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1,2,5-THIADIAZOLE-1-OXIDES. V. RING TRANSFORMATIONS TO PYRAZINE, 1,2,4-THIADIAZOLE AND PYRROLE

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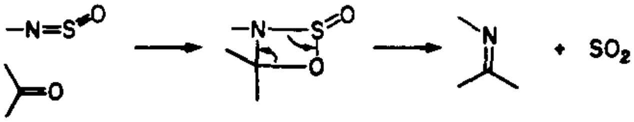
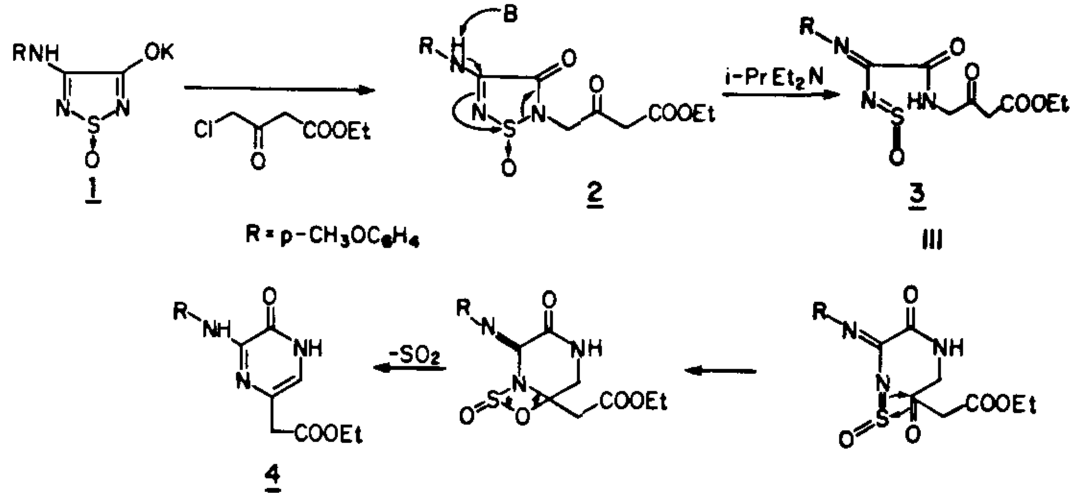
Abstract - Rearrangement of 2-alkyl-1,2,5-thiadiazole-3-on-1-oxides to pyrazine, 1,2,4-thiadiazole and pyrrole derivatives is described. Ring opening to a sufinylamine and cyclization by cycloaddition or nucleophilic addition is the postulated mechanism.

In a previous paper[1] we described the conversion of 1,2,4-thiadiazole-1-oxides into thiatriazole and thiatriazene oxides, a process involving ring opening to a sulfinylamine intermediate followed by cyclization with nitrogen nucleophiles. In this paper ring transformations to 1,2,4-thiadiazole, pyrazine and pyrrole derivatives are described. It is envisioned that these reactions take place by similar base initiated ring opening followed by cyclization with other reactive functions.

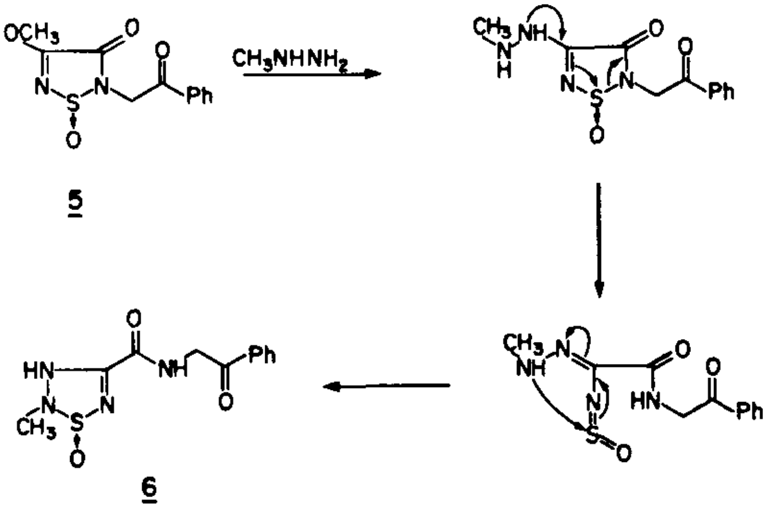
Condensation of sulfinylamines with carbonyl compounds by 2 + 2 cycloaddition to afford imines is a well known reaction.[2]



