

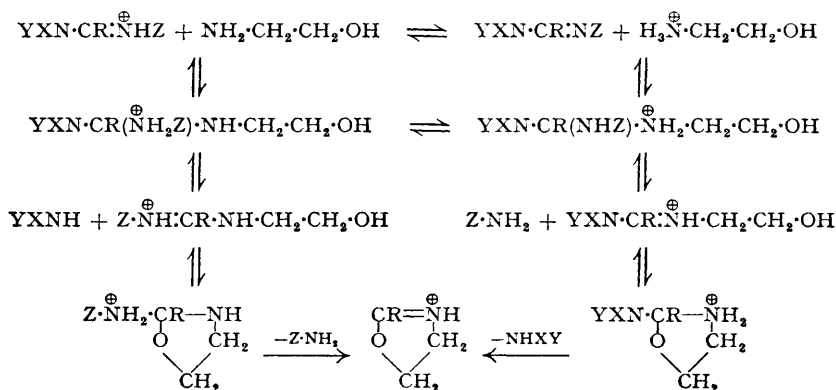
225. Amidines. Part XIV. Preparation of 2-Substituted Δ^2 -Oxazolines and 4:5-Dihydro-1:3-Oxazines from Hydroxyalkylamines and N-Substituted Amidines or Ketoxime Sulphonates.

By P. OXLEY and W. F. SHORT.

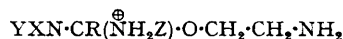
2-Substituted Δ^2 -oxazolines may be prepared from N-substituted amidinium salts or ketoxime sulphonates and 2-hydroxyethylamines. N-Phenyl-p-methylsulphonylbenzamidinium toluene-p-sulphonate and 3-hydroxypropylamine afford 2-p-methylsulphonylphenyl-4:5-dihydro-1:3-oxazine.

METHODS for the synthesis of Δ^2 -oxazolines (4:5-dihydro-oxazoles) have recently been reviewed by Wiley and Bennett (*Chem. Reviews*, 1949, **44**, 449) and follow the usual pattern for the formation of heterocyclic compounds. As a sequel to the investigation of the action of alkylenediamines on N-substituted amidinium salts and on ketoxime sulphonates (Part XIII; *J.*, 1950, 859), we examined the action of 2-hydroxyethylamine on these compounds and found that it leads to new syntheses of Δ^2 -oxazolines.

The reaction between an N-substituted amidinium salt and 2-hydroxyethylamine occurs at 100–140° and may yield a free 2-substituted Δ^2 -oxazoline or its salt, depending on the relative strength of the bases produced. We suggest that the reaction may be formulated as follows, the formation of cyclic intermediates being postulated because 4:5-dihydroglyoxalines are not formed simultaneously.



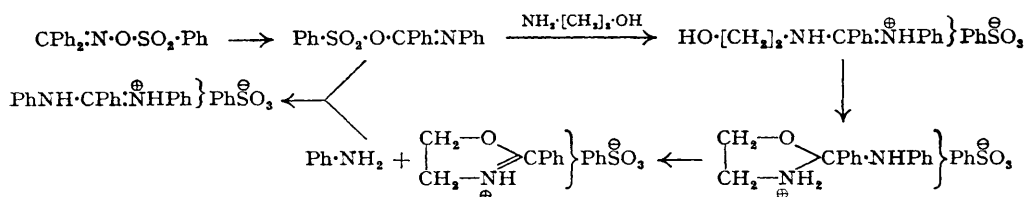
Alternative routes involving the production of ethers of the type



may also play some part in the reaction.

A number of 2-substituted Δ^2 -oxazolines has been prepared from N-substituted amidinium salts and 2-hydroxyethylamine, and 2-p-methylsulphonylphenyl-4:4-dimethyl- Δ^2 -oxazoline was obtained in 79% yield from N-ethyl-p-methylsulphonylbenzamidinium toluene-p-sulphonate and 2-aminoisobutyl alcohol. 3-Hydroxypropylamine and N-phenyl-p-methylsulphonylbenzamidinium chloride similarly gave a 34% yield of 2-p-methylsulphonylphenyl-4:5-dihydro-1:3-oxazine.

Benzophenone oxime benzenesulphonate and 2-hydroxyethylamine in boiling benzene afforded 2-phenyl- Δ^2 -oxazoline (56%), NN'-diphenylbenzamidine (23%), and aniline. In conformity with the reaction mechanisms discussed in Parts VI (*J.*, 1947, 497) and XIII (*loc. cit.*), the formation of these products may be represented as follows:



EXPERIMENTAL.*

2-Benzyl- Δ^2 -oxazoline.—*N*-cycloHexylphenylacetamidinium chloride (1.26 g.) and 2-hydroxyethylamine (1.0 g., 3.3 mols.) were heated for 30 minutes in a bath at 140°, and the product was mixed with water and extracted with benzene giving a brown oil (0.5 g.) which afforded a picrate (0.25 g., 13%), m. p. 132.5–133°, on neutralisation with alcoholic picric acid. Elfeldt (*Ber.*, 1891, **24**, 3222) states that this picrate has m. p. 130–131°.

