Schiff Bases. Part II.† Some Ketimines prepared by Decarboxylation of α-Amino-acids in the Presence of Ketones and their Reaction and that of Aldimines with Phenyl Isocyanate

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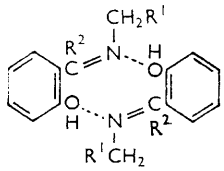
Some ketimines prepared by thermal decarboxylation of amino-acids in the presence of aromatic ketones, or directly from the corresponding amines, are described. In the case of β-hydroxy-amines, ring closure takes place to give oxazolidines. Aromatic ketimines derived from *o*-hydroxyacetophenone react with phenyl isocyanate to give coumarin derivatives. Aldimines prepared from *o*- and *p*-hydroxy- and -methoxy-substituted benzaldehydes react with phenyl isocyanate to give *s*-triazine derivatives.

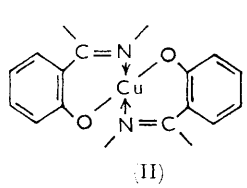
WHEN α-amino-acids are heated with carbonyl compounds the first formed carboxylated Schiff bases undergo decarboxylation to give the Schiff bases or ketimines of the corresponding amines. We have prepared a number of these derived from aromatic ketones, directly from the amino-acids and also from the corresponding amines. In many cases it was advantageous to start with the amino-acid, since the reaction temperatures when amines were used were above the boiling points of the amines.

These Schiff bases were very weak bases, and gave neither hydrochlorides nor picrates in all but a few cases. With the exception of the compound obtained from 2,2'-dimethoxybenzophenone and phenylalanine, only those from *o*-hydroxyacetophenone and benzophenones with an *o*-hydroxy-substituent were obtained crystalline. The u.v. absorption spectra of these were comparable with those of the acetophenone derivatives previously described [1] and showed maxima in the range 2540—3900 Å which were absent in the spectra of the secondary amines prepared from them by hydrogenation of the C=N bond. Lysine, as expected, gave the di-Schiff base and showed anomalous behaviour in its u.v. absorption spectrum, as did the Schiff bases derived from 2,4-dihydroxybenzophenone (Table 1).

The i.r. absorption spectra showed broad maxima at about 2500 cm.$^{-1}$, which, according to Heinert and Martell [2] are due to intermolecular hydrogen bonding as shown in (I). This absorption band was absent in the



(I)

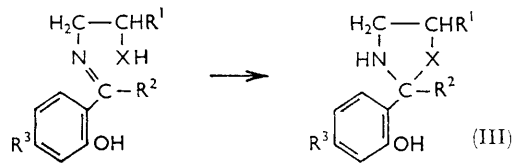


(II)

spectra of the corresponding *O*-methylated compounds, most of which were non-crystalline oils at room temperature, and in those of the copper co-ordination complexes (II).

The C=N absorption band in the i.r. spectra normally to be found [3] in the range 1690—1635 cm.$^{-1}$ occurred at 1600—1620 cm.$^{-1}$. This shift may have been caused by conjugation with the aromatic ring.[2]

The β-hydroxy-amino-acids, serine, phenylserine and threonine, when decarboxylated in the presence of aromatic ketones, gave crystalline products which yielded picrates and unstable hydrochlorides. These substances were also obtainable from the corresponding amines. Their u.v. absorption spectra had no distinct band in the 2600 Å region analogous to that shown by the derivatives of non-hydroxylated amino-acids, but showed a plateau at about 2300—2650 Å. The i.r. spectra indicated no intermolecular hydrogen bonding, but intramolecular bonding was suggested by the absorption band at 3200 cm.$^{-1}$. There was no indication of alcoholic OH absorption normally to be expected at 3625 cm.$^{-1}$. Their lower R_F values on silica gel confirmed their basicity to be greater than that of the corresponding derivatives from non-hydroxylated amino-acids. They were also much more resistant to hydrogenation. Taking these factors into consideration we have proposed for them oxazolidine structures (III; R^1 = H, Me, or Ph, R^2 = Me or Ph, R^3 = H or OMe, X = O). Analogous compounds have been obtained from ethanolamine by use of aliphatic ketones [4] and substituted benzaldehydes,[5] but the proposed oxazolidine structure was later questioned.[6]



(III)

Hydrolysis of these oxazolidines readily gave the corresponding hydroxy-amines and ketones. Under mild conditions, cysteine behaved in an analogous manner with acetophenone and *o*-methoxyacetophenone and gave the thiazolidines (III; X = S). With 2,4-dihydroxyacetophenone, oxidation took place to give the di-Schiff base corresponding to cystine.

