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Chemistry of Amino Acids. IV.[1] Decarboxylation of 1,2,3,4-Tetrahydroisoquinoline-3-carboxylic Acid and Its Derivatives[2]

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Decarboxylation of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivatives, I, II, III, IV and IV hydrochloride, in acetophenone and benzaldehyde as solvents, was examined. It was found that in the case of IV hydrochloride, 4-substituted isoquinoline derivatives were formed in moderate yield according to the solvent used.

It is well known that amino acids are readily decarboxylated by enzymes in a living body.[4] But satisfactory results are not necessarily obtained by chemical decarboxylation of amino acids, in spite of the fact that numerous modifications have been reported.[5]

We have been studying how to utilize the amino acids especially optically active ones, now being produced cheaply, as the starting materials for the synthesis of various kinds of optically and biologically active compounds, such as chloramphenicol from L-phenylalanine,[6] and l-norephedrine from D-phenylalanine.[7]

Compounds containing the 1,2,3,4-tetrahydroisoquinoline structure bearing asymmetric center at the position 1, have been of great interest in connection with their occurrence in certain alkaloids and their biological activities. If the decarboxylation of 1-substituted 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivatives proceeds smoothly, the corresponding 1,2,3,4-tetrahydroisoquinoline derivatives are to be easily prepared from phenylalanine derivatives.

This paper, aiming at this point, reports a preliminary attempt which has been made to investigate the chemical decarboxylation of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (I) and its derivatives (II—IV) as the model compounds.

K. Dose[8] reported that amines were obtained in good yield by refluxing the corresponding amino acids with *p*-dimethylaminobenzaldehyde in nitrobenzene. Later, G. Chatelus[9]

1) Part III: *Chem. Pharm. Bull.* (Tokyo), **15**, 1948 (1967).
2) This work was presented at the Annual Meeting of Pharmaceutical Society of Japan, October, 1965, Tokushima.
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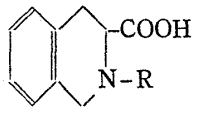
4) J.P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," Vol. 1, John Wiley & Sons, Inc., New York, 1961, p. 593.
5) E. Waser, *Helv. Chim. Acta.*, **8**, 758 (1925); H. Hunsdiecker, C. Hunsdiecker, and E. Vogt, U.S.P 2,176,181 (1939), [*C.A.*, 34, 1685 (1940)]; A. Schönberg and R. Moubacher, *Chem. Rev.*, **50**, 261 (1952); S. Kanao and K. Shinozuka, *Yakugaku Zasshi*, **67**, 218 (1947); S. Kanao, *Yakugaku Zasshi*, **67**, 243 (1947); T. Suyama and S. Kanao, *Yakugaku Zasshi*, **84**, 1012, 1014 (1964), **85**, 531 (1965); K. Heyns and K. Stange, Z. Naturforsch., **7b**, 677 (1952), **10b**, 129, (1955), **10b**, 245 (1955); E.W. Chappelle and J.M. Luck, *J. Biol. Chem.*, **229**, 171 (1957); N. Königsberg, G. Stevenson, and J.M. Luck, *J. Biol. Chem.*, **235**, 1341 (1960); G.W. Stevenson and J.M. Luck, *J. Biol. Chem.*, **236**, 715 (1961); M, Mazelis, *Nature*, **189**, 305 (1961); A.F. Beecham, *J. Am. Chem. Soc.*, **79**, 3257 (1957); S. Emoto, *Nippon Nôgei Kagaku Kaishi*, **35**, 667 (1961).
6) S. Yamada, K. Koga, and H. Matsuo, *Chem. Pharm. Bull.* (Tokyo), **11**, 1140 (1963).
7) K. Koga, H. Matsuo, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **14**, 243 (1966).
8) K. Dose, *Ber.*, **90**, 1251 (1957).
9) G. Chatelus, *C.r.*, **248**, 690 (1959).

also showed that the decarboxylation occurred smoothly by refluxing amino acids with acetophenone at 150°, and J.W. Clark-Lewis, *et al.*[10] obtained 4-hydroxypiperidine from 4-hydroxypipecolic acid in 38% yield by the modification of the method of G. Chatelus.

