ISOLATION OF Δ^3-1,2,3-THIADIAZOLIN-1-ONES, A KEY INTERMEDIATE OF THE HURD-MORI REACTION

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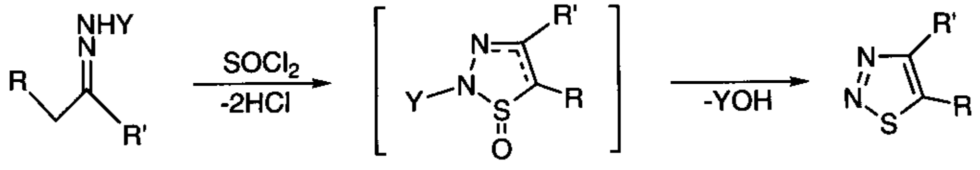
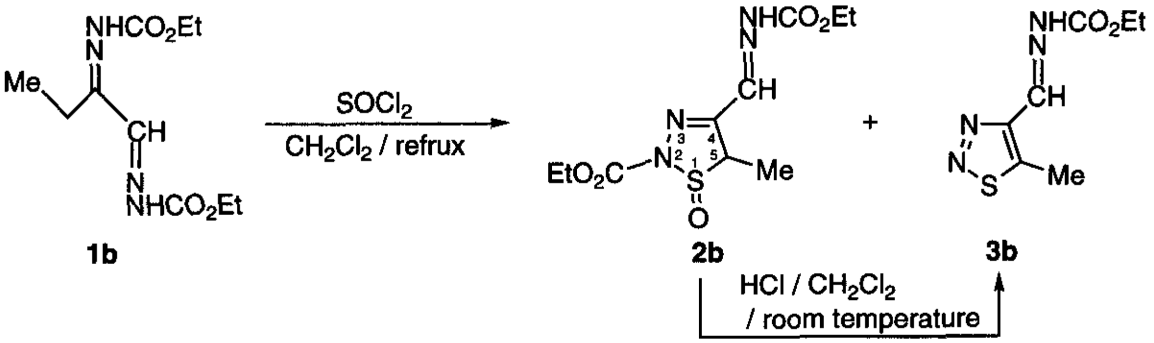
Abstract - The Hurd-Mori reaction of *N*-ethoxycarbonyl- or *p*-toluenesulfonylhydrazones of 1,2-alkanediones (**1**) gave Δ^3-1,2,3-thiadiazolin-1-ones (**2**) as each sole isolable product. Upon HCl treatment **2b** was converted into 1,2,3-thiadiazole, an expected product of the Hurd-Mori reaction.

The Hurd-Mori reaction[1] is the one which converts hydrazones into 1,2,3-thiadiazoles using thionyl chloride and has attracted synthetic[2,3] and mechanistic interest. It is assumed that the reaction proceeds *via* Δ^2- or Δ^3-1,2,3-thiadiazolin-1-one (**I**), which then aromatizes to 1,2,3-thiadiazole (**II**).[1,4,5] However, no evidence has been available that supports the formation of **I** or the conversion of **I** into **II**.[6,7] Herein we report that the Hurd-Mori reaction of an appropriate hydrazone allows us to isolate 1,2,3-thiadiazolin-1-one which can be converted successfully into 1,2,3-thiadiazole.