† Part I, A. F. Al-Sayyab and A. Lawson, preceding Paper.

[1] M. Abella, R. P. Ossorio, and V. Sanchez del Olmo, *Anales real Soc. espan. Fis. Quim.*, 1964, **60**, 17 (*Chem. Abs.*, 1964, **61**, 10,569).

[2] D. Heinert and A. E. Martell, *J. Amer. Chem. Soc.*, 1962, **84**, 3257.

[3] A. D. Cross, 'Practical Infra-Red Spectroscopy,' Butterworth, London, 1960.

[4] A. C. Cope and E. M. Hancock, *J. Amer. Chem. Soc.*, 1942, **64**, 1503.

[5] L. H. Goodson and H. Christopher, *J. Amer. Chem. Soc.*, 1949, **71**, 1117.

[6] G. E. McCasland and E. C. Horswill, *J. Amer. Chem. Soc.*, 1951, **73**, 3923.

TABLE 1

Schiff bases obtained by decarboxylation of amino-acids with ketones

Ketone	Decarboxylation temp.	M. p.	Yield (%)	Found (%) C	H	N	Required (%) C	H	N	Formula	Schiff base	$\lambda_{max.}$ (Å)	Log ε	$\nu_{max.}$
							DL-Phenylglycine							
o-Hydroxyacetophenone	215°	125°	80	80·4	6·6		80·0	6·7		$C_{15}H_{15}NO$	*N*-[1-(*o*-Hydroxyphenyl)ethylidene]benzylamine *	2540	3·73	2490 1610
o-Hydroxybenzophenone	220	78	78			4·8			4·8	$C_{20}H_{17}NO$	*N*-[α-(*o*-Hydroxyphenyl)benzylidene]benzylamine	2600	5·63	
2,2′-Dihydroxybenzophenone	220	192	75	79·4	5·7		79·2	5·6		$C_{20}H_{17}NO_2$	*N*-[*o*-Hydroxy-α-(*o*-hydroxyphenyl)benzylidene]benzylamine *	2600	4·1	2500 1605
2,4-Dihydroxybenzophenone	178	218	70	79·3	5·9	4·5	79·2	5·6	4·6	$C_{20}H_{17}NO_2$	*N*-[α-(2,4-Dihydroxyphenyl)benzylidene]benzylamine	3100	4·1	
							DL-β-Phenylalanine							
o-Hydroxyacetophenone	210	142	80	69·3	6·6		69·6	6·5		$C_{16}H_{17}NO$,HCl	*N*-[1-(*o*-Hydroxyphenyl)ethylidene]phenethylamine, HCl	2720	4·0	
2,2′-Dihydroxybenzophenone	185	185	81	78·8	5·9		79·5	5·9		$C_{21}H_{19}NO_2$	*N*-[Di-(*o*-hydroxyphenyl)methylene]phenethylamine	2600	4·84	
2,4-Dihydroxybenzophenone	190	235	75			4·3			4·4	$C_{21}H_{19}NO_2$	*N*-[α-(2,4-Dihydroxyphenyl)benzylidene]phenethylamine	3100	4·01	
2,2′-Dimethoxybenzophenone	160	104	60	79·8	6·7		80·0	6·7		$C_{23}H_{23}NO_2$	*N*-[Di-(*o*-methoxyphenyl)methylene]phenethylamine	2580	3·94	
							L-Tyrosine							
o-Hydroxybenzophenone	220	245	70	79·2	6·1	4·4	79·5	5·9	4·5	$C_{21}H_{19}NO_2$	*N*-[α-(*o*-Hydroxyphenyl)benzylidene]-*p*-hydroxyphenethylamine	2600	3·99	
2,2′-Dihydroxybenzophenone	220	260	67	75·29	5·82	4·23	75·7	5·7	4·2	$C_{21}H_{19}NO_3$	*N*-[Di-(*o*-hydroxyphenyl)methylene]-*p*-hydroxyphenethylamine	2600	3·75	
							L-Histidine							
2,2′-Dihydroxybenzophenone	230	187	50	72·1	5·6	10·4	70·3	5·3	13·6	$C_{18}H_{17}N_3O_2$	*N*-[Di-(*o*-hydroxyphenyl)methylene]histamine	2600	4·44	
							DL-Tryptophan							
o-Hydroxyacetophenone	215	117	80	77·52	6·72		77·69	6·47		$C_{18}H_{18}NO_2$	*N*-[1-(*o*-hydroxyphenyl)ethylidene]tryptamine	2750	4·46	
o-Hydroxy-n-butyrophenone	235	120	75	77·8	7·3		78·4	7·18		$C_{20}H_{22}NO_2$	*N*-[1-(*o*-Hydroxyphenyl)butylidene]tryptamine	2800	4·27	
2,2′-Dihydroxybenzophenone	195	187	78	77·83	5·9	7·6	77·6	5·6	7·9	$C_{23}H_{20}N_2O_2$	*N*-[Di-(*o*-hydroxyphenyl)methylene]tryptamine	2800	3·18	
							DL-Methionine							
2,2′-Dihydroxybenzophenone	200	160	65	67·38	6·02		67·77	6·3		$C_{17}H_{19}NO_2S$	*N*-[*o*-Hydroxy-α-(*o*-hydroxyphenyl)benzylidene]-3-methylthiopropylamine	2580	3·91	
							L-Lysine							
o-Hydroxyacetophenone	180	115	60	74·5	8·0		74·6	7·7		$C_{21}H_{26}N_2O_2$	*NN*′-Bis-[1-(*o*-hydroxyphenyl)ethylidene]pentane-1,5-diamine	3900	3·73	
							L-Leucine							
o-Hydroxyacetophenone	210	111	75	76·0	9·3		76·1	9·3		$C_{13}H_{19}NO$	*N*-[1-(*o*-Hydroxyphenyl)ethylidene]isopentylamine	—	—	

