The Beckmann Rearrangement of Substituted Benzylideneacetone Oximes.

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The synthesis and Beckmann rearrangement of a number of *para*-substituted benzylideneacetone oximes have been studied. *N*-*p*-Methoxy- and *N*-*p*-nitro-styrylacetamide have been prepared.

N-STYRYLACETAMIDE has been prepared by the Beckmann rearrangement of benzylidene-acetone α-oxime (Auwers *et al.*, *J. pr. Chem.*, 1932, **133**, 154) and this method has now been applied to the synthesis of *N*-*p*-methoxy- and *N*-*p*-nitro-styrylacetamide.

Oximation of benzylideneacetone under both acidic and alkaline conditions yields only the α-oxime. The β-oxime has been obtained by neutralisation of a hydrochloride prepared from the α-oxime in absolute ethanol (Auwers *et al.*, *loc. cit.*). Oximation of *p*-methoxybenzylideneacetone under alkaline conditions gives the α-oxime, but acidic conditions lead to a mixture of the α- and the β-oxime (65 : 35). These structures have been determined from the products of Beckmann rearrangement of the oximes. Under the action of phosphorus pentachloride, the β-oxime of *p*-methoxybenzylideneacetone is rearranged to *p*-methoxy-*N*-methylcinnamamide, and the α-oxime to *N*-*p*-methoxy-styrylacetamide. Oximation of *p*-nitrobenzylideneacetone under both acidic and alkaline conditions yields only the α-oxime, which has been isomerized to *N*-*p*-nitrostyrylacetamide. The hydrochlorides, prepared in anhydrous ether, and the benzoates of the aforementioned oximes all regenerated the parent oxime on mild alkaline hydrolysis.

Recently, Brady and Benger (*J.*, 1953, 3612) have suggested that hydrogen bonding plays an important part in stabilizing one isomeride relative to the other in a series of substituted cinnamaldoximes; *e.g.*, cinnamaldehyde on oximation in alkaline solution gives a mixture of the α- and the β-oxime in which the latter predominates, but *o*-, *m*-, and *p*-nitrocinnamaldehydes under these conditions give mainly the α-aldoximes. Structures (I) and (II) are proposed for the possible isomerides. A similar explanation can account for our observations concerning the stability of the benzylideneacetone oximes already described. In these cases it is suggested that a lone pair of electrons of the oxygen atom may be associated either with the methine-hydrogen H_α (IV) or with a hydrogen of the terminal methyl group (III).
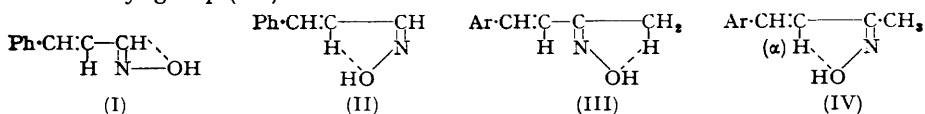
The α-isomeride (III) represents the stable form of benzylideneacetone oxime, and the only form of *p*-nitrobenzylideneacetone oxime. In the latter case the electron-withdrawing influence of the nitro-group will militate against hydrogen bonding, although a hydrogen bond with the most electron-deficient hydrogen atom should be possible. Because of the inductive and possible hyperconjugative effects of the terminal methyl group, hydrogen bonding may take place with a methyl hydrogen (III). This could provide an explanation for the occurrence of only the α-isomeride of *p*-nitrobenzylideneacetone oxime. With an electron-repelling methoxyl group in the *para*-position, which should help to promote hydrogen bonding, *p*-methoxybenzylideneacetone gives a mixture of isomerides, with the α-form still predominating.

EXPERIMENTAL

p-Methoxybenzylideneacetone α-Oxime.—Hydroxylamine hydrochloride (2 g.) and *p*-methoxy-benzylideneacetone (1 g.) (*Org. Synth.*, Coll. Vol. I, 2nd Edn., p. 77) were added to aqueous sodium hydroxide (20 c.c.; 5%), and sufficient alcohol (10 c.c.) to give a clear solution was added. After

being heated on a water-bath for 15 min. the mixture was diluted with water (200 c.c.), and the oxime separated. Recrystallisation from xylene gave colourless needles of the α-oxime, m. p. 123—124°. Harries and Tietz (*Annalen*, 1902, **320**, 242) record m. p. 119—120° for this compound : their specimen obviously contained some of the β-isomeride. p-*Methoxybenzylideneacetone α-oxime benzoate* (prepared by use of benzoyl chloride in pyridine) crystallised from methanol in plates, m. p. 125° (Found : C, 73·1 ; H, 5·8. $C_{18}H_{17}O_3N$ requires C, 73·2 ; H, 5·8%).

