

208. Researches on Acetylenic Compounds. Part IX. Heterocyclic Compounds derived from Ethynyl Ketones.

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With reagents such as hydrazine, hydroxylamine, guanidine, diazomethane, and ammonium carbonate, ethynyl ketones yield the expected heterocyclic products, identical in most cases with those obtained under similar conditions from the hydroxymethylene derivatives of the corresponding methyl ketones.

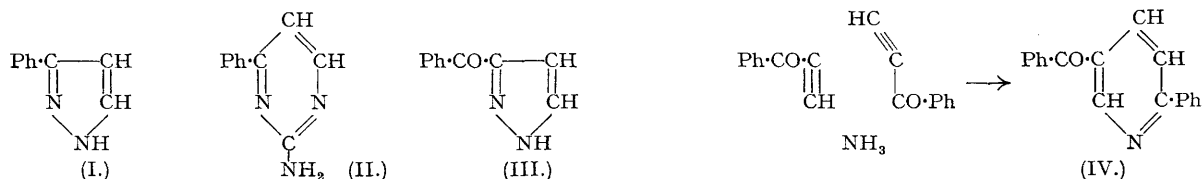
THE close similarity between the reactions with amines of ethynyl ketones and hydroxymethylene derivatives, *i.e.*,



(Bowden, Braude, Jones, and Weedon, this vol., p. 45) suggested that the ethynyl ketones should be converted readily into heterocyclic compounds with appropriate reagents. This has now been found to be so, provided that the reactions are effected under only weakly basic conditions, readily attained by gradually liberating the bases into refluxing aqueous alcoholic solutions of the ketones.

With hydrazine, phenyl ethynyl ketone gives a 70% yield of 3-phenylpyrazole (I), the corresponding 5-phenylisooxazole being obtained in 90% yield by using hydroxylamine (*cf.* Claisen, *Ber.*, 1903, **36**, 3665; Moureu and Delange, *Bull. Soc. chim.*, 1904, **31**, 347, 1335; Moureu and Brachin, *ibid.*, p. 343; André, *Ann. Chim.*, 1913, **29**, 590, for similar reactions with substituted acetylenic ketones). Guanidine under similar conditions gives 2-amino-4-phenylpyrimidine (II) in 25% yield, identical with the product obtained by interaction of hydroxymethyleneacetophenone and guanidine nitrate (Benary, *Ber.*, 1930, **63**, 2601).

Hüttel (*Ber.*, 1941, **74**, 1680) has shown that propargyl aldehyde reacts with diazoacetic ester, diazomethane, hydrozoic acid, and phenyl azide, addition taking place exclusively at the acetylenic linkage. Phenyl ethynyl ketone combines with diazomethane at ordinary temperatures giving 3-benzoylpyrazole (III) in 85% yield.



In Part VIII (this vol., p. 945) the simple addition reaction between phenyl ethynyl ketone and liquid ammonia was described. When the ketone is refluxed in alcoholic solution with ammonium carbonate, reaction occurs between two molecules of the ketone and one of ammonia giving 5-benzoyl-2-phenylpyridine (IV) identical with that obtained from the interaction of the sodio-derivative of hydroxymethyleneacetophenone and ammonium acetate (Benary and Psille, *Ber.*, 1924, **57**, 830).

EXPERIMENTAL.

3-Phenylpyrazole (I).—Phenyl ethynyl ketone (6.5 g.) and hydrazine sulphate (6.5 g.) were refluxed with alcohol (75 c.c.) and sufficient water to render the mixture homogeneous. Sodium carbonate (5.3 g.) dissolved in the minimum volume of water was added dropwise to the boiling solution during 1 hour and refluxing was continued for a further 3 hours. After dilution with water and isolation with ether the crude product was purified by sublimation at 50° (bath temp.)/10⁻⁴ mm. followed by crystallisation from light petroleum (b. p. 40–60°) giving 3-phenylpyrazole (5 g.), m. p. 78°. Both this compound and its picrate showed no depression of m. p. on admixture with authentic specimens obtained by the method of Knorr (*Ber.*, 1895, **28**, 691) from the sodium salt of hydroxymethyleneacetophenone and hydrazine sulphate.

5-Phenylisooxazole.—Phenyl ethynyl ketone (3.25 g.) was dissolved in alcohol (50 c.c.) to which hydroxylamine hydrochloride (1.75 g.) had been added. Whilst refluxing, a small amount of water was added to make the mixture homogeneous. Sodium carbonate (1.3 g.) dissolved in the minimum amount of water was added during 1 hour, and after 9 hours' refluxing the product was isolated with ether. Distillation gave 5-phenylisooxazole (3 g.), m. p. 23°, b. p. 130°/11 mm. (Claisen and Stock, *Ber.*, 1891, **24**, 135, give m. p. 22–23°). The isooxazole (*ca.* 0.25 g.) was authenticated by warming with methyl alcohol (5 c.c.) to which a small amount of sodium had previously been added. Neutralisation with acetic acid followed by evaporation gave a solid which after crystallisation from water yielded *o*-cyanoacetophenone, m. p. 80–81° (Claisen and Stock, *loc. cit.*, give m. p. 80–81°).

2-Amino-4-phenylpyrimidine (II).—Phenyl ethynyl ketone (6.5 g.) was refluxed in alcohol (50 c.c.) with guanidine nitrate (6.1 g.), water being added to give a clear solution, and sodium carbonate (2.65 g.), in the minimum quantity of water, was added whilst refluxing during 2 hours. Refluxing was continued for a further 10 hours and the product was isolated with benzene giving needles of 2-amino-4-phenylpyrimidine (2 g.), m. p. 164°, undepressed on admixture with an authentic specimen obtained from the sodium salt of hydroxymethyleneacetophenone and guanidine nitrate (Benary, *loc. cit.*).

3-Benzoylpyrazole (III).—An ethereal solution of diazomethane, prepared from nitrosomethylurea (5.25 g.), was added dropwise to phenyl ethynyl ketone (3.25 g.) in ether (25 c.c.) at 0–5° until a permanent yellow colour remained. After 12 hours, evaporation of the solution gave a pale yellow solid (3.6 g.) which on sublimation at 65° (bath temp.)/10⁻⁴ mm. yielded long needles of 3-benzoylpyrazole, m. p. 98° (Found: N, 16.4. C₁₀H₉ON₂ requires N, 16.4%).

5-Benzoyl-2-phenylpyridine (IV).—Ammonium carbonate (0.72 g.) was dissolved in the minimum quantity of water and phenyl ethynyl ketone (1.3 g.) added in alcohol (15 c.c.). The mixture was refluxed for 2 hours, the solvent removed under reduced pressure, and the product isolated with ether and crystallised from aqueous methyl alcohol followed by

sublimation at 10^{-4} mm. to give 5-benzoyl-2-phenylpyridine (0.75 g.), m. p. 84—85° (Found: N, 5.25. Calc. for $C_{18}H_{15}ON$: N, 5.4%). No depression of m. p. was observed upon admixture with an authentic specimen, m. p. 85° (Benary and Psille, *loc. cit.*). Light absorption in alcohol: Maxima, 2600, 3000 μ ; ϵ = 8,500 and 28,000 respectively (identical with that of the authentic specimen). The picrate had m. p. 175°, undepressed on admixture with an authentic specimen (Found: N, 11.2. Calc. for $C_{24}H_{18}O_8N_4$: N, 11.45%).

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