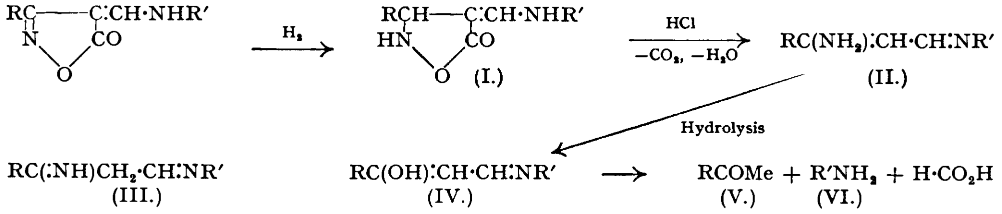
## 225. iso*Oxazolones. Part II.* iso*Oxazolidones.*

By G. Shaw.

The compounds formerly regarded as arylaminomethyl*iso*oxazolones (*J.*, 1950, 720) have now been shown to be arylaminomethylene*iso*-oxazolidones. The latter when treated with hydrogen chloride in acetic acid afforded anils of substituted β-amino-acraldehydes (II). Similarly the product of the palladium-catalysed reduction of 4-benzylidene-3-methyl-*iso*oxazol-5-one with hydrogen chloride afforded 3-imino-1-phenylbutene, suggesting the formation of an *iso*oxazolidone which however was not isolated. *iso*Oxazolones under the same conditions did not react with hydrogen chloride.

In a preliminary paper (*J.*, 1950, 720), which is regarded as Part I of this series, it was shown that hydrogenation of the *iso*oxazolone nucleus produces a reactive anhydride-like compound postulated as an *iso*oxazolidone; this postulate has now been confirmed. It has been found that the compounds formerly assumed to be arylaminomethyl*iso*oxazolones are in fact arylaminomethylene*iso*oxazolidones (I), since hydrolysis afforded the arylamine in good yield. In addition when a solution of (I; R = R′ = Ph), (I; R = Me, R′ = Ph), (I; R = $CH_2Ph$, R′ = Ph), or (I; R = Me, R′ = *o*-tolyl) in dry acetic acid was saturated with dry hydrogen chloride at room temperature, evaporation of the solvent afforded the yellow crystalline hydrochloride of the base (II). The hydrochlorides of (I) were obtained as white solids by triturating the *iso*oxazolidones with hydrochloric acid.

The free bases (II; R = R′ = Ph) and (II; R = $CH_2Ph$, R′ = Ph) were precipitated as crystalline solids when aqueous solutions of the corresponding hydrochlorides were treated with sodium hydrogen carbonate solution, whereas the bases (II; R = Me, R′ = Ph) and (II; R = Me, R′ = *o*-tolyl) were obtained as oils. Ethereal solutions of the bases with hydrogen chloride gave precipitates of the unchanged salts.



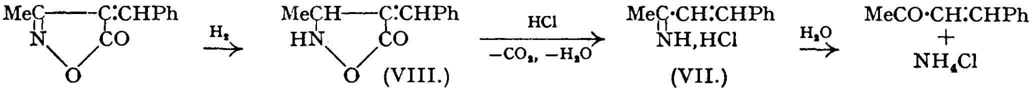
(I.) (II.) $RC(NH_2){:}CH{\cdot}CH{:}NR'$

(III.) $RC({:}NH)CH_2{\cdot}CH{:}NR'$

(IV.) $RC(OH){:}CH{\cdot}CH{:}NR' \longrightarrow RCOMe + R'NH_2 + H{\cdot}CO_2H$ (V.) (VI.)

That the bases were anils of substituted β-aminoacraldehyde (II) followed from their hydrolysis, which afforded the ketones (V), the amines (VI), and ammonia. The analogous keto-anils (IV) are known to hydrolyse in a similar manner (Claisen and Fischer, *Ber.*, 1888, **21**, 1136). The alternative imino-structure (III) for the bases is unlikely since compounds of this type are generally very unstable in the presence of water.