Table I



I : R=H
II : R=-CO·CH$_3$
III : R=-CO·C$_6$H$_5$
IV : R=CH$_3$

Run	Compound	Reaction Temperature (°C)	Reaction Time (hr)	Percentage of Decarboxylation (%)	Products and Yield
1	I	150	2.5	80	Isoquinoline 16% Tetrahydroisoquinoline 15% Picrate mp 156—157°C
2	I-HCl	150	6.0	80	Tetrahydroisoquinoline 32% Picrate (13%) mp 157—158.5°C
3	II	150—170	18.0	30	Recovery of starting material 54% Picrate (15%) mp 159—161°C
4	III	150—180	5.0	13	Recovery of starting material 60%
5	IV	190—210	3.5	25	Recovery of starting material 77%
6	IV-HCl	190	9.0	70	4-(α-phenethyl)isoquinoline 60% Picrate mp 159—161°C

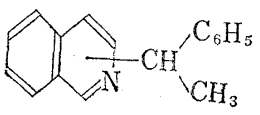
a) temperature of oil bath *b*) measured by the weight of $BaCO_3$

Compound I is considered to be a kind of cyclic α-amino acid, and decarboxylation of I and its derivatives II, III and IV, was investigated according to some modifications of the Chatelus procedure. The results are shown in Table I.

The considerable differences observed in the decarboxylation of tetrahydroisoquinoline derivatives, I—IV, should be noted. The tetrahydroisoquinoline-3-carboxylic acid (I) and its hydrochloride proved to be decarboxylated at a relatively low temperature (150°) to afford tetrahydroisoquinoline in 15% and 30% yields, respectively under 80% of CO_2 evolution per mole of amino acids. Although the reaction was performed in a nitrogen atmosphere, the oxidized product, isoquinoline, was also formed in 16% yield in the case of I. On the other hand in the case of I hydrochloride only a detectable amount of isoquinoline was observed in the ultraviolet (UV) spectrum. In addition to these products, a small amount of a base which formed picrate mp 156—158° was obtained through alumina chromatography.

Decarboxylation of 2-acyl derivatives, such as 2-acetyl (II), and 2-benzoyl (III) derivatives, was found to be much more difficult than that of I and its hydrochloride. They were not decarboxylated at 150°, and the amount of CO_2 evolved was only 10—30% with more than half of the starting material recovered even at 150—180°. These facts suggested that an introduction of an acyl group at the N atom made it difficult to permit decarboxylation.

Decarboxylation of 2-methyl derivative (IV) and its hydrochloride was also difficult, they did not undergo decarboxylation below 190°. The free amino acid IV did not give a definite product except for the recovery of the starting material and evolution of CO_2 was only 25%. However, in the case of IV hydrochloride, evolution of CO_2 began to take place gradually at 190° and the CO_2 evolved was about 70% of the theoretical amount for 9 hours. Basic colorless crystals were obtained as a main product having a melting point of 86°. This base formed picrate mp 159—161°, identical with those obtained from the decarboxylation of I, I hydrochloride and II as a



Compound A

10) J.W. Clark-Lewis and P.I. Mortimer, *J. Chem. Soc.*, **1961**, 189.

small amount of by-product (Table I). Elementary analysis and molecular weight determination by the Rast method showed its composition to be $C_{17}H_{15}N$. The UV spectrum of this compound had λ_{max}^{EtOH} (log ε) 284 (3.22), 308 (3.20), 322 (3.26), and no C=O absorption was observed in the IR spectrum. Thus the structure of this compound would be supposed to be compound A.

No derivative bearing the α-phenethyl group at 1, 3 or 4 position of isoquinoline has been previously reported, whereas, isoquinoline derivatives substituted at 1, 3 or 4 position by a benzyl group have been already reported,[11-14] the UV spectra of which are listed in Table II.

