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

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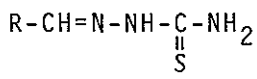
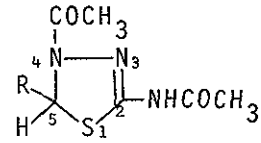
N.m.r. spectroscopy showed that the compounds obtained by reaction of thiosemicarbazones (I) with acetic anhydride are 2-acetylamino-4-acetyl-1,3,4-thiadiazolines (II) and not N^4, S-diacetyl-thiosemicarbazones (III) as thought previously.

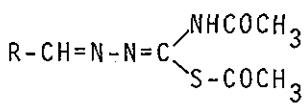
It has been reported that the reaction of thiosemicarbazones (I) with excess acetic anhydride gave N^4, S-diacetyl-thiosemicarbazones (III).[1,2,3,4] We found that the n.m.r. spectrum of the diacetyl compound (mp 222-223°, lit.[1] mp 222-224°) obtained by reaction of benzaldehyde thiosemicarbazone (Ia) 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



(I)



(II)



(III)

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

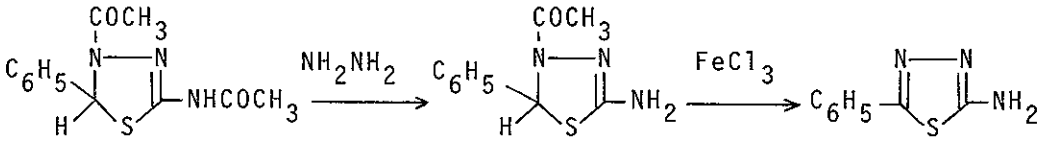
b: R=2-Pyridyl, f: R=p-ClC_6H_4

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-H), 6.72(2H, s, NH_2), 7.26(5H, s, C_6H_5), 2.10(3H, s, $COCH_3$)]. 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).



(IIa) (IV) (V)

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<u>H</u>=N-	Product	Mp(°C)	Yield (%)	n.m.r. (DMSO-d_6)δ: C_5-<u>H</u>
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 $COCH_3$), 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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