729. *The Synthesis of* DL-*Baikiain.*

By N. A. Dobson and R. A. Raphael.

The synthesis of baikiain (1 : 2 : 3 : 6-tetrahydropyridine-2-carboxylic acid) from but-2-yne-1 : 4-diol is described.

The amino-acid baikiain (XIII) was first isolated from the heartwood of Rhodesian teak (*Baikiaea plurijuga*) by King, King, and Warwick [1] and shown by degradation to be L-1 : 2 : 3 : 6-tetrahydropyridine-2-carboxylic acid. Biogenetically it has been suggested as an intermediary between the 4- and 5-hydroxypipecolic acid.[2] An attempted synthesis of baikiain [1] led only to an impure concentrate in which the required compound was shown by paper chromatography to be present in small amount. Alternative synthetic routes based on acetylenic intermediates were therefore examined.

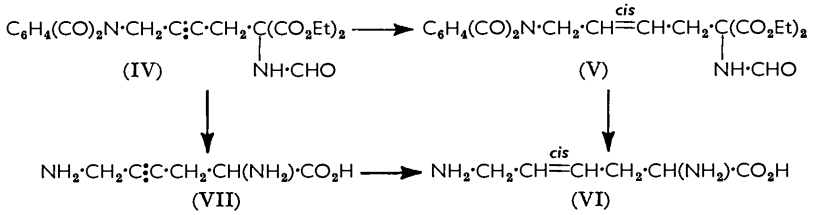
The well-known ready cyclisation of 1 : 5-amino-alcohols to the corresponding piperidines [3] suggested that an analogous dehydration of *cis*-1-amino-5-hydroxypent-3-ene-1-carboxylic acid (III) would proceed with ease to yield baikiain. Accordingly the former compound was synthesised in the following manner. Condensation of 1-benzoyloxy-4-bromobut-2-yne (prepared from but-2-yne-1 : 4-diol by Fraser and Raphael's method [4]) with ethyl sodiophthalimidomalonate produced the expected ester (I) which, by acid

$$\underset{\text{(I)}}{BzO\cdot CH_2\cdot C{:}C\cdot CH_2\cdot C(CO_2Et)_2\,[N(CO)_2C_6H_4]} \longrightarrow \underset{\text{(II)}}{HO\cdot CH_2\cdot C{:}C\cdot CH_2\cdot CH(NH_2)\cdot CO_2H} \longrightarrow \underset{\text{(III)}}{HO\cdot CH_2\cdot \overset{cis}{CH{=}CH}\cdot CH_2\cdot CH(NH_2)\cdot COH_2}$$

hydrolysis, gave the acetylenic acid (II). Partial catalytic hydrogenation of the latter gave the required *cis*-amino-5-hydroxypent-3-ene-1-carboxylic acid (III). The structure of this product was confirmed by its hydrogenation to the known 1-amino-5-hydroxypentane-1-carboxylic acid.[5] All attempts to cyclise the acid (III) by acidic or basic dehydrating agents proved fruitless. That its zwitterion nature was not the prime cause was shown by the similar resistance to dehydration of the methyl ester. The reason is indeed obscure, in view of the successful closely analogous ring closure of 1-amino-4-hydroxybutane-1-carboxylic acid to proline.[6]

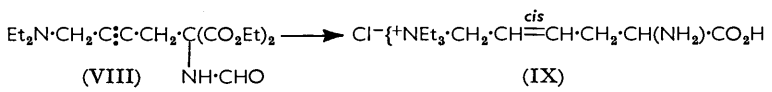
[1] King, King, and Warwick, *J.*, 1950, 3590.
[2] Witkop, *Chem. Soc. Special Publ.* No. 3, 1955, p. 81.
[3] *E.g.*, Woods and Sanders, *J. Amer. Chem. Soc.*, 1946, **68**, 2111.
[4] Fraser and Raphael, *J.*, 1955, 4280.
[5] Gaudry, *Canad. J. Res.*, 1948, **26**, *B*, 387.
[6] Plieninger, *Chem. Ber.*, 1950, **83**, 271.