Table II

Compound	mμ (log ε)		
Isoquinoline	267 (3.55)	305 (3.36)	317 (3.51)
1-Benzylisoquinoline[11]	271 (3.76)	310 (3.55)	321 (3.60)
2-Benzylisoquinolinium Salt[a]	270 (3.69)	278 (3.69)	338 (3.69)
3-Benzylisoquinoline[12]	259.5 (3.63)	312 (3.44)	323 (3.50)
4-Benzylisoquinoline[13]	273 (3.25)	308 (3.20)	322 (3.26)
Compound A	273 (3.25)	308 (3.20)	323 (3.26)

a) UV spectrum of this compound was measured as perchlorate prepared by the procedure described in Experimental.

In order to obtain structural information, the UV spectrum of compound A was compared with those of the above mentioned benzyl-substituted isoquinoline derivatives. The spectrum of compound A was found to be quite similar to that of 4-benzylisoquinoline, therefore it may be posited that an α-phenethyl group of compound A should be attached at the 4 position of isoquinoline nuclei.

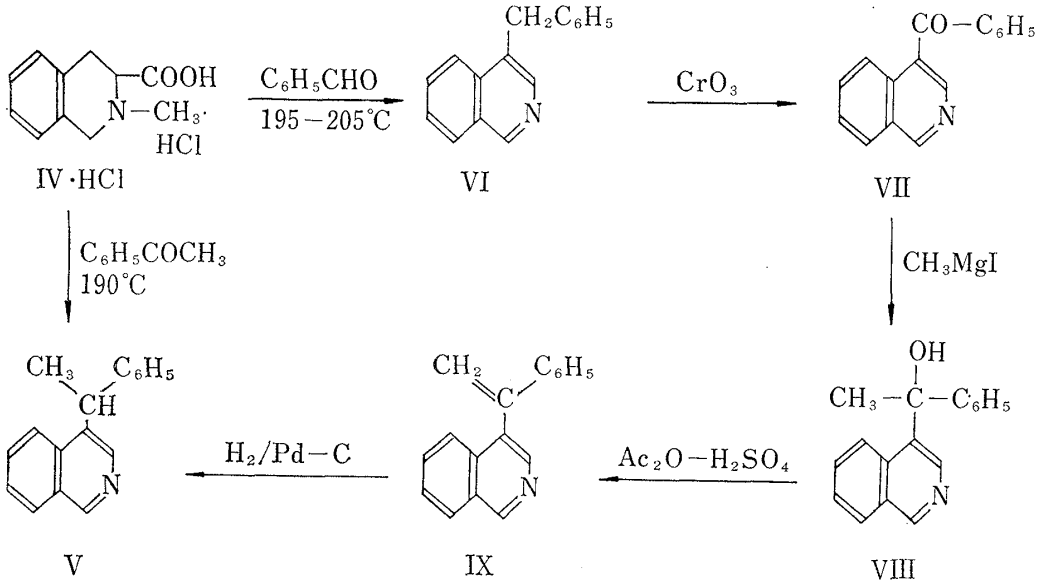
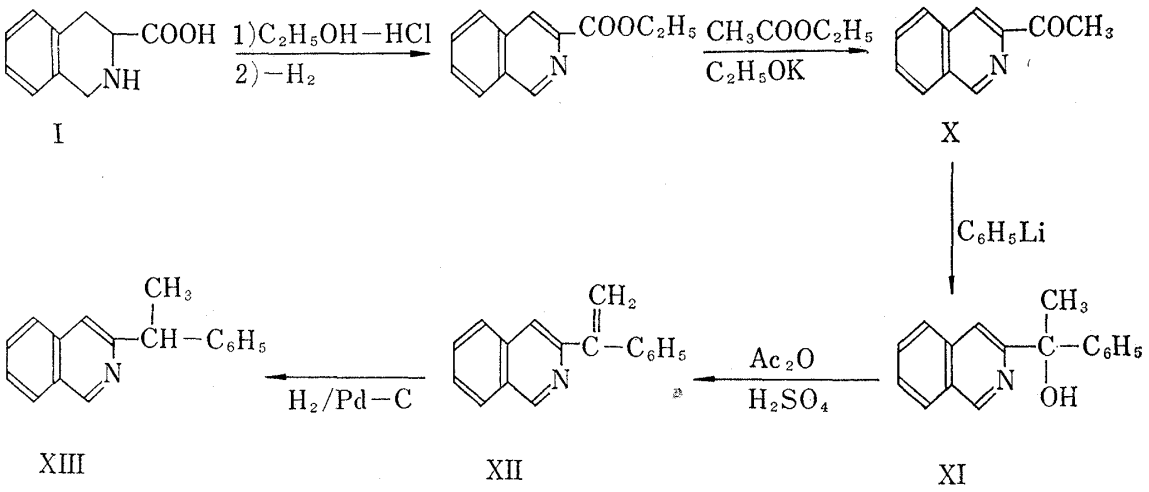


