MESOMERICALLY STABILIZED THIOALDEHYDES. 3-THIOFORMYLINDOLE AND ITS ALKYL AND PHENYL DERIVATIVES

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3-Thioformylindole and its previously unknown 2-methyl-, 2-phenyl-, and 1-ethyl substituted derivatives have been synthesized by the thiolysis of the corresponding indolylmethylenimmonium perchlorates. The thioaldehydes containing no substituent at the nitrogen atom were isolated as crystalline solvates with DMSO and DMF. Monitoring of 3-thioformylindole formation was effected by polarography and spectrophotometry.

In the first example of a stable thioaldehyde, viz. 5-thioformyldipyrrylmethane, it was established that the extremely unstable thioformyl group may be stabilized by conjugation with a heterocyclic system [1]. This enabled a series of stable heterocyclic thioaldehydes to be synthesized subsequently [2-5]. The chemistry of thioaldehydes is currently attracting much attention among investigators [6-8].

It was shown previously in [9] that under the conditions of making thioformyl substituted indolizines [2] and pyrrolo[2,1-b]thiazoles [3] by the reaction of the appropriate methinimmonium salts with an aqueous solution of sodium hydrosulfide, N-[(3-indolyl)methylene]-N,N-dimethylimmonium perchlorate (Ia) is hydrolyzed to 3-formylindole. 3-Thio-formylindole (IIa) was synthesized by the action of anhydrous sodium hydrosulfide or hydrogen sulfide on salt (Ia) in DMSO and DMF.

Before our investigations 3-thioformyl-1,2-dimethylindole (IIb) was the only known thioformyl derivative of indole [10]. Compound (IIb) was the only known thioformyl derivative of indole [10]. Compound (IIb) is an orange powder and is capable of storage in monomeric form over a long period. The unsubstituted thioaldehyde (IIa) synthesized by us was isolated as weakly colored solvated crystals $3(IIa) \ L$ (IIIa, $L = Me_2NCHO$; IIIb, $L = Me_2SO$). It exists as the monomeric form only in solution. This indicates that in the case of compound (IIb) the electron donating substituents at position 1 and 2 of the indole ring stabilize the thioaldehyde function.

We have synthesized 2-methyl-, (IIc), 2-phenyl- (IId), and 1-ethyl- (IIe) 3-thioformylindoles to obtain additional information on the effect of substituents on the stability of 3-thioformyl-substituted indoles. The most convenient method of obtaining them, as in the case of 3-thioformylindole (IIa), proved to be thiolysis of the corresponding methinimmonium salts (Ic, d, e). The reaction was effected in a dipolar aprotic solvent (DMF, DMSO), usually at 20°C. The yields of solvated crystals of thioaldehydes (IIc, d) and of free thioaldehyde (IIe) exceeded 90%. The known thioformylindole (IIb) was obtained by the same route.

Compounds (IIc) and (IId) containing no substituent on the nitrogen atom were isolated like (IIa) as complexes of type (III) with DMF or DMSO. They readily dissociated in solution with the formation of the monomeric form of the corresponding thioaldehyde as indicated by the intense red coloration of the solution and by ¹H NMR spectral data. The thioaldehydes (IIb) and (IIe) having no alkyl group at the nitrogen atom did not form complexes (III) with the solvents investigated. 1-Ethyl-3-thioformylindole (IIe) was isolated either as the monomer or mixed with the trimer depending on the reaction temperature.

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Compound	Electronic spectrum, $\lambda(\varepsilon)$	Polarographic reduction in DMF, $E_{1/2}$ (i/c)
la	264 (4,01)	-1,520 (3,38)
	275 (4,02)	-2,530 (3,50)
	281 (3,75)	
	342 (4,25)	
lla	275 (4,02)	-0,925 (3,40)
	283 (3,97)	-1,700 (5,00)
	374 (4,40)	-2,480 (8,17)
	512 (1,56)	
IIIa	275 (3,95)	-1,650 (2,09)
	277,8 (3,90)	-2,530 (2,12)
	375 (4,34)	

 TABLE 1. Polarographic Characteristics and Electronic Spectral Data of Compounds

 (Ia)-(IIIa)

The conversion of N-[(3-indolyl)methylene]-N,N-dimethylimmonium perchlorate (Ia) into 3-thioformylindole (IIa) was followed by polarography and spectrophotometry. The characteristics given in Table 1 indicate that the solvated crystals of (IIIa) (3IIa·Me₂NCHO) isolated from the reaction have parameters different from the free (IIa) formed during the reaction. In the case of the former the band for the $n \rightarrow \pi^*$ transition was absent, the size of log ε for the $\pi \rightarrow \pi^*$ band was significantly less, the potential of the first reduction wave was displaced towards the cathode by 0.7 V, and the sizes of the i/c values were less. These data confirm the formation of stable associate with the solvent.



