697. iso*Oxazolones. Part V.* Arylaminoalkyl(or aryl)idene-*iso*oxazolones and -*iso*oxazolidones.*

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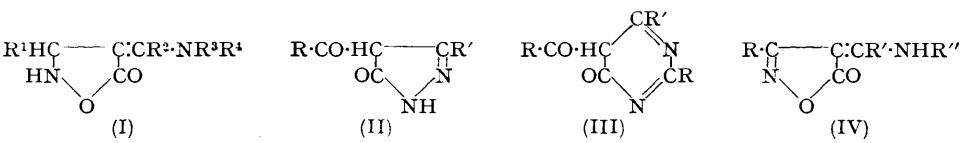
The reaction of *NN'*-diphenylacetamidine and benzamidine with 3-phenyl-*iso*oxazol-5-one gave the *iso*oxazolones (IV; R = R'' = Ph, R' = Me and Ph), and similar products (V; R = Me and Ph) were obtained from 3-methyl-1-phenylpyrazol-5-one. Hydrolysis, hydrogenation, and methylation of the products have been studied.

The reaction of arylaminomethylene*iso*oxazolidones (I; R^2 = H) with hydrazines and aromatic amidines has been shown (Part III, *J.*, 1952, 3428) to give acyl-pyrazolones and -pyrimidones (respectively II and III; R' = H). This has now been extended in an attempt to prepare other pyrazolones and pyrimidones; syntheses were required of arylaminoalkyl(or aryl)idene-*iso*oxazolones (IV; R' = alkyl, etc.) and -*iso*oxazolidones (I; R^2 = alkyl, etc.) and of *N*-alkyl- or *N*-aryl-*iso*oxazolidones (I; R^3 and R^4 = alkyl or aryl), which could not undergo the base-catalysed rearrangement characteristic of (I; R^2 = R^3 = H, R^4 = aryl), a limiting factor in the preparation of the pyrimidines.



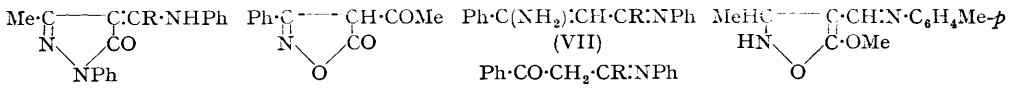
Equimolar parts of 3-phenyl*iso*oxazol-5-one and *NN'*-diphenylacetamidine, kept at 120—130° for 1 hour, gave smoothly the *iso*oxazolone (IV; R = R'' = Ph, R' = Me). The reaction, analogous to that of *NN'*-diaryl-formamidines with reactive methylene groups, namely, $>CH_2 + Ar{\cdot}N{:}CR{\cdot}NHAr \longrightarrow C{:}CR{\cdot}NHAr + ArNH_2$, does not appear to have been recorded previously; its generality was confirmed by the preparation, in a similar manner, of (IV; R = R' = R'' = Ph) from the phenyl*iso*oxazolone and *NN'*-diphenylbenzamidine, and of the compounds (V; R = Me and Ph) from 3-methyl-1-phenylpyrazol-5-one and the appropriate amidines. Ethyl acetoacetate and *NN'*-diphenylacetamidine reacted, however, with difficulty, to give a high-melting compound to which no simple structure could be assigned. The amidines failed to remove the benzylidene group in 4-benzylidene-3-methyl*iso*oxazol-5-one below 150°, and above this temperature decomposition resulted. Similar experiments with (*a*) methyl-*NN'*-diphenyl*iso*thiourea, *NN'*-diphenylguanidine, and *NN'N''*-triphenylguanidine and (*b*) phenyl*iso*oxazolone were also unsuccessful, the first-mentioned compound reacting with loss of methanethiol, and the others with decomposition.