Chart 1

11) C.I. Brodrick and W.F. Short, *J .Chem. Soc.*, **1949**, 2587.
12) T. Haginiwa, I. Murakoshi, and Y. Ôbe, *Yakugaku Zasshi*, **79**, 1578 (1959).
13) M. Avramoff and Y. Sprinzak, *J. Am. Chem. Soc.*, **78**, 4090 (1956).
14) W.D. Burrows and E.P. Burrows, *J. Org. Chem.*, **28**, 1180 (1963). These authors reported that UV spectrum of 4-benzylisoquinoline had λ_{max}: 265 (sh), 274, 285, 298, 310, 318, 323 mμ, ε_{max}: 4480, 5130, 4270, 2070, 3910, 3870, 5480.

To confirm this suggestion, decarboxylation of IV hydrochloride was carried out by using benzaldehyde instead of acetophenone; refluxing IV hydrochloride in benzaldehyde at 190° for 6 hours in a nitrogen atmosphere. The product had the identical melting point and IR spectrum with those of the authentic 4–benzylisoquinoline (VI) prepared by the Avramoff method.[13] This is strong support for the structure of compound A as 4–(α–phenethyl)isoquinoline (V). The following alternative synthesis of V, as shown in Chart 1 was investigated for the identification of this structure.

Oxidation of 4–benzylisoquinoline (VI) with anhydrous chromic acid gave 4–benzoylisoquinoline (VII) which underwent the Grignard reaction with methylmagnesium iodide to give 4–isoquinolylphenylmethylcarbinol (VIII).[15] This compound VIII was dehydrated with acetic anhydride–sulfuric acid, followed by reduction with Pd–charcoal to afford 4–(α–phenethyl)isoquinoline (V) which was identical with the sample prepared by the reaction of IV hydrochloride with acetophenone, as confirmed by its infrared (IR) spectrum and mixed melting point.



I X XIII XII XI

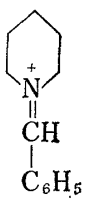
Chart 2

Moreover, 3–(α–phenethyl)isoquinoline (XIII) was synthesized from 3–acetylisoquinoline by the scheme shown in Chart 2. But the product obtained, XIII, having a mp of 75—77°, was quite different from V.

Rügheimer[16] reported that benzaldehyde was condensed with N–benzoylpiperidine at a high temperature to give 3,5–dibenzylpyridine, and E.P. Burrows, *et al.*[17] showed that condensation of piperidine and 1,2,3,4–tetrahydroisoquinoline with benzaldehyde in the presence of a trace of acetic acid in refluxing toluene yield 3,5–dibenzylpyridine and 4–benzylisoquinoline in 25% and 34% yields, respectively.

The proposed mechanism by Burrows, *et al.*[14] involved that the first stage of the reaction is the formation of immonium ion (XIV), since the starting amines are secomdary.

It would be inadequate to suppose such an immonium cation as the first stage intermediate in this reaction because the tertiary amine is the starting material. It is very difficult to assume the mechanism of this reaction from the aforementioned results and the references cited here. However, the procedure reported by Burrows *et al.*,[14] gave 4–substituted isoquinoline in poorer yield (30—40%) but the present procedure gave the same derivatives in fairly good yield (60—80%), hence, this reaction would appear to have important synthetic potential.



XIV

15) J.J. Padburg and H.G. Lindwall, *J. Am. Chem. Soc.*, **67**, 1268 (1945). The reported mp 168.5—170°.
16) L. Rügheimer, *Ann*, **328**, 326 (1903) mp 117.5—118°.
17) E.P. Burrows, R.F. Hutton, and W.D. Burrows, *J. Org. Chem.*, **27**, 316 (1962).

