

Department of Chemistry, Saint Francis Xavier University

Ring Fission of 4-Hydroxypyrazolo[3,4-d] pyrimidines by Hydrazine (1)

Brian M. Lynch and Allan J. Robertson

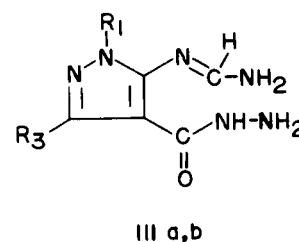
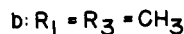
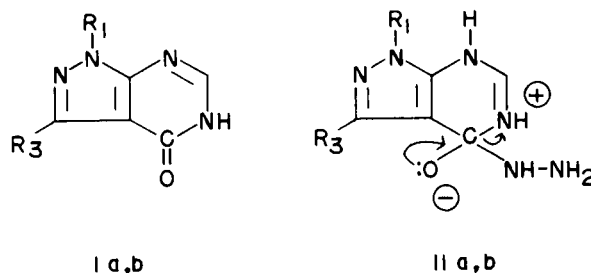
Sir:

Hydrazine effects ring-fission of several heterocyclic lactams: thus 4-quinolone yields 5-(*o*-aminophenyl)pyrazole after recyclization (2), and uracil yields pyrazolone (3,4). We find that the 4-hydroxypyrazolo[3,4-d]pyrimidines Ia and Ib are converted by refluxing hydrazine hydrate into products assigned as IIIa (5-formamidino-4-pyrazolecarboxhydrazide) and its 1,3-dimethyl derivative IIIb (5). The suggested course of reaction is ring-fission of the C₄-N₅ bond after initial nucleophilic attack at C-4: the intermediates or transition states IIa and IIb are consistent with previous demonstrations (6,7) that nucleophilic attack in pyrazolo[3,4-d]pyrimidines occurs most readily at the 4-position, and possess arrangements of electron-donating and electron-accepting groups likely to promote C₄-N₅ bond fission.

The 60 Mc p.m.r. spectrum of the product from compound Ib is in good agreement with its formulation as IIIb: a solution in dimethylsulfoxide-d₆ shows signals at δ 2.23 from the three 3-methyl protons, at δ 3.50 from the three 1-methyl protons, at δ 4.30 (broad: width 9 c/s at half intensity) from the two protons of the formamidino-NH₂ group (the broadening is ascribed to coupling with the C-H proton of the formamidino group, in addition to quadrupole broadening), at δ 6.07 from the two protons of the hydrazide-NH₂ group, and at δ 8.05 (broad: width 5 c/s at half intensity) from the C-H proton of the formamidino group. The absence of a signal from the -NH- proton in the -C(:O)-NH-NH₂ group, and also the absence of coupling between the -NH and -NH₂ protons, may be explained readily since a proton of this type would be expected to exchange rapidly with the solvent (*cf.* (8)).

The infrared spectrum (potassium chloride discs) of the products are also consistent with the structures III: several strong bands appear in the 3180-3460 cm⁻¹ region (N-H stretching); IIIa shows intense peaks at 1618 and 1560 cm⁻¹, and IIIb at 1608 and 1538 cm⁻¹; IIIa also shows a strong peak at 935 cm⁻¹, characteristic of a free hydrogen atom in a pyrazole ring (9). Benzoylhydrazine, a homocyclic model for these products, shows corresponding absorption: 3160-3330, 1613, and 1550 cm⁻¹.

The ring-fission, which proceeds in good yields in a one-step process, promises to provide interesting candidate substances for biological testing, in view of results with other heterocyclic acylhydrazides (10).



Acknowledgments.

We thank the National Research Council, Ottawa, for support of this work, and Dr. Roland K. Robins, who supplied the samples of 4-hydroxypyrazolo[3,4-d]pyrimidines.

REFERENCES

- (1) Based upon the honours research thesis of A. J. R., to be submitted in fulfillment of the B.Sc. requirements.
- (2) G. de Stevens, A. Halamandaris, M. Bernier, and H. M. Blatter, *J. Org. Chem.*, **28**, 1336 (1963).
- (3) R. Fosse, A. Hienke, and L. W. Bass, *Compt. rend.*, **178**, 811 (1924).
- (4) F. Baron and D. M. Brown, *J. Chem. Soc.*, 2855 (1955).
- (5) IIIa has m.p. 225°, IIIb m.p. 212-214°. Satisfactory analyses were obtained on these compounds.
- (6) R. K. Robins, *J. Am. Chem. Soc.*, **78**, 784 (1956).
- (7) R. K. Robins, *ibid.*, **79**, 6407 (1957).
- (8) A. J. Boulton, A. R. Katritzky, A. M. Hamid, and S. Oksne, *Tetrahedron*, **20**, 2835 (1964).
- (9) M. A. Khan, B. M. Lynch, and Y. Hung, *Can. J. Chem.*, **41**, 1540 (1963).
- (10) E. Jucker, *Pure and Appl. Chem.*, **6**, 409 (1963).

Received January 20, 1965

Antigonish, Nova Scotia