

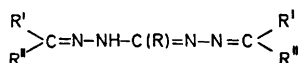
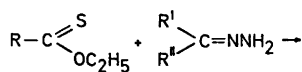
## Preparation and Characterisation of $N^2,N^4$ -Dialkylidene Hydrazidines

PALLE JAKOBSEN

Medicinsk-Kemisk Institut, University of Copenhagen, Rådmandsgade 71, DK-2200 Copenhagen, Denmark

The reactions between hydrazones and aliphatic thioacid-*O*-esters have been investigated. Substituted benzophenone hydrazones form  $N^2,N^4$ -dialkylidene hydrazidines with high yields, while the main product from the reactions with aliphatic hydrazones are the corresponding azines.  $^1\text{H}$  NMR, IR, MS, and in two cases  $^{13}\text{C}$  NMR spectra have been recorded.

In the literature <sup>1-5</sup> it has been established that *N*-substituted thiohydrazides are stable, while the aliphatic *N*-unsubstituted thiohydrazides are unstable, but the aromatic ones stable.<sup>2,3</sup> Attempts to prepare the benzylidene derivative of a thiohydrazide by reaction of dithioesters with benzalhydrazone has been reported as unsuccessful.<sup>2</sup> Mayer and Orgis<sup>6</sup> demonstrated the efficiency of *O*-ethyl thioformate in the preparation of thioformamide and later Walter<sup>4</sup> showed that *O*-ethyl thioformate could be used in the preparation of *N*-substituted thioformhydrazides. The purpose of this investigation was to try to prepare the alkylidene derivatives of thioformhydrazides by the reaction of *O*-ethyl thioformate with hydrazones. It turned out, however, that equimolar amounts of hydrazone and *O*-ethyl thioformate gave  $N^2,N^4$ -dialkylidene formohydrazide hydrazones (I) as the main product under conditions suitable for thioformylation of hydrazines.



I (a-g)

Several hydrazidines have been reported as unstable intermediates in formazane formation<sup>7-11</sup> but no dialkylidene derivatives have been reported in the literature. Therefore, a closer investigation of the chemical and physical properties of I was carried out.

*O*-Ethyl thioformate and an *N*-unsubstituted benzophenone hydrazone in benzene or ethanol solution react at room temperature under instantaneous evolution of hydrogen sulfide. Reasonable yields of the hydrazidine derivatives (I) can be isolated after stirring for few hours (Table 1).

Mixtures of products are obtained if the reactions are carried out under cooling. It is clear from the IR and  $^1\text{H}$  NMR spectra of these mixtures that one of the components is the expected hydrazidine derivative. One of the other components has spectroscopical properties that might fit a thioformylated hydrazone. Attempts to isolate the components by preparative layer chromatography gave no thioformylated hydrazone.

The reaction was carried out with hydrazones of aliphatic, aromatic, and mixed aliphatic-aromatic ketones. With aliphatic hydrazones the corresponding azine was the main product and no hydrazidine was isolated. This is in accordance with the wellknown instability of aliphatic hydrazones and with results of other reactions with hydrazones.<sup>12,13</sup>

Mixtures of the corresponding azine and the hydrazidine (I) were formed when acetophenone hydrazone or dibenzylketone hydrazone were reacted with *O*-ethyl thioformate. In the latter case the two compounds were separated by PLC.



cm<sup>-1</sup>. (the aromatic protons and the hydrogen attached to CN double bond). In the region 1638–1580 cm<sup>-1</sup> two to three strong and broad absorption-bands were found which possibly arise from C=N-stretching and the aromatic skeletal vibrations. This region seems to be in accordance with that quoted in Bellamy.<sup>16</sup> Some other characteristic absorptions are given in the experimental part.

The mass spectra all gave a molecular ion corresponding to the actual molecular weight (variable intensity 0.2–26 % of base peak). The fragmentation pattern is in accordance with structure I.

## EXPERIMENTAL

Microanalyses were carried out in the micro-analysis department of Chemical Laboratory II, the H. C. Ørsted Institute. <sup>1</sup>H NMR spectra were obtained on a Varian A-60 or a JEOL JNM-MH 60/II instrument with TMS as internal reference. IR spectra were recorded on a Perkin-Elmer model 225 grating spectrograph. Mass spectra were taken on a Finnigan 1015 S/L or an AEI-902 instrument operating at 70 eV. <sup>13</sup>C NMR spectra were recorded on a Bruker WH 90 instrument. Melting points were taken on a Büchi melting point apparatus and are uncorrected.