Experimental[18]

1,2,3,4-Tetrahydroisoquinoline-3-carboxylic Acid (I)——Prepared according to the method described by A. Pictet and T. Spengler.[19]

2-Acetyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic Acid (II)——Prepared according to the method reported by S. Archer.[20] Recrystallized from aq. acetone to colorless cubic crystals, mp 171—172°. Reported. mp 173.2—175.8° (corr.).[20]

2-Benzoyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic Acid (III)——Prepared by hydrolysis of ethyl 2-benzoyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylate, mp 78—79°, synthesized by the method reported by G.R. Clemo and S.P. Popli[21] with KOH-EtOH. Recrystallized from 40% aq. EtOH to white bulky crystals, mp 158—160°. Reported mp 170—172°.[22]

2-Methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic Acid (IV)—A mixture of I hydrochloride (3.0 g) in formaline (20 ml) and 80% HCOOH (40 ml) was refluxed for 8 hr to give a red brown clear solution. After adding 20% HCl (30 ml) the solution was evaporated to dryness *in vacuo*. The residue was recrystallized from EtOH to give IV hydrochloride (2.5 g), mp 204—206° (decomp.) in 80% yield. *Anal.* Calcd. for $C_{11}H_{13}O_2N \cdot HCl$: C, 58.02; H, 6.20; N, 6.15; Cl, 16.01. Found: C, 57.89; H, 5.76; N, 5.92; Cl, 15.48.

Decarboxylation

General Procedure: Adding the acid to freshly distilled acetophenone, 5—10 times the weight of the acid, this suspension was stirred in a N_2 atmosphere and oil bath heated at 150° or above, evolved CO_2 was introduced into baryts water and collected as $BaCO_3$. The rate of decarboxylation was calculated from this weight.

At the end of CO_2 evolution the reaction mixture was acidified with HCl, acetophenone was removed by steam distillation, the residual aqeous layer was made alkaline with K_2CO_3, and extracted with benzene, the benzene extract was then dried over Na_2SO_4 and benzene was distailled off to give the crude base.

(1) Decarboxylation of 1,2,3,4-tetrahydroisoquinoline-3-carboxylic Acid (I): A mixture of I (5.0 g) in acetophenone (50 ml) was heated in an oil bath at 150°. After evolution of CO_2 ceased the reaction mixture was treated by the general procedure to give $BaCO_3$ (4.1 g, 80%) and crude base (3.2 g). The latter was chromatographed on Al_2O_3 with benzene to afford a yellowish-red oil which proved to contain 50—60% of isoquinoline in it by determination with UV spectrum absorption at λ_{max}^{EtOH} (mμ) 318. With the separation of secondary and tertiary amines in crude base, the Hinsberg method[23] was carried out.[24] The secondary amine was tosylated with *p*-toluenesulfonylchloride to give 2-*p*-toluenesulfonyl-1,2,3,4-tetrahydroisoquinoline. First recrystallization from EtOH afforded colorless needles, mp 137—140°, 1.3 g (16%). Repeated recrystallization from EtOH gave colorless needles, mp 142—143° (mp 142° reported by F.G. Hollimann).[25] Untosylated tertiary amine formed picrate which was first recrystallized from aq. EtOH to give yellow needles (1.1 g, 16%), mp 202—207°, repeated recrystallization from aq. EtOH afforded isoquinoline picrate, mp 222—223° identical with the authentic sample.

(2) Decarboxylation of 1,2,3,4-tetrahydroisoquinoline-3-carboxlic acid hydrochloride (I-hydrochloride): A mixture of I hydrochloride (5.0 g) and acetophenone (40 ml) was heated at 150° for 6 hr. The reaction mixture was worked up similar to the general procedure to give $BaCO_3$ (2.3 g, 80%) and crude base (3.0)g, distillation of which gave colorless oil (1.4 g), bp 110—130° (20 mmHg), remaining the undistilled residue (1.5 g). The distillate, whose UV spectrum hardly showed the presence of isoquinoline, was tosylated with *p*-toluenesulfonyl chloride to obtain 2-*p*-toluenesulfonyl-1,2,3,4-tetrahydroisoquinoline (2.2 g, 32%), mp 138—141° from EtOH. Undistilled residue (1.5 g) was dissolved in benzene and the solution was passed through a column of Al_2O_3 (20 g) to remove impurities. The red oil (0.7 g) obtained afforded picrate, mp 157—158° from ethanol with the yield of 1.3 g, 13%.