The structures of the compounds synthesized were confirmed by the results of elemental analysis and NMR data. The ¹H NMR spectra of thioformylindoles (Ia-e) contain a signal for the thioaldehyde proton at 11.29-11.41 ppm. In the ¹³C NMR spectrum of 3-thioformylindole (IIa) the thioaldehyde carbon resonates at 185.17 ppm which is in good agreement with the literature data for 2-amino-3-thioformylindoles [4].

Reaction of thioformylindoles (IIa, b) with 2,4-dinitrophenylhydrazine in DMF gave the corresponding hydrazones.

EXPERIMENTAL

The ¹H NMR spectra were recorded on a JEOL FX 90Q spectrometer, internal standard being HMDS. The ¹³C NMR spectrum was recorded on a Bruker WP 200SY spectrometer. The IR spectra were taken on a UR 75 instrument in KBr disks. The electronic spectra were obtained on a UV-vis spectrophotometer. The electrochemical investigations were carried out on an LP 7 polarograph with a dropping mercury electrode. A check on the course of reactions and the purity of the compounds obtained was effected by TLC on Silufol UV 254 plates in the system chloroform – ethyl acetate, 3:1, visualization was with UV light.

The initial indolylmethylenimmonium perchlorates (Ia-e) were obtained by the Wilsmeier-Haack method [11].

N-[(3-Indolyl)methylene-N,N-dimethylimmonium Perchlorate (Ia). Yield was 92%, mp 231-233°C. Found, %: C 48.91, H 4.77, Cl 12.64, N 10.25. $C_{11}H_{13}CIN_2O_4$. Calculated, %: C 48.44, H 4.77, Cl 13.03, N 10.28.

N-{[3-(1,2-Dimethyl)indolyl]methylene}-N,N-dimethylimmonium Perchlorate (Ib). Yield was 94%, mp 178-179°C (from acetonitrile). Found, %: C 51.47, H 5.61, Cl 12.02, N 9.71. $C_{13}H_{17}CIN_2O_4$. Calculated, %: C 51.91, H 5.66, Cl 11.81, N 9.32.

N-{[3-(2-Methyl)indolyl]methylene}-N,N-dimethylimmonium Perchlorate (Ic). Yield was 87%, mp 182-183°C (from acetonitrile). Found, %: C 50.71, H 5.26, Cl 12.10, N 9.73. $C_{12}H_{15}CIN_2O_4$. Calculated, %: C 50.26, H 5.24, Cl 12.39, N 9.77.

 $N-\{[3-(2-Phenyl)indolyl]methylene)-N, N-dimethylimmonium Perchlorate (Id). Yield was 84\%, mp 245-247°C (from acetonitrile). Found, %: C 58.51, H 5.15, Cl 10.39, N 8.02, C₁₇H₁₇ClN₂O₄. Calculated, %: C 58.54, H 4.88, Cl 10.19, N 8.03.$

 $N-\{[3-(1-Ethyl)indolyl]methylene\}-N, N-dimethylimmonium Perchlorate (Ie). Yield was 93\%, mp 278-280°C (from acetonitrile). Found, \%: C 51.20, H 5.68, Cl 11.70, N 9.36. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl 11.81, N 9.32. C_{13}H_{17}ClN_2O_4. Calculated, \%: 51.91, H 5.66, Cl$

Bands were present in the IR spectra of salts (Ia-e) at 3120, 1500, 1400, 1250, 750-785 (indole ring); 1630-1660 (C=N⁺); 1080-1100 (stretching vibrations of CIO in the perchlorate anion); 3250 cm⁻¹ [N-H, in (Ia, c, d)].

Solvated Crystals of 3-Thioformylindole (IIa) with DMF (IIIa) and with DMSO (IIIb). A current of dry hydrogen sulfide was passed for 30 min into a solution of salt (Ia) (2.1 g: 0.0077 mole) in DMF (12 ml) at 20°C. The dark red reaction mixture was poured into ice water, the precipitated bright cream solid was filtered off, washed thoroughly with water, and dried in vacuum over P_2O_4 . Solvated crystals (IIIa) (1.42 g: 98%) were obtained, mp 108-110°C (with decomposition). PMR spectrum (DMSO-D₆): 7.37-7.59 (3H, m, 5-, 6-, and 7-H), 8.40 (1H, s, 2-H), 8.75 (1H, m, 4-H), 11.36 (1H, s, CH=S), 12.62 ppm (1H, br s, NH). Found, %: C 64.26, H 5.22, N 10.46, S 17.13. (C₉H₇NS)₃:C₃H₇NO. Calculated, %: C 64.75, H 5.04, N 10.07, S 17.27.