* The same compounds were prepared directly from the amine corresponding to the amino-acid and the ketone.

TABLE 2

Oxazolidines formed by decarboxylation of α-amino-β- hydroxy-acids in the presence of aromatic ketones

Ketone	Amino-acid	Yield (%)	M. p. of product	Found (%) C	Found (%) H	Reqd. (%) C	Reqd. (%) H	Formula	Oxazolidine
o-Hydroxyacetophenone	DL-Serine	52	97°	67·3	7·4	67·0	7·3	$C_{10}H_{13}NO_2$	2-(*o*-Hydroxyphenyl)-2-methyloxazolidine
o-Hydroxyacetophenone	DL-Serine		165	46·7	3·8	47·0	3·9	$C_{16}H_{16}N_4O_9$	2-(*o*-Hydroxyphenyl)-2-methyloxazolidine picrate
o-Hydroxy-*p*-methoxyacetophenone	DL-Serine	60	178	53·1	4·2	52·8	4·0	$C_{22}H_{20}N_4O_{10}$	2-(*o*-Hydroxy-*p*-methoxyphenyl)-2-phenyloxazolidine picrate
o-Hydroxyacetophenone	DL-β-Phenylserine	50	115	75·6	6·8	75·3	6·7	$C_{16}H_{17}NO_2$	2-(*o*-Hydroxyphenyl)-2-methyl-5-phenyloxazolidine
o-Hydroxyacetophenone	DL-Threonine	75	103	68·4	7·9	68·4	7·8	$C_{11}H_{15}NO_2$	2-(*o*-Hydroxyphenyl)-2,5-dimethyloxazolidine
o-Hydroxyacetophenone	DL-Threonine		136	48·5	4·3	48·3	4·3	$C_{17}H_{18}N_4O_9$	2-(*o*-Hydroxyphenyl)-2,5-dimethyloxazolidine picrate

