1,2,4-Triazoles from Formic Acid-Induced Rearrangement of 6-(Phenylhydrazino)uracils

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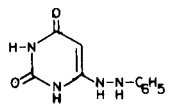
The structure of a rearrangement product of 6-(phenylhydrazino)uracil + formic acid has been proved to be 1-phenyl-3-carboxamidomethyl-1,2,4-triazole: hydrolysis of this compound and thermal decarboxylation of the intermediate acid gave the known 1-phenyl-3-methyl-1,2,4-triazole. Yields of triazoles from substituted 6-(phenylhydrazino)uracils follow inversely yields of pyrimidoindoles derived from Fischer-type cyclization [*J. Heterocyclic Chem.*, 13, 539 (1976)]. The lack of formation of a triazole from 3-methyl-6-(phenylhydrazino)uracil suggests that an intermediate in this rearrangement, *i.e.*, that resulting from formylation of the anilino nitrogen atom followed by intramolecular cyclization involving the uracil 1-nitrogen atom, must undergo conjugate elimination of water to generate the triazole ring.

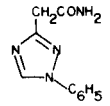
J. Heterocyclic Chem., 14, 701 (1977).

Sir:

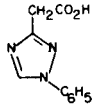
In a recent report (1) on the acid-catalyzed cyclization of I and derivatives to 9*H*-pyrimido[4,5-*b*]indole-2,4-diones, we suggested that the product of a competing reaction in refluxing formic acid was the triazole, II. We now offer proof that II is 1-phenyl-3-carboxamidomethyl-1,2,4-triazole, and that the proposed mechanism accounts for the formation of it and analogous compounds.



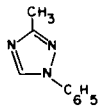
I



II



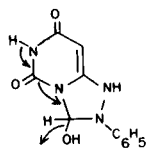
III



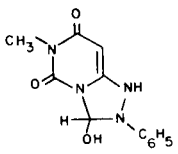
IV

Compound II was heated at reflux in *N* sodium hydroxide for 10 minutes, and, after neutralization, the acid III was isolated in 92% yield, m.p. 189-191°; nmr (DMSO-d_6; internal TMS): 12.50 δ (bd s, 1H), 9.19 δ (s, 1H), 7.4-7.8 δ (m, 5H), 3.74 δ (s, 2H). Decarboxylation of III was effected by heating it at 230° for 30 minutes; sublimation of the residue (80°, 1 mm.) gave 81% of 1-phenyl-3-methyl-1,2,4-triazole, IV, m.p. 85-86°, lit. (2) m.p. 86.5°; nmr (DMSO-d_6; internal TMS): 9.11 δ (s, 1H), 7.4-7.8 δ (m, 5H), 2.36 δ (s, 3H).

The initial step in the formation of II was proposed (1) to be formylation of the anilino nitrogen atom of I. (Thus, no triazole was obtained when this nitrogen atom was substituted with a methyl group.) Intramolecular cyclization would produce an intermediate V from which conjugate elimination of water could serve to open the uracil ring. (Hydrolysis of the resulting acyl isocyanate, decarboxylation and tautomerization complete the formation of II.) Structure V is a likely intermediate in this reaction because no triazole has been detected in reactions of 3-methyl-6-(phenylhydrazino)uracil with formic acid; the intermediate, VI, derived from this compound could not undergo dehydration.



V



VI

Triazoles have been isolated from the reactions of derivatives of I with formic acid, *e.g.* 1-(*p*-tolyl)- (20%, m.p. 187-191°), 1-(*p*-bromophenyl)- (69%, m.p. 189-191°). It is not clear what the driving force is for this unusual rearrangement, although the yields of triazoles follow inversely the yields of pyrimidoindoles in these reactions. Studies of triazole formation in substituted analogs of I may help to resolve this problem.

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REFERENCES AND NOTES

(1) G. E. Wright, *J. Heterocyclic Chem.*, 13, 539 (1976).

(2) G. Pellizzari, *Gazz. Chim. Ital.*, 41, II, 20 (1911).