(3) Decarboxylation of 2-acetyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (II): The suspension of II (2.0 g) in acetophenone (15 ml) was heated at 150° for 6 hr, no evolution of CO_2 occurred, hence heating was continued at 170° for 12 hr. The yield of $BaCO_3$ was 0.5 g (30%). The reaction mixture, diluted with benzene, was shaken with aq. $NaHCO_3$ to recover the unreacted starting material (0.9 g, 54%). Crude base (0.5 g) obtained by general procedure was dissolved in benzene and the solution was passed through a column of Al_2O_3 (10 g) to remove impurities. The yellow oil (0.3 g) obtained gave picrate (0.6 g, 15%), mp 159—161° from ethanol.

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18) All melting points are uncorrected.
19) A. Pictet and T. Spengler, *Ber.*, **44**, 2030 (1911).
20) S. Archer, *J. Org. Chem.*, **16**, 430 (1951).
21) G.R. Clemo and S.P. Popli, *J. Chem. Soc.*, **1951**, 1406.
22) R.B. Mc Griff and C. Niemann, *J. Am. Chem. Soc.*, **82**, 1830 (1960).
23) O. Hinsberg, *Ber.*, **23**, 2962 (1890). **33**, 3526 (1900); O. Hinsberg and J. Kessler, *Ber.*, **38**, 906 (1905).
24) Direct separation of secondary and tertiary amines was tried, all trials failed. When crude base was chromatographed on Al_2O_3, third base which formed picrate mp 156—157° was separated.
25) F.G. Hollimann and F.G. Mann, *J. Chem. Soc.*, **1942**, 737.

(4) Decarboxylation of 2-benzoyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (III): The suspension of III (2.0 g) in acetophenone (15 ml) was heated at 150—180° for 2 hr and at 180° for another 2 hr, yielding 0.18 g, 13% of $BaCO_3$. The starting material (1.2 g, 60%) was recovered by the same treatment as described for II. Crude base 0.3 g obtained by the general procedure was passed through a column of Al_2O_3, but purification was unsuccessful.

(5) Decarboxylation of 2-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (IV): The suspension of IV (3.5 g) in acetophenone (35 ml) was heated at *ca.* 190° for 5.5 hr. Since no evolution of CO_2 occurred, the whole was further heated at a slightly higher temperature, 190—210° for 3.5 hr yielding 0.9g (25%) of $BaCO_3$. The reaction mixture was worked up as described above, and the recovery of the starting material was 2.7 g (77%). The purification of the crude base (0.8 g) through Al_2O_3 chromatography was not successful, no definite product was obtained.

(6) Decarboxylation of 2-methyl-1,2,3,4-tetrahydroisoquinoline hydrochloride (IV-hydrochloride): IV hydrochloride (3.0 g) in acetophenone (20 ml) was heated at 190° for 9 hr, decarboxylation did not take place below 190°. The crude base (2.2 g) and $BaCO_3$ (1.8 g, 70%) were obtained according to general procedure as described above. The crude base was chromatographed on Al_2O_3 with benzene to give colorless needles (1.8 g, 60%), mp 86° from *n*-hexane, which was shown to be identical with the authentic sample 4-(α-phenethyl)isoquinoline by its mixed melting point and comparison of the IR spectra of the both samples. Picrate, mp 159—161°. *Anal.* Calcd. for $C_{17}H_{15}N \cdot C_6H_3O_7N_3$: N, 12.12. Found: N, 12.09. The melting point of this picrate was not depressed by admixture with the picrates above-described in (1), (2) and (3), and the IR spectra of picrates were essentially superimposable.

