Schiff Bases. Part I. Thermal Decarboxylation of α-Amino-acids in the Presence of Ketones

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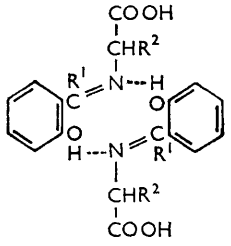
A number of Schiff bases derived from α-amino-acids and hydroxy-substituted aromatic ketones have been prepared. Their infrared spectra suggest that their relative stability to hydrolysis as compared with those from ketones with no hydroxy-groups is due to hydrogen bonding. The thermal decomposition of α-amino-acids in the presence of ketones, followed by hydrolysis produces the amines corresponding to the amino-acids or the ketones (transamination) or both, depending on the nature of the amino-acid and the ketone used and also on the method of hydrolysis. In the case of amino-acids with a quaternary α-carbon atom, transamination is the principal reaction. The preparation of tyramine, tryptamine, and histamine in good yield from the corresponding amino-acids is described.

SCHIFF bases have been prepared from a number of amino-acids and aldehydes including pyridoxal. Apart from one described by Emoto and Ando,[1] who employed 2-hydroxynaphthaldehyde, these have in most cases been isolated either as salts,[2,3] or as derivatives which arise by ring closure of the original Schiff base, as in the cases of tryptophan [4] and histidine.[5]

We have attempted to prepare similar derivatives from ketones of various kinds; whilst in most cases products were obtainable, these proved unstable when purification was attempted, and only in the case of *o*-hydroxy-substituted aromatic ketones were pure derivatives isolated (Table 1). Evidence for the structure of these substances was provided by the infrared spectra, which showed absorption bands in the region 2500 cm.$^{-1}$. This suggests the presence of intermolecular hydrogen bonding and accounts for the stability of the structure (I; R^1 = Me or Ph) as compared with that of the corresponding non-hydroxylated compounds.

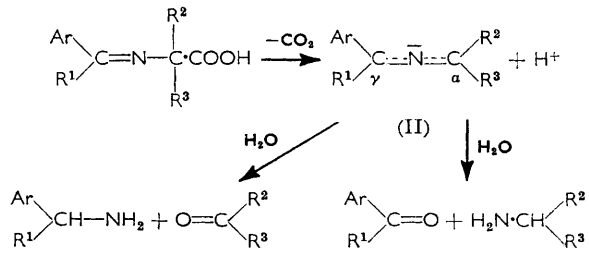


(I)

Most of these substances also showed absorption maxima in the region 2520—2740 Å (Table 1), which, according to Heinert and Martell [5] and Abella *et al.*,[6] is characteristic of azomethine compounds. Hydrogenation caused disappearance of these maxima. These carboxylated Schiff bases did not react with phenyl isocyanate or benzoyl chloride.

There seems little doubt that these substances are intermediates when α-amino-acids are decarboxylated by heating with carbonyl compounds. Their decarboxylation, however, takes place at a much lower temperature than is required when the amino-acids are heated directly with the carbonyl compounds, a reaction which has been studied by Franke,[7] Baddar *et al.*,[8] Dose,[9] and Chatelus.[10]

Baddar was interested mainly in the degradation or transamination of amino-acids, *i.e.*, the formation of the aldehydes or ketones corresponding to the amino-acids. He heated the amino-acid in aqueous pyridine with the carbonyl compound and examined the effect of substituent groups in the aromatic ring of the ketone or aldehyde on the potentially prototropic system present in the decarboxylated Schiff base (II; R^1 = H, Me, or Ph, R^2 = Me or Ph, R^3 = H or Me), which was shown by the nature of the products of hydrolysis.



He showed that a nitro-group in the *o*- or *p*-position favoured the degradation by its negative inductive effect.

Dose used, as the carbonyl component, benzaldehydes with *p*-substituted electron-donating groups (OH, OMe, and Me) and showed by electrophoresis of the hydrolysates that transamination took place to a much less extent than with benzaldehyde itself; the simple decarboxylation, *i.e.*, formation of the amine corresponding to the amino-acid, was the main reaction.