When the product from the palladium-catalysed hydrogenation of 4-benzylidene-3-methyl-*iso*oxazol-5-one was treated with dry hydrogen chloride in acetic acid a white crystalline hydrochloride was obtained. This was soluble in water giving a clear solution which after 2—3 minutes became turbid and deposited a crystalline precipitate of benzylideneacetone. The hydrochloride readily evolved ammonia when treated with cold sodium hydroxide solution, and can be formulated as the imine (VII).



Neither 4-benzylidene- nor 4-benzyl-3-methyl*iso*oxazol-5-one showed any signs of reaction with dry hydrogen chloride under the conditions used for the corresponding *iso*oxazolidones, hence the imine (VII) must have arisen from a precursor, such as the *iso*oxazolidone (VIII) which has not yet been isolated in crystalline form.

The complete hydrogenation of 4-benzylidene-3-methyl*iso*oxazol-5-one to 4-phenylbutan-2-one and of 4-anilinomethylene-3-methyl*iso*oxazol-5-one to 4-anilinobutan-2-one has been dealt with previously (cf. Part I). It would thus appear that hydrogenation of the *iso*oxazolone nucleus results first in the saturation of the endocyclic double bond to afford an *iso*oxazolidone with anhydride properties which are stabilised by an exocyclic double bond in the 4-position. Saturation of the exocyclic double bond then results in the formation of a reactive system which combines readily with water or alcohol (cf. Part I). Initial saturation of the exocyclic double bond may also occur to a small extent since a low yield of 4-benzyl-3-methyl*iso*oxazol-5-one was obtained by hydrogenation of 4-benzylidene-3-methyl*iso*oxazol-5-one (Part I).

The anils (II) inhibited the growth of *Staphylococcus aureus* at a dilution of about 1 in 20,000.

## EXPERIMENTAL.

4-*Anilinomethylene*-3-*benzyl*iso*oxazolid*-5-*one* (I; R = Ph·CH₂, R′ = Ph).—4-Anilinomethylene-3-benzyl*iso*oxazol-5-one (2 g.) was reduced with hydrogen and 5% palladium–charcoal for 1 hour (Uptake, 170 ml. Calc. for 1 mol., 161 ml.). Evaporation of the filtered solution *in vacuo* gave 4-*anilinomethylene*-3-*benzyl*iso*oxazolid*-5-*one* (2 g.) which separated from water as very pale yellow needles, m. p. 166—168° (decomp.) (Found: N, 9·7. $C_{17}H_{16}O_2N_2$ requires N, 10%). The *iso*oxazolidone (0·5 g.) was triturated with 2N-hydrochloric acid (5 ml.), giving the *hydrochloride* (0·35 g.), which separated from ethanol–ether as white needles, m. p. 170°, sparingly soluble in water (Found: N, 8·8. $C_{17}H_{16}O_2N_2$,HCl requires N 8·85%).

4-*Anilinomethylene*-3-*phenyl*iso*oxazolid*-5-*one* (I; R = R′ = Ph).—4-Anilinomethylene-3-phenyl*iso*oxazol-5-one (2 g.) when similarly reduced gave 4-*anilinomethylene*-3-*phenyl*iso*oxazolid*-5-*one* (2 g.) which separated from water as fine pale yellow needles, m. p. 170° (Found: C, 72·0; H, 5·45; N, 10·35. $C_{16}H_{14}O_2N_2$ requires C, 72·2; H, 5·3; N, 10·5%).

3-*Methyl*-4-m-*toluidinomethylene*iso*oxazolid*-5-*one* (I; R = Me, R′ = *m*-tolyl).—This product separated from water in pale yellow needles of the *monohydrate*, m. p. 98—100° (decomp.) (Found: N, 12·1. $C_{12}H_{14}O_2N_2$,$H_2O$ requires N, 11·85%).