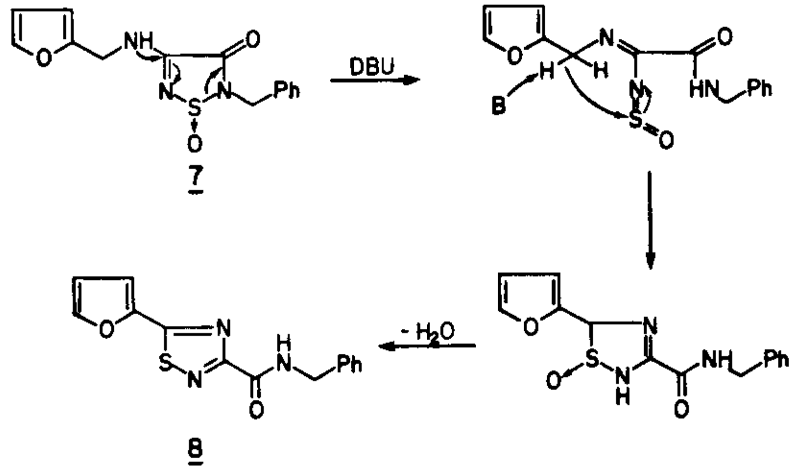
It appeared plausible, therefore, that the sulfinylamine 3 generated in an equilibrium by base catalyzed ring opening of 2, can be trapped by a suitably placed keto function. The keto ester derivative 2 was prepared by alkylation of 1 in DMF at room temperature for 2 days in 55% yield. When this compound was allowed to stand at room temperature for 3 days in the presence of Hunig's base, pyrazine 4 was generated in 30% yield[3]. Other analogous compounds reacted similarly.



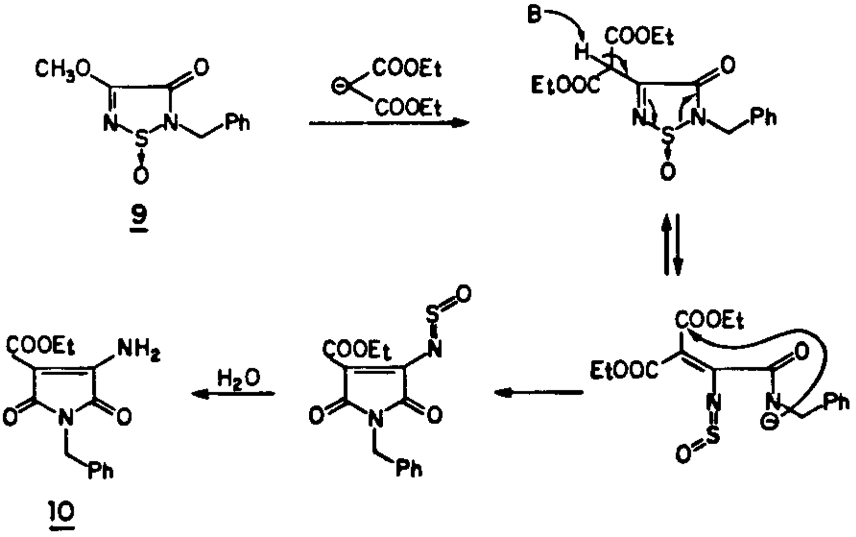
Similar rearrangements could be expected when phenacyl derivative 5 was treated with an alkylhydrazine. In this case, however, cyclization with the strongly nucleophilic nitrogen took preference over cycloaddition[1]. Thiatriazole oxide 6 was isolated from this reaction in 65%



A formally analogous rearrangement took place when compound 7 was treated with strong base, producing 1,2,4-thiadiazole derivative 8 in poor yield. In this case, the cyclization took place by carbanion addition to the sulfinylamine. The reaction was carried out by heating 7 and a trace of DBU in refluxing xylene for 5 h, followed by chromatographic isolation of the product.