p-*Methoxybenzylideneacetone* β-*Oxime.*—*p*-Methoxybenzylideneacetone (5 g.) and hydroxylamine hydrochloride (5 g.) in absolute alcohol (50 c.c.) were refluxed for 5 hr. and then kept overnight in an ice-chest, a yellow precipitate of the oxime hydrochloride separating. Hydrolysis of this with water (50 c.c.) liberated p-*methoxybenzylideneacetone* β-*oxime* (35% yield) which after recrystallisation from ethanol had m. p. 157—158° (Found : C, 68·8 ; H, 6·9 ; N, 6·9. $C_{11}H_{13}O_2N$ requires C, 68·75 ; H, 6·8 ; N, 7·3%). The filtrate after removal of the above hydrochloride was poured into water (150 c.c.), and the resulting precipitate of the α-oxime collected. It had m. p. 123—124° after recrystallisation from xylene (yield 65%). p-*Methoxybenzylideneacetone* β-*oxime benzoate*, prepared by the method described for the α-oxime, crystallised as plates from methanol, m. p. 125°, depressed on admixture with the benzoate from the α-oxime (Found : C, 73·0 ; H, 5·8 ; N, 4·6. $C_{18}H_{17}O_3N$ requires C, 73·2 ; H, 5·8 ; N, 4·75%).

N-p-*Methoxystyrylacetamide.*—*p*-Methoxybenzylideneacetone α-oxime (2 g.) was dissolved in dry ether, phosphorus pentachloride (2 g.) added, and the mixture shaken for 20 min., separation of a dull red powder from the ether layer then being complete. Ether (20 c.c.) and chipped ice (20 g.) were added, and the shaking continued until the decomposition of the complex was complete. The ether layer was separated, washed with water, and dried (Na_2SO_4). The ether solution was concentrated until a red oil separated, and the ethereal liquors were decanted therefrom. Complete removal of the ether gave oily crystals of N-p-*methoxystyrylacetamide*, which crystallised as small plates, m. p. 114—115°, after repeated crystallisation from benzene (Found : C, 68·9 ; H, 6·5. $C_{11}H_{13}O_2N$ requires C, 68·75 ; H, 6·8%).

Rearrangement of *p*-methoxybenzylideneacetone β-oxime in the same manner gave p-*methoxy*-N-*methylcinnamamide*, m. p. 164° (from water), undepressed with a specimen prepared from *p*-methoxycinnamoyl chloride and methylamine (Found : C, 68·9 ; H, 6·8. $C_{11}H_{13}O_2N$ requires C, 68·75 ; H, 6·8%).

p-*Nitrobenzylideneacetone.*—*p*-Nitrobenzaldehyde (1 g.) was dissolved in acetone (12 c.c.), and the solution cooled below 5°. An aqueous solution of sodium hydroxide (1·2 c.c. ; 1%) was added dropwise with stirring, which was continued for a further 15 min., and the solution was then made acid with 2N-sulphuric acid. After removal of most of the acetone by distillation, the solution of 4-hydroxy-4-*p*-nitrophenylbutan-2-one was heated with N-sulphuric acid (7 c.c.). *p*-Nitrobenzylideneacetone separated and after crystallisation from alcohol had m. p. 110° (Baeyer and Becker, *Ber.*, 1883, **16**, 1968, record m. p. 110°). Oximation by the methods already described gave in each case p-*nitrobenzylideneacetone* α-*oxime*, m. p. 185° after crystallisation from ethanol (Found : C, 58·85 ; H, 4·85 ; N, 13·45. $C_{10}H_{10}O_3N_2$ requires C, 58·25 ; H, 4·85 ; N, 13·6%) ; its *benzoate*, prepared by use of benzoyl chloride in pyridine, crystallised from ethanol in lemon-yellow needles, m. p. 155° (Found : C, 65·9 ; H, 4·1. $C_{17}H_{14}O_4N_2$ requires C, 65·8 ; H, 4·5%).

N-p-*Nitrostyrylacetamide.*—*p*-Nitrobenzylideneacetone α-oxime (5 g.) was dissolved in dry ether (100 c.c.), phosphorus pentachloride (5 g.) added, and the mixture shaken for 2 hr., then poured on crushed ice (20 g.) ; the ether layer was separated, washed with water, and dried (Na_2SO_4). Evaporation gave N-p-*nitrostyrylacetamide* as a bright orange microcrystalline solid, m. p. 155°, after crystallisation from benzene (Found : C, 58·5 ; H, 4·4 ; N, 13·3. $C_{10}H_{10}O_3N_2$ requires C, 58·25 ; H, 4·85 ; N, 13·6%). N-*Methyl*-p-*nitrocinnamamide*, synthesised by reaction of *p*-nitrocinnamoyl chloride with methylamine, had m. p. 203—204° (from ethanol) (Found : C, 57·75 ; H, 5·1 ; N, 13·4. $C_{10}H_{10}O_3N_2$ requires C, 58·25 ; H, 4·85 ; N, 13·6%).