Chatelus, with acetophenone, propiophenone, or benzophenone as the carbonyl component, was mainly interested in the effect of the groups R^2 and R^3 on the course of the reaction. He first claimed [10] that when R^2 and R^3 were both methyl, no transamination was apparent, but that when R^2 was changed to ethyl, transamination was complete. With R^2 = Ph and R^3 = Me there was no transamination. These findings,

[1] S. Emoto and M. Ando, *J. Agric. Chem. Soc. Japan*, 1961, **35**, 957 (*Chem. Abs.*, 1964, **60**, 8119).
[2] M. Bergman and E. Zervas, *Z. physiol. Chem.*, 1926, **152**, 282.
[3] D. Heinert and A. E. Martell, *J. Amer. Chem. Soc.*, 1963, **85**, 183.
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[5] A. Neuberger, *Biochem. J.*, 1944, **38**, 313.
[6] M. Abella, R. P. Ossorio, and V. S. del Olmo, *Anales real Soc. espan. Fis. Quim.*, 1964, **60**, 17 (*Chem. Abs.*, 1964, **61**, 10,569).
[7] W. Franke, *Biochem. Z.*, 1933, **258**, 280.
[8] F. G. Baddar and Z. Iskandar, *J. Chem. Soc.*, 1954, 209.
[9] K. Dose, *Chem. Ber.*, 1957, **90**, 1251.
[10] G. Chatelus, *Compt. rend.*, 1961, **253**, 1588.

TABLE 1

Schiff bases from various amino-acids and various aromatic ketones

Amino-acid	Aromatic ketone	Yield (%)	Purification method	Decomp. temp.	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H	Formula	Schiff base	$\lambda_{max.}$ (Å)	log ε
DL-Valine	*o*-Hydroxyacetophenone	85	A	245°	58·7	6·5	58·6	6·4	$C_{13}H_{16}NO_3Na,\frac{1}{2}H_2O$	DL-*N*-[1-(*o*-Hydroxyphenyl)ethylidine]valine	2740	3·62
DL-Valine	2,2′-Dihydroxybenzophenone	78	B	125	68·6	6·3	69·0	6·1	$C_{18}H_{19}NO_4$	DL-*N*-[Di-(*o*-hydroxyphenyl)methylene]valine	2580	3·71
DL-Leucine	*o*-Hydroxyacetophenone	80	A	240	60·4	6·9	60·0	6·8	$C_{14}H_{18}NO_3Na,\frac{1}{2}H_2O$	DL-*N*-[1-(*o*-Hydroxyphenyl-ethylidene]leucine	2740	3·58
DL-Leucine	2,2′-Dihydroxybenzophenone	76	B	101	69·6	6·5	69·7	6·4	$C_{19}H_{21}NO_4$	DL-*N*-[Di-(*o*-hydroxyphenyl)methylene]leucine	2600	3·65
Phenylglycine	*o*-Hydroxyacetophenone	89	A	150	71·4	5·8	71·4	5·6	$C_{16}H_{15}NO_3$	*N*-[1-(*o*-Hydroxyphenyl)ethylidene]-phenylglycine	2520	2·68
Phenylglycine	2,2′-Dihydroxybenzophenone	86	B	97	71·8	5·6	72·6	4·9	$C_{21}H_{17}NO_4$	*N*-[Di-(*o*-hydroxyphenyl)methylene]-phenylglycine	2600	2·74
Phenylglycine	2-Hydroxy-4-methoxybenzophenone	76	A	160	66·1	5·0	65·8	4·8	$C_{22}H_{18}NO_4Na,H_2O$	*N*-[α-(2-Hydroxy-4-methoxyphenyl)-benzylidene]phenylglycine	3020 3080	3·2
DL-β-Phenylalanine	2,2′-Dihydroxybenzophenone	78	A	180	71·1	5·8	71·4	5·4	$C_{22}H_{19}NO_4$	*N*-[Di-(*o*-hydroxyphenyl)methylene]-phenylglycine	2600	2·34
L-Histidine	*o*-Hydroxybenzophenone	75	B	205	67·7	5·4	67·9	5·4	$C_{19}H_{18}N_3O_3$	L-*N*-[α-(*o*-Hydroxyphenyl)benzylidene]histidine	2600	3·69
L-Histidine	2,2′-Dihydroxybenzophenone	76	B	200	64·4	5·2	64·7	5·1	$C_{19}H_{18}N_3O_4$	L-*N*-[Di-(*o*-hydroxyphenyl)methylene]histidine	2600	3·82