In the previous examples ring opening was initiated by the action of base on an acidic N-H group. The rearrangement outlined below is rationalized[4] by analogous ring opening triggered by formation of a carbanion. The rearrangement is completed by condensation of the amide anion with the ester group, to afford pyrrole 10. Thus, when sodiomalonate, generated with NaH in DMF, was allowed to react with 9 in CH_3CN at 0°C and room temperature for 2 h, 10 was obtained in 60% yield.



These papers[1] demonstrate the remarkable ability of the 1,2,5-thiadiazole-1-oxides to undergo rearrangements. No doubt, further studies will lead to new discoveries in this fertile area.

ACKNOWLEDGEMENT

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REFERENCES AND NOTES

1) S. Karady, J. S. Amato, R. A. Reamer and L. M. Weinstock, *Tetrahedron Letters*, 1985, **26**, 6155.

2) For review see: "Organic Compounds of Sulfur, Selenium and tellurium" (Specialist Periodical Reports) The Chemical Society, London, Vol. 2, 1973, p. 336-338, Vol 4, 1977, p. 105.

3) Satisfactory C, H, N and S analysis and spectral data (NMR, IR, and mass) were obtained on all intermediates. Melting points are uncorrected. Diagnostic data are summarized here. $\underline{4}$: mp 140°C; MS m/z 303 (M+); ^{1}H NMR ($CDCl_3$) δ 4.45 (s, 2H,-CH_2-), 6.6 (s, 1H,=CH) and the usual signals for OCH_2CH_3 and $pCH_3OC_6H_4N$; ^{13}C NMR ($CDCl_3$) δ_c 39.9 ($\underline{CH_2}$-COO-), 112.4 (NH$\underline{CH}$=C-), 128.4 (=N-$\underline{C}$=CH-), 147.5 (NH-C=0), 155.4 (N=$\underline{C}$-CO-); $\underline{6}$ (p-$\overline{Cl-}C_6H_4$ analog): mp 157-158°C; MS m/z 314 (M^+), 266 (M^+-SO); ^{1}H NMR (DMSO-d_6) δ 3.4 (s, 3H, -N-CH_3) 4.8 (d, J=5 Hz, 2H, NH-$\underline{CH_2}$), 7.6 and 8.1 (two br d, J=8 Hz, 4 H, p-Cl-C_6H_4-), 8.8 (t, J=5 Hz, 1H, $\underline{NH}$-CH_2). $\underline{8}$: mp 111-112°C; MS m/z 285 (M+); ^{1}H NMR: in accord with structure. ^{13}C NMR ($CDCl_3$) δ_c 43.8 (CH_2-N), 113.0 and 113.5 (C_3 and C_4 of furane), 146.1 (C_2 of furane), 146.3 (C_5 of furane), 158.1 (N-C=0), 167.3 (N=C-N), 177.96 (N=C-S). $\underline{10}$: mp 148-149°C; MS m/z 274 (M+); ^{13}C NMR (DMSO-d_6) δ_c 40.5 ($\underline{PHCH_2}$-N), 87.4 (NH_2-C=$\underline{C}$-), 155.1 (NH_2-$\underline{C}$=C-), 162.6 (NH_2-C=C-$\underline{C}$=0), 164.2 (0=$\underline{C}$-CNH_2=C).

4) It was shown in an earlier paper that carbanions displace methoxy groups in this system: S. Karady, J. S. Amato, D. Dortmund and L. M. Weinstock, *Heterocycles*, 1981, **16**, 1561.

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