*O*-Ethyl thioformate was prepared according to the literature.<sup>14</sup>

*O*-Ethyl thioacetate. This compound was prepared from ethyl acetoimidate hydrochloride and hydrogen sulfide according to the literature.<sup>17</sup> The acetoimidate hydrochloride was prepared following the method described in *Organic Syntheses*<sup>18</sup> with small modifications. Thus after the calculated amount of HCl-gas had been added to the solution the resulting oily mass was evaporated to dryness on a rotavapor and further dried *in vacuo* for 1 h. The resulting crystalline mass was used without further purification.

2-Chlorobenzophenone hydrazone was prepared from 2-chlorobenzophenone (0.03 mol 8.65 g) and excess hydrazine (8.7 g 95 %) in 25 ml abs. ethanol. The mixture was refluxed for 8 h, stirred overnight at room temperature, cooled and filtered. The precipitate was recrystallized from ethanol. Yield 74 %, m.p. 126 °C. (Found: 67.60; H 4.49; N 12.18. Calc. for C<sub>13</sub>H<sub>11</sub>N<sub>2</sub>Cl: C 67.68; H 4.81; N 12.14).

The other hydrazones were prepared in a similar way, their physical constants were found in accordance with literature values.<sup>19–23</sup>

N<sup>2</sup>,N<sup>4</sup>-Bis(diphenylmethylene)-formohydrazone (Ia). Benzophenone hydrazone (19.6 g, 0.1 mol) was dissolved in 70 ml ethanol (abs.). *O*-Ethyl thioformate (9.0 g, 0.1 mol)

was added dropwise over a period of 10 min at room temperature. The mixture was stirred until the evolution of hydrogen sulfide ceased. The precipitate was filtered off and the mother-liquor concentrated to give additional crystals. The compound was recrystallized from abs. ethanol.

(Ia) is insoluble in water, pentane, ether and soluble in benzene and chloroform.

IR(KBr, in cm<sup>-1</sup>): 3310m, 1610s, 1583s, 1554m, 1491m, 1488m, 1443s, 1392m, 1118m.

<sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 7.25–7.67 (20 H, m); 7.80 (1 H, d); 9.40 (1 H, d); J<sub>CH-NH</sub> = 9.5 Hz.

<sup>13</sup>C NMR: δ 162.3, 150.0, 138.1, 137.1, 135.6, 132.5, 129.8, 129.7, 129.4, 129.1, 128.7, 128.3, 127.9, 127.1.

MS *m/e*, (% of base peak): 402(38)M<sup>+</sup>, 401(29), 325(15), 22(3) 207(5), 195(35), 180(100), 165(31), 104(17), and 77(67).

N<sup>2</sup>,N<sup>4</sup>-Bis-(4,4'-dimethyldiphenylmethylene)-formohydrazone hydrazone (Ib) was prepared from equimolar amounts (0.1 mol) of 4,4'-dimethylbenzophenone hydrazone and *O*-ethyl thioformate in 70 ml ethanol as described for Ia. The mixture was stirred overnight and subsequently evaporated to dryness. The residual crystals were recrystallized from abs. ethanol.

IR(KBr, in cm<sup>-1</sup>): 3300w, 1610sh, 1599s, 1582s, 1508m, 1240m, 1122w, 1110w.

<sup>1</sup>H NMR(CDCl<sub>3</sub>): δ 6.9–7.6 (16 H, m); 2.36 (s) 2.50 (s) 3 H, intensity 3/1; 7.76 (1 H, d); 9.40 (1 H, d); J<sub>CH-NH</sub> = 9.5 Hz.

<sup>13</sup>C NMR: δ 149.6, 139.5, 139.0, 138.8, 138.1, 135.7, 132.8, 130.3, 129.6, 128.9, 128.6, 127.1, 21.3.

MS *m/e* (% of base peak): 458(20)M<sup>+</sup>, 457(21), 367(4), 223(30), 208(77), 194(20), 179(32), 178(29), 165(13), 118(26), 91(100).

N<sup>2</sup>,N<sup>4</sup>-Di(2-chlorophenylphenylmethylene)-formohydrazone hydrazone (Ic). Prepared from 2-chlorobenzophenone hydrazone and *O*-ethyl thioformate as described for Ib.

IR(KBr, in cm<sup>-1</sup>): 3320w, 1610s, 1585s, 1565m, 1442m, 1392m, 1124m, 1060w.

<sup>1</sup>H NMR(CDCl<sub>3</sub>): δ 7.6–7.67(18 H, m); 7.80 (1 H, d); 9.21 (1 H, d) J<sub>CH-NH</sub> = 9.5 Hz.

MS *m/e* (% of base peak): 472(0.2), 471(0.2), 470(0.2), 435(2.5), 229(5), 214(18), 195(52), 180(4), 165(38), 138(7), 111(16), 104(13), 77(100).