Reaction of the *iso*oxazolone (IV; R = R'' = Ph, R' = Me) with boiling dilute alkali, was similar to that of the *iso*oxazolones (IV; R' = H) (Cook and Shaw, *J.*, 1952, 4466), and gave the ketone (VI), which was converted back into (IV; R = R'' = Ph, R' = Me) by hot aniline. The *iso*oxazolone (IV; R = R' = R'' = Ph), however, was remarkably resistant and was recovered unchanged from 2N-sodium hydroxide solution after 4 hr.' boiling; continued boiling with aqueous-alcoholic hydrogen chloride opened the *iso*oxazol-

* Part IV, preceding paper.

one ring, to form dibenzoylmethane; it is interesting that 4-anilinomethylene-3-methyl-1-phenylpyrazol-5-one (Dains and Brown, *J. Amer. Chem. Soc.*, 1909, **31**, 1148) was not hydrolysed by alkali, also that recovery of the *iso*oxazolone (IV; R = R′ = R″ = Ph) from alkaline solution by acidification was attended by the precipitation of a bright yellow solid [possibly an enol ·C(OH):C·CR′:NR″] which after a few seconds had changed to the colourless *iso*oxazolone.

Hydrogenation of the *iso*oxazolone (IV; R = R″ = Ph, R′ = Me) in ethanol at a platinum catalyst gave the *iso*oxazolidone (I; $R^1 = R^3 = Ph$, $R^2 = Me$, $R^4 = H$) which was readily hydrolysed to the anil (VIII; R = Me) or benzoylacetone. The *iso*oxazolidone with hydrazine readily gave the pyrazolone (II; R = Ph, R′ = Me) in rather low yield, but with aromatic and aliphatic amidines or with sodium hydroxide the base (VII; R = Me) was obtained almost quantitatively; this structure followed from acid hydrolysis to benzoylacetone, ammonia, and aniline. Hydrogenation of the *iso*oxazolone (IV; R = R′ = R″ = Ph) in ethanol or ethyl acetate gave the base (VII; R = Ph) exclusively and this furnished ammonia, aniline, and dibenzoylmethane on hydrolysis. These experiments suggest that the introduction of increasingly large substituents R^2 in (I) is accompanied by an increased tendency of the *iso*oxazolidone to rearrange, presumably to the acid $RC(NH_2):CH(CO_2H)\cdot CR:NR$, and thence to the base (VII).



(V) (VI) (VII) (VIII) (IX)

Possible routes to the required *iso*oxazolidones (I; $R^3 = R^4$ = alkyl or aryl) included the condensation of *N*-alkyl-*NN*′-diarylformamidines with an *iso*oxazolone, or alkylation of the available *iso*oxazolones (IV; R = H) and hydrogenation of the products, or alkylation of *iso*oxazolidones (I; $R^2 = R^3 = H$, R^4 = aryl). *N*-Methyl-*NN*′-di-*p*-tolylformamidine was prepared, in rather poor yield, from *NN*′-di-*p*-tolylformamidine and methyl iodide (Lander, *J.*, 1904, **85**, 996); an attempt to prepare the amidine by desulphurisation of *N*-methyl-*NN*′-di-*p*-tolylthiourea with Raney nickel in benzene failed, although we have frequently used this method successfully for the preparation of *NN*′-diarlyformamidines from corresponding thioureas. The *N*-methylformamidine reacted with 3-phenyl*iso*oxazol-5-one but the product was an intractable gum which did not have the physical properties expected of the required *iso*oxazolone. Attempted methylation of 3-methyl-4-*p*-toluidinomethylene*iso*oxazol-5-one with methyl iodide or methyl sulphate, alone or in the presence of a base, or with diazomethane, was also unsuccessful. 3-Methyl-4-*p*-toluidinomethylene*iso*oxazolid-5-one (I; $R^1 = Me$, $R^2 = R^3 = H$, $R^4 = p$-tolyl), however, reacted slowly with diazomethane, to give a basic compound with the required molecular formula; hydrolysis of this substance with hydrochloric acid gave ammonia, *p*-toluidine, and acetone, indicating that it was the methoxy*iso*oxazoline (IX); the *iso*oxazoline was readily hydrogenated to a substance, possibly $C_{11}H_{15}O_4N$, to which no simple structure could be assigned.

