Tetrahedron Letters,Vol.24,No.51,pp 5763-5766,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

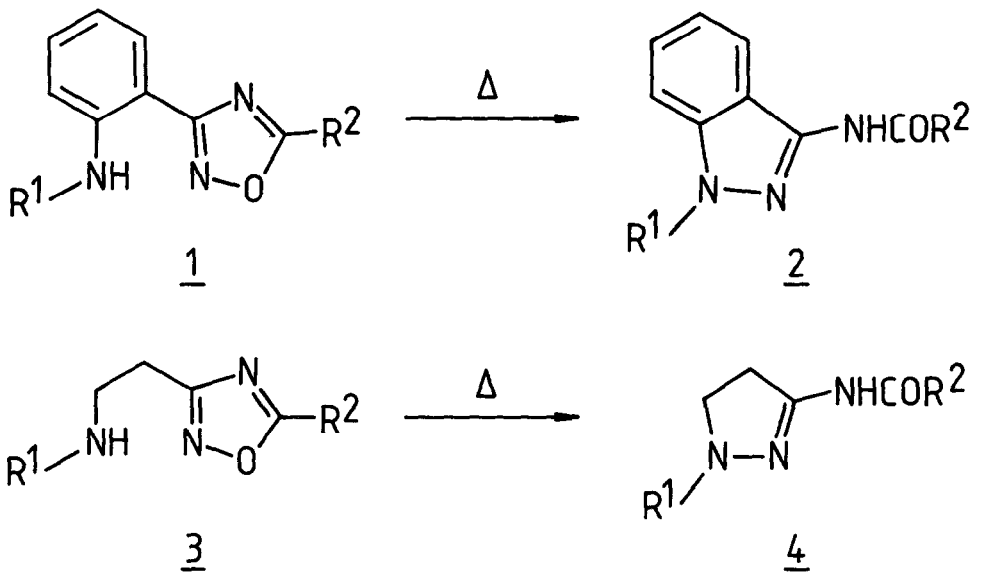
A NOVEL RING TRANSFORMATION: 1,2,4-OXADIAZOLES FROM PYRIMIDINE-N-OXIDES

Dezső Korbonits* and Kálmán Simon
Chinoin Research Centre, H-1325, P.O.B. 110, Budapest, Hungary

Pál Kolonits
Institute for Organic Chemistry, Technical University, H-1111,
Budapest, Hungary

Summary: Tetrahydropyrimidine-N-oxides (9) rearranged on heating to the azolines 8. In contrary to the azoles 1 and 3, the corresponding azolines (6 and 8) failed to transform to 3-aminopyrazoles and pyrazolines, respectively.

Recently we reported that the compounds of type 1 and 3 can be readily rearranged to the aminopyrazoles 2 and aminopyrazolines 4[1,2].

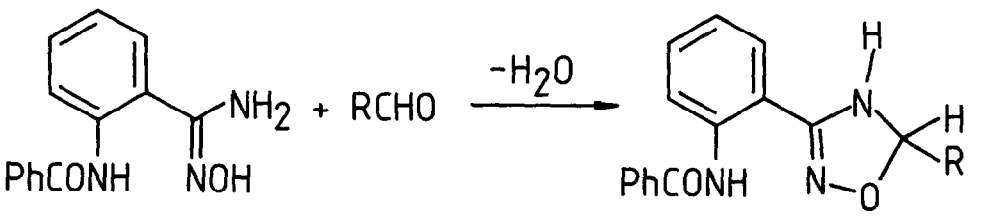


Our earlier results also indicated that the delocalized π-electron system in the parent compound was important for the success of ring isomerizations. Now the models 6 and 8 were studied which differed from 1 and 3 only in the partial saturation of the azole ring.

The azolines 6 and 8 failed to isomerize under conditions which were effective with the azoles 1 and 3. 1 → 2 (R^1 = PhCO, R^2 = Me), k = 1.95 10^{-3} s^{-1} in DMF at 150°C; no reaction for 6a,b within 8 h. 3 → 4 (R^1 = R^2 = Ph) k = 1.13 10^{-4} s^{-1} in BuOH at 115°C; no reaction for 8a-c within 8 h[3].

