcd. 12.50%.

As many of the reactions are violently exothermic, due precaution must be exercised when adding the amine to the acetonyl acetone. Often it is necessary to leave the trap out of the system, adding the amine slowly by pouring through the condenser. After the reaction has subsided the trap is connected and the water removed. Also, with low-boiling amines it is necessary to reflux for a sufficient period to complete the reaction before inserting the trap.

Even with mixtures containing 68% aqueous ethylenediamine, this method has proved very satisfactory. Also, this method has the advantage that the pyrrole, either liquid or solid, may be poured from the reaction flask and purified directly, or for practical purposes used without further purification. In these cases the yield is essentially 100%.

Negative results have been encountered in the preparation of dimethyl pyrroles by this method with urea,[1b] thiourea, phenyl thiourea, dicyandiamide, aminoguanidine bicarbonate, hydrazine,[3] melamine, benzene sulfonamide and 2-aminopyridine.

Seven new di-pyrroles and thirteen new mono-pyrroles with their properties and analytical data are listed in the following Tables I and II.

The following 1-R-2,5-dimethylpyrroles have also been prepared but not included in the table for lack of analytical data: R equals, allyl, b. p. 88° (22 mm.); octadecyl, m. p. 38–39°; *p*-hydroxyphenyl, m. p. 105–105.4; 3-hydroxybutyl, b. p. 128(7); and ω-hydroxydiethyleneimine, m. p. 42.5–43.0, b. p. 164°(6).

Appreciation is expressed to Mr. F. C. Koch of these Laboratories for the nitrogen analyses.

(3) Blaise, *Compt. rend.*, **170**, 1324 (1920), believes the reaction product to be a dimer of dimethyl pyridazine.

(4) Knorr and Rabe, German Patent, 116, 335 *Frdl.*, **6**, 1215.

(5) See (1b) who reports a m. p. of 196-198° and pale pink color; Gilman and O'Donnell, THIS JOURNAL, **66**, 840, 1944; m. p. 196–197°.

(6) Knorr, *Ber.*, **22**, 170 (1889), reports m. p. 90–92°.

BELL TELEPHONE LABORATORIES, INC.
MURRAY HILL, NEW JERSEY RECEIVED AUGUST 22, 1945

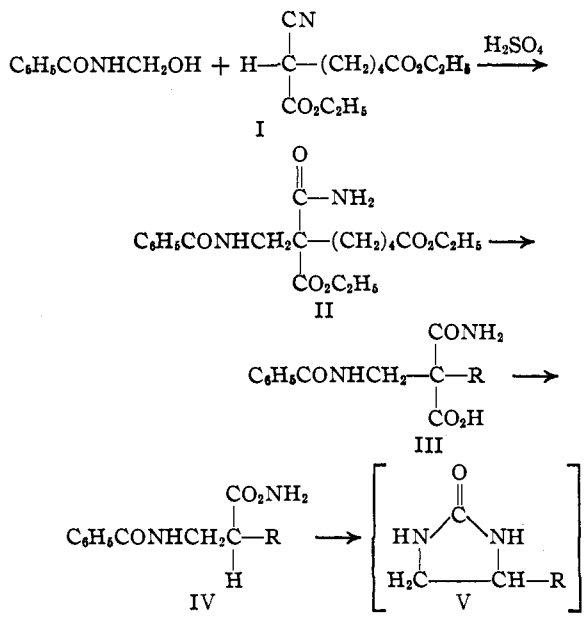
The Preparation of 7-Benzoylamino-6-carbamylheptylic Acid

BY JACKSON P. ENGLISH AND RICHARD C. CLAPP

It seemed possible that nordesthiobiotin (V, R = $(CH_2)_5COOH$)[1] might be synthesized by the

(1) Dittmer and du Vigneaud, *Science*, **100**, 129 (1944).

following series of reactions.



Since a supply of ethyl δ-bromovalerate was available, from which diethyl α-cyanopimelate (I) was readily prepared, the synthesis of the next lower homolog (V, R = $(CH_2)_4COOH$)[1] was attempted. In practice, the conversion of IV (R = $(CH_2)_4COOH$) into V (R = $(CH_2)_4COOH$) was not achieved by the method of Kanewskaja[2] for the conversion of β-benzoylaminopropionamide (IV; R = H) into ethyleneurea (V, R = H). An interesting and efficient synthesis of the penultimate compound IV (R = $(CH_2)_4COOH$) was, however, accomplished.