Solvated crystals of (IIIb) were obtained similarly in DMSO solution in 98% yield, mp 114-116°C (with decomposition). PMR spectrum (DMF-D₇): 7.44-7.64 (m, 5-, 6-, and 7-H), 8.44 (1H, s, 2-H), 8.80 (1H, m, 4-H), 1141 (1H, s, CH=S), 12.64 ppm (1H, br. s, NH). Found, %: C 62.03, H 4.95, N 8.30, S 22.45. $(C_9H_7NS)_3 \cdot C_2H_6OS$. Calculated, %: C 62.03, H 4.81, N 7.49, S 22.82.

The solvated crystals (IIIa,b) formed red hydrazones with 2,4-dinitrophenylhydrazine in DMF and had mp 310°C (from methanol). Found, %: C 55.19, H 3.75, N 21.86. C₁₅H₁₁N₅O₄. Calculated, %: C 55.38, H 3.38, N 21.54.

Solvated crystals of 2-methyl-3-thioformylindole (IIc) with DMF (IIIc) were obtained by the procedure given above for (IIIa) from salt (Ic) in DMF solution. Yield was 95%, mp 109-110°C (with decomposition). PMR spectrum (DMSO-D₆): 2.76 (3H, s, 2-Me), 7.30-7.47 (3H, m, 5-, 6-, and 7-H), 8.78 (1H, m, 4-H), 11.29 (1H, s, CH=S), 12.53 ppm (1H, br s, NH). Found, %: C 66.26, H 6.29, N 8.87, S 16.45. (C₁₀H₉NS)₃·C₃H₇NO. Calculated, %: C 66.22, H 5.69, N 9.36, S 16.05.

The dark red hydrazone was obtained with 2,4-dinitrophenylhydrazine in DMF and had mp 355°C (from methanol). Found, %: 56.37, H 3.64, N 20.28. $C_{16}H_{13}N_5O_4$. Calculated, %: C 56.64, H 3.83, N 20.65.

Solvated crystals of 2-phenyl-3-thioformylindole (IId) with DMF (IIId) were obtained analogously to solvate (IIIa) from salt (Id) in DMF solution. Yield was 93%, mp 142-145°C. PMR spectrum (DMF-D₇): 7.36-7.78 (8H, m, 5H_{Ph}, 5-, 6-, and 7-H), 8.94 (1H, m, 4-H), 11.29 ppm (1H, s, CH=S). Found, %: 73.17, H 5.42, N 7.27, S 12.80. ($C_{15}H_{11}NS$)₃· $C_{3}H_{7}NO$. Calculated, %: C 73.47, H 5.10, N 7.14, S 12.25.

1-Ethyl-3-thioformylindole (IIe) was obtained similarly to the solvate (IIIa) from salt (Ie) in DMF solution but at -20° C. Yield was 96%, mp 122-125°C (with decomposition). PMR spectrum (DMSO-D₆): 1.50 (3H, t, NCH₂CH₃), 4.36 (2H, q, N<u>CH₂CH₃), 7.33-7.67 (3H, m, 5-, 6-, and 7-H), 8.42 (1H, s, 2-H), 8.74 (1H, m, 4-H), 11.27 ppm (1H, CH=S).</u> Found, %: C 69.29, H 5.85, N 7.64, S 16.77. C₁₁H₁₁NS. Calculated, %: C 69.84, H 5.82, N 7.41, S 16.93.

The trimer $(IIe)_3$ was obtained at 20°C from salt (I) in DMF [see synthesis of (IIIa)] and was isolated as a bright yellow powder, poorly soluble in DMF and DMSO. The signal for the thioformyl proton was absent from its PMR spectrum (CDCl₃) and the signals for the other protons were broadended. The data of elemental analysis for the trimer and for compounds (IIe) coincide.

1,2-Dimethyl-3-thioformylindole (IIb) was synthesized analogously to (IIIa) from salt (Ib). Yield was 97%, mp 157-159°C (with decomposition). Literature gives decomposition temperature > 160°C [10]. PMR spectrum (DMSO-D₆): 2.81 (3H, s, 2-Me), 3.86 (3H, s, N-Me), 7.46-7.67 (3H, m, 5-, 6-, and 7-H), 8.94 (1H, m, 4-H), 11.35 ppm (1H, s, CH=S); see [10].

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