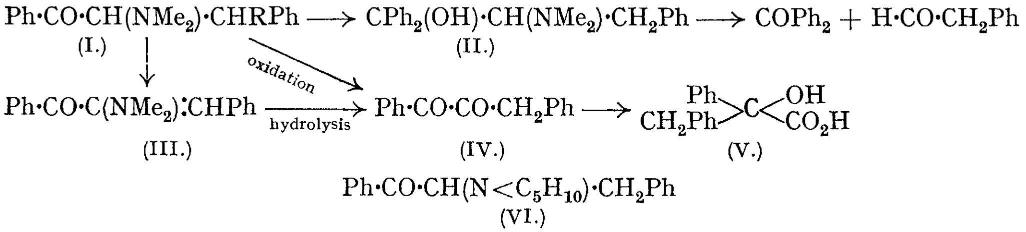
177. *Reactions of α-Amino-ketones.*

By Thomas S. Stevens and B. Arthur Hems.

In establishing the constitutions of substances analogous to (I) it was difficult to prove that the nitrogen atom occupied the α- and not the β-position with respect to the carbonyl group (Stevens, J., 1930, 2109). A feasible procedure is now described, together with some incidental observations.

The *hydroxy-amine* (II), prepared from (I, R = H) by the Grignard reaction, was comparatively stable even to acid permanganate, but it was oxidised very readily by persulphate, or by manganese dioxide and sulphuric acid, to benzophenone and phenylacetaldehyde. This reaction, which establishes the point at issue, was not brought about by other oxidising agents; nor could a similar oxidation of (I) itself be achieved. The nature of the breakdown, and the reagents employed, recall the oxidative fission of narcotine and its analogues, which, like (II), contain the group $\cdot O\cdot CAr\cdot C\cdot NAlk_2$. A similar series of reactions was carried out with (I, R = Me) and with (VI), but it failed in the case of (I, R = Ph), probably because the required aldehyde was not volatile enough to be protected from further oxidation.



$$\underset{\text{(I.)}}{Ph\cdot CO\cdot CH(NMe_2)\cdot CHRPh} \longrightarrow \underset{\text{(II.)}}{CPh_2(OH)\cdot CH(NMe_2)\cdot CH_2Ph} \longrightarrow COPh_2 + H\cdot CO\cdot CH_2Ph$$

$$\underset{\text{(III.)}}{Ph\cdot CO\cdot C(NMe_2)\colon CHPh} \xrightarrow[\text{hydrolysis}]{} \underset{\text{(IV.)}}{Ph\cdot CO\cdot CO\cdot CH_2Ph} \longrightarrow \underset{\text{(V.)}}{\begin{matrix}Ph\\CH_2Ph\end{matrix}\!>\!C\!<\!\begin{matrix}OH\\CO_2H\end{matrix}}$$

(I.) → (III.); (I.) $\xrightarrow{\text{oxidation}}$ (IV.)

$$\underset{\text{(VI.)}}{Ph\cdot CO\cdot CH(N{<}C_5H_{10})\cdot CH_2Ph}$$

Air slowly oxidised alkaline solutions of (I), yielding, by a curious dehydrogenation, the unsaturated *base* (III), together with phenylbenzylglycollic (V) and benzoic acids. The constitution of (III) follows from its hydrolysis to phenylbenzylglyoxal (IV) and its synthesis from phenyl bromostyryl ketone and dimethylamine. The acid (V) presumably arose by benzilic transformation of (IV) (compare Widman, *Ber.*, 1916, **49**, 477; Jörlander, *ibid.*, 1917, **50**, 416). Independent experiments showed that (III) was not produced from dimethylamine and (IV), nor (V) from (III) *via* (IV), under the conditions of the dehydrogenation. A similar result could not be achieved by other oxidising agents, and other bases, *e.g.* (I, R = Me), could not be oxidised in an analogous manner.

The allyl radical, and others containing a similarly situated unsaturated centre, are detached from tertiary bases by cyanogen bromide with special facility. From (I, R = H) which contains a *carbonyl* double bond in a position corresponding to that of the olefinic double bond in an allylamine, cyanogen bromide removed on the contrary a methyl group; and in the case of (VI) the usually stable piperidine ring was opened.

Experimental.

2-*Dimethylamino*-1-*hydroxy*-1 : 1 : 3-*triphenylpropane* (II).—The base (I, R = H) was added to excess of phenylmagnesium bromide in ether, the vigorous reaction completed by 1 hour's boiling, and after treatment with ice and ammonium chloride the product (II) was extracted from the ethereal layer by acid; yield, almost quantitative. It crystallised from ligroin or methyl alcohol in small prisms, m. p. 75°, whose solutions in concentrated sulphuric acid changed from orange-red to colourless to bluish-green in a few seconds (Found : N, 4·0. $C_{23}H_{25}ON$ requires N, 4·2%). The *picrate* formed irregular yellow prisms from alcohol, m. p. 188° with previous softening (Found : $C_6H_3O_7N_3$, 41·1. $C_{23}H_{25}ON,C_6H_3O_7N_3$ requires $C_6H_3O_7N_3$, 40·9%). The analogous hydroxy-amines described below were prepared in the same way.