Experimental

4-1′-*Anilinoethylidene*-3-*phenyl*iso*oxazol*-5-*one* (IV; R = R″ = Ph, R′ = Me).—A finely ground mixture of 3-phenyl*iso*oxazol-5-one (2·7 g.) and *NN*′-diphenylacetamidine (3·5 g.) was kept at 120—130° (bath) for 1 hr., then cooled. The hard red glass dissolved in boiling ethanol (40 ml.); when cooled, the solution gave crystalline 4-1′-*anilinoethylidene*-3-*phenyl*iso*oxazol*-5-*one* (1·5 g.) which recrystallised from ethanol as plates, m. p. 184—185° (Found: C, 73·15; H, 5·1; N, 10·25. $C_{17}H_{14}O_2N_2$ requires C, 73·35; H, 5·05; N, 10·05%). A further quantity (0·5 g.) separated from the filtrate overnight.

4-1′-*Anilinobenzylidene*-3-*phenyl*iso*oxazol*-5-*one* (IV; R = R′ = R″ = Ph).—3-Phenyl*iso*oxazol-5-one (3 g.) and *NN*′-diphenylbenzamidine (5 g.) at 140—150° (bath) (1 hr.) gave 4-1′-*anilinobenzylidene*-3-*phenyl*iso*oxazol*-5-*one* (2·5 g.), plates (from ethanol), m. p. 238° (decomp.) (Found: C, 77·5; H, 4·6; N, 8·3. $C_{22}H_{16}O_2N_2$ requires C, 77·65; H, 4·75; N, 8·25%).

4-1′-*Anilinoethylidene*-5-*methyl*-2-*phenylpyrazol*-3-*one* (V; R = Me).—5-Methyl-2-phenyl-

pyrazol-3-one (0·8 g.) and *NN'*-diphenylacetamidine (1 g.) at 160° (1 hr.) gave the *pyrazolone* (1 g.), yellow laths (from ethanol), m. p. 184—185° (Found: C, 73·9; H, 5·75; N, 14·3. $C_{18}H_{17}ON_3$ requires C, 74·2; H, 5·9; N, 14·4%).

4-1'-*Anilinobenzylidene*-5-*methyl*-2-*phenylpyrazol*-3-*one* (V; R = Ph).—The *pyrazolone* was obtained similarly as yellow prisms (from ethanol), m. p. 161—162° (Found: C, 78·1; H, 5·2; N, 11·8. $C_{23}H_{19}ON_3$ requires C, 78·15; H, 5·4; N, 11·9%).

Reaction of NN'-*Diphenylacetamidine with Ethyl Acetoacetate.*—Ethyl acetoacetate (3·25 g.) and *NN'*-diphenylacetamidine (5·25 g.) were heated together at 200° (bath) for 1 hr. (little or no reaction occurred below this temperature); the cooled melt with excess of ether gave a *substance* (0·5 g.) which separated from pyridine as pale yellow needles, m. p. 296—300° (decomp.) (Found: C, 73·6; H, 4·8; N, 11·1%).

4-*Acetyl*-3-*phenyl*iso*oxazol*-5-*one* (VI).—A suspension of 4-1'-anilinoethylidene-3-phenyl*iso*oxazol-5-one (1 g.) in 2% sodium carbonate solution was distilled until a small volume (*ca.* 15 ml.) remained; the *iso*oxazolone slowly dissolved and aniline appeared in the distillate. Acidification of the ice-cold residual solution gave 4-*acetyl*-3-*phenyl*iso*oxazol*-5-*one* (0·55 g.) which crystallised from water or benzene–light petroleum as laths, m. p. 136—137° (Found: C, 65·45; H, 4·6; N, 7·1. $C_{11}H_9O_3N$ requires C, 65·0; H, 4·45; N, 6·9%). The ketone gave a red colour and precipitate with ferric chloride in aqueous alcohol. The 2:4-*dinitrophenylhydrazone* separated from methanol as pale yellow laths, m. p. 212° (decomp.) (Found: C, 53·1; H, 3·3; N, 18·05. $C_{17}H_{13}O_6N_5$ requires C, 53·25; H, 3·4; N, 18·25%), and the *phenylhydrazone* from methanol–water as colourless needles, m. p. 167° (Found: C, 69·4; H, 5·15; N, 14·35. $C_{17}H_{15}O_2N_3$ requires C, 69·6; H, 5·15; N, 14·35%). The ketone (0·1 g.) and aniline (0·1 g.), heated together at 150° (bath) for 10 min. and then acidified, gave 4-1'-anilinoethylidene-3-phenyl*iso*oxazol-5-one (0·1 g.), m. p. 185° alone or mixed with the material prepared as above.

