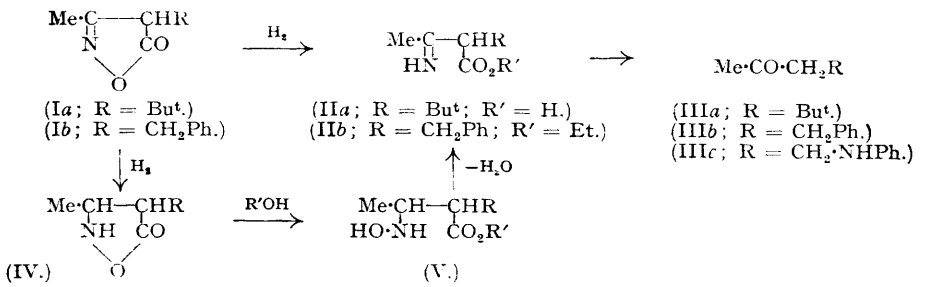
146. *The Hydrogenation of Some* iso*Oxazolones.*

By G. Shaw.

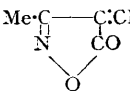
Hydrogenation of 4-benzylidene-3-methyl- and 3-methyl-4-anilinomethylene-*iso*oxazolones using a palladium catalyst affords the 4-benzyl- and 4-anilinomethyl-*iso*oxazolones. When a platinum catalyst is used in moist solvents, disruption of the *iso*oxazolone nucleus occurs and linear ketones are obtained; in anhydrous ethanol hydrogenation of the 4-benzylidene- and 4-benzyl-*iso*oxazolones affords ethyl α-benzylacetoacetate, suggesting the formation of a reactive anhydride-like substance, possibly an *iso*oxazolidone (IV). Hydrogenation of propiophenone oxime acetate affords the corresponding acylketimine. Oxidation of propiophenone acetylimine with potassium permanganate in acetone, in an attempt to reverse the last-mentioned reaction, gives *N*-acetylbenzamide.

It has been shown recently (Panizzi, *Gazzetta*, 1946, **76**, 44) that hydrogenation of 3-methyl-4-*tert.*-butyl*iso*oxazol-5-one (I*a*), using a large excess of platinum as catalyst and acetic acid as solvent, affords *tert.*-butylacetone (III*a*); Panizzi points out the unexpected lability of oxygen in the *iso*oxazolone nucleus and suggests that ketone formation is preceded by formation of β-imino-α-*tert.*-butylbutyric acid (II*a*). Evidence is now presented which suggests that hydrogenation of the *iso*oxazolone system produces a reactive anhydride-like substance, possibly the *iso*oxazolidone (IV) which may yield (II) *via* the hydroxylamine derivative (V).

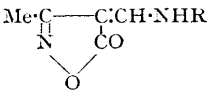


Hydrogenation of 4-benzylidene-3-methyl*iso*oxazol-5-one (VI) over 5% palladium–charcoal in ethanol or ethyl acetate at room temperature resulted in the absorption of only 1 mole of hydrogen and formation of 4-benzyl-3-methyl*iso*oxazol-5-one (I*b*). Hydrogenation of the basic arylaminomethylene*iso*oxazolones (VII*a*—*c*) under the same conditions afforded quantit-

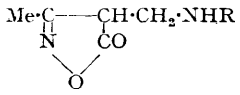
ative yields of the corresponding *arylaminomethyl*iso*oxazolones* (VIII*a*—*c*) which readily formed *picrates*.



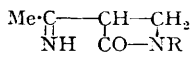
(VI.)



(VII*a*; R = Ph.)
(VII*b*; R = *o*-tolyl.)
(VII*c*; R = *p*-tolyl.)



(VIII*a*; R = Ph.)
(VIII*b*; R = *o*-tolyl.)
(VIII*c*; R = *p*-tolyl.)



(IX.)