TABLE 3

NN'-Diphenylmalonamide ketimines (V)

R^1	R^2	R^3	M. p.	Yield (%)	Found (%) C	Found (%) H	Found (%) N	Formula	Required (%) C	Required (%) H	Required (%) N	$\lambda_{max.}$ (Å)
Pr^n	*p*-MeO·C_6H_4	H	173°	41	72·7	6·1	9·9	$C_{26}H_{27}N_3O_3$	72·7	6·3	9·8	
Pr^n	*o*-HO·C_6H_4	Me	140	60	72·8	6·4	—	$C_{26}H_{27}N_3O_3$ *	72·7	6·3	9·8	
Pr^n	*o*-HO·C_6H_4	H	137	67	72·1	6·3	9·9	$C_{25}H_{25}N_3O_3$ *	72·3	6·0	10·1	2410
Pr^n	*o*-HO·C_6H_4	Me	167	65	72·4	6·4	9·4	$C_{26}H_{27}N_3O_3$	72·6	6·3	9·8	
Pr^n	*o*-HO·C_6H_4	Et	140	75	73·0	6·7	9·5	$C_{27}H_{29}N_3O_3$	73·1	6·5	9·5	
$PhCH_2$	*o*-HO·C_6H_4	H	150	70	74·8	5·5	9·4	$C_{29}H_{25}N_3O_3$	75·1	5·4	9·1	
$PhCH_2$	*p*-HO·C_6H_4	H	157	30	75·0	5·7	—	$C_{29}H_{25}N_3O_3$	75·1	5·4		2700, 3240
$PhCH_2$	*o*-MeO·C_6H_4	H	175	40	75·6	5·5	8·7	$C_{30}H_{27}N_3O_3$	75·4	5·7	8·8	2800, 3220
$PhCH_2$	*o*-HO·C_6H_4	Me	159	50	75·6	5·9	—	$C_{30}H_{27}N_3O_3$	75·4	5·7		

* $\nu_{max.}$ 2950 (OH), 1965 (C=O) (cm.$^{-1}$).

TABLE 4

Hexahydro-1,3,5-triazines formed from aldimines and phenyl isocyanate

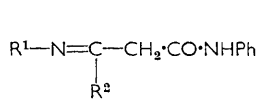
Aldehyde	Amine	M. p.	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N	Formula	Triazine	$\lambda_{max.}$ (Å)	Log ε
Salicylaldehyde	Methylamine	187	70·3	5·1	11·4	70·7	4·9	11·4	$C_{29}H_{24}N_4O_4$	1-Methyl-3,5-diphenyl-6-(*o*-phenylcarbamoyloxy)phenylhexahydro-1,3,5-triazine-2,4-dione		
Salicylaldehyde	Ethylamine	173	70·9	5·4	10·8	71·1	5·1	11·0	$C_{30}H_{26}N_4O_4$	1-Ethyl-3,5-diphenyl-6-(*o*-phenylcarbamoyloxy)phenylhexahydro-1,3,5-triazine-2,4-dione	2350—2500	4·53
Salicylaldehyde	n-Propylamine	175	71·3	5·5	10·8	71·6	5·4	10·8	$C_{31}H_{28}N_4O_4$	3,5-Diphenyl-6-(*o*-phenylcarbamoyloxy)phenyl-1-n-propylhexahydro-1,3,5-triazine-2,4-dione	2350—2400	4·55
Salicylaldehyde	Benzylamine	211 * (decomp.)			9·9			9·9	$C_{35}H_{28}N_4O_4$	1-Benzyl-3,5-diphenyl-6-(*o*-phenylcarbamoyloxy)phenylhexahydro-1,3,5-triazine-2,4-dione	2360—2370	4·53
p-Hydroxybenzaldehyde †	Benzylamine	143 (decomp.)	74·3	5·3		74·0	4·9		$C_{35}H_{28}N_4O_4$	1-Benzyl-3,5-diphenyl-6-(*p*-phenylcarbamoyloxy)phenylhexahydro-1,3,5-triazine-2,4-dione	2375—2400	4·90
p-Methoxybenzaldehyde	Propylamine	88	72·2	6·2	10·2	72·3	6·0	10·1	$C_{25}H_{25}N_3O_3$	6-(*p*-Methoxyphenyl)-3,5-diphenyl-1-propylhexahydro-1,3,5-triazine-2,4-dione		