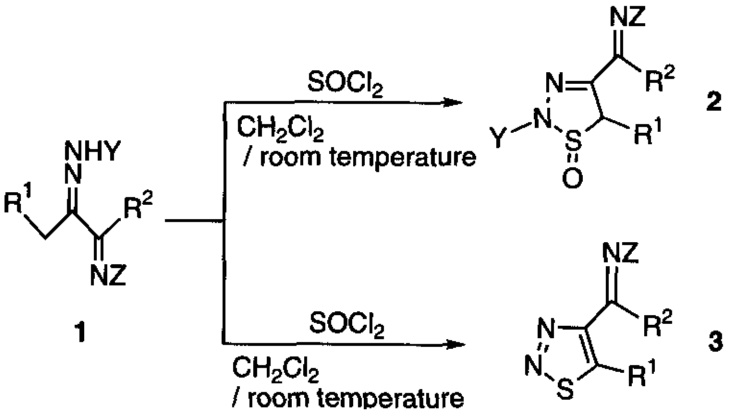


I **II**

Whereas bis(*N*-ethoxycarbonylhydrazone) of propane-1,2-dione (**1a**) afforded a normal Hurd-Mori product as a sole product,[2] the reaction of bis(*N*-ethoxycarbonylhydrazone) of butane-1,2-dione (**1b**) with 3 mol eq. of thionyl chloride under reflux in CH_2Cl_2 gave 1,2,3-thiadiazolin-1-one (**2b**) as a major product in 44% yield along with 1,2,3-thiadiazole **3b** (6%). The structure of **2b** was assigned as Δ^3-isomer based on its ^{1}H and ^{13}C nmr spectra.[8] The compound (**2b**) was converted into **3b** in 63% yield by treatment with dry HCl in CH_2Cl_2.



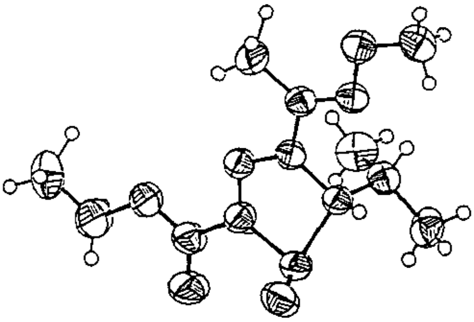
Similar reaction of methoxyiminohydrazones (**1c**; R^1 = Me, R^2 = Me, Y = CO_2Et, Z = OMe) afforded Δ^3-1,2,3-thiadiazolin-1-one (**2c**) in 38% yield with no trace of formation of 1,2,3-thiadiazole (**3**), but **1d** (R^1 = Me, R^2 = Ph, Y = CO_2Et, Z = Me) gave normal product (**3d**) in 26% yield, hereby 1,2,3-thiadiazolin-1-one being not detected.

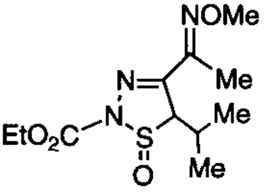


c: R^1 = Me, R^2 = Me,
Y = CO_2Et, Z = OMe

d: R^1 = Me, R^2 = Ph,
Z = OMe

Hydrazones having various alkyl groups for R^1 and R^2 gave the corresponding Δ^3-1,2,3-thiadiazolin-1-ones (**2**): R^1 = R^2 = Me, Y = Tos, Z = OMe (**2e**): 69% yield; R^1 = R^2 = Et, Y = CO_2Et, Z = OMe (**2f**): 48% yield; R^1 = R^2 = Et, Y = Tos, Z = OMe (**2g**): 57% yield; R^1 = i-Pr, R^2 = Me, Y = CO_2Et, Z = OMe (**2h**): 60% yield; R^1 = i-Pr, R^2 = Me, Y = Tos, Z = OMe (**2i**): 38% yield. In all cases, **2** was not accompanied by **3**. Thus, Δ^3-1,2,3-thiadiazolin-1-one (**2**) was a single isolable product particularly when Y was CO_2Et or Tos.[9] The structure of **2h** was confirmed by X-ray crystallographic analysis as shown in Figure 1.