N<sup>2</sup>,N<sup>4</sup>-Di(4-chlorophenylphenylmethylene)-formohydrazone hydrazone (Id). Prepared from 4-chlorobenzophenone hydrazone and *O*-ethyl thioformate as described for Ib.

IR(KBr, in cm<sup>-1</sup>): 3305m, 1600s, 1580s, 1552m, 1484s, 1445m, 1395m, 1118m, 1085m, 998m.

<sup>1</sup>H NMR(CDCl<sub>3</sub>): δ 7.17–7.67 (18 H, m); 7.78 (1 H, d); 9.47 (1 H, d).

MS *m/e* (% of base peak): 472(10), 471(26), 470(26), 469(40), 408(17), 393(10), 359(10), 258(10), 231(21), 230(28), 229(54), 216(44), 215(19), 214(100), 199(10), 195(7), 180(25), 165(39), 119(21), 111(23), 105(17), 104(19), 91(21), 77(86).

$N^2,N^4$ -Bis(dibenzylmethylene)-formohydrazide hydrazone (Ie). The procedure described for Ib yielded a crystalline mass which was a mixture of (Ie) and dibenzylketone azine. The two compounds were separated on silica gel plates using  $CHCl_3$  as eluent. The azine was identified by m.p. and IR, superimposable with IR of an authentic sample.

IR(KBr, in  $cm^{-1}$ ): 3382m 1638s, 1620s, 1599m, 1491s, 1451s, 1425m, 1340m, 1218m, 1091m, 1072m.

$^1H$  NMR ( $CDCl_3$ ):  $\delta$  the  $CH_2$  protons occurred as 4 singlets of equal intensity at 3.35, 3.41, 3.59 and 3.83; 6.9–7.4 (20H,m); 7.62 (1H,d); 9.05 (1H,d);  $J_{CH-NH}$  = 9.0 Hz.

MS *m/e* (% of base peak): 458(0.7) $M^+$  416(6), 326(3), 325(8), 235(2), 206(6), 130(10), 117(11), 116(10), 115(7), 103(5), 92(31), 91(100), 77(8).

$N^2,N^4$ -Bis(diphenylmethylene)-acetohydrazide hydrazone (If). Benzophenone hydrazone (7.45 g, 0.038 mol) was dispersed in 30 ml of abs. ethanol. *O*-Ethyl thioacetate (2 g, 0.019 mol) in 1 ml abs. ethanol was added dropwise at room temperature. The mixture was refluxed for 6 h. Standing for three days at room temperature and an additional few hours in the freezer caused precipitation of If, which was recrystallized from ethanol. The residue which could be isolated from the mother liquor was a mixture of unreacted hydrazone and If according to the NMR spectrum.

IR(KBr, in  $cm^{-1}$ ): 3295w, 1599s, 1591s, 1572s, 1548s, 1440m, 1410m, 1125m, 1038m, 1028m, 1022m.

$^1H$  NMR ( $CDCl_3$ ):  $\delta$  2.33(3 H, s); 7.0–7.67 (20 H, m); 9.88(1 H, s).

MS *m/e* (% of base peak): 416(4) $M^+$ , 339(3), 211(1), 196(4), 195(4), 180(87), 165(27), 152(5), 104(16), 78(14), 77(100).

$N^2,N^4$ -Di-(methylphenylmethylene)-acetohydrazide hydrazone (Ig). Acetophenone hydrazone (6.7 g, 0.05 mol) was dissolved in 20 ml abs. ethanol. *O*-Ethyl thioacetate (5.2 g, 0.05 mol) was added dropwise over a period of 5 min. After standing overnight at room temperature with stirring, crystals were formed. These were filtered off and identified as acetophenone azine by m.p. and IR spectrum.

The mother liquor was evaporated to dryness and from the formed crystalline mixture Ig was isolated by separation on silica gel plates with  $CHCl_3$  as eluent.

IR(KBr, in  $cm^{-1}$ ): 3332w, 1608m, 1578m, 1558m, 1492m, 1418m, 1282m, 1142m, 1045m, 1040m.

$^1H$  NMR( $CDCl_3$ ):  $\delta$  2.23, 2.33, 2.40, 2.47, 2.52 (9 H, singlets) 7.17–7.57 and 7.63–7.87 (10 H, m); 9.50–9.84 (1 H, s).

MS *m/e* (% of base peak): 292(15) $M^+$ , 277(40), 236(33), 221(44), 215(8), 180(6), 176(8), 159(13), 134(13), 133(15), 199(19), 118(100), 104(17), 103(17), 92(6), 91(8), 77(75).

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