* Crystallised from dimethylformamide. † The intermediate *aldimine* had m. p. 204° (from ethanol) (Found: C, 79·6; H, 6·2 $C_{14}H_{13}NO$ requires C, 79·6; H, 6·2%).

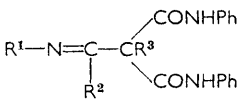
Moszew and Inasinki [7] investigated the reaction of anils of acetophenone with isocyanates. By use of vigorous conditions they obtained the monoamides (IV; $R^1 = R^2 =$ Ph or *p*-MeC_6H_4) and the diamides (V; $R^1 =$ Ph or *p*-MeC_6H_4, $R^2 =$ Ph or *p*-MeC_6H_4, $R^3 = H$). We have found that Schiff bases prepared from α-amino-acids or the corresponding amines and *o*- and *p*-hydroxy- and -methoxy-substituted aryl alkyl ketones react exothermically with phenyl isocyanate at room temperature to give the *NN'*-diphenylmalonamide

[7] J. Moszew and A. Inasinki, *Zestyty nauk., Uniw. Jagiel., Ser. Nauk. chem.*, 1962, **7**, 121 (*Chem. Abs.*, 1965, **63**, 11,290).

derivatives (V; R^1 = alkyl or CH_2Ph, R^2 = *o*- or *p*-$HO{\cdot}C_6H_4$ or -$MeO{\cdot}C_6H_4$, R^3 = H or alkyl) (Table 4). These substances on hydrolysis gave the original ketones, the corresponding alkylphenylureas and aniline. Under the same conditions the Schiff bases from *m*-hydroxy and -methoxyacetophenone, like those from the unsubstituted acetophenone, reacted only to produce the original ketones and the *NN'*-disubstituted ureas.

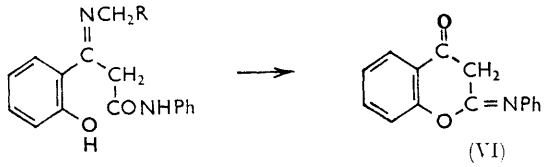


(IV)



(V)

The products obtained with the *o*-hydroxy-ketones were unstable to heat. The propiophenone and butyrophenone derivatives decomposed to give diphenylurea and the original ketones. On the other hand, the acetophenone derivatives, when heated at 90—100° cyclised with formation of the *N*-alkyl-*N'*-phenylureas to give 2-phenyliminochroman-4-one (VI) which could be obtained in higher yield directly without isolation of the diamide, possibly by cyclisation of the intermediate monoamide. Hydrogenation of (VI) gave a dihydro-derivative.

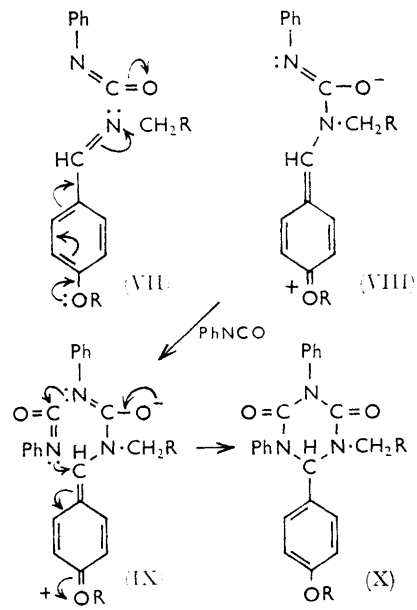


(VI)