however, were modified in the following paper,[11] and he concluded that the course of the reaction was determined by the nature of the groups R^2 and R^3 in the amino-acid and was independent of the carbonyl compound. We have examined the system (II) by varying the nature of both the carbonyl component and the amino-acid, and have extended the range of amino-acids. In a number of cases the Schiff bases from the decarboxylation were isolated and characterised (see following Paper). These Schiff bases were hydrolysed by four methods, *viz.*, with boiling dilute hydrochloric acid, boiling concentrated hydrochloric acid, concentrated hydrochloric acid under pressure, or aqueous alcoholic sodium hydroxide. In most cases the resulting amine mixture was examined quantitatively by non-aqueous titration and qualitatively by electrophoresis. In a few cases gas chromatography was employed. The results are shown in Tables 2—11.

Apart from the case of α-amino-acids with quaternary α-carbon atoms such as α-aminoisobutyric acid and α-amino-α-methylbutyric acid, thermal decarboxylation of α-amino-acids in the presence of acetophenone or benzophenone followed by hydrolysis gives in general both simple decarboxylation and transamination. Introduction of electron-donating groups such as hydroxyl or methoxyl into the *o*- and *p*-positions of the aromatic ring reduces the extent of transamination. These

[11] G. Chatelus, *Bull. Soc. chim. France*, 1964, 2523.

TABLE 2

Results of hydrolysis of product obtained by decarboxylation of phenylglycine with various ketones

Ketone	Method of hydrolysis	Yield (%) of benzylamine, HCl	Transamination (%) (by non-aqueous titration) *
Acetophenone	b	67	16 †
o-Hydroxyacetophenone	a	76	0
o-Hydroxyacetophenone	c	70	18 †
o-Methoxyacetophenone	c	80	Some
p-Methoxyacetophenone	b	85	0
p-Nitroacetophenone	a, b	Poor ‡	
p-Nitroacetophenone	c	Poor	
o-Nitroacetophenone	a, b	Poor ‡	
o-Nitroacetophenone	c	Poor	
Benzophenone	b	70	20 §
Benzophenone	c	76	33
o-Hydroxybenzophenone	a	51	0
o-Hydroxybenzophenone	c	33	15
2,2′-Dihydroxybenzophenone	a	45	0
2,4-Dihydroxybenzophenone	a	55	0
4,4′-Dihydroxybenzophenone	a	42	0
4,4′-Dihydroxyacetophenone	c	39	12·5
4-Methoxybenzophenone	b	85	0
4,4′-Dimethoxybenzophenone	b	78	0

* In all cases the hydrolysis products were examined qualitatively by electrophoresis. † Verified by gas chromatography. ‡ Identified by picrate from electrophoresis eluate. § The amine (diphenylmethylamine) resulting from transamination was isolated as the hydrochloride from the cooled hydrolysate (m. p. 270°).

