

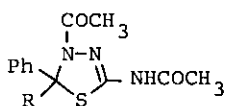
NOVEL REARRANGEMENT OF 3-ACYL-5-ACYLAMINO-2,3-DIHYDRO-1,3,4-THIADIAZOLE 1-OXIDES INTO 1,3,4-OXADIAZOLES

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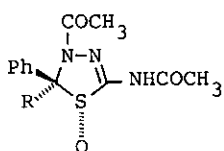
Abstract — Thermally, or in the presence of p-toluenesulfonic acid, 3-acyl-5-acylamino-2,3-dihydro-1,3,4-thiadiazole 1-oxides are transformed into 1,3,4-oxadiazoles, carbonyl compounds and sulfur.

In the previous communication,¹ we reported that the oxidation of 3-acetyl-5-acetamido-2-phenyl-2,3-dihydro-1,3,4-thiadiazole (1) and the 2-methyl-2-phenyl derivative (2) with m-chloroperbenzoic acid (m-CPBA) gave single isomers of the S-oxides (3) and (4), respectively. We now report a novel rearrangement of these S-oxides into 1,3,4-oxadiazoles. Previously, we reported that 3-acetyl-5-methylsulfonyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (5) was converted into 2-methylsulfonyl-5-phenyl-1,3,4-thiadiazole (6) in ethanol in the presence of base at room temperature or by heating in dimethylsulfoxide (DMSO) at 100°C.²



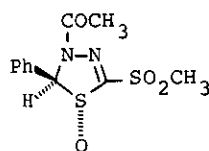
1 R = H

2 R = CH₃

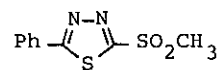


3 R = H

4 R = CH₃



5

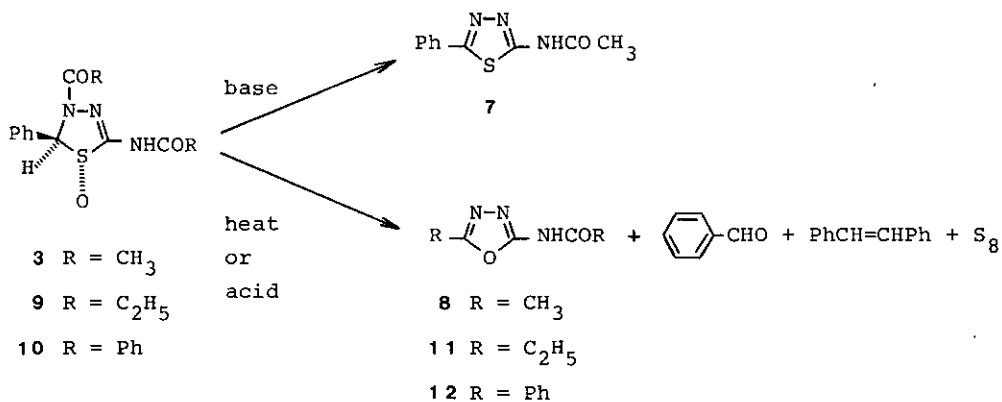


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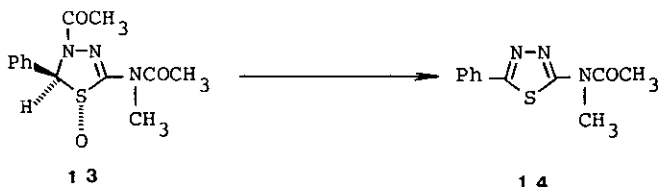
We examined a similar reaction of 3-acetyl-5-acetamido-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (3). Treatment of compound (3) with a base in ethanol gave 2-acetamido-5-phenyl-1,3,4-thiadiazole (7)³ in a 70 % yield (with pyridine) or in a 90 % yield (with triethylamine). However, heating compound (3) in DMSO

at 100°C for 3 h gave 2-acetamido-5-methyl-1,3,4-oxadiazole (8), mp 179-180°C (lit.⁴, mp 180-181°C), in 74 % yield along with benzaldehyde, trans-stilbene and sulfur.

This novel rearrangement was also observed when compound (3) was heated in dimethylformamide at 100°C for 3 h (77 % yield). Similarly, 5-propionamido-3-propionyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (9)⁵ and 5-benzamido-3-benzoyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (10),⁶ which were obtained by oxidation of the corresponding 3-acyl-5-acylamino-2-phenyl-2,3-dihydro-1,3,4-thiadiazoles³ with m-CPBA, were also transformed into 2-ethyl-5-propionamido-1,3,4-oxadiazole (11)⁷ in 60 % yield and 5-benzamido-2-phenyl-1,3,4-oxadiazole (12), mp 198-200°C (lit.⁴, 201-202°C), in 78 % yield, respectively, when heated in DMSO at 100°C for 3 h.