The chromanone (VI) can obviously exist in a *cis*- or a *trans*-form depending on the configuration about the C=N bond. The n.m.r. spectrum indicated that the compound isolated was that with the *trans*-configuration. The protons of the methylene group in the heterocyclic ring showed a difference in chemical shift of 1·03 p.p.m. (J = *ca.* 2 c./sec.). This large difference is explicable in terms of a marked deshielding of that proton which lies nearer to the plane of the =NPh group than the other and hence is more under the influence of the aromatic ring current. These considerations require the =NPh group to be *trans* with respect to the oxygen of the heterocyclic ring.

s-Triazines are formed [8] when phenyl isocyanate is heated under pressure with aldimines such as *N*-benzylidene-ethylamine. Because of practical difficulties and poor yield this method of preparing triazines has been little used. In contrast, the reaction between *p*-methoxybenzylidene alkylamines with phenyl isocyanate takes place exothermically at room temperature to give the corresponding triazines, *e.g.*, (X; R = alkyl or Ph). Under the same conditions analogous Schiff bases derived from *m*-hydroxy-, *m*-methoxy-, and *o*-, *p*-, and *m*-nitrobenzaldehydes did not react. The mechanism [(VII) ⟶ (X); R = alkyl or Ph] is proposed. The charges in intermediate (VIII) can be neutralised either internally to give a (strained) four-membered ring or externally by addition of another isocyanate molecule to give (X), by the mechanism indicated (IX).

These triazines showed a broad band in the region 2350—2500 Å in their u.v. spectra. Hydrolysis of (X; R = alkyl or Ph) gave *p*-methoxybenzaldehyde, aniline, and the corresponding amine.



The reaction of Schiff bases derived from salicylaldehyde with phenyl isocyanate (three molecules in this case) again took place readily to give the corresponding *s*-triazines with a phenylcarbamoyloxy-substituent. In these compounds hydrolysis of the triazine ring did not take place so readily, but the carbamoyloxy-group could be cleaved to give the corresponding *o*-hydroxyphenyl-*s*-triazine.

EXPERIMENTAL

Preparation of Schiff bases.—(a) *By decarboxylation of amino-acids.* The amino-acid (10 mmoles) was mixed with the ketone (20 mmoles) and heated under a stream of nitrogen at the minimum temperature required for decarboxylation. The course of the reaction was followed by passing the gas stream through a solution of calcium hydroxide, and the resulting material was taken up in ethanol. The bases obtained crystalline are described in Table 1.

(b) *By condensation of the amine with the ketone.*—The amine (10 mmoles) was mixed with the ketone (20 mmoles) in dry toluene and the mixture was refluxed under a water separator till the reaction was complete. In some cases a catalytic amount of the amine hydrochloride was added to promote the reaction. After removal of the toluene the product was distilled or recrystallised from ethanol.

Copper Complexes of Schiff Bases.—The Schiff base (10 mmoles) in ethanol (60 ml.) was added to an aqueous ethanolic solution (50 ml.) of copper acetate (5 mmoles) and sodium acetate (10 mmoles). The dark coloured precipitate was filtered off, washed with alcohol and ether, and

[8] N. A. Lange, *J. Amer. Chem. Soc.*, 1926, **48**, 2440.

recrystallised from dimethylformamide–ethanol. *Bis*-{-[N-1-(o-*hydroxyphenyl*)*ethylidene*]*benzylaminato*}*copper* had m. p. 210° (decomp.) (Found: C, 70·1; H, 5·5; Cu, 12·3. $C_{30}H_{28}CuN_2O_2$ requires C, 70·4; H, 5·5; Cu, 12·4%), $\lambda_{max.}$ 2680 Å (log ε 4·36). *Bis*-{N-[α-(o-*hydroxy*-p-*methoxy*)-*benzylidene*]*benzylaminato*}*copper* had m. p. 190° (decomp.) (Found: C, 72·1; H, 5·5; Cu, 9·1. $C_{42}H_{36}CuN_2O_4$ requires C, 72·5; H, 5·2; Cu, 9·1%), $\lambda_{max.}$ 2920—2960 Å (log ε 4·48). *Bis*-{N-[*di*-(o-*hydroxyphenyl*)*methylene*]*benzylaminato*}*copper* had m. p. 170° (decomp.) (Found: Cu, 9·8. $C_{40}H_{32}CuN_2O_4$ requires Cu, 9·5%), $\lambda_{max.}$ 2708 Å (log ε 3·93).