TABLE 3

Results of hydrolysis of Schiff bases formed during decarboxylation of DL-β-phenylalanine with various ketones

Ketone	Method of hydrolysis	Yield (%) of 2-phenylethylamine HCl	Transamination (%) (by non-aqueous titration) *
Acetophenone	b	82	—
o-Hydroxyacetophenone	a	72	0
o-Hydroxyacetophenone	c	70·5	12
o-Methoxyacetophenone	c	90	Some
p-Methoxyacetophenone	b	80	0
o-Nitroacetophenone	a, b	Poor †	—
o-Nitroacetophenone	c	Poor	—
Benzophenone	b	76	12
Benzophenone	c	70	20
o-Hydroxybenzophenone	a	33	0
o-Hydroxybenzophenone	c	50	13
2,2′-Dihydroxybenzophenone	a	60	0
2,4′-Dihydroxybenzophenone	a	50	0
2,4′-Dihydroxybenzophenone	c	55	5
4-Hydroxybenzophenone	a	33	0
4-Hydroxybenzophenone	c	37	10·5
4,4′-Dihydroxybenzophenone	a	33	0
4,4′-Dihydroxybenzophenone	c	39	4
2,2′-Dimethoxyacetophenone	b	88	0

* In all cases the hydrolysis products were identified by electrophoresis. † Identified by picrate from electrophoresis eluate.

TABLE 4

Results of hydrolysis of Schiff bases formed during decarboxylation of L-tyrosine with various aromatic ketones

Ketone	Method of hydrolysis	Yield of of tyramine, HCl	Transamination (%) (by non-aqueous titration *
Acetophenone	b	85	17
o-Methoxyacetophenone	b	80	0
Benzophenone	b	75	17
o-Hydroxybenzophenone	a	75	0
o-Hydroxybenzophenone	c	61·5	12
2 2′-Dihydroxybenzophenone	a	60	0
2 2′-Dihydroxybenzophenone	c	63	3
2,4-Dihydroxybenzophenone	a	50	0
4-Hydroxybenzophenone	c	53	10
4 4′-Dihydroxybenzophenone	a	45	0
4,4′-Dihydroxybenzophenone	c	55	12
4-Methoxybenzophenone	b	82	0
2,2′-Dimethoxybenzophenone	b	89	0

* In all cases the hydrolysis products were identified by electrophoresis.

results are in general agreement with those of Ingold *et al.*[12] on the effect of substituents on the system (II) as applied to azomethines derived from benzaldehydes and benzylamines, although in these azomethines R^1 and either R^2 or R^3 was always H. The results confirm the work of Dose [9] and Baddar [8] but differ in detail from that of Chatelus,[10] in that we found that except in the cases of α-amino-α-methylbutyric and α-aminoisobutyric acids, the nature of the products depends on all three factors, the constitution of the carbonyl compound, the structure of the amino-acid, and the medium of hydrolysis.

TABLE 5

Results of hydrolysis of Schiff bases formed during decarboxylation of DL-α-phenyl-α-alanine with various ketones

Ketone	Decomp. temp.	Method of hydrolysis	Yield (%) of 1-phenylethylamine	Transamination (%) (by non-aqueous titration) *
Benzophenone	180°	b	62	25
2,2′-Dimethoxybenzophenone	192	b	79	0
o-Hydroxyacetophenone	205	a	41	0
o-Methoxyacetophenone	195	a	83	0
p-Methoxyacetophenone	187	c	92	0

* In all cases the products were identified by electrophoresis and gas chromatography.

TABLE 6

Results of hydrolysis of product formed during decarboxylation of L-histidine with various aromatic ketones

Ketone *	Method of hydrolysis	Yield (%) of histamine, HCl	Transamination (%) (by non-aqueous titration)
o-Methoxyacetophenone	b	61—81	0
p-Methoxyacetophenone	b	25	0
p-Hydroxyacetophenone	a	Poor	0
p-Methoxypropiophenone	c	20	0
p-Hydroxyvalerophenone	a	Poor	
o-Hydroxyacetophenone	a	50	0
o-Hydroxyacetophenone	c	54	7
Benzophenone	c	15	14
p-Methoxybenzophenone	b	25	
2,2′-Dimethoxybenzophenone	b	32	
2,2′-Dihydroxybenzophenone	a	30	
2,4-Dihydroxybenzophenone	c	25	9
2,4-Dihydroxybenzophenone	a	30	0
o-Hydroxybenzophenone	a	31	0
o-Hydroxybenzophenone	c	34	8
4-Hydroxybenzophenone	c	33	10
4-Hydroxybenzophenone	a	23	0

* The molar ratio of ketone to histidine was 2/1.