Another, though less ready, synthesis of piperidine systems, involves the elimination of ammonia from 1 : 5-diamines.[7] The elaboration of the requisite diamino-acid (VI) started from 1 : 4-dichlorobut-2-yne which with one equivalent of potassium phthalimide in dimethylformamide gave a low yield of 1-chloro-4-phthalimidobut-2-yne. Interaction



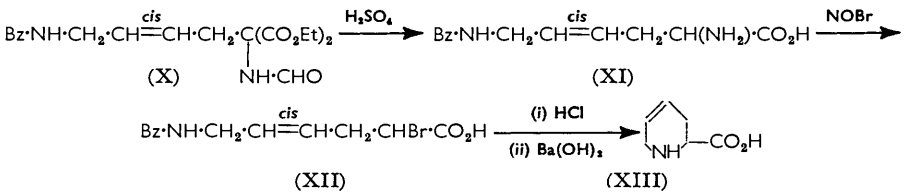
with ethyl sodioformamidomalonate then produced the expected acetylenic ester (IV) which, by partial catalytic hydrogenation, followed by acid hydrolysis of the resulting *cis*-ester (V), gave the required *cis*-1 : 5-diaminopent-3-ene-1-carboxylic acid (VI) best isolated as its crystalline sulphate. The structure was confirmed by catalytic hydrogenation to DL-lysine. That no stereomutation of the *cis*-ethylene had occurred during the relatively drastic hydrolysis was confirmed by hydrolysis of the ester (IV) to the acetylenic diamino-acid (VII) and partial catalytic hydrogenation of this to the same product (VI). Later it was found that the acid (VI) could be obtained more easily in much higher yield by using 1-benzamido-4-chlorobut-2-yne instead of the phthalimido-derivative; this starting material was readily made by treating 1 : 4-dichlorobut-2-yne with hexamine [8] and benzoylating the resulting 1-amino-4-chlorobut-2-yne. Attempts to cyclise the diamino-acid (VI) to baikiain by removing the elements of ammonia failed.

In a variant of this approach the quaternary ammonium chloride (IX) was obtained by interaction of formaldehyde, diethylamine, and ethyl α-formamido-α-propargylmalonate to give the ester (VIII), followed by partial catalytic hydrogenation, quaternisation, and acid-hydrolysis. Treatment of this quaternary salt (IX) with hot alkali did indeed result in the elimination of triethylamine but no baikiain could be detected in the product.



The successful synthesis arose from the observation that, under carefully controlled conditions, selective hydrolysis of diethyl *cis*-5-benzamido-1-formamidopent-3-ene-1 : 1-dicarboxylate (X) to *cis*-1-amino-5-benzamidopent-3-yne-1-carboxylic acid (XI) could be effected in high yield by sulphuric acid. Surprisingly the *free* amino-acid (XI) crystallised from the acid reaction medium.

The free amino-group in (XI) was smoothly replaced by treatment with nitrosyl bromide, to give the crystalline bromo-acid (XII). Hydrolysis of the benzamido-group, followed by base-catalysed elimination of hydrogen bromide, then furnished a crystalline



product identical with baikiain in melting point, chromatographic behaviour, ninhydrin coloration, and infrared absorption. The *N*-benzoyl derivatives of the synthetic and the

[7] Elderfield, " Heterocyclic Compounds," Vol. I, Chapman and Hall Ltd., London 1950, p. 642 *et seq.*

[8] Marszak-Fleury, *Compt. rend.*, 1955, **241**, 752.

natural product were also identical in m. p., mixed m. p., and infrared spectra. The *N*-benzoyl derivative was also obtained by the direct cyclisation of the benzamido-acid (XII) with barium hydroxide. The absence of depression in melting point in mixtures of the synthetic DL- and the natural L-baikiain and of the corresponding derivatives seems to indicate that the optical enantiomorphs of baikiain and its derivatives form a continuous series of mixed crystals, the racemic form being neither a eutectic nor a true compound. The overall yield of DL-baikiain from but-2-yne-1 : 4-diol in seven stages was over 6%.