Hydrogenation of Schiff Bases.—The Schiff base (5 mmoles) was dissolved in glacial acetic acid (25 ml.) and shaken with platinum oxide (0·1 g.) under hydrogen at atmospheric pressure. When hydrogenation was complete (3 hr.), the filtered solution was evaporated under reduced pressure and the residue was crystallised from ethanol–ether. N-[1-(o-*Hydroxyphenyl*)*ethyl*]*benzylamine acetate* had m. p. 125° (Found: C, 70·8; H, 7·3. $C_{17}H_{21}NO_3$ requires C, 71·1; H, 7·3%). In the case of the derivative from *o*-hydroxyacetophenone and tryptamine, the hydrogenated product was benzoylated to give N-*benzoyl*-N-[1-(o-*hydroxyphenyl*)*ethyl*]*tryptamine*, m. p. 180° (Found: C, 78·4; H, 6·2. $C_{25}H_{24}N_2O_2$ requires C, 78·2; H, 6·3%).

Preparation of Oxazolidines from Schiff Bases.—The α-amino-β-hydroxy-acids (10 mmoles) were mixed with the ketone and heated under nitrogen to the minimum temperature required for decarboxylation (*ca.* 200°). The dark coloured residue was taken up in ethanol and the filtered solution was decolourised with charcoal, concentrated and cooled. The product (Table 2) if crystalline was recrystallised from ethanol. In some cases the oxazolidine was isolated as the picrate, which was recrystallised from ethanol.

Hydrolysis of Oxazolidines.—Hydrolysis was effected by boiling with concentrated hydrochloric acid under reflux; the solution was extracted with benzene to remove the ketone, and the hydroxy-amine hydrochloride was isolated after evaporation of the aqueous layer.

Preparation of Thiazolidines from Cysteine.—Cysteine (20 mmoles) was decarboxylated by heating with acetophenone (40 mmoles) under nitrogen for 18 hr. The product was taken up in toluene and the solution was filtered and evaporated under reduced pressure. The oily residue dissolved in cold ether was treated with a cold ethereal solution of hydrogen chloride to give 2-*methyl*-2-*phenylthiazolidine hydrochloride* (25%), m. p. 182° (from ethanol) (Found: C, 55·6; H, 6·6. $C_{10}H_{13}NS$,HCl requires C, 55·7; H, 6·5%. By the same procedure *o*-methoxyacetophenone and cysteine gave 2-(o-*methoxyphenyl*)-2-*methylthiazolidine hydrochloride*, m. p. 175° (from ethanol–ether) (Found: C, 53·6; H, 6·5; N, 5·7. $C_{11}H_{15}NOS$,HCl requires C, 53·8; H, 6·5; N, 5·7%), $\lambda_{max.}$ 2740 Å (log ε 3·52).

NN′*Bis*-[α-(2,4-*dihydroxyphenyl*)*benzylidene*]-2,2′-*dithiodi*(*ethylamine*).—When 2,4-dihydroxybenzophenone was used with cysteine in the above reaction, the only product isolated was the *di-Schiff base* corresponding to cystine, m. p. 242° (decomp.) (Found: C, 65·9; H, 5·5. $C_{30}H_{28}N_2O_4S_2$ requires C, 66·2; H, 5·2%).

Preparation of the NN′-*Diphenylmalonamide Derivatives.*—The Schiff bases produced from the ketones and amines (or the corresponding amino-acids) (10 mmoles) were mixed with phenyl isocyanate (20 mmoles) at room temperature. When the exothermic reaction had subsided the mixture was heated on a steam-bath for a few min., and the product was crystallised from ethanol (Table 3).

Hydrolysis of the NN′-*Diphenylmalonamide Derivatives.*—These ketimines were hydrolysed by heating on a steam-bath with concentrated hydrochloric acid for 3 hr. The solution was diluted with water and extracted with ether; the extracts were evaporated to give the original ketone, identified as its 2,4-dinitrophenyl hydrazone, and the corresponding alkylphenylurea. Aniline hydrochloride was identified in the aqueous layer.