With α-amino-α-methylbutyric and α-aminoisobutyric acids, the nature of the carbonyl component did not affect the result; transamination only was observed (Table 10). This is to be expected in view of the electronic effect of two alkyl groups on the α-position of the system (II) in producing at the γ-position a higher electron density to attract the proton. In the case of α-phenylalanine, Chatelus concluded that, irrespective of the ketone used, transamination always took place. We have found that whilst this is so in the case of

[12] C. K. Ingold and C. W. Shoppee, *J. Chem. Soc.*, 1929, 1199.

TABLE 7

Results of hydrolysis of product formed during decarboxylation of DL-tryptophan with various aromatic ketones

Ketone	Method of hydrolysis	Yield (%) of tryptamine, HCl	Transamination (%) (by non-aqueous titration) *
o-Hydroxy-n-butyrophenone	c	30	9
Benzophenone	†	25	15
o-Hydroxybenzophenone	c	34	6
2,2′-Dimethoxybenzophenone	†	40	0
4-Hydroxybenzophenone	c	35	7
2,4-Dihydroxybenzophenone	c	30	10
4,4′-Dihydroxybenzophenone	c	45	0
4-Methoxybenzophenone	c	40	6
4,4′-Dimethoxybenzophenone	†	46	0
Acetophenone	†	50	15
o-Hydroxyacetophenone	c	40	9
o-Methoxyacetophenone	†	63	0
o-Methoxyacetophenone	c	50	0
p-Methoxyacetophenone	†	45	0
p-Hydroxyacetophenone	c	30	10·5
p-Nitroacetophenone	†	0	
p-Nitroacetophenone	c	0	

* Amines were identified by electrophoresis. † In these cases the hydrolysis was carried out with 3N-hydrochloric acid at 50° for 1 hr.

TABLE 8

Results of hydrolysis of product formed during decarboxylation of DL-methionine with various aromatic ketones

Ketone	Method of hydrolysis	Yield (%) of 3-methylthio-n-propylamine, HCl	Transamination (%) (by non-aqueous titration)
2,2′-Dihydroxybenzophenone	a	10	0
2,2′-Dihydroxybenzophenone	c	31	11
2,4-Dihydroxybenzophenone	a	Poor	0
2,4-Dihydroxybenzophenone	c	27	8

TABLE 9

Results of hydrolysis of product formed during decarboxylation of DL-leucine with various aromatic ketones

Ketone	Method of hydrolysis	Yield (%) of isopentylamine, HCl	Extent of transamination (%)
o-Hydroxyacetophenone	a	60	0
o-Hydroxyacetophenone	c	53	9
o-Methoxyacetophenone	b	86	0
o-Methoxyacetophenone	c	90	0
4-Hydroxybenzophenone	a	41	0
4-Hydroxybenzophenone	c	30	11
4,4′-Dihydroxybenzophenone	a	47	0

acetophenone, the introduction of a *p*-methoxy-group [*i.e.*, (II; R^1 = Me, R^2 = Ph, R^3 = Me, Ar = C_6H_4·OMe)] is sufficient to overcome the inductive effect of the methyl groups on the α-carbon atom and inhibit completely the transamination.

As reagents for the production of amines corresponding to simple decarboxylation products of amino-acids, methoxy-substituted aromatic ketones were found to be the most useful in that the amines, including tyramine, tryptamine, and histamine, could be isolated as salts in good yield from the cheaper amino-acids. The case of histamine is noteworthy; previous workers have recorded its isolation from histidine only as the dipicrolonate. On the other hand the use of α-amino-acids with a quaternary α-carbon atom offers a general method of preparing amines by transamination from the corresponding ketones.