Experimental

Diethyl 5-Benzoyloxy-1-phthalimidopent-3-yne-1 : 1-dicarboxylate (I).—To a solution of sodium (2·22 g.) in dry ethanol (200 ml.) ethyl phthalimidomalonate [9] (29·4 g.) was added and the mixture heated for 1 hr. The solvent was taken off under reduced pressure and the ethanol of crystallisation removed by heating the residual solid for 1 hr. at 150°/0·5 mm. The sodio-derivative thus formed was finely powdered and suspended in dry toluene (500 ml.). 1-Benzoyloxy-4-bromobut-2-yne [4] (20·4 g.) was added and the mixture heated under reflux for 72 hr. After hot filtration through charcoal the solution was acidified with acetic acid (2 ml.). The cooled solution was washed with N-sulphuric acid and sodium hydrogen carbonate solution, dried ($MgSO_4$), and evaporated, to give a semi-solid residue which was dissolved in ethanol (40 ml.) and cooled to −15°. The almost pure *ester* (I) (26·5 g., 69%) crystallised; an analytical sample crystallised from *n*-butyl ether as plates, m. p. 63—64° (Found: C, 65·2; H, 4·7. $C_{26}H_{23}O_8N$ requires C, 65·4; H, 4·8%).

1-*Amino-5-hydroxypent-3-yne-1-carboxylic Acid* (II).—The ester (I) (6·7 g.) was heated in ethanol (50 ml.) and 12N-hydrochloric acid (10 ml.) under reflux for 9 hr. with further additions of 12N-hydrochloric acid at 30-minute intervals (10 × 10 ml.). The filtered mixture was reduced to 5 ml. under reduced pressure and the hygroscopic amino-acid hydrochloride precipitated by addition of acetone (150 ml.). This was dissolved in a little water and treated with ion-exchange resin (Amberlite IR-4B) until the solution was neutral. Evaporation of the filtrate under reduced pressure gave a residue of the crude amino-hydroxy-acid contaminated with a little glycine; this impurity was conveniently removed by sublimation at 180°/10^{-5} mm. Crystallisation of the residue from methanol furnished the pure *amino-hydroxy-acid* (II) as needles (1·5 g., 75%), m. p. 192° (decomp.) (Found: C, 50·0; H, 6·5; N, 9·3. $C_6H_9O_3N$ requires C, 50·3; H, 6·3; N, 9·7%). Microhydrogenation showed 2·2 double bonds. The corresponding 3-*phenyl-2-thiohydantoin* prepared by Edman's technique [10] crystallised from water in pale-yellow prisms, m. p. 171—172° (Found: N, 10·8. $C_{13}H_{12}O_2N_2S$ requires N, 10·8%).

cis-1-*Amino-5-hydroxypent-3-ene-1-carboxylic Acid* (III).—A solution of the acetylenic acid (II) (1·086 g.) in water (20 ml.) was catalytically hydrogenated (10% palladium–charcoal) until 1 mol. of hydrogen had been absorbed. Filtration, evaporation, and crystallisation of the residue from methanol gave the ethylenic *acid* (III), m. p. 227° (decomp.) (Found: C, 49·6; H, 7·9; N, 9·7. $C_6H_{11}O_3N$ requires C, 49·6; H, 7·6; N, 9·7%). Complete hydrogenation of this in water using Adams catalyst gave 1-amino-5-hydroxypentane-1-carboxylic acid, crystallising from water in needles, m. p. 254—260° (decomp.) [lit.,[5] m. p. 260—262° or 245—248° (decomp.) depending on the rate of heating]. The phenylureido-derivative crystallised from water in plates, m. p. 138° (lit.,[5] m. p. 141°) (Found: N, 10·8. Calc. for $C_{13}H_{18}O_4N_2$: N, 10·5%).

The following methods of converting the amino-hydroxy-acid (III) into baikiain were tried without success; pyrolysis of the acid and its methyl ester, hot acid and alkaline treatment of the acid, fusion with urea, ammonium carbonate, or zinc chloride, and treatment with phosphoric oxide in triethylamine.

1-*Chloro-4-phthalimidobut-2-yne*.—A stirred solution of 1 : 4-dichlorobut-2-yne [11] (57 g.) in dimethylformamide (350 ml.) was heated at 95° and powdered potassium phthalimide (88 g.) was added during 2 hr.; heating and stirring were continued for a further 8 hr. Water (1·5 l.) was added to the cooled mixture, and the filtered solid washed with water. This product (*ca.* 160 g.) was heated with glacial acetic acid (300 ml.) and filtered hot. Most of the 1 : 4-diphthalimidobut-2-yne [12] remained undissolved and was filtered off; the cooled solution

[9] Osterberg, *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 271.
[10] Edman, *Acta Chem. Scand.*, 1950, **4**, 277.
[11] Johnson, *J.*, 1946, 1009.
[12] Fraser and Raphael, *J.*, 1952, 226.

deposited more of this compound. To the filtrate water (1 l.) was added and the precipitated solid filtered off and crystallised from ethanol; the pure 1-*chloro*-4-*phthalimidobut*-2-*yne* (30—40%) formed pale yellow needles, m. p. 116—117° (Found: C, 62·0; H, 3·4. $C_{12}H_8O_2NCl$ requires C, 61·7; H, 3·4%).