(7) Decarboxylation of IV hydrochloride in benzaldehyde: IV hydrochloride (3.0 g) in benzaldehyde (25 ml) was heated at 195—205° in a N_2 atmosphere. The initial suspension became transparent and the evolution of CO_2 occurred at the temperature of reflux, ceasing after 6 hr. The yield of $BaCO_3$ was 2.6 g (100%). Crude base obtained by the general procedure was chromatographed on Al_2O_3 with benzene to give yellow crystals (2.2 g, 73%). Recrystallization from benzene or ethanol yield colorless crystals of 4-benzylisoquinoline (VI), mp 116—118°. UV λ_{max}^{EtOH} mμ (log ε) 265 (3.24), 273 (3.25), 284 (3.22), 308 (3.20), 322 (3,26). Admixture with the authentic sample prepared according to the method described by M. Avramoff, *et al.*[13] showed no depression, and IR and UV spectra of the two samples were superimposable. Picrate, mp 191—193° from a large amount of EtOH–AcOEt, showed no depressed melting point with the picrate of the authentic sample.[13]

4-Benzoylisoquinoline (VII)——A solution of CrO_3 (3.5 g, 0.022 mole) in AcOH (20 ml) was added dropwise at 0° to a solution of VI (4.4 g, 0.02 mole) in conc. H_2SO_4 (10 ml) and AcOH (20 ml) and the whole was stirred at 0—10° for 1 hr, at room temperature for an additional 1 hr and at 40—50° for another 1 hr. The reaction mixture was poured into H_2O, the solution was made alkaline with 20% aq. NaOH and extracted with benzene and AcOEt. The combined extract was dried over Na_2SO_4 and evaporated to yield reddish oil (4.0 g). This oil dissolved in benzene was chromatographed on Al_2O_3 (40 g). Benzene eluates yielded crude VII (3.5 g, 77%) which was recrystallized from hexane to give colorless needles, mp 76—78°. *Anal.* Calcd. for $C_{16}H_{11}ON$: C, 82.38; H, 4.75; N, 6.01. Found: C, 82.55; H, 5.00; N, 5.99. IR cm^{-1}: $\nu_{C=O}$ 1653 (Nujol).

4-Isoquinolylmethylphenylcarbinol (VIII)——A solution of VII (1.3 g) in benzene (20 ml) was added dropwise to a solution of Grignard's reagent prepared from Mg 0.5 g and CH_3I 3.0 g in a mixture of ether and benzene, under cooling below 15°. The mixture was refluxed for 3 hr in a N_2 atmosphere, allowed to stand overnight and poured into sat. aq. NH_4Cl to decompose a complex. The product was extracted with benzene, the combined extract was dried over anhyd. K_2CO_3 and evaporated. The residue was recrystallized from benzene to give colorless cubic crystals (0.5 g, 36%), mp 165—167° (lit. mp 168.5—170°[15]).

4-α-Styrylisoqinoline (IX)——A mixture of VIII (0.45 g), Ac_2O (15 ml) and conc. H_2SO_4 (0.5 ml) was refluxed for 25 min. Ac_2O was removed under reduced pressure. The residue was added to H_2O, made alkaline with NaOH, extracted with benzene, and the extract was dried over Na_2SO_4 and evaporated. The reddish residue (0.4 g) was chromatographed on Al_2O_3 employing *n*-hexane and benzene–hexane (1:1) as eluting solvent system, the eluate furnished IX (0.25 g) which was recrystallized from hexane to give colorless needles, mp 93—94.5°. *Anal.* Calcd. for $C_{17}H_{13}N$: C, 88.28; H, 5.67; N, 6.06. Found: C, 88.09; H, 5.63; N, 5.94. IR cm^{-1}: δ>C=CH_2 914 ($CHCl_3$).

4-(α-phenethyl)isoquinoline (V)——A solution of IX (0.13 g) in EtOH (30 ml) was shaken in a H_2 atmosphere over a small amount of 30% Pd-C, H_2 (24 ml) was absorbed during the 3 hr. After filtration of catalyst, EtOH was evaporated in reduced pressure and the residue was chromatographed on Al_2O_3 (5 g) with benzene to give V which was recrystallized from hexane to afford colorless plates (0.08 g., 66%) of mp 85—86°. *Anal.* Calcd. for $C_{17}H_{15}N$: C, 87.51; H, 6.48; N, 6.00. Found: C, 87.84; H, 6.39; N, 6.04. UV λ_{max}^{EtOH} mμ (log ε) 265 (3.23), 273 (3.26), 284 (3.21), 308 (3.20), 317 (3.21), 322 (3.27). Picrate, mp 158—160° from EtOH. *Anal.* Calcd. for $C_{17}H_{15}N \cdot C_6H_3O_7N_3$: C, 59.74; H, 3.92; N, 12.12. Found: C, 59.28; H, 4.20; N, 12.25. This base and its picrate are indentical with V and its picrate prepared from decarboxylation of 1,2,3,4-tetrahydroisoquinoline derivatives as observed by the mixed melting points, UV and IR spectra.