TABLE 10

Results of hydrolysis of Schiff bases formed during decarboxylation of L-lysine with various ketones

Ketone	Method of hydrolysis	Yield (%) of pentane-1,5-diamine 2HCl	Transamination (%) (by non-aqueous titration)
o-Hydroxyacetophenone	b	Poor	0
o-Hydroxyacetophenone	c	20	8
o-Methoxyacetophenone	b	25	0
o-Methoxyacetophenone	c	24	0
4-Hydroxybenzophenone	b	Poor	0
4-Hydroxybenzophenone	c	15	10
4,4′-Dihydroxybenzophenone	c	21	11

TABLE 11

Amines obtained on hydrolysis after decarboxylation of DL-α-aminoisobutyric (A) and DL-α-amino-α-methylbutyric (B) acids in the presence of various ketones

	Ketone	Amine	Yield (%) of hydrochloride
A.	*o*-Hydroxyacetophenone	1-(*o*-Hydroxyphenyl)-ethylamine	45
	o-Methoxyacetophenone	1-(*o*-Methoxyphenyl)-ethylamine	51
	p-Methoxyacetophenone	1-(*p*-Methoxyphenyl)-ethylamine	56
	Benzophenone	Diphenylmethylamine	62
	Benzyl methyl ketone	1-Benzylethylamine	14
B.	*o*-Methoxyacetophenone	1-(*o*-Methoxyphenyl)-ethylamine	78
	p-Methoxyacetophenone	1-(*p*-Methoxyphenyl)-ethylamine	75
	Benzophenone	Diphenylmethylamine	68
	p-Methoxybenzophenone	α-(*p*-Methoxyphenyl)-benzylamine	82
	Benzyl methyl ketone	1-Benzylethylamine	30

EXPERIMENTAL

Preparation of Schiff Bases of α-Amino-acids.—The amino-acid (0·01 mole) was added to sodium (0·23 g.) in ethanol (30 ml.) containing just sufficient water to give a clear solution, and the ketone (0·01 mole) was added to the mixture heated on the water-bath. The solution was heated for about 20 min. under reflux then set aside to evaporate. Those Schiff bases which were decomposed by dilute acid were isolated as the sodium salts. In the other cases, the sodium salts were neutralised with cold 1N-acetic acid and the yellow product was filtered off and either crystallised

from aqueous ethanol (method A) or, when non-crystalline, washed several times with water, and then with warm benzene (method B) (see Table 1).

Decarboxylation of Amino-acids in the Presence of Ketones.—The amino-acid (0·01 mole) was intimately mixed with the ketone (0·01 mole) and heated in a nitrogen stream with stirring at the minimum temperature required for decarboxylation. When no more carbon dioxide was evolved the mixture was cooled and hydrolysed by one of the following methods.

(a) *By concentrated hydrochloric acid under pressure.* The residue from the decarboxylation with concentrated hydrochloric acid (25 ml.) was heated in a sealed tube at 150—160° for 3 hr. and filtered. The residue of amine hydrochloride left after removal of the acid under reduced pressure was washed with hot ethanol–acetone (1 : 10) and crystallised from ethanol–ether.

(b) *By boiling hydrochloric acid.* The residue was boiled with concentrated hydrochloric acid (25 ml.) for 3 hr. The cooled solution was then diluted with water and extracted twice with benzene. The aqueous layer was evaporated to dryness under reduced pressure, and the amine hydrochloride was recovered as described above.

(c) *By alkali.* The residue was dissolved in alcoholic 3N-sodium hydroxide (25 ml.) and heated under reflux for 3 hr. The solution was then acidified with 3N-hydrochloric acid and extracted with benzene. The resulting aqueous layer was evaporated to dryness under reduced pressure. All but traces of inorganic material was removed by repeated evaporation with ethanol followed by filtration from hot ethanol, and the small amount of sodium chloride remaining in the amine hydrochlorides was determined by flame photometry.