Diethyl 1-*Formamido*-5-*phthalimidopent*-3-*yne*-1 : 1-*dicarboxylate*.—Ethyl formamidomalonate (16·3 g.) was added to ethanol (300 ml.) in which sodium (1·84 g.) had been dissolved, and the solution warmed at 50° for 1 hr. 1-Chloro-4-phthalimidobut-2-yne (18·7 g.) was added and the stirred mixture heated under reflux for 14 hr. The volume was reduced to 100 ml. and acetic acid (1 ml.) added. Addition of water precipitated the crude product as an oil which became semi-solid after some time at 0°. Crystallisation proved difficult and tedious but the pure *ester* (IV) (30—40%) was finally obtained as needles, m. p. 122° [from light petroleum (b. p. 60—80°)–ethanol (9 : 1)] (Found: C, 60·1; H, 4·8. $C_{20}H_{20}O_7N_2$ requires C, 60·0; H, 5·0%). The sodium hydride method (see below) gave a lower yield.

Diethyl cis-1-*Formamido*-5-*phthalimidopent*-3-*ene*-1 : 1-*dicarboxylate* (V).—A solution of the acetylenic ester (IV) (7·1 g.) in ethyl acetate (150 ml.) was subjected to partial catalytic hydrogenation in the presence of Lindlar catalyst [13] (2 g.). Removal of catalyst and solvent, followed by crystallisation of the residue from light petroleum (b. p. 60—80°)–ethanol (9 : 1), gave the *cis*-ethylenic *ester* (6·6 g., 92%) as needles, m. p. 110° (Found: C, 59·5; H, 5·3. $C_{20}H_{22}O_7N_2$ requires C, 59·7; H, 5·5%).

Dihydrochloride of 1 : 5-*Diaminopent*-3-*yne*-1-*carboxylic Acid* (VII).—The acetylenic ester (IV) (5 g.) was heated under reflux for 6 hr. with 6N-hydrochloric acid (40 ml.). The volume was reduced to 10 ml. under reduced pressure and the phthalic acid was filtered off. After further concentration of the filtrate to 3 ml. the crude product was precipitated by addition of acetone. Crystallisation from aqueous ethanol (90%) gave the *diamino-acid dihydrochloride* (2·04 g., 76%) as needles, m. p. 192—194° (decomp.) with preliminary softening at 120—140° (Found: C, 33·7; H, 5·65; N, 13·05. $C_6H_{10}O_2N_2,2HCl$ requires C, 33·7; H, 5·85; N, 13·05%). The NN′-*dibenzoyl derivative* prepared by the Schotten–Baumann procedure crystallised from aqueous ethanol as prisms, m. p. 176° (Found: N, 8·2. $C_{20}H_{18}O_4N_2$ requires N, 8·0%).

Salts of cis-1 : 5-*Diaminopent*-3-*ene*-1-*carboxylic Acid* (VI).—(*a*) The *cis*-ethylenic ester (V) (1·6 g.) was heated under reflux for 6 hr. with dilute sulphuric acid (2 ml. of concentrated acid and 17 ml. of water). The volume was then reduced under reduced pressure to 4 ml.; cooling to 0° precipitated phthalic acid which was filtered off. Ethanol (75 ml.) was added to the filtrate and the solution set aside at −5° for 48 hr. The resulting solid was purified by dissolution in the minimum quantity of hot water and addition of boiling ethanol until a turbidity was formed. Slow cooling then gave the *diamino-acid sulphate* (0·57 g., 59%) as feathery needles, m. p. 235° (decomp.) (Found: C, 29·8; H, 6·1; N, 11·7. $C_6H_{12}O_2N_2,H_2SO_4$ requires C, 29·8; H, 5·8; N, 11·6%). The NN′-*dibenzoyl derivative*, prepared by the Schotten–Baumann procedure, yielded prisms, m. p. 180—181° (from water) (Found: N, 8·1. $C_{20}H_{20}O_4N_2$ requires N, 7·95%). Complete hydrogenation of the sulphate in water over palladium–charcoal, followed by benzoylation, gave *NN′*-dibenzoyl-DL-lysine, crystallising from aqueous acetone (90%) in needles, m. p. 145—146° (lit.,[14] m. p. 145—146°).

