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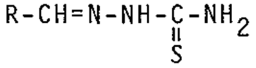
ACETYL-1,3,4-THIADIAZOLINES FROM THE REACTION OF THIOSEMICARBAZONES WITH ACETIC ANHYDRIDE

Seiju Kubota*, Kazuichi Fujikane, Masayuki Uda,
and Tamiya Yoshioka

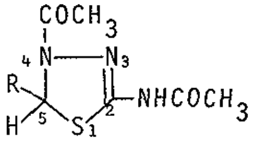
Faculty of Pharmaceutical Sciences, University of Tokushima,
Shomachi, Tokushima, Japan

N.m.r. spectroscopy showed that the compounds obtained by reaction of thiosemicarbazones (I) with acetic anhydride are 2-acetylamino-4-acetyl-1,3,4-thiadiazolines (II) and not N^4, S-diacetyl-thiosemicarbazones (III) as thought previously.

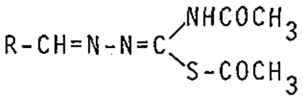
It has been reported that the reaction of thiosemicarbazones (I) with excess acetic anhydride gave N^4, S-diacetyl-thiosemicarbazones (III).[1,2,3,4] We found that the n.m.r. spectrum of the diacetyl compound (mp 222-223°, lit.[1] mp 222-224°) obtained by reaction of benzaldehyde thiosemicarbazone (Ia) with excess acetic anhydride showed the signal of methine proton at δ 6.80. This δ value is 1.24 ppm to a higher field than that of the methine proton of the starting thiosemicarbazone (Ia) and is in good agreement with those of C-5 protons of 1,3,4-thiadiazoline derivatives.[5] The signals of the aromatic protons of


$R\text{-}CH{=}N\text{-}NH\text{-}C(=S)\text{-}NH_2$

(I)



(II)


$R\text{-}CH{=}N\text{-}N{=}C(NHCOCH_3)(S\text{-}COCH_3)$

(III)

I,II,IIIa: R=C_6H_5, e: R=p-$NO_2C_6H_4$

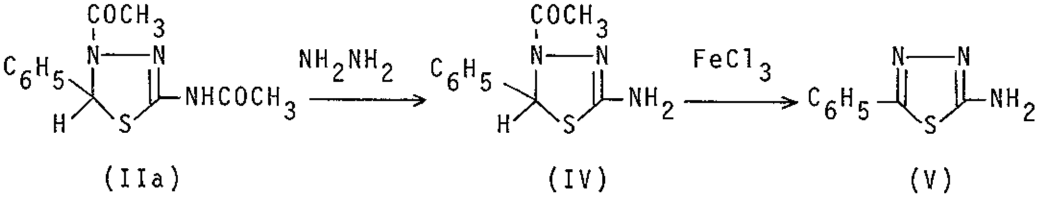
b: R=2-Pyridyl, f: R=p-ClC_6H_4

c: R=3-Pyridyl, g: R=p-$MeOC_6H_4$

d: R=4-Pyridyl, h: R=p-$Me_2NC_6H_4$

the diacetyl compound appeared as a multiplet centered at δ 7.27, whereas those of the aromatic protons of (Ia) were separated in two broad multiplets centered at δ 7.36 and 7.78 in a ratio of 3:2, due to the effect of the adjacent -CH=N- group. The spectral data described above indicate that the product is 2-acetylamino-4-acetyl-5-phenyl-1,3,4-thiadiazoline (IIa) and not benzaldehyde N^4, S-diacetyl-thiosemicarbazone (IIIa).

The reaction of IIa with excess hydrazine hydrate (85%) at room temperature gave 2-amino-4-acetyl-5-phenyl-1,3,4-thiadiazoline (IV), mp 160-161°, n.m.r. spectrum [δ(DMSO-d_6): 6.97 (1H, s, C_5-$\underline{H}$), 6.72(2H, s, NH_2), 7.26(5H, s, C_6H_5), 2.10(3H, s, $COC\underline{H}_3$)]. Treatment of IV with ferric chloride solution gave 2-amino-5-phenyl-1,3,4-thiadiazole(V).^{6} This chemical evidence also supports the structure (IIa).



Similarly, the δ values of the methine protons of the products obtained in the reaction of thiosemicarbazones (Ib-Ih) with acetic anhydride indicate that structures (IIb-IIh) are reasonable for the products (Table). The signals of the aromatic protons of the products also support the cyclized structure (II).

Table

Starting material	n.m.r. ($DMSO-d_6$)δ: -C$\underline{H}$=N-	Product	Mp(° C)	Yield (%)	n.m.r. ($DMSO-d_6$)δ: C_5-$\underline{H}$
Ia	8.04	IIa	222-223	78	6.80
Ib	8.11	IIb	206-208*	78	6.79
Ic	8.10	IIc	179-180**	66	6.89
Id	8.04	IId	220-222	54	6.84
Ie	8.11	IIe	210-211	57	6.95
If	8.02	IIf	229-233	68	6.82
Ig	8.06	IIg	168-169	76	6.76
Ih	7.88	IIh	222***	76	6.70

* lit.[1] 208-211°, ** lit.[1] 188-190°, *** decomp.

Reaction of acetophenone thiosemicarbazone with acetic anhydride gave a diacetyl compound, mp 216-217°, in 73% yield, n.m.r. spectrum [δ(DMSO-d_6): 2.02, 2.20 (each 3H, each s, 2 X COC$\underline{H}_3$), 2.28 (3H, s, C_5-CH_3), 11.75 (1H, s, NH)]. The diacetyl compound was also concluded to be 2-acetylamino-4-acetyl-5-methyl-5-phenyl-1,3,4-thiadiazoline, because the signals of its aromatic protons appeared at δ 7.32 as a singlet, whereas those of the starting thiosemicarbazone were separated in two broad multiplets centered at δ 7.36 and 7.90 in a ratio of 3:2.

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