Preparation of the model compounds 8 led to the observation of a novel ring isomerization, namely the transformation of tetrahydropyrimidine-N-oxides to dihydro-1,2,4-oxadiazoles.

6 was prepared (by analogy)[4] by reacting the amidoxime 5 with aldehydes[5].



5 6

R

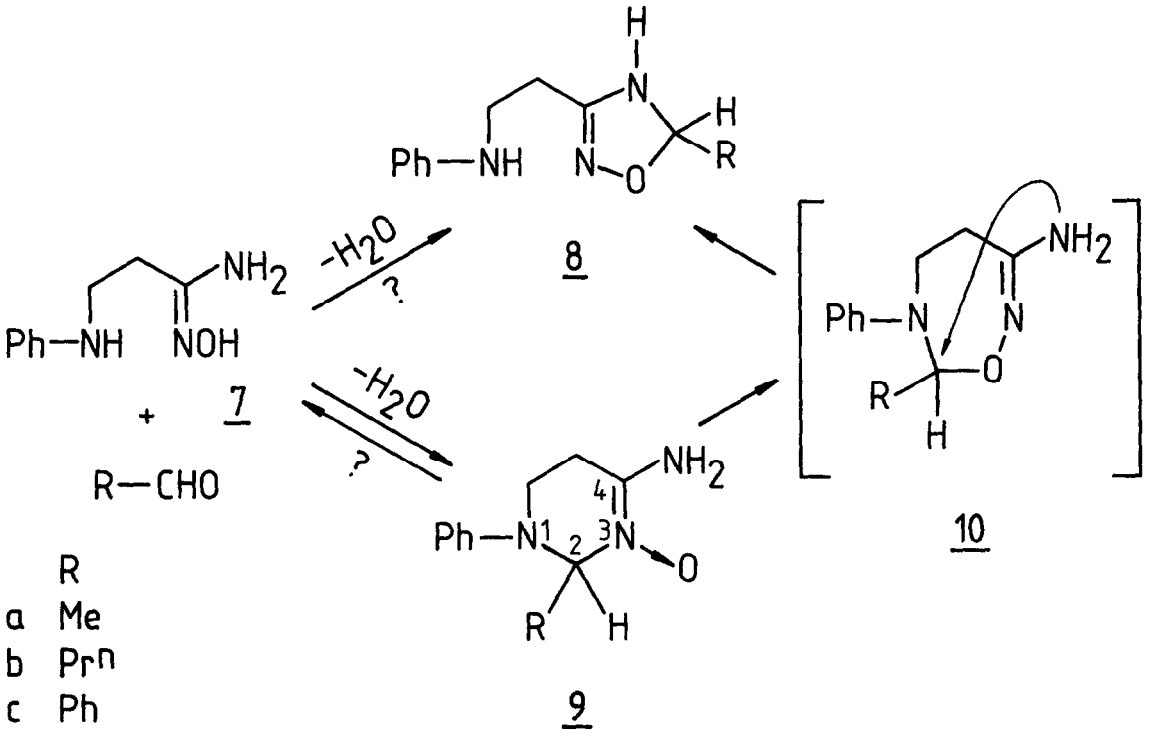
a Me

b Pr^n

Preparation of 8 by the same method was not straightforward since the corresponding amidoxime (7) and aldehydes reportedly gave tetrahydropyrimidine-N-oxides (9)[7]. Having repeated this reaction, we were, however, surprised to find that when we heated 9 in water, ethanol or toluene to 70-95°C for 4-5 h the N-oxides isomerized to the required azolines 8 in excellent yield[8].

X-ray analysis of 9c confirmed the N-oxide type structure and that among the bonds around N(3) the C(2)-N(3) bond is unusually long (1.48 Å) which suggested that ring transformation was initiated at this point[9]. Ring-expansion followed by ring-contraction of N-oxides and also the transannular ring-contraction of aminodiazepin derivatives are well documented[10-13]. Considering the above arguments we suppose that isomerization of 9 to 8 involves the oxadiazepin 10.