(*b*) A solution of the dihydrochloride (3·93 g.) of the acetylenic diamino-acid (VII) in water (40 ml.) was catalytically hydrogenated over 10% palladium–charcoal (1 g.). After absorption of 1 mol. of hydrogen and removal of catalyst the filtrate was reduced to 5 ml. under reduced pressure. Addition of acetone (100 g.) then precipitated an oil which solidified on being warmed with ethanol. Crystallisation from aqueous ethanol (95%) gave the *diamino-acid monohydrochloride* (1·57 g., 53%) as prisms, m. p. 257—258° (decomp.) (Found: C, 39·9; H, 7·0; N, 15·6. $C_6H_{12}O_2N_2,HCl$ requires C, 39·9; H, 7·25; N, 15·5%). Addition of acetone to the crystallisation mother-liquors precipitated an extremely hygroscopic solid (1 g.) which was shown by a chlorine estimation to be mainly composed of the corresponding dihydrochloride. This hygroscopic dihydrochloride was also obtained by hydrochloric acid hydrolysis of the ethylenic ester (V). Both hydrochlorides gave the same *NN′*-dibenzoyl derivative identical with that prepared from the sulphate as in (*a*), and both were converted into this sulphate by successive treatment with ammonia and sulphuric acid.

Attempts to cyclise the diamino-acid salts to baikiain by methods similar to those detailed above for the corresponding hydroxyamino-acid were unsuccessful. In addition, treatment of

[13] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.
[14] von Braun, *Ber.*, 1909, **42**, 845.

the diamino-acid monohydrochloride with nitrosyl chloride under conditions similar to those used to convert lysine into pipecolic acid [15] gave no detectable trace of baikiain.

Diethyl cis-5-*Diethylamino*-1-*formamidopent*-3-*ene*-1 : 1-*dicarboxylate*.—A solution of ethyl α-formamido-α-propargylmalonate [16] (8 g.) and diethylamine (3 g.) in dioxan (10 ml.) was heated with paraformaldehyde (1·5 g.) in a sealed tube by steam for 12 hr. The dioxan was removed under reduced pressure, the residue dissolved in ether, and the solution filtered from a small amount of gum. The ether was evaporated off and the residue heated at 100° under a high vacuum for 30 min. On cooling, the residue solidified and crystallised from benzene–light petroleum (b. p. 60—80°), to give *diethyl* 5-*diethylamino*-1-*formamidopent*-3-*yne*-1 : 1-*dicarboxylate* (VIII) (68%) as prisms, m. p. 70°, readily soluble in dilute acid (Found: C, 58·8; H, 7·9; N, 9·0. $C_{16}H_{26}O_5N_2$ requires C, 58·9; H, 8·0; N, 8·6%). This material was partially catalytically hydrogenated in ethyl acetate with 10% palladium–charcoal. Removal of catalyst and solvent gave a gum which slowly solidified. Crystallisation from benzene–light petroleum (b. p. 60—80°) gave the cis-*ester* as cream needles, m. p. 73—74° (Found: C, 58·6; H, 8·7; N, 8·3. $C_{16}H_{28}O_5N_2$ requires C, 58·5; H, 8·6; N, 8·5%). Heating this ester with ethanolic ethyl iodide gave the corresponding quaternary salt which was then hydrolysed by hot hydrochloric acid to the hygroscopic *N*-(5-amino-5-carboxypent-2-*cis*-enyl)triethylammonium chloride (IX). This product was unaffected by warm 0·5N- or N-alkali but 50% aqueous sodium hydroxide at 100° caused rapid evolution of triethylamine. Paper-chromatographic investigation of the product showed no trace of baikiain.