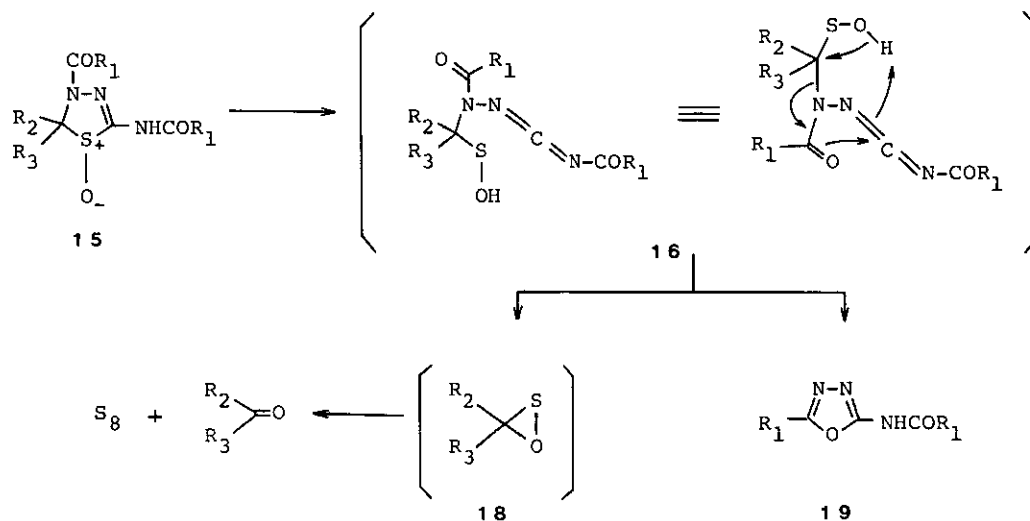


Refluxing compound (3) in dioxane for 20 h or in toluene for 1 h in the presence of a catalytic amount of p-toluenesulfonic acid gave the 1,3,4-oxadiazole (8) in 49 % or in 54 % yield, respectively, along with benzaldehyde and sulfur. Heating 3-acetyl-5-acetamido-2-methyl-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (4)¹ in DMSO at 100°C gave many decomposition products, and the expected oxadiazole derivative was not detected. However, refluxing compound (4) in dioxane for 20 h or in toluene for 1 h in the presence of catalytic amount of p-toluenesulfonic acid gave the oxadiazole (8) in 49 % or in 35 % yield, along with acetophenone and sulfur. 3-Acetyl-5-(N-methylacetamido)-2-phenyl-2,3-dihydro-1,3,4-thiadiazole 1-oxide (13)⁸



which was obtained from 3-acetyl-5-(N-methylacetamido)-2-phenyl-2,3-dihydro-1,3,4-thiadiazole³ by oxidation with m-CPBA did not change at 100°C in DMSO, but was converted into 2-(N-methylacetamido)-5-phenyl-1,3,4-thiadiazole (14), mp 191-193°C (lit.³, 191-192°C), in 40 % yield at 150°C in DMSO for 5 h.

This fact suggests that the presence of an NH proton in acylamino side chain is necessary for this rearrangement. A possible mechanism to explain the formation of the oxadiazole is shown in the following scheme.



The ring expansion reaction which occurs on heating heterocyclic sulfoxides containing β -hydrogen atoms is well documented,⁹⁻¹³ and the initial step of these reaction is the thermal ring opening to a sulfenic acid intermediate. In the present reaction, the intermediate sulfenic acid (16) would be produced from the sulfoxide (15) by a prototropic rearrangement or by the initial protonation with p-toluenesulfonic acid. The subsequent intramolecular reaction of 16 affords the oxadiazole (17) and the thermally highly unstable oxathirane (18)^{14,15} which is converted into the corresponding carbonyl compounds and sulfur.

ACKNOWLEDGEMENT

This work was supported in part by a Grant in Aid for Scientific Research from the Ministry of Education, Science and Culture, Japan, which is gratefully acknowledged.

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5. Compound 9 : yield 90 % ; mp 149.5-151.0 °C (decomp.). IR (KBr): 1705, 1685 (C=O), 1025 (SO) cm⁻¹. ¹H-NMR (CDCl₃): δ 1.11 (3H, t, CH₂CH₃), 1.18 (3H, t, CH₂CH₃), 2.36 (2H, q, CH₂CH₃), 2.80 (2H, q, CH₂CH₃), 6.63 (1H, s, C₂-H), 7.05-7.46 (5H, m, C₆H₅), 9.35 (1H, br.s, NH). All new compounds in this paper gave satisfactory elemental analyses.
6. Compound 10 : yield 82 % ; mp 158.5-160.0 °C (decomp.). IR (KBr): 1690, 1660 (C=O), 1030 (SO) cm⁻¹. ¹H-NMR (Me₂SO-d₆): δ 7.06 (1H, s, C₂-H), 7.32-8.12 (15H, m, ArH), 12.40 (1H, br.s, NH).
7. Compound 11 : mp 127.5-129.0 °C. MS m/z: 169 (M⁺). IR (KBr): 1660 (C=O) cm⁻¹. ¹H-NMR (CDCl₃): δ 1.23 (3H, t, CH₂CH₃), 1.37 (3H, t, CH₂CH₃), 2.59 (2H, q, CH₂CH₃), 2.86 (2H, q, CH₂CH₃), 11.82 (1H, br.s, NH).
8. Compound 13 : yield 84 % from 3-acetyl-5-acetylmethylamino-2-phenyl-2,3-dihydro-1,3,4-thiadiazole. mp 144.0-145.0 °C (decomp.). MS m/z: 293 (M⁺). IR (KBr): 1690, 1675 (C=O), 1065 (SO) cm⁻¹. ¹H-NMR (CDCl₃): δ 2.33 (3H, s, COCH₃), 2.49 (3H, s, COCH₃), 3.51 (3H, s, N-CH₃), 6.62 (1H, s, C₂-H), 6.96-7.52 (5H, m, ArH).
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Received, 2nd September, 1985