4-1'-*Anilinoethylidene*-3-*phenyl*iso*oxazolid*-5-*one* (I; $R^1 = R^3 =$ Ph, $R^2 =$ Me, $R^4 =$ H).—A suspension of 4-1'-anilinoethylidene-3-phenyl*iso*oxazol-5-one (1 g.) in ethanol (50 ml.) was hydrogenated over platinum until 1 mol. of hydrogen had been absorbed (2 hr.), a clear solution being obtained; evaporation *in vacuo* gave a crystalline residue; 4-1'-*anilinoethylidene*-3-*phenyl*iso*oxazolid*-5-*one* (0·8 g.) separated from ethyl acetate as pale yellow needles, m. p. 143—144° (decomp.) (Found: C, 73·0; H, 5·9; N, 10·25. $C_{17}H_{16}O_2N_2$ requires C, 72·85; H, 5·75; N, 10·0%). The *iso*oxazolidone (0·1 g.) dissolved in warm N-hydrochloric acid (20 ml.) to a clear solution which after 1 hr. had deposited a crystalline solid; 1-*benzoyl*-2-*phenyliminopropane* (0·05 g.) separated from light petroleum as pale yellow plates, m. p. 112° (Found: N, 5·85. $C_{16}H_{15}ON$ requires N, 5·9%). The *iso*oxazolidone (0·5 g.) was boiled with N-hydrochloric acid (10 ml.) for 10 min., to give an emulsion which when cooled gave benzoylacetone (0·3 g.) as colourless prisms (from water), m. p. and mixed m. p. 61—62°. Basification of the filtrate with sodium hydroxide solution gave ammonia and aniline.

4-*Acetyl*-5-*methylpyrazol*-3-*one* (II; R = Ph, R' = Me).—4-1'-Anilinoethylidene-3-phenyl-*iso*oxazolid-5-one (0·28 g.) was added to a solution prepared from hydrazine sulphate (0·13 g.), water (1 ml.), ethanol (10 ml.), and sodium (0·05 g.), and the mixture was boiled under reflux for 15 min.; ammonia was freely evolved and some ammonium carbonate sublimed into the condenser. The solution was evaporated *in vacuo* to a small volume, and water (5 ml.) added to precipitate a solid; the solid was dissolved in N-sodium hydroxide (2 ml.), the solution filtered from a small residue, the filtrate acidified with hydrochloric acid, and the precipitated 4-*acetyl*-5-*methylpyrazol*-3-*one* (0·05 g.) crystallised from ethanol–water as needles, m. p. 280° (decomp.) (Found: C, 65·2; H, 4·9; N, 13·6. $C_{11}H_{10}O_2N_2$ requires C, 65·4; H, 5·0; N, 13·85%). The pyrazolone gave a red colour with ferric chloride in aqueous alcohol.

Reaction of 4-1'-*Anilinoethylidene*-3-*phenyl*iso*oxazolid*-5-*one with Amidines.*—A solution of the *iso*oxazolidone (0·28 g.) and *p*-methanesulphonylbenzamidine (0·2 g.) in ethanol (5 ml.) was boiled under reflux for 15 min., ammonium carbonate subliming into the condenser; the clear solution with an equal volume of water gave 1-*amino*-1-*phenyl*-3-*phenyliminobut*-1-*ene* (0·1 g.) which separated from ethanol–water as pale yellow needles, m. p. 83° (Found: C, 81·35; H, 6·8; N, 11·95. $C_{16}H_{16}N_2$ requires C, 81·35; H, 6·8; N, 11·85%). A solution of the base (0·1 g.) in ether (5 ml.) with concentrated hydrochloric acid (1 drop) gave the *hydrochloride* (0·1 g.) as pale yellow needles (from ethanol–ether), m. p. 220° (decomp.) (Found: N, 10·1. $C_{16}H_{16}N_2$,HCl requires N, 10·3%). The base when boiled for a few minutes with dilute hydrochloric acid gave benzoylacetone. The same base was also obtained by reaction of the *iso*oxazolidone with acetamidine, benzamidine, guanidine, or sodium hydroxide.