*Hydrolysis of the Arylaminomethylene*iso*oxazolidones*.—The *iso*oxazolidones (I; R = R′ = Ph; R = Me, R′ = Ph; R = Ph·CH₂, R′ = Ph) (2 g.) were refluxed with N-hydrochloric acid (20 ml.) for 1 hour, and the solutions were made alkaline with 5N-sodium hydroxide and extracted with ether. Evaporation of the extracts afforded, in each case, an oil which had an odour of aniline and when benzoylated gave benzanilide (60—80% of the theoretical amount), m. p. 160° not depressed on admixture with an authentic specimen. Similarly the *iso*oxazolidones (I; R = Me, R′ = *o*-tolyl; R = Me, R′ = *m*-tolyl; and R = Me, R′ = *p*-tolyl) when hydrolysed gave the corresponding toluidines.

*Reaction of the Arylamino*iso*oxazolidones with Hydrogen Chloride*.—1-*Amino*-1-*phenyl*-3-*phenylimino-propene* (II; R = Ph, R′ = Ph). Dry hydrogen chloride was passed into a solution of 4-anilino-methylene-3-phenyl*iso*oxazolid-5-one (3 g.) in acetic acid (20 ml.) until the gas was no longer absorbed; no attempt was made to cool the solution, the temperature of which rose as the gas was absorbed. The solution was left overnight, then evaporated to dryness *in vacuo*, giving a solid residue of 1-*amino*-1-*phenyl*-3-*phenyliminopropene hydrochloride* (2·2 g.) which separated from ethanol–ether as yellow needles, m. p. 210° (decomp.) (Found: C, 69·3; H, 6·0; N, 10·4. $C_{15}H_{14}N_2$,HCl requires C, 69·6; H, 5·85; N, 10·8%). The hydrochloride (1 g.) in water (20 ml.) was treated with excess of sodium hydrogen carbonate solution whereupon a yellow precipitate was obtained; the 1-*amino*-1-*phenyl*-3-*phenylimino-propene* (0·8 g.) separated from light petroleum as bright-yellow plates, m. p. 167° [Found: C, 80·85;

H, 6·6; N, 12·8%; *M* (Rast), 217. $C_{15}H_{14}N_2$ requires C, 81·05; H, 6·35; N, 12·6%; *M*, 222]. A solution of the base (0·1 g.) in ether when treated with dry hydrogen chloride gave a precipitate of the hydrochloride, m. p. 210° (decomp.) not depressed on admixture with the sample prepared as above.

*Hydrolysis of the imine.* The base (2 g.) was refluxed with N-hydrochloric acid (20 ml.) for 30 minutes, and the cooled solution extracted with ether. Evaporation of the extract gave acetophenone (2 : 4-dinitrophenylhydrazone, m. p. 249—250° not depressed when mixed with an authentic specimen, m. p. 250°). The aqueous solution was concentrated to a small volume and made alkaline with 5N-sodium hydroxide; ammonia was evolved and was removed by aeration. The solution was shaken with benzoyl chloride giving benzanilide, m. p. 160° not depressed on admixture with an authentic specimen.

1-*Amino*-1-*methyl*-3-*phenyliminopropene* (II; R = Me, R′ = Ph).—4-Anilinomethylene-3-methyl*iso*oxazolid-5-one (2 g.) when treated with hydrogen chloride as above gave 1-*amino*-1-*methyl*-3-*phenyliminopropene hydrochloride dihydrate* (1·55 g.) which separated from ethanol–ether as bright-yellow needles, m. p. 98—99° (decomp.) (Found: C, 52·4; H, 7·5; N, 12·2. $C_{10}H_{12}N_2,HCl,2H_2O$ requires C, 52·15; H, 7·35; N, 12·05%). Basification of a solution of the hydrochloride gave an oil which did not crystallise; a solution of the oil in ether, however, when treated with hydrogen chloride, gave the unchanged salt. Hydrolysis of the hydrochloride with acid gave acetone, ammonia, and aniline.