Qualitative Determination of the Extent of Transamination.—The crude amine hydrochloride was subjected to paper electrophoresis in acetate buffer (pH 4·9) with an applied voltage of 500. The paper was developed by spraying with ninhydrin and heating to 60° for 1 hr.

Quantitative Determination of the Extent of Transamination.—A known weight of the amine hydrochloride (*ca.* 0·001 mole) was dissolved in glacial acetic acid and titrated with 0·1N-perchloric acid in glacial acetic acid. Since the molecular weights of the two amines expected in any particular case were known, the composition of the mixture could be calculated.

Gas Chromatographic Analysis of the Amine Hydrochloride Mixture.—This was done with a Pye Argon Chromatograph with a column of 10% Carbowax on alkali-coated Celite, 100—120 mesh. The flow rate was 40 ml./min. and the temperature, voltage, and sensitivity were chosen to suit each particular mixture. The amines liberated from their salts were applied to the column as a 10% solution in benzene.

Decarboxylation of α-Aminoisobutyric and α-Amino-α-methylbutyric Acids.—The amino-acid (0·005 mole) was intimately mixed with the ketone (0·005 mole) and heated under nitrogen with stirring to 245°. Decarboxylation was complete after 1 hr. The cooled oily red product was refluxed with concentrated hydrochloric acid (30 ml.) for 3 hr. and the acid was removed by evaporation to dryness. The residue containing the amine hydrochloride was crystallised from ethanol–ether (see Table 11). No isopropylamine or isobutylamine was detectable by paper chromatography.

Preparation of Amines.—Amines required for identification purposes were prepared from the corresponding ketoximes by reduction with lithium aluminium hydride [13] or Raney nickel alloy.[14] 1-(o-*Hydroxyphenyl*)*ethylamine hydrochloride* (65%) had m. p. 213° (decomp.) (Found: C, 55·2; H, 6·7. $C_8H_{11}NO,HCl$ requires C, 55·3; H, 6·9%). 1-(o-*Methoxyphenyl*)*ethylamine hydrochloride*, (65%) had m. p. 136—137° (Found: C, 57·8; H, 7·3. $C_9H_{13}NO,HCl$ requires C, 57·7; H, 7·5%). α-(p-*Hydroxyphenyl*)*benzylamine hydrochloride* (60%) had m. p. 164° (Found: C, 66·1; H, 5·9. $C_{13}H_{13}NO,HCl$ requires C, 66·3; H, 5·9%). [*Di*-(o-*hydroxyphenyl*)*methyl*]*amine hydrochloride* had m. p. 203° (Found: C, 62·0; H, 5·7. $C_{13}H_{13}NO_2,HCl$ requires C, 62·1; H, 5·6%).

Hydrogenation of the Amino-acid Schiff Bases.—The sodium salt of the Schiff base (5 mmoles) in ethanol (50 ml.) was hydrogenated at atmospheric pressure in the presence of platinum oxide (0·1 g.). After 20 hr., the solution was filtered, and most of the solvent was removed under reduced pressure. The gummy residue was neutralised with dilute acetic acid and the product (60—76%) was crystallised from aqueous ethanol. In this way were prepared DL-N-[1-(o-*hydroxyphenyl*)*ethyl*]*leucine*, m. p. 240° (Found: C, 66·9; H, 8·5. $C_{14}H_{21}NO_3$ requires C, 66·9; H, 8·4%), and DL-N-[*di*-(o-*hydroxyphenyl*)*methyl*]*leucine*, m. p. 160° (Found: C, 69·2; H, 6·9. $C_{19}H_{23}NO_4$ requires C, 69·3; H, 7·0%). DL-N-[1-(o-*hydroxyphenyl*)*ethyl*]*tryptophan*, m. p. 208° (decomp.) (Found: C, 69·1; H, 6·4. $C_{19}H_{20}N_2O_3$ requires C, 70·0; H, 6·2%), was obtained under similar conditions except that the hydrogenation was carried out at 10 atm. for 12 hr.

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[14] B. Staskun and T. van Es, *J. Chem. Soc.* (*C*), 1966, 531.