1-*Benzamido*-4-*chlorobut*-2-*yne*.—Hexamine (14 g.), 1 : 4-dichlorobut-2-yne (12·3 g.), and chloroform (100 ml.) were heated under reflux for 20 min., then cooled. The hexamine complex was filtered off; evaporation of the filtrate to smaller bulk gave a second crop (total yield, 93%). The product formed white irregular crystals, m. p. 200—210° (with discoloration after 185°) (Found: N, 20·6. Calc. for $C_{10}H_{16}N_4Cl_2$: N, 20·9%). A solution of the complex (128 g.) in ethanol (960 ml.) was shaken for 24 hr. at room temperature with concentrated hydrochloric acid (170 ml.). The precipitate of ammonium chloride was filtered off and the filtrate concentrated under reduced pressure until crystallisation was incipient. Addition of dry ether then precipitated the hydrochloride (55 g., 74%) of 1-amino-4-chlorobut-2-yne as white plates; purification was attained by dissolution in the minimum quantity of ethanol and precipitation by ether (Found: C, 34·0; H, 5·2; N, 9·7. Calc. for C_4H_6NCl,HCl: C, 34·3; H, 5·05; N, 10·0%). The amine hydrochloride (120 g.) was dissolved in water (500 ml.). 30% Sodium hydroxide solution (2·5 mols.) was then added, followed immediately by benzoyl chloride, with vigorous shaking and cooling. Care was taken that the mixture remained alkaline throughout the reaction. After 15 minutes' further shaking the initially oily precipitate solidified and was filtered off, washed with water, and dried in a vacuum-desiccator. Crystallisation from benzene–*cyclo*hexane (1 : 3) gave 1-*benzamido*-4-*chlorobut*-2-*yne* (147 g., 82%) as white plates, m. p. 95—96° (Found: C, 63·4; H, 4·75; N, 6·5. $C_{11}H_{10}ONCl$ requires C, 63·4; H, 4·85; N, 6·7%).

Diethyl 5-*Benzamido*-1-*formamidopent*-3-*yne*-1 : 1-*dicarboxylate*.—To a suspension of sodium hydride (3·84 g.) in dry benzene (10 ml.) was added a solution of ethyl formamidomalonate (29·2 g.) in benzene (50 ml.) and the mixture stirred at gentle reflux for 30 min. A solution of 1-benzamido-4-chlorobut-2-yne (29·2 g.) in benzene (50 ml.) was then added and refluxing continued for 5 hr. A small quantity of ethanol was then added to the cooled solution to decompose excess of hydride, followed by water (100 ml.). Sometimes the product crystallised almost immediately; where this did not occur the benzene layer was separated and evaporated to half its bulk. The separated *ester* (74%) was filtered off and crystallised from benzene as needles, m. p. 134° (Found: C, 61·3; H, 5·95; N, 7·6. $C_{19}H_{22}O_6N_2$ requires C, 61·0; H, 5·9; N, 7·5%).

Diethyl cis-5-*Benzamido*-1-*formamidopent*-3-*ene*-1 : 1-*dicarboxylate* (X).—A solution of the corresponding acetylenic ester (7·5 g.) in ethyl acetate (150 ml.) was partially catalytically hydrogenated with 10% palladium–charcoal (0·5 g.). After 1 mol. of hydrogen had been absorbed, catalyst and solvent were removed to give the product which rapidly solidified. Crystallisation was best effected by dissolution in a small quantity of warm benzene followed by addition of 5 volumes of dry ether. At 0° the ethylenic *ester* (X) (93%) crystallised as needles or rods, m. p. 85° (Found: C, 60·5; H, 6·15; N, 7·65. $C_{19}H_{24}O_6N_2$ requires C, 60·6; H, 6·4;

[15] Schiedt and Hoss, *Z. physiol. Chem.*, 1957, **308**, 179.
[16] Gerston, Shapira, Meek, and Dittmar, *J. Amer. Chem. Soc.*, 1954, **76**, 3484.