Fast but reversible formation of 9 followed by conversion under thermodynamic control (via 7 or an aldehyde-ammonia type intermediate) to 8 cannot be completely ruled out. The fact, however, that 9 can be converted to 8 even in toluene favours the pathway 9 → 10 → 8[14].



References and notes

1 D. Korbonits, I. Kanzel-Szvoboda, and K. Horváth, J. Chem. Soc. Perkin 1, 1982, 759.

2 D. Korbonits, E.M. Bakô, and K. Horváth, J. Chem. Research, 1979, (S) 64; (M) 2801.

3 As its congeners the azoles 1 and 3 corresponding to 6b and 8a, can be easily isomerized but no detailed kinetics are available as yet[1,2].

4 F. Tiemann, Ber. 22, 2412 (1889).

5 Reduction of 1 and 3 has to be ruled out since it generally involves ring opening. A method for the selective saturation of the $N^4 = C^5$ bond[6] cannot be applied for our substrates.

6 H.L. Yale and E.R. Spitzmiller, J. Het. Chem. 15, 1373 (1978).

7 H. Goncalves and M. Bon, C.R. Acad. Sci. Paris, 280 (C) 141 (1975).

8 Structures 6, 8, and 9 were supported by elementary analysis, IR, ^{1}H-, ^{13}C-, and ^{15}N-NMR data.[15] As reference NMR data for 5-methyl-3-phenyl-4,5-dihydro-1,2,4-oxadiazole[4] were used: $\delta_{1H}(CDCl_3)$: 5.76m (1H, CH); $\delta_{13C}(CDCl_3)$: 89.7 (C-3); 156.3 (C-5); $\delta_{15N}(CDCl_3)$: 90.2 (N-4); 298.6 (N-2). Characteristic NMR data: 6: $\delta_{1H}((CD_3)_2SO)$: 1.47d (3H, CH_3); 5.83m (1H, CH); 7.9bs (1H, NH); 11.4s (1H, NH-CO); $\delta_{13C}((CD_3)_2SO)$: 88.8(C-3); 156.4(C-5); 165.0(CO-NH).

8a: $\delta_{1H}(CDCl_3)$: 5.57m (1H, CH); $\delta_{13C}(CDCl_3)$: 89.0 (C-3); 156.2(C-5); $\delta_{15N}(CDCl_3)$: 96.5 (N-4); 293.2 (N-2); 65.4 (Phenyl-NH). 9a: $\delta_{1H}(CDCl_3)$: 5.2q (1H, CH): $\delta_{13C}((CD_3)_2SO)$: 74.0 (C-2); 143.9 (C-4); $\delta_{15N}((CD_3)_2SO)$: 77.1 (N-1); 215.4 (N-3); 70.4 (NH_2).

9 X-ray analysis was performed at the Central Research Institute for Chemistry, Hungarian Academy of Sciences; relevant data are deposited (Tetrahedron Letters, 1978, 3081).

10 H.C. Van Der Plas, Ring Transformation of Heterocycles, Chapter 4., Academic Press, 1973.

11 L.D. Quin and F.A. Shelburne, J. Org. Chem., 30, 3135 (1965).

12 J. Feijen and H. Wynberg, Rec. Trav. Chim. 89, 639 (1970).

13 W. Metlesics, R.F. Tawares, and L.H. Sternbach, J. Org. Chem. 30, 1311 (1965)

14 Analogue but reversed transformation to the 9 → 10 ring-expansion has been published recently: C. Deshayes and S. Gelin, Tetrahedron Letters, 1981, 2557.

15 Microanalyses are acknowledged to Dr. I. Remport, I. R. spectra to Mrs G. Kovács, technical assistance to Mrs G. Héja and to Mr Cs. Kertész.

(Received in UK 7 October 1983)