2-Phenyl- Δ^2 -oxazoline.—(1) From *NNN'*-trimethylbenzamidinium toluene-*p*-sulphonate (2.33 g., 1.0 mol.) were heated on the steam-bath for 30 minutes, methylamines being evolved. The cold product was dissolved in water and mixed with 2*M*-lithium picrate, and the precipitate was collected after several hours and crystallised from acetone, giving 2-phenyl- Δ^2 -oxazolinium picrate (0.78 g., 21%), m. p. and mixed m. p. 178° (decomp.). The 2-hydroxyethylammonium toluene-*p*-sulphonate used in the experiment was prepared from hydrated toluene-*p*-sulphonic acid and an equivalent of 2-hydroxyethylamine in isopropanol. Water was removed by azeotropic distillation with isopropanol and the salt was recrystallised from this solvent. After being dried at 50°/1 mm. the salt (yield, 86%) had m. p. 101° (Found: N, 6.2. $C_9H_{11}O_4NS$ requires N, 6.0%).

(2) From benzophenone oxime benzenesulphonate. A solution of the oxime ester (15 g.) and 2-hydroxyethylamine (5.45 g., 2 mols.) in dry benzene (100 c.c.) separated into two layers when it was boiled for 30 minutes. The product was shaken with water, and the residue obtained by evaporating the dried benzene solution was distilled giving (i) aniline (1.5 g.), b. p. up to 60°/1 mm., (ii) 2-phenyl- Δ^2 -oxazoline (3.7 g., 56.5%), b. p. 77–78°/1 mm., giving a picrate, m. p. 178–181° (decomp.) (Found: N, 14.9. Calc. for $C_{15}H_{13}O_3N_4$: N, 14.9%) (Wenker, *J. Amer. Chem. Soc.*, 1935, **57**, 1079, states that the picrate has m. p. 177°, and (iii) a residue (4.4 g.) which afforded *NN'*-diphenylbenzamidinium, m. p. and mixed m. p. 147° (2.8 g., 23%) on crystallisation from benzene.

2-p-Methylsulphonylphenyl- Δ^2 -oxazoline.—(1) *N*-Phenyl-*p*-methylsulphonylbenzamidinium benzenesulphonate (4.32 g.) and 2-hydroxyethylamine (3 g., 5 mols.) were heated on the steam-bath for 4 hours; the solid obtained by triturating the product with water was crystallised from acetone, giving 2-*p*-methylsulphonylphenyl- Δ^2 -oxazoline (82%), m. p. 190° (Found: N, 6.3, 6.4. $C_{10}H_{11}O_3NS$ requires N, 6.2%). The picrate, which was very sparingly soluble in water and organic solvents, had m. p. 213° (decomp.) (Found: N, 12.3. $C_{16}H_{14}O_4N_4S$ requires N, 12.3%).

(2) 2-*p*-Methylsulphonylphenyl- Δ^2 -oxazoline was obtained in 18% yield by heating *p*-methylsulphonylphenyl cyanide and 2-hydroxyethylamine (1 mol.) in a bath at 200° for 45 minutes.

2-p-Methylsulphonylphenyl-4:4-dimethyl- Δ^2 -oxazoline.—A mixture of *N*-ethyl-*p*-methylsulphonylbenzamidinium toluene-*p*-sulphonate (3.98 g.) and 2-aminoisobutyl alcohol (2.5 g., 2.8 mols.) was heated at 140° for 30 minutes; the solid which separated when the cold melt was diluted with water was crystallised from light petroleum-benzene, giving colourless needles of 2-*p*-methylsulphonylphenyl-4:4-dimethyl- Δ^2 -oxazole (2 g., 79%), m. p. 102° (Found: N, 5.5. $C_{12}H_{15}O_3NS$ requires N, 5.5%).

2-3':4'-Dimethoxyphenyl- Δ^2 -oxazoline.—Ammonia was evolved when *N*-phenylveratramidinium benzenesulphonate (2.07 g.) and 2-hydroxyethylamine (2.0 g., 7.5 mols.) were heated on the steam-bath, and after 3 hours the homogeneous mixture was cooled, diluted with water (10 c.c.), and extracted with chloroform. The oil obtained from the chloroform solution was mixed with isopropanolic picric acid and the precipitate was crystallised several times from methanol, giving 2-3':4'-dimethoxyphenyl- Δ^2 -oxazolinium picrate (1.25 g., 57%), m. p. 185.5° (Found: N, 13.0. $C_{17}H_{16}O_6N_4$ requires N, 12.8%).

2-p-Methylsulphonylphenyl-4:5-dihydro-1:3-oxazine.—The mixture obtained by heating *N*-phenyl-*p*-methylsulphonylbenzamidinium chloride (3.1 g.) and 3-aminopropanol (1.5 g., 2 mols.) at 140° for 30 minutes was crystallised from 50% aqueous methanol giving colourless needles (0.81 g., 34%) of 2-*p*-methylsulphonylphenyl-4:5-dihydro-1:3-oxazine, m. p. 131.5° (Found: C, 55.4; H, 5.45; N, 6.0. $C_{11}H_{13}O_3NS$ requires C, 55.2; H, 5.4; N, 5.9%). The picrate separated from methanol in needles, m. p. 182° (Found: N, 12.2. $C_{17}H_{16}O_6N_4S$ requires N, 12.0%).

RESEARCH LABORATORIES, MESSRS. BOOTS PURE DRUG CO. LTD.,
NOTTINGHAM.

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