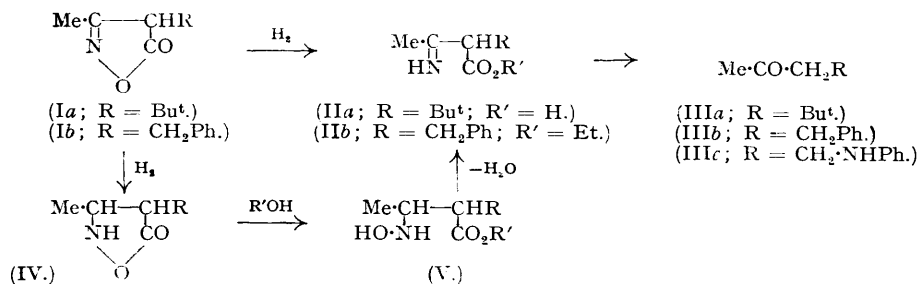


146. The Hydrogenation of Some isoOxazolones.

By G. SHAW.

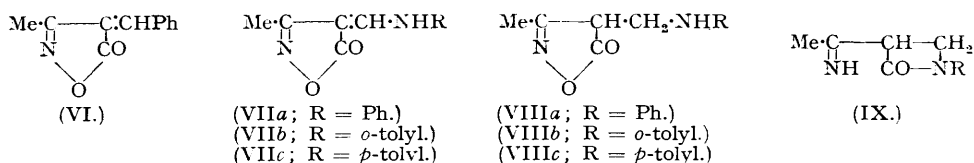
Hydrogenation of 4-benzylidene-3-methyl- and 3-methyl-4-anilinomethylene-*isooxazolones* using a palladium catalyst affords the 4-benzyl- and 4-anilinomethyl-*isooxazolones*. When a platinum catalyst is used in moist solvents, disruption of the *isooxazolone* nucleus occurs and linear ketones are obtained; in anhydrous ethanol hydrogenation of the 4-benzylidene- and 4-benzyl-*isooxazolones* affords ethyl α -benzylacetoacetate, suggesting the formation of a reactive anhydride-like substance, possibly an *isooxazolidone* (IV). Hydrogenation of propiophenone oxime acetate affords the corresponding acylketimine. Oxidation of propiophenone acetyl-imine 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.*-butylisooxazol-5-one (Ia), using a large excess of platinum as catalyst and acetic acid as solvent, affords *tert.*-butylacetone (IIIa); Panizzi points out the unexpected lability of oxygen in the *isooxazolone* nucleus and suggests that ketone formation is preceded by formation of β -imino- α -*tert.*-butylbutyric acid (IIa). Evidence is now presented which suggests that hydrogenation of the *isooxazolone* system produces a reactive anhydride-like substance, possibly the *isooxazolidone* (IV) which may yield (II) *via* the hydroxylamine derivative (V).



Hydrogenation of 4-benzylidene-3-methylisooxazol-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-methylisooxazol-5-one (Ib). Hydrogenation of the basic arylaminomethyleneisooxazolones (VIIa—c) under the same conditions afforded quant-

ative yields of the corresponding *arylaminoethylisooxazolones* (VIIIa—c) which readily formed *picrates*.



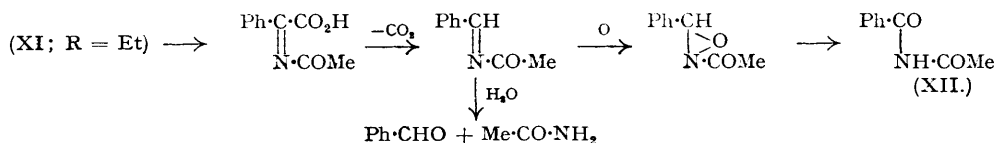
It soon appeared that Adams's platinum catalyst was required for the disruption of the *isooxazolone* nucleus: when thus reduced in ethanol or ethyl acetate, (VI) absorbed 2 moles of hydrogen affording ammonia and an oil consisting largely of 4-phenylbutan-2-one (IIIb). Under the same conditions 4-benzyl-3-methylisooxazol-5-one (Ib) absorbed 1 mole of hydrogen and gave the same products. In these experiments no special precautions were taken to exclude moisture. When (Ib) 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 (IIb). 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 (Ib) showed evidence of reaction with ethanol at room temperature. Hydrogenation of 3-methyl-4-anilinomethyleneisooxazol-5-one (VIIa) in moist solvents afforded ammonia and 4-anilinobutan-2-one (IIIc), 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 *isooxazolidone* (IV; R = CH₂·NHPh).

The isolation of ethyl α -benzylacetoacetate by reduction of (Ib) 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 *isooxazolidone* (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 $\text{--C}\cdot\text{N}\cdot\text{O}\cdot\text{CO--}$ 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



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:



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-methylisooxazol-5-one (VI).—The *isooxazolone* (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-methylisooxazol-5-one (Ib) (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-methylisooxazol-5-one (Ib) 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 -benzylacetimidooacetate (Iib).

3-Methyl-4-anilinomethylisooxazol-5-one (VIIA).—3-Methyl-4-anilinomethylisooxazol-5-one (VIIA) (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-anilinomethylisooxazol-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. $C_{11}H_{12}O_2N_2 \cdot 2H_2O$ requires N, 11.65%). This lost water when heated at 50°/1 mm. for 1 hour to give the anhydrous isooxazolone 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-anilinomethylisooxazol-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-toluidinomethylisooxazol-5-one (VIIIC).—3-Methyl-4-p-toluidinomethylisooxazol-5-one (VIIIC) (1 g.), when reduced with hydrogen-palladium as above, afforded 3-methyl-4-p-toluidinomethylisooxazol-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-toluidinomethylisooxazol-5-one (VIIIB).—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 tile, and recrystallised from water as needles, m. p. 125°, undepressed when mixed with an authentic sample of propiophenone *N*-acetylamine (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 5*N*-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*-Acetylamine (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.

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