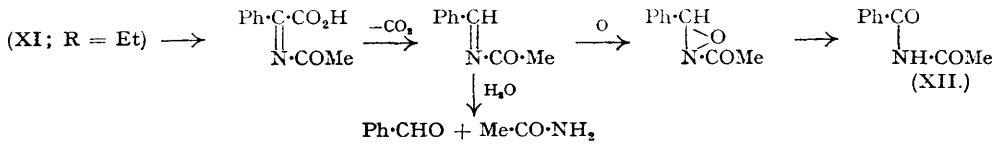
It soon appeared that Adams's platinum catalyst was required for the disruption of the *iso*oxazolone nucleus: when thus reduced in ethanol or ethyl acetate, (VI) absorbed 2 moles of hydrogen affording ammonia and an oil consisting largely of 4-phenylbutan-2-one (III*b*). Under the same conditions 4-benzyl-3-methyl*iso*oxazol-5-one (I*b*) absorbed 1 mole of hydrogen and gave the same products. In these experiments no special precautions were taken to exclude moisture. When (I*b*) was reduced with hydrogen–platinum in absolute ethanol under anhydrous conditions 1 mole of hydrogen was absorbed but no ammonia was formed, and from the reaction mixture was isolated ethyl α-benzylacetoacetate and a base which was rapidly hydrolysed to the keto-ester and was probably its imine (II*b*). The identity of the keto-ester was confirmed by conversion by warm concentrated sulphuric acid into 1-methylindene-2-carboxylic acid (von Pechmann, *Ber.*, 1883, **16**, 516; Roser, *Annalen*, 1888, **247**, 157). The keto-ester was also obtained by reduction of (VI) under anhydrous conditions in absolute ethanol, but neither (VI) nor (I*b*) showed evidence of reaction with ethanol at room temperature. Hydrogenation of 3-methyl-4-anilinomethylene*iso*oxazol-5-one (VII*a*) in moist solvents afforded ammonia and 4-anilinobutan-2-one (III*c*), but in anhydrous solvents a viscous liquid was obtained which could not be satisfactorily identified; work in this direction is being pursued to ascertain the possibility of formation of an azetidinone or β-lactam (IX) which might conceivably arise by rearrangement of the hypothetical *iso*oxazolidone (IV; R = CH_2·NHPh).

The isolation of ethyl α-benzylacetoacetate by reduction of (I*b*) and (VI) in ethanol implies the intermediate formation of an anhydride-like substance capable of combining with the solvent and this substance is postulated provisionally as the *iso*oxazolidone (IV). Attempts to isolate such a compound by carrying out the reduction in anhydrous ethyl acetate were unsuccessful, a viscous oil being obtained from which benzylacetone alone could be isolated.

The system $-C{:}N{\cdot}O{\cdot}CO-$ exists in the acyloximes (X) and hydrogenation of these substances was next attempted in the hope that the stable acylketimines (XI) might be obtained. Moureu

(X.) Ph·CR:N·O·COMe Ph·CR:N·COMe (XI.)

and Mignonac (*Compt. rend.*, 1913, **156**, 1805; 1920, **170**, 1354) showed that reduction of oximes with hydrogen–platinum afforded the ketimines and prepared a number of acylketimines by acylation of these substances and also by an independent method. In presence of platinum in ethanol propiophenone oxime acetate (X; R = Et) absorbed 1 mole of hydrogen during 4 hours, to afford propiophenone *N*-acetylimine (XI; R = Et), identical with a sample prepared from phenylmagnesium bromide, propionitrile, and acetyl chloride (Moureu and Mignonac, *loc. cit.*). Hydrogenation of acetophenone oxime acetate (X; R = Me) under the same conditions afforded an oil which was presumably the ketimine (XI; R = Me) since it gave acetophenone, ammonia, and acetic acid when hydrolysed. In an attempt to reverse the latter reaction, propiophenone *N*-acetylimine (XI; R = Et) was treated with potassium permanganate in acetone, but, instead of the expected oxime acetate, *N*-acetylbenzamide (XII) was obtained in good yield, together with a small amount of benzaldehyde. This suggests that the oxidation may proceed according to the scheme:



(XI; R = Et) → Ph·C(N·COMe)·CO_2H —$-CO_2$→ Ph·C(N·CO·Me)H —O→ Ph·CH(O)(N·COMe) → Ph·CO(NH·COMe) (XII.)

Ph·C(N·CO·Me)H —H_2O→ Ph·CHO + Me·CO·NH_2

Experimental.

Hydrogenations were carried out at room temperature and atmospheric pressure; the recorded volumes of hydrogen refer to N.T.P.

Hydrogenation of 4-*Benzylidene*-3-*methyl*iso*oxazol*-5-*one* (VI).—The *iso*oxazolone (1 g.; Dains and