Preparation of 2-*Phenyliminochroman*-4-*one.*—The Schiff base from *o*-hydroxyacetophenone and the amine (10 mmoles) was mixed with phenyl isocyanate (40 mmoles) and heated on a steam-bath for 3 hr. The product gave 2-*phenyliminochroman*-4-*one* (80%), m. p. 163° (from benzene or ethanol) (Found: C, 75·8; H, 4·8; N, 5·8. $C_{15}H_{11}NO_2$ requires C, 76·0; H, 4·6; N, 5·9%), $\lambda_{max.}$ 2380 Å (log ε 4·4), $\nu_{max.}$ (KCl) 1720 (C=O) and 1620 (C=N) cm.$^{-1}$, τ 5·17 and 6·18 (both d, J = 1—2 c./sec.). The mother-liquor from this material when concentrated deposited the corresponding *N*-alkyl-*N*′-phenylurea. The same substance was also obtained (50%) by heating the diamides (above) obtained from *o*-hydroxyacetophenone on a steam-bath for 2 hr. The substance was very readily hydrolysed by dilute aqueous acid or alkali to the original hydroxyacetophenone, aniline, and carbon dioxide. When hydrogenated in the presence of platinum oxide, hydrogen (1 mol.) was taken up to give 2-*phenylaminochroman*-4-*one*, m. p. 135° (from ethanol) (Found: C, 72·2; H, 6·2; N, 4·9. $C_{15}H_{13}NO_2$,C_2H_5OH requires C, 71·6; H, 6·7; N, 4·9%), $\lambda_{max.}$ 2670 and 2740 Å, $\nu_{max.}$ (KCl) 1720 (C=O), 3420 (NH), and 1350 (C–N) cm.$^{-1}$. The hydrogenated product gave a *dinitrophenylhydrazone*, m. p. 200° (from ethanol (Found: C, 59·8; H, 4·1. $C_{21}H_{17}N_5O_5$ requires C, 60·1; H, 4·1%).

Preparation of Hexahydro-1,3,5-*triazines.*—The aldehyde (20 mmoles) was refluxed with an excess of the amine in ethanol for 1 hr. The product left after removal of the ethanol and the excess of amine was mixed at room temperature with phenyl isocyanate (40 mmoles). When the exothermic reaction had subsided, the mixture was heated on a water-bath for 1 hr. and crystallised from ethanol. Yields were >85%. The results are shown in Table 4.

Hydrolysis of Carbamoyloxy-groups.—The triazine (4·0 mmole) was vigorously stirred with 5N-hydrochloric acid (30 ml.) for 30 min. at 70—75° and the solid product was filtered off, washed, and recrystallised from ethanol.

1-*Benzyl*-6-(o-*hydroxyphenyl*)-3,5-*diphenylhexahydro*-1,3,5-*triazine*-2,4-*dione* had m. p. 195° (Found: C, 74·9; H, 5·1; N, 9·1. $C_{28}H_{23}N_3O_3$ requires C, 74·8; H, 5·1; N, 9·4%), $\lambda_{max.}$ 2370—2390 Å (log ε 4·4). 1-*Benzyl*-6-(p-*hydroxyphenyl*)-3,5-*diphenylhexahydrotriazine*-2,4-*dione* had m. p. 168° (Found: C, 74·5; H, 5·1; N, 9·8. $C_{28}H_{23}N_3O_3$ requires C, 74·8; H, 5·1; N, 9·4%), $\lambda_{max.}$ 2400 Å (log ε 4·8).

Hydrolysis of Hexahydrotriazines.—The material was heated under reflux with concentrated hydrochloric acid for 2 hr. and the original aldehyde was identified in the steam distillate of the hydrolysate as its 2,4-dinitrophenylhydrazone. Aniline and the original amine were identified as hydrochlorides after evaporation of the hydrolysate to dryness and fractional crystallisation from acetone–water.

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