1-*Amino*-1-*benzyl*-3-*phenyliminopropene* (II; R = Ph·CH$_2$, R′ = Ph).—4-Anilinomethylene-3-benzyl*iso*oxazolid-5-one (2 g.) with hydrogen chloride gave 1-*amino*-1-*benzyl*-3-*phenyliminopropene hydrochloride hydrate* (1·4 g.) which separated from ethanol–ether as yellow needles, m. p. 98—100° (decomp.) (Found: C, 65·95; H, 7·0; N, 9·5. $C_{16}H_{16}N_2,HCl,H_2O$ requires C, 66·1; H, 6·6; N, 9·65%). Basification of an ice-cold aqueous solution of the hydrochloride (1 g.) with sodium hydrogen carbonate gave 1-*amino*-1-*benzyl*-3-*phenyliminopropene* (0·6 g.) as a crystalline precipitate which separated from a small amount of light petroleum on cooling to 0° as very pale yellow laths, m. p. 39—40° (Found: C, 81·1; H, 7·0; N, 12·0. $C_{16}H_{16}N_2$ requires C, 81·35; H, 6·8; N, 11·85%). Hydrolysis of the base with dilute acid gave benzyl methyl ketone, ammonia, and aniline.

1-*Amino*-1-*methyl*-3-o-*tolyliminopropene* (II; R = Me, R′ = *o*-tolyl).—3-Methyl-4-*o*-toluidinomethylene*iso*oxazolid-5-one (10 g.) with hydrogen chloride gave 1-*amino*-1-*methyl*-3-o-*tolyliminopropene hydrochloride* (7 g.) which separated from ethanol–ether as pale yellow needles, m. p. 160° (Found: N, 13·35. $C_{11}H_{14}N_2,HCl$ requires N, 13·3%). Hydrolysis of the salt gave acetone, ammonia, and *o*-toluidine.

*Reaction of the Reduction Product of* 4-*Benzylidene*-3-*methyl*iso*oxazol*-5-*one with Hydrogen Chloride.*—4-Benzylidene-3-methyl*iso*oxazol-5-one (3 g.) in dry acetic acid (30 ml.) was reduced with hydrogen and 5% palladium–charcoal (Uptake, 385 ml. Calc. for 1 mol., 375 ml.). Dry hydrogen chloride was passed through the filtered solution until the gas was no longer absorbed, and the solution was set aside overnight and then evaporated to dryness *in vacuo*, giving an oil which soon crystallised. 3-*Imino*-1-*phenylbut*-1-*ene hydrochloride hydrate* (1·1 g.) separated from ethanol–ether as white, hair-like needles, m. p. 61—62° (Found: N, 6·8. $C_{10}H_{11}N,HCl,H_2O$ requires N, 7·0%). The hydrate lost water when heated at 56°/15 mm., to give a glass-like material which readily solidified when rubbed with moist ether affording the hydrated hydrochloride. The imine (0·4 g.) was dissolved in water (0·5 ml.) giving a clear solution which after a few minutes deposited a crystalline precipitate of benzylideneacetone (0·2 g.), m. p. 42° not depressed on admixture with an authentic specimen, m. p. 42°. The imine readily afforded ammonia when warmed with sodium hydroxide solution, and with semicarbazide it gave benzylideneacetone semicarbazone (as white plates from methanol), m. p. 184—185°, undepressed on admixture with an authentic specimen, m. p. 185°, obtained as laths from methanol; a solution of the plates gave laths when seeded therewith. After a few days the solid hydrochloride had crumbled to a white powder of benzylideneacetone and ammonium chloride.

*Treatment of* 4-*Benzyl*-3-*methyl*iso*oxazol*-5-*one with Hydrogen Chloride.*—A solution of the *iso*oxazolone (2 g.) in dry acetic acid was saturated with dry hydrogen chloride at room temperature. After 3 days the solution was evaporated to dryness *in vacuo* giving the unchanged *iso*oxazolone (1·8 g.). Under the same conditions 4-benzylidene-3-methyl*iso*oxazol-5-one did not react with hydrogen chloride.

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