N, 7·45%). Complete hydrogenation of a small quantity of this material gave the corresponding saturated *ester*, prisms, m. p. 83° (from benzene) (Found: C, 60·4; H, 6·75; N, 7·3. $C_{19}H_{26}O_6N_2$ requires C, 60·3; H, 6·9; N, 7·4%). Acid hydrolysis of the latter, followed by benzoylation, gave *NN'*-dibenzoyl-DL-lysine, m. p. and mixed m. p. 143—144°.

cis-1-*Amino*-5-*benzamidopent*-3-*ene*-1-*carboxylic Acid* (XI).—The *cis*-ester (X) (5·5 g.) was heated under reflux with dilute sulphuric acid (15 g. of concentrated acid and 100 ml. of water) for 2·5 hr. and the solution then chilled. The precipitated benzoic acid was filtered off and the filtrate extracted with ether. The total amount of benzoic acid thus obtained showed that there had been about 18% hydrolysis of the benzoyl group. The bulk of the sulphuric acid in the solution was removed by the addition of 95% of the theoretical amount of warm barium hydroxide solution. The acidic filtrate was evaporated to small bulk under reduced pressure and the product (2·5 g., 68%) crystallised from the chilled concentrate. The *amino-acid* (XI) crystallised from water in plates, m. p. 234° (Found: C, 62·6; H, 6·3; N, 10·9. $C_{13}H_{16}O_3N_2$ requires C, 62·9; H, 6·5; N, 11·3%). The *benzoyl derivative* crystallised from water in prisms, m. p. 183—185° (Found: C, 68·4; H, 5·7; N, 7·95. $C_{20}H_{20}O_4N_2$ requires C, 68·2; H, 5·7; N, 7·95%). Catalytic hydrogenation of this derivative gave *NN'*-dibenzoyl-DL-lysine.

cis-1-*Bromo*-5-*benzamidopent*-3-*ene*-1-*carboxylic Acid* (XII).—To a chilled (0°) solution of the *cis*-amino-acid (XI) (1·24 g.) in 2·5N-sulphuric acid (10 ml.) containing potassium bromide (2 g.), sodiium nitrite (0·55 g.) was added in portions during 30 min. The precipitated gum was isolated with ether and slowly solidified on being set aside. Crystallisation from benzene gave the *bromo-acid* (XII) (58%) as needles, m. p. 103—104° (Found: C, 49·8; H, 4·45; N, 4·7. $C_{13}H_{14}O_3NBr$ requires C, 50·0; H, 4·5; N, 4·5%).

DL-*Baikiain* (XIII).—The above bromo-acid (XII) (0·6 g.) was heated under reflux for 12 hr. with 10% hydrochloric acid (10 ml.). The mixture was evaporated under reduced pressure and the residue washed with dry ether. It was then dissolved in a little water and neutralised with ion-exchange resin (Amberlite IR-4B). After removal of the resin the filtrate was treated with N-barium hydroxide (10 ml.) and warmed at 50° for 30 min. A slight excess of 2N-sulphuric acid was then added, the barium sulphate removed, and the filtrate neutralised with resin (Amberlite IR-4B). The neutral solution was evaporated to dryness and the resulting solid dissolved in methanol and reprecipitated with acetone. Crystallisation from methanol gave DL-*baikiain* (51%) as prisms, m. p. 273—274° (decomp.) undepressed on admixture with authentic L-baikiain [m. p. 273—274° (decomp.)]. The infrared absorption curves of the two compounds in potassium bromide discs were identical. Paper chromatograms of the natural and the synthetic compound, with aqueous phenol as the mobile phase, gave spots identical in position, shape, and ninhydrin coloration. Benzoylation of the synthetic amino-acid gave N-*benzoyl*-DL-*baikiain*, crystallising from ethyl acetate in prisms, m. p. 179—180°, undepressed on admixture with *N*-benzoyl-L-baikiain, m. p. 178—179° (Found: C, 67·6; H, 5·4; N, 5·75. $C_{13}H_{13}O_3N$ requires C, 67·5; H, 5·65; N, 6·05%). The same derivative was obtained (23%) by direct dehydrobromination of the bromo-acid (XII) with barium hydroxide. Hydrolysis of the benzoyl derivative with hot 20% hydrochloric acid gave DL-baikiain hydrochloride (87%), m. p. 264° (decomp.) (from ethanol–ether). The m. p. was undepressed by admixture with L-baikiain hydrochloride [m. p. 264° (decomp.)].

We thank Dr. M. M. Fraser for assistance in the initial stages of this work and Dr. F. E. King, F.R.S., for kindly providing samples of L-baikiain and its derivatives. We are also indebted to the Colonial Products Council for a studentship (N. A. D.), to the Chemical Society for a research grant, and to the Rockefeller Foundation for an equipment grant.

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[*Received, May 21st,* 1958.]