Griffin, *J. Amer. Chem. Soc.*, 1913, **35**, 959) in 90—95% ethanol (30 ml.) was reduced with hydrogen and 5% palladium–charcoal (0·1 g.), hydrogen (131 ml. Calc. for 1 mol., 120 ml.) being absorbed during 1 hour. Evaporation of the filtered solution *in vacuo* gave an oil which partly crystallised. 4-Benzyl-3-methyl-*iso*oxazol-5-one (I*b*) (0·2 g.) separated from benzene as needles, m. p. 106°, undepressed when mixed with an authentic specimen, m. p. 107°, prepared according to Schiff and Viciana (*Ber.*, 1897, **30**, 1161; *Gazzetta*, 1897, **27**, 73). When (VI) (2 g.) in 90—95% ethanol (30 ml.) was reduced with hydrogen–platinum (Adams's catalyst) (0·1 g.), hydrogen (244 ml. Calc. for 2 mols., 240 ml.) was absorbed during 4 hours; the resultant solution had a strong ammoniacal odour. Evaporation of the filtered solution *in vacuo* afforded an oil which readily gave crystalline benzylacetone semicarbazone (1·3 g.) which separated from ethanol as needles, m. p. 142°, undepressed on admixture with an authentic sample. The same compound was also obtained by reduction in ethyl acetate. 4-Benzyl-3-methyl*iso*oxazol-5-one (I*b*) did not absorb hydrogen in the presence of palladium, but in presence of a platinum catalyst 1 mole of hydrogen was absorbed with formation of ammonia and benzylacetone. (VI) (2 g.) in anhydrous ethanol (30 ml.) was reduced with hydrogen–platinum, with exclusion of moisture; hydrogen (245 ml. Calc. for 1 mol., 240 ml.) was absorbed during 3 hours and the solution became slightly alkaline but there was no odour of ammonia. Evaporation of the filtered solution *in vacuo* gave an oil (1·9 g.) which gave a purple colour with alcoholic ferric chloride. The oil in ether (20 ml.) was extracted successively with 2% sodium hydrogen carbonate solution (2 × 10 ml.), 2% hydrochloric acid (2 × 10 ml.), and water (10 ml.). Evaporation of the dried solution afforded ethyl α-benzylacetoacetate (1·3 g.), b. p. 165—169°/12 mm. (Leuchs, *Ber.*, 1911, **44**, 1510, gives b. p. 164—165°/12 mm.). The oil (0·5 g.) and concentrated sulphuric acid (3 ml.) were heated on a water-bath for 10 minutes, then cooled, and poured into ice-water (100 ml.); 1-methylindene-2-carboxylic acid (0·25 g.) was obtained as a white precipitate, which separated from ethanol as needles, m. p. 200°, undepressed when mixed with an authentic specimen, m. p. 200°, prepared from ethyl α-benzylacetoacetate and sulphuric acid (von Pechmann, *loc. cit.*; Roser, *loc. cit.*). Acidification of the sodium hydrogen carbonate solution, extraction with ether, and evaporation afforded only a trace of gum, indicating absence of acid. The acid extract when kept for a few hours deposited an oil (0·2 g.) (insoluble in sodium hydrogen carbonate solution), which afforded 1-methylindene-2-carboxylic acid when treated with sulphuric acid and was probably ethyl α-benzylacetoacetate, the basic precursor being presumably ethyl α-benzylacetimidoacetate (II*b*).

3-*Methyl*-4-*anilinomethyl*iso*oxazol*-5-*one* (VIII*a*).—3-Methyl-4-anilinomethylene*iso*oxazol-5-one (VII*a*) (1 g.; Dains and Griffin, *loc. cit.*) in 90—95% ethanol (30 ml.) was reduced in presence of 5% palladium–charcoal (0·1 g.), hydrogen (110 ml. Calc. for 1 mol., 111 ml.) being absorbed in 2 hours. Evaporation of the filtered solution *in vacuo* gave 3-*methyl*-4-*anilinomethyl*iso*oxazol*-5-*one dihydrate* as a pale yellow solid (1 g.) which separated from water as fine pale yellow needles, m. p. 101—102° (decomp.) (Found: N, 11·6. $C_{11}H_{12}O_2N_2,2H_2O$ requires N, 11·65%). This lost water when heated at 50°/1 mm. for 1 hour to give the anhydrous *iso*oxazolone as a very pale yellow powder, m. p. 150°; the anhydrous material was extremely deliquescent (rapidly reverting to the dihydrate in moist air) and could not be recrystallised satisfactorily, but when it, or the dihydrate, was added to a saturated solution of picric acid in ethanol, the *picrate* was precipitated as a yellow solid which separated from ethanol as prisms, m. p. 167—168° (decomp.) (Found: N, 16·3. $C_{17}H_{15}O_9N_5$ requires N, 16·15%). 3-Methyl-4-anilinomethylene*iso*oxazol-5-one (2 g.) in 90—95% ethanol (40 ml.) was reduced with platinum (0·1 g.), hydrogen (225 ml. Calc. for 2 mols., 222 ml.) being absorbed in 3 hours. Evaporation of the filtered solution (which possessed an ammoniacal odour) *in vacuo* gave almost colourless 4-anilinobutan-2-one, b. p. 149—155°/14 mm. (1·5 g.), which became brown in the air (Found: N, 8·4. Calc. for $C_{10}H_{13}ON$: N, 8·6%). Bayer and Co. (*Zentr.*, 1913, II, 1832) give b. p. 140—145°/10 mm.