Oxidation. A solution and suspension of the base (II) in 0·05*N*-sulphuric acid (1 equiv.) was distilled with gradual addition of a slight excess of 0·5% ammonium persulphate solution. The ethereal extract of the distillate yielded 10% of phenylacetaldehyde, separated as bisulphite compound and identified as semicarbazone (mixed m. p.), and also much benzophenone, characterised as dinitrophenylhydrazone (mixed m. p.).

2-*Dimethylamino*-1-*hydroxy*-1 : 1 : 3-*triphenylbutane*.—This base, prepared from (I, R = Me) (α-form; Stevens, *loc. cit.*), was a gum. The sparingly soluble *hydrochloride* crystallised from methyl alcohol–ether in stout irregular plates, m. p. 226—231° (decomp.) (Found: HCl, 9·6. $C_{24}H_{27}ON,HCl$ requires HCl, 9·6%). The base was oxidised in the same way as its lower homologue, except that 0·02*N*-sulphuric acid was used, and α-phenylpropaldehyde (prepared for comparison according to Tiffeneau, *Ann. Chim. Phys.*, 1907, **10**, 351) and benzophenone were isolated and identified similarly.

2-*Piperidino*-1-*hydroxy*-1 : 1 : 3-*triphenylpropane* (VI), prepared from ω-piperidino-ω-benzylacetophenone (Stevens, *loc. cit.*), formed prisms from ligroin, m. p. 145—147° (Found: N, 3·8. $C_{26}H_{29}ON$ requires N, 3·8%). The oxidation and the identification of the products were performed as in the previous case.

2-*Dimethylamino*-1-*hydroxy*-1 : 1 : 3 : 3-*tetraphenylpropane*, prepared from (I, R = Ph) (Stevens, *loc. cit.*), and purified through its insoluble sulphate, crystallised from ligroin in warty masses, m. p. 105° (Found: N, 3·5. $C_{29}H_{29}ON$ requires N, 3·4%). Oxidised in the same way as (II), it gave only benzophenone, and neither diphenylacetaldehyde nor diphenylacetic acid could be detected.

ω-*Dimethylamino*-ω-*benzylideneacetophenone* (III) was readily prepared by the method of Dufraisse and Moureu (*Bull. Soc. chim.*, 1927, **41**, 469), the piperidine being replaced by 10% ethereal dimethylamine. It crystallised from alcohol in scarlet needles, m. p. 62° [Found: N, 5·4; *M* (Rast), 240. $C_{17}H_{17}ON$ requires N, 5·6%; *M*, 251]. The base (I), in 10 parts of 2·5*N*-alcoholic sodium ethoxide solution, was oxidised by a slow current of pure dry air for 6 hours at 70°. The ethereal extract of the diluted mixture yielded (III) (mixed m. p.) on evaporation. This base gave dimethylamine picrate (mixed m. p.) with alcoholic picric acid, and ethereal oxalic acid (compare Dufraisse and Moureu, *loc. cit.*) converted it into phenylbenzylglyoxal (IV), m. p. 60° (quinoxaline, m. p. and mixed m. p. 98°). The alkaline aqueous-alcoholic liquors from the oxidation gave a mixture of acids resolved by crystallisation from benzene into more soluble benzoic acid (mixed m. p.) and less soluble phenylbenzylglycollic acid (V) (mixed m. p.), which yielded benzophenonedinitrophenylhydrazone (mixed m. p.). When the sodium ethoxide solution was replaced by alcoholic potash, the products were the same, but the yield of the acid (V) was negligible.

Action of Cyanogen Bromide on (I).—The base was refluxed for 30 minutes with cyanogen bromide (1½ mols.) in ether. After removal of ether and cyanogen bromide in a vacuum, the residual ω-*methylcyanoamido*-ω-*benzylacetophenone* was crystallised from methyl alcohol; m. p. 110° (Found: N, 10·7. $C_{17}H_{16}ON_2$ requires N, 10·6%). By 5 minutes' boiling with 10% sulphuric acid, the cyanoamide was completely converted, without dissolving, into the related *urea*, 226° (Found: N, 10·1. $C_{17}H_{18}O_2N_2$ requires N, 9·9%). On similar treatment, ω-piperidino-ω-benzylacetophenone (VI) yielded ω-(ε-*bromoamylcyanoamido*)-ω-*benzylacetophenone*, m. p. 83° after crystallisation from methyl alcohol (Found: N, 7·0; Br, 20·7. $C_{21}H_{23}ON_2Br$ requires N, 7·0; Br, 20·1%).

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THE UNIVERSITY, GLASGOW.

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