The Synthesis of Substituted Thiosemicarbazones Containing Ferrocenyl Group

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Received 27 December 1991

We have reported on the preparation of ten thiosemicarbazones, which contain ferrocenyl group and have not been described so far, by condensation of 1-acetylferrocene or 1,1′-diacetylferrocene with various substituted thiosemicarbazides. The compositions and structures have been characterized by elemental analysis, IR and ^{1}H NMR spectra.

A large number of thiosemicarbazones have been synthesized by condensation of aliphatic, aromatic or heterocyclic aldehydes or ketones with thiosemicarbazides in recent years. Many of them exhibit a wide spectrum of bioactivities including antitumour [1], antiviral [2], antimalarial [3], antifungal [4], anticoccidal [5], *etc.* There were also a few reports about thiosemicarbazones containing ferrocenyl group. One of the authors of this paper had reported on some substituted semicarbazones and thiosemicarbazones which contain ferrocenyl group and found out that they have bacteriostatic activities [6]. We continued in the work and prepared another ten thiosemicarbazones of acetylferrocenes which have not been reported previously.

EXPERIMENTAL

Acetylation of ferrocene gave 1-acetylferrocene (AF) and 1,1′-diacetylferrocene (DAF) [7].

A series of 4-substituted thiosemicarbazides (TSC) were synthesized from the appropriate amines in the mixture of ethanol and NH_4OH under cooling by the action of CS_2 and hydrazine hydrate in the presence of sodium chloroacetate [8] and crystallized from ethanol. $NH_2NHCSNHC_6H_4R$: R = *p*-CH_3, m.p. = 138—139 °C (Ref. [9] gives m.p. = 138 °C), R = *p*-EtO, m.p. = 148—150 °C (145 °C [10]), R = *p*-CH_3O, m.p. = 144 °C (144 °C [8]), R = *o*-CH_3, m.p. = 144 °C (147 °C [9]), R = *o*-CH_3O, m.p. = 156 °C (156 °C [11]). We have some doubts of the compound where R = *p*-EtO which has higher melting point than that given in the literature. So in this case the elemental analysis was done (w_i(calc.): 51.16 % C, 6.20 % H, 19.89 % N; w_i(found): 51.10 % C, 6.28 % H, 19.87 % N) and the agreement with the formula $C_9H_{13}N_3OS$ was shown.

The infrared spectra of the compounds were obtained with a Nicolet FT-5DX instrument ($\tilde{\nu}$ = 400—4000 cm^{-1}, KBr), NMR spectra were obtained on a Varian FT-80A spectrometer (solvent: $CDCl_3$, internal standard: TMS). The melting points were determined using Kofler apparatus. The elemental analyses were carried out on an Erba instrument, model 1106.

Substituted Thiosemicarbazones *I*—*X*

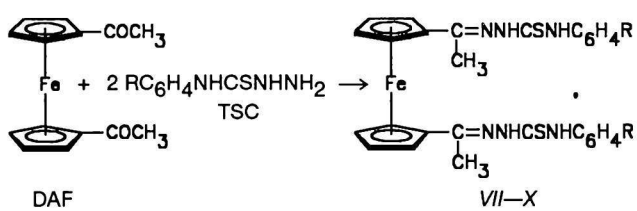
AF or DAF (2 mmol) in pyridine (1.2 cm^3) was mixed with a solution of a TSC (2 mmol) in warm 95 % ethanol (20 cm^3). Hydrochloric acid was added to adjust pH to 4—5 with rapid shaking. After the solution was allowed to stand for several hours, the precipitate was formed. Then it was filtered, washed with aqueous ethanolic solution, dried and recrystallized with ethanol or methanol.

RESULTS AND DISCUSSION

The condensation reactions of AF or DAF with various substituted thiosemicarbazides in the presence of hydrochloric acid are carried out as follows

$$\underset{\text{AF}}{FcCOCH_3} + \underset{\text{TSC}}{RC_6H_4NHCSNHNH_2} \rightarrow \rightarrow FcC(CH_3){=}NNHCSNHC_6H_4R \quad (I\text{—}VI)$$

where Fc = ferrocenyl, R = H (*I*); *p*-CH_3 (*II*); *p*-CH_3O (*III*); *p*-EtO (*IV*); *o*-CH_3 (*V*); *o*-CH_3O (*VI*).



DAF VII—X

where R = H (*VII*); *o*-CH_3 (*VIII*); *p*-CH_3O (*IX*); *o*-CH_3O (*X*).

Table 1. Characterization of the Studied Compounds

Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%			Yield/%	M.p./°C	Colour
			C	H	N			
I	$C_{19}H_{19}FeN_3S$	377.3	60.49	5.08	11.14	63.1	169—170	orange red
			60.84	5.14	11.39			
II	$C_{20}H_{21}FeN_3S$	391.3	61.39	5.41	10.74	49.4	159.8—160.5	dark-red
			61.37	5.44	10.80			
III	$C_{20}H_{21}FeN_3OS$	407.3	58.98	5.20	10.32	46.3	156.5—157	orange
			58.72	5.21	10.22			
IV	$C_{21}H_{23}FeN_3OS$	421.3	59.86	5.50	9.97	52.9	125.5—127	dark-red
			60.30	5.59	10.42			
V	$C_{20}H_{21}FeN_3S$	391.3	61.39	5.41	10.74	79.4	176—176.8	orange
			61.17	5.38	10.49			
VI	$C_{20}H_{21}FeN_3OS$	407.3	58.98	5.20	10.32	70.2	141—142	dark-red
			58.99	5.13	10.25			
VII	$C_{28}H_{28}FeN_6S_2$	568.5	59.15	4.96	14.78	90	174—174.5	dark-red
			59.45	5.07	14.55			
VIII	$C_{30}H_{32}FeN_6S_2$	556.6	60.40	5.41	14.09	91	178—178.5	dark-red
			60.20	5.32	13.82			
IX	$C_{30}H_{32}FeN_6O_2S_2$	628.6	57.32	5.13	13.37	91.5	175—175.5	golden
			57.55	5.22	12.97			
X	$C_{30}H_{32}FeN_6O_2S_2$	628.6	57.32	5.13	13.37	88.7	206 (decomp.)	orange red
			57.17	5.08	13.19			