This synthesis was based on the condensation of N-hydroxymethylbenzamide with diethyl α-cyanopimelate in the presence of concentrated sulfuric acid. Previous instances of the reaction of N-hydroxymethylbenzamide with compounds containing active methylene groups have been reported by Monti.[3]

Experimental[4,5]

Diethyl α-Cyanopimelate (I).—To a solution of 4.25 g. (0.185 atom) of sodium in 230 cc. of absolute alcohol was added 21.4 g. (0.189 mole) of ethyl cyanoacetate (Eastman Kodak Co.) and 39 g. (0.186 mole) of ethyl δ-bromovalerate.[6] After refluxing for three and one-half hours the neutral mixture was concentrated to about one-half its original volume. Water was added and the oily layer which separated was taken up in ether. After washing and drying, the ether was distilled from this solution and the residue was distilled under reduced pressure. The fraction (19.7 g.) boiling from 160 to 200° at 3 mm. was collected. Redistillation gave 16.7 g. (37% yield) of a colorless liquid, b. p. 161–165° (3 mm.).

Anal. Calcd. for $C_{12}H_{19}NO_4$: N, 5.8. Found: N, 5.9, 6.1.

Diethyl α-Benzoylaminomethyl-α-carbamylpimelate (II).—To a mixture of 10 cc. of cold concentrated sulfuric acid and 2.4 g. (0.01 mole) of diethyl α-cyanopimelate, cooled in ice, was added 1.58 g. of N-hydroxymethylbenzamide.[7] The solution was allowed to stand at 5° for fifteen hours and was then poured onto ice. Crystallization of the precipitate from aqueous alcohol gave small white needles; 3.07 g. (91% yield), m. p. 99–102°. This melting point was raised to 103–105° by several further crystallizations.

Anal. Calcd. for $C_{20}H_{28}N_2O_6$: C, 61.2; H, 7.2; N, 7.1. Found: C, 61.8, 61.6; H, 7.4, 7.4; N, 7.3, 7.3.

α-Benzoylaminomethyl-α-carbamylpimelic Acid (III, R = $(CH_2)_4COOH$).—Two grams of II was dissolved in 50 cc. of a solution prepared by shaking absolute alcohol with excess sodium hydroxide pellets for fifteen minutes. A white solid began to precipitate after about ten minutes at room temperature. After standing for fifteen hours water was added and the resulting solution was acidified in the cold. The product precipitated on standing in the cold; 1.44 g. (84% yield), m. p. 176°, dec. Crystallization from water gave fine white needles, m. p. 177°, dec.

Anal. Calcd. for $C_{15}H_{20}N_2O_6$: C, 57.1; H, 6.0; N, 8.3; neut. equiv., 168. Found: C, 56.9; H, 5.8; N, 8.3; neut. equiv., 170.

7-Benzoylamino-6-carbamylheptylic Acid (IV, R = $(CH_2)_4COOH$).—Decarboxylation of 7.11 g. of II began at a bath temperature of 175° and proceeded smoothly while the temperature was held at 175–182°. Approximately one mole of gas was collected. The cooled residue was dissolved in dilute sodium hydroxide and the solution was acidified to precipitate the product. Crystallization from aqueous alcohol gave 4.48 g. (73% yield) of fine white needles. This product did not have a definite melting point after several crystallizations, appearing to melt at 145.5–147°, to resolidify partially and to melt completely at 155–156°.

Anal. Calcd. for $C_{15}H_{20}N_2O_4$: C, 61.6; H, 6.9; N, 9.6; neut. equiv., 292. Found: C, 61.5, 61.7; H, 7.2, 6.9; N, 9.8, 9.6; neut. equiv., 294.

When 7-benzoylamino-6-carbamylheptylic acid reacted with one or two moles of bromine in potassium hydroxide solution,[2] the starting product was recovered. Treatment with larger quantities of bromine and the use of barium hydroxide or of methanolic alkali also failed to effect the reaction.

(2) Kanewskaja, *Ber.*, **69**, 266 (1936).

(3) Monti, *Gazz. chim. ital.*, **60**, 39 (1930); *C. A.*, **24**, 4013 (1930).

(4) All melting points are corrected.

(5) The microanalyses were performed in these Laboratories under the direction of Dr. J. A. Kuck, to whom we are indebted.

(6) Merchant, Wickert and Marvel, THIS JOURNAL, **49**, 1828 (1927).

(7) Einhorn, Bischkopff and Szelinski, *Ann.*, **343**, 207 (1905).

STAMFORD RESEARCH LABORATORIES
AMERICAN CYANAMID COMPANY
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An Improved Synthesis of γ-(3,4-Ureylenecyclohexyl)-butyric Acid

BY J. P. ENGLISH, R. C. CLAPP, Q. P. COLE AND J. KRAPCHO

γ-(3,4-Ureylenecyclohexyl)-butyric acid (VI) had been previously synthesized[1] in the course of work on the preparation of compounds which would inhibit the utilization of biotin by microorganisms. Further quantities of this compound were desired, and the low yield in the first step of the earlier process led to the development of the present method.

The principal new features of this synthesis are contained in the steps leading to the preparation

(1) English, Clapp, Cole, Halverstadt, Lampen and Roblin, THIS JOURNAL, **67**, 295 (1945).