Hydrogenation of 4-1'-*Anilinobenzylidene*-3-*phenyl*iso*oxazol*-5-*one.*—A suspension of the *iso*oxazolone (1 g.) in ethanol (50 ml.) was hydrogenated over platinum until 1 mol. of hydrogen

had been absorbed (3 hr.); a clear solution was obtained; evaporation *in vacuo* gave a crystalline residue; 1-*amino*-1 : 3-*diphenyl*-3-*phenyliminopropene* (0·8 g.) separated from ether–light petroleum as yellow needles, m. p. 127° (Found : C, 84·85; H, 6·05; N, 9·1. $C_{21}H_{18}N_2$ requires C, 84·55; H, 6·1; N, 9·4%). The base (0·1 g.) gave, as above, the *hydrochloride* (0·1 g.), pale yellow needles (from ethanol–ether), m. p. 215° (decomp.) (Found : N, 8·45. $C_{21}H_{18}N_2$,HCl requires N, 8·35%). The base (0·1 g.) was boiled with N-hydrochloric acid (3 ml.) for a few min.; a clear solution was obtained which rapidly became turbid and when cooled gave dibenzoylmethane (0·05 g.) as colourless prisms (from ethanol–water), m. p. 77° not depressed when admixed with an authentic specimen of m. p. 76—77°.

5-*Methoxy*-3-*methyl*-4-p-*toluidinomethylene*iso*oxazoline* (IX).—A suspension of finely ground 3-methyl-4-*p*-toluidinomethylene*iso*oxazolid-5-one (1 g.) in ether (50 ml.) containing methanol (1 ml.) was set aside with an excess of ethereal diazomethane at room temperature with occasional shaking until a clear solution was obtained (2 days). Evaporation then gave a solid residue; 5-*methoxy*-3-*methyl*-4-p-*toluidinomethylene*iso*oxazoline* (0·75 g.) separated from ethanol–water as pale yellow needles, m. p. 138° (Found : C, 66·8; H, 6·7; N, 12·0. $C_{13}H_{16}O_2N_2$ requires C, 67·2; H, 6·95; N, 12·05%). This (0·1 g.) gave, as above, the *hydrochloride* (0·1 g.), yellow needles (from ethanol–ether), m. p. 184° (decomp.) (Found : C, 58·15; H, 6·35; N, 10·5. $C_{13}H_{16}O_2N_2$,HCl requires C, 58·1; H, 6·4; N, 10·4%). The *iso*oxazoline (0·5 g.) was boiled under reflux with 2N-hydrochloric acid (20 ml.) for 1 hour and the solution distilled until the volume was about 10 ml. The distillate contained acetone and gave the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 122°, thereof (Found : C, 45·55; H, 4·1. Calc. for $C_9H_{10}O_4N_4$: C, 45·4; H, 4·25%). The hydrolysis solution was basified with sodium hydroxide solution, and air aspirated through it, the vapour being condensed in dilute hydrochloric acid; evaporation of the acid solution gave ammonium chloride (0·1 g.). The alkaline solution was extracted with ether (2 × 10 ml.) to give a base, the acetyl derivative of which had m. p. 145°, undepressed when mixed with aceto-*p*-toluidide, m. p. 146°. A solution of the *iso*oxazoline (1 g.) in methyl acetate (20 ml.) was hydrogenated over platinum until 1 mol. of hydrogen had been absorbed (2 hr.); evaporation *in vacuo* and addition of ether gave a *substance* (0·25 g.), which separated from ethanol as pale yellow needles, m. p. 210° (Found : C, 58·3; H, 6·55; N, 6·0. $C_{11}H_{15}O_4N$ requires C, 58·65; H, 6·7; N, 6·2%).

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