All the products *I*—*X* are coloured, having sharp melting point or decomposing before melting, soluble in $CHCl_3$, CH_2Cl_2, DMSO, warm alcohols; insoluble in water, petroleum ether or ethyl ether. They are stable in the solid form as well as in the solution. Their physical properties, elemental analyses, and spectral data are given in Tables 1 and 2. The IR spectrum is characterized by strong

Table 2. IR and ^{1}H NMR Spectral Data of Compounds *I*—*X*

Compound	$\tilde{\nu}$/cm^{-1}	Chemical shifts δ
I	1595 w ν(C=N)	4.21 (s, C_5H_5), 4.45, 4.63 (t, XC_5H_4),
	1525 s ν(C=S)	7.26—7.77 (m, C_6H_5), 9.33 (br, XNH),
	3325 m, 3220 m ν(N—H)	2.24 (s, CH_3)
II	1588 w ν(C=N)	4.21 (s, C_5H_5), 4.46, 4.62 (t, XC_5H_4),
	1525 s ν(C=S)	7.15, 7.22, 7.51, 7.61 (m, C_6H_4), 9.25
	3325 m, 3220 m ν(N—H)	(br, XNH), 2.37, 2.24 (2 × s, 2 × CH_3)
III	1609 w ν(C=N)	4.22 (s, C_5H_5), 4.45, 4.63 (t, XC_5H_4),
	1518 s ν(C=S)	6.89, 6.99, 7.50, 7.60 (m, C_6H_4), 9.17
	3346 m, 3177 m ν(N—H)	(br, XNH), 2.25 (s, CH_3), 3.83 (s, OCH_3)
IV	1616 w ν(C=N)	4.21 (s, C_5H_5), 4.42, 4.62 (t, XC_5H_4),
	1525 s ν(C=S)	7.18—7.29 (m, C_6H_4), 10.11 (br, XNH),
	3339 m, 3177 m ν(N—H)	2.22 (s, CH_3), 3.39 (s, OCH_3)
V	1588 m ν(C=N)	4.19 (s, C_5H_5), 4.42, 4.62 (t, XC_5H_4),
	1546 s ν(C=S)	7.18—7.29 (m, C_6H_4), 9.17 (br, XNH),
	3360 m, 3297 m ν(N—H)	2.37, 2.24 (2 × s, 2 × CH_3)
VI	1602 m ν(C=N)	4.19 (s, C_5H_5), 4.43, 4.67 (t, XC_5H_4),
	1546 s ν(C=S)	7.00—7.09 (m, C_6H_4), 10.11 (br, XNH),
	3360 m, 3255 m ν(N—H)	2.22 (s, CH_3), 3.96 (s, OCH_3)
VII	1595 m ν(C=N)	4.44, 4.67 (t, XC_5H_4), 9.28 (br, XNH),
	1532 s ν(C=S)	7.28—7.75 (m, C_6H_5), 2.20 (s, CH_3)
	3135 m, 3296 m ν(N—H)	
VIII	1581 m ν(C=N)	4.43, 4.64 (t, XC_5H_4), 9.32 (br, XNH),
	1532 s ν(C=S)	7.23—7.78 (m, C_6H_4), 2.20, 2.35 (2 × s,
	3247 m, 3289 m ν(N—H)	2 × CH_3)
IX	1605 w ν(C=N)	4.41, 4.62 (t, XC_5H_4), 9.07 (br, XNH),
	1516 s ν(C=S)	6.84, 6.95, 7.43, 7.54 (m, C_6H_4),
	3360 m, 3248 m ν(N—H)	2.16 (s, CH_3), 3.79 (s, OCH_3)
X	1592 m ν(C=N)	4.44, 4.66 (t, XC_5H_4),
	1539 s ν(C=S)	6.93—7.11 (m, C_6H_4), 10.11 (br, XNH),
	3360 m, 3248 m ν(N—H)	2.15 (s, CH_3), 3.93 (s, OCH_3)

bands of ν(C=N) vibrations between $\tilde{\nu}$ = 1588—1616 cm^{-1}, ν(C=S) bands between 1516—1546 cm^{-1}, and ν(N—H) bands between 3120—3360 cm^{-1}. We have observed that the different substituted group (alkyl or alkoxyl) in benzene ring of the title compounds has little effect on the $\tilde{\nu}$(ν(C=S)) value. Only the groups in *ortho* position exhibit more changes, such as in *V*, *VI*, *X*, they are at 1546 cm^{-1}, 1546 cm^{-1}, and 1539 cm^{-1} compared with 1525 cm^{-1} at other compounds. The ^{1}H NMR spectrum is also in agreement with the proposed structures.

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