3-Acethylisoquinoline (X)——Prepared according to the method described by G.R. Clemo, *et al.*[21]

3-Isoquinolylmethylphenylcarbinol (XI)——To a ethereal solution of phenyllithium prepared from Li (0.16 g, 0.023 atom) and bromobenzene (2.0 g, 0.016 mol) was slowly added a solution of X (0.6 g, 0.0035 mol) in ether (10 ml) at room temperature. After 1 hr of stirring, the reaction mixture was refluxed for an additional 1 hr, then poured into H_2O to decompose the complex and the product was extracted with ether. The ether layer was extracted with 10% HCl, the aq. acidic layer was then made alkaline with K_2CO_3 and extracted with benzene and dried over anhyd. K_2CO_3. Benzene was removed leaving a reddish-yellow oil (0.9 g). Attempts to crystallize the oil were unsuccessful and this material was employed without further purification in the subsequent reactions.

3-α-Styrylisoquinoline (XII)——A mixture of XI (0.9 g), Ac_2O (10 ml) and conc. H_2SO_4 (0.3 ml) was refluxed for 5 min. After removal of Ac_2O *in vacuo*, the resulting mixture was diluted with H_2O, made alkaline with K_2CO_3 and then extracted with benzene which was dried over Na_2SO_4. Benzene was removed giving a reddish oil (0.75 g). The oily product obtained was submitted to chromatography on Al_2O_3 (30 g). Elution with benzene–hexane (1:1) and recrystallization from hexane gave XII (0.5 g, 60%) as colorless crystals, mp 87—89° *Anal.* Calcd. for $C_{17}H_{13}N$: C, 88.28; H, 5.67; N, 6.06. Found: C, 88.74; H, 5.86; N, 6.02. IR cm^{-1}: δ>C=CH_2 905 ($CHCl_3$).

3-(α-Phenethyl)isoquinoline (XIII)——A solution of XII (0.3 g) in EtOH (20 ml) was shaken in a H_2 atmosphere over 30% Pd–C (0.1 g), absorbing H_2 (50 ml) for 4 hr. After filtration of the catalyst, the solution was removed under reduced pressure, the residue was recrystallized from hexane to give colorless plates XIII (0.25 g, 85%), mp 76—77°. *Anal.* Calcd. for $C_{17}H_{15}N$: C, 87.51; H, 6.48; N, 6.00. Found: C, 87.16; H, 6.57; N, 6.01. UV λ_{max}^{EtOH} mμ (log ε): 260 (3.30), 273 (3.28), 312 (3.19), 325 (3.22). Picrate, mp 156—158° from EtOH. *Anal.* Calcd. for $C_{17}H_{15}N \cdot C_6H_3O_7$: C, 59.74; H, 3.92; N, 12.12. Found: C, 60.12; H, 4.17; N, 12.16.

2-Benzylisoquinolinium Perchlorate——Isoquinoline (2.0 g) was refluxed in acetone (30 ml) together with benzyl chloride (2.0 g) for 10 hr. As the yellowish oil was separated, acetone was decanted off, the residue was added to 5 ml sat. ammonium perchlorate aqueous solution to give 2-benzylisoquinolinium perchlorate, after recrystallization from MeOH, colorless plates were formed, mp 165.5—167°. *Anal.* Calcd. for $C_{16}H_{14}O_4NCl$: C, 59.90; H, 4.42; N, 4.38. Found: C, 59.49; H, 4.50; N, 4.33. UV λ_{max}^{EtOH} (log ε) 270 (3.69), 338 (3.69).

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