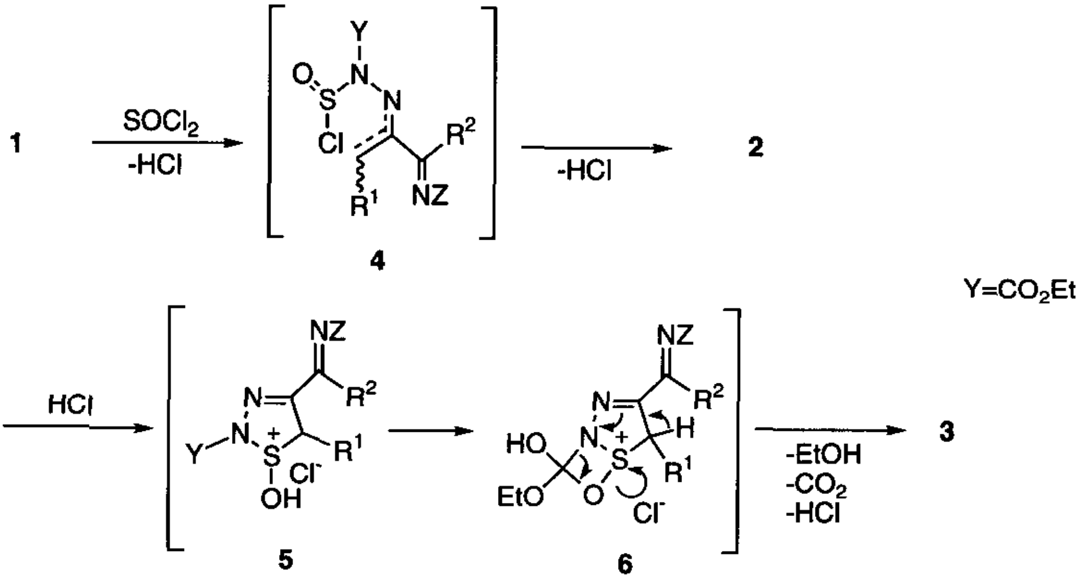




2h

Figure 1.

The most plausible mechanism of the Hurd-Mori reaction is as follows: The reaction of hydrazone (**1**) with thionyl chloride gives **4** which undergoes cyclization to afford 1,2,3-thiadiazolin-1-one (**2**). Protonation of **2** gives rise to sulfonium salt (**5**) that converts into **6** by intramolecular addition.[1] Final compound 1,2,3-thiadiazole (**3**) may be produced from **6** by the elimination of EtOH, CO$_2$, and HCl.



The reaction of **1a** and **1b** suggests that an alkyl group at 5-position (R^1), in contrast to the case in which R^1 is hydrogen, stabilizes the sulfonium cation (**5**) or (**6**) which could revert to **2** after work-up, and makes it difficult to convert **5** or **6** into **3**. However, in cases of R^1 = alkyl, **3d** was not accompanied by **2**, showing that a phenyl group for R^2 facilitates the production of aromatic compound (**3**). Substituents R^1 and R^2 play an important role in the isolation of 1,2,3-thiadiazolin-1-one (**2**).

The study reported herein clearly demonstrates that an intermediate of the Hurd-Mori reaction is 1,2,3-thiadiazolin-1-one. These findings should be useful for the synthesis of a variety of Δ^3-1,2,3-thiadiazolin-1-one.[10]

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6. Ref. 1 reported that intermediates isolated in the Hurd-Mori reaction were Δ^2-1,2,3-thiadiazolin-1-ones on the basis of elemental analysis. Ref. 7 also reported the isolation of a Δ^2-1,2,3-thiadiazolin-1-one derivative whose structure was determined by elemental analysis and ^{1}H nmr only, but one product in ref. 1 was later corrected to be a TosOH salt of 1,2,3-thiadiazole in ref. 5.

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8. ^{1}H Nmr ($CDCl_3$) δ 1.33 (t, J = 7.1 Hz, 3H), 1.43 (t, J = 7.1 Hz, 3H), 1.47 (d, J = 7.8 Hz, 3H), 4.29 (q, J = 7.1 Hz, 2H), 4.47 (q, J = 7.1 Hz, 2H), 4.58 (q, J = 7.8 Hz, 1H), 8.04 (s, 1H), 8.80 (br s, 1H); ^{13}C nmr (DMSO d_6) δ 11.0 (q), 14.3 (q), 14.5 (q), 61.2 (t), 63.9 (t), 69.3 (d), 135.6 (d), 151.5 (s), 152.9 (s), 155.8 (s); ms *m/z* 304 (M^+); ir(KBr) 1040 cm^{-1} (S=O); Anal. Calcd for $C_{10}H_{16}N_4O_5S$: C, 39.47; H, 5.30; N, 18.41; S, 10.54. Found: C, 39.80; H, 5.33: N, 18.24; S, 10.44.

9. Ethoxycarbonylhydrazones and tosylhydrazones have been used as the starting material of the Hurd-Mori reaction.

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