3-*Methyl*-4-p-*toluidinomethyl*iso*oxazol*-5-*one* (VIII*c*).—3-Methyl-4-*p*-toluidinomethylene*iso*oxazol-5-one (VII*c*) (1 g.), when reduced with hydrogen–palladium as above, afforded 3-*methyl*-4-p-*toluidinomethyl*iso*oxazol*-5-*one* (0·95 g.) which separated from water as fine, very pale yellow needles, m. p. 181—182° (decomp.) (Found: N, 12·7. $C_{12}H_{14}O_2N_2$ requires N, 12·8%). The *picrate* crystallised from ethanol as prisms, m. p. 167—169° (decomp.) (Found: N, 15·4. $C_{18}H_{17}O_9N_5$ requires N, 15·65%).

3-*Methyl*-4-o-*toluidinomethyl*iso*oxazol*-5-*one* (VIII*b*).—This *product* separated from water as fine pale yellow needles, m. p. 163—164° (decomp.) (Found: N, 12·65%). The *picrate* separated from ethanol as yellow prisms, m. p. 150° (decomp.) (Found: N, 15·45%).

Propiophenone Oxime Acetate (X; R = Et).—Propiophenone oxime (13·5 g.) and acetic anhydride (15 ml.) were heated on the water-bath for 3 hours. Evaporation of the solution *in vacuo* gave an oil which soon crystallised; *propiophenone oxime acetate* (10·5 g.) separated as needles (from light petroleum), m. p. 57° (Found: N, 7·25. $C_{11}H_{13}O_2N$ requires N, 7·35%). The acetate (5 g.) was reduced with hydrogen and platinum (0·2 g.) in ethanol (100 ml.) until 1 mole of hydrogen (585 ml.) had been absorbed, this requiring 5 hours. The filtered solution was evaporated *in vacuo* to afford a pale brown oil, which partly crystallised on being kept overnight. The crystals (1·4 g., 31%) were separated from oil by spreading the mixture over a porous title, and recrystallised from water as needles, m. p. 125°, undepressed when mixed with an authentic sample of propiophenone *N*-acetylimine (XI; R = Et), m. p. 126°.

Hydrogenation of Acetophenone Oxime Acetate (X; R = Me).—The acetate (2 g.) in ethanol (30 ml.) was reduced with platinum (0·1 g.) until 1 mole of hydrogen (252 ml.) had been absorbed (4 hours). Evaporation of the filtered solution gave an oil (1·9 g.). A solution of this in ether was extracted successively with sodium hydrogen carbonate solution, hydrochloric acid, and water; evaporation of the dried ethereal solution gave an oil (1·3 g.) which failed to crystallise. The oil (1 g.) was boiled under reflux with N-hydrochloric acid (10 ml.) for 30 minutes, and the cooled solution extracted with ether (20 ml.). Evaporation of the extract afforded acetophenone (0·5 g.) (2 : 4-dinitrophenylhydrazone, m. p. 248°, undepressed when mixed with an authentic specimen, m. p. 250°). The aqueous solution was evaporated to a small volume and made alkaline with 5N-sodium hydroxide, whereupon ammonia was evolved; neutralisation of the solution and addition of ferric chloride produced a red colour, and boiling the mixture precipitated basic ferric acetate.

Oxidation of Propiophenone N-*Acetylimine* (XI; R = Et).—A solution of the acylketimine (1 g.) in acetone (100 ml.) was boiled under reflux, and solid potassium permanganate added until a lasting pink

colour was obtained (about 3 g. were required). The solution was filtered, the filtrate decolorised with sulphur dioxide and re-filtered, and the filtrate evaporated to dryness *in vacuo*, to yield crystalline *N*-acetylbenzamide (0·8 g.) which separated from water as laths, m. p. 116°, undepressed when mixed with an authentic specimen, m. p. 116° (Titherley and Holden, *J.*, 1912, **101**, 1880). The filtrate from the above crystallisation had an odour of benzaldehyde and gave the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 235°, thereof.

TECHNICAL COLLEGE, SYDNEY, N.S.W., AUSTRALIA. [*Received, October 25th*, 1949.]