SYNTHESIS AND TRANSFORMATIONS OF 1,3-DITHIOL-2-YLIDENEISOPROPYLIDENE MALONATES

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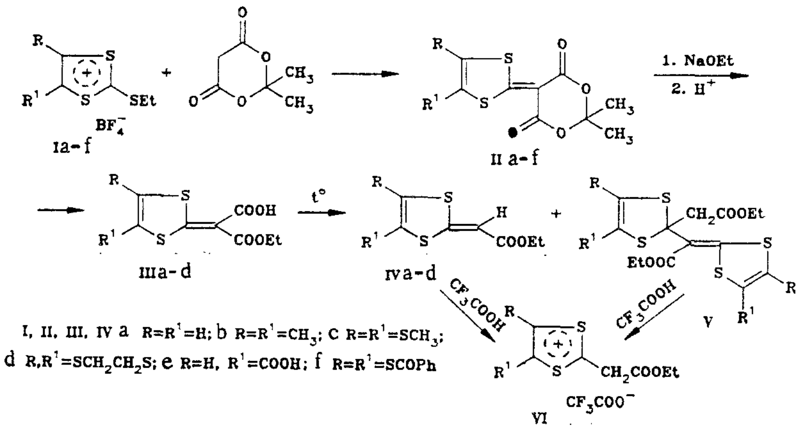
UDC 547.461.2'738.07

The reaction of 2-alkylthio-1,3-dithiolium salts with Meldrum's acid gave 1,3-dithiol-2-ylideneisopropylidene malonates, which were converted successively to monoethyl esters of 1,3-dithiol-2-ylidenemalonic acids and esters of 1,3-dithiol-2-ylideneacetic acid. 2-Methyl-1,3-dithiolium salts are formed when 1,3-dithiol-2-ylideneisopropylidene malonates are heated with acids.

Biologically active compounds (hepatoprotectors, fungicides) have been detected among 1,3-dithiol-2-ylidenemalonic acid esters [1]. Two methods are used for their synthesis: the reaction of 2-alkylthio-1,3-dithiolium salts with malonic esters in the presence of bases [1] and alkylation in DMSO of the product of the reaction of malonic ester and carbon disulfide in the presence of alkali with trihaloethanes [2] or dihaloethylenes [3]. 1,3-Dithiol-2-ylideneisopropylidene malonates II have not been described in the literature but are of special interest not only as potential biologically active compounds but also as promising starting compounds for obtaining various derivatives of 2-methylidene-1,3-dithiole and 2-methyl-1,3-dithiolium salts – intermediates for the synthesis of dyes [4].

Isopropylidene malonates IIa-f were obtained in high yields by the action of Meldrum's acid on 2-ethylthio-1,3-dithiolium tetrafluoroborates Ia-f in solution in acetonitrile in the presence of pyridine. The compounds have the intense absorption in their UV spectra at 370-420 nm that is characteristic for 1,3-dithiol-2-ylidene derivatives [5] (Table 1).



The sodium salts of 1,3-dithiol-2-ylidenemalonic acid monoethyl ester, which were converted to the corresponding acids IIIa-d (Table 2), were obtained by the action of sodium ethoxide on IIa-d (Table 2). Heating acids IIIa-d at temperatures above 140°C or refluxing in diglyme (30 min to 1 h) leads to the undescribed 1,3-dithiol-2-ylideneacetic acid esters IVa-d, which decompose readily (Table 3). Dimeric compound V was isolated as a side product in the decarboxylation of acid IIIb in dyglyme. The dimerization of 1,3-dithiole-2-methylidene was previously observed when benzodithiolemethylidene was distilled [6]. Judging from the PMR spectrum of a solution in trifluoroacetic acid, dimer V dissociates with the formation of salt VI.

Riga Polytechnical Institute, Riga 226355. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1621-1624, December, 1988. Original article submitted May 22, 1987; revision submitted December 25, 1987.

TABLE 1. Characteristics of 1,3-dithiol-2-ylideneisopropylidene Malonates IIa-f

Compound	Empirical formula	mp,* °C	IR spectrum cm^{-1}	UV spectrum, λ_{max}, nm (log ε) in ethanol	PMR spectrum, ppm	Yield, %
IIa	$C_9H_8O_4S_2$	235...237	1649	246 (4,25), 368 (4,46)	1,73 (s, 6H), 7,44 (s, 2H)	86
IIb	$C_{11}H_{12}O_4S_2$	208...210	1679	228 (4,29), 241 (3,98), 381 (4,49)	1,73 (s, 6H), 2,33 (s, 6H)	95
IIc	$C_{11}H_{12}O_4S_4$	187...189	1674	231 (4,11), 284 (3,87), 392 (4,19)	1,73 (s, 6H), 2,58 (s, 6H)	59
IId	$C_{11}H_{10}O_4S_4$	259...260	1648	226 (4,14), 298 (4,0), 420 (4,13)	1,71 (s, 6H), 3,4 (s, 4H)	67
IIe	$C_{10}H_8O_6S_2$	209...210	1696, 1658, 1592, 1562, 1517	230 (4,13), 298 (3,18), 367 (4,47)	1,71 (s, 6H), 8,56 (s, 1H), 10 (1H)	81
IIf	$C_{23}H_{16}O_6S_4$	190...192	1670	246 (4,55), 268 (4,37), 368 (4,47)	1,76 (s, 6H), 7,56 (m, 6H), 7,93 (m, 4H)	52

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*Compounds IIa-c, e were recrystallized from ethanol while IIf was recrystallized from acetonitrile; IId was reprecipitated from chloroform by means of hexane.

TABLE 2. Characteristics of 1,3-Dithiol-2-ylidenemalonic Acid Monoethyl Esters IIIa-d

Compound	Empirical formula	mp,* °C	IR spectrum, cm^{-1}		UV spectrum, λ_{max}, nm (log ε) in ethanol	PMR spectrum, ppm	Yield, %
			COOR	COOH			
IIIa	$C_8H_8O_4S_2$	165...166	1692	1624	224 (4,33), 363 (4,43)	1,41 (t 3H), 4,42 (q, 2H), 7,55 (s, 2H)	87
IIIb	$C_{10}H_{12}O_4S_2$	122...124	1711	1595	227 (4,30), 377 (4,40)	1,45 (t, 3H), 2,24 (s, 6H), 4,43 (q, 2H)	93
IIIc	$C_{10}H_{12}O_4S_4$	134...136	1692	1605	229 (4,08), 273 (3,79), 308 (3,60), 374 (4,13)	1,44 (t, 3H), 4,44 (q, 2H), 2,55 (s, 6H)	85
IIId	$C_{10}H_{10}O_4S_4$	162...163	1679	1590	231 (4,20), 288 (3,94), 402 (4,10)	1,44 (t, 3H), 3,35 (s, 4H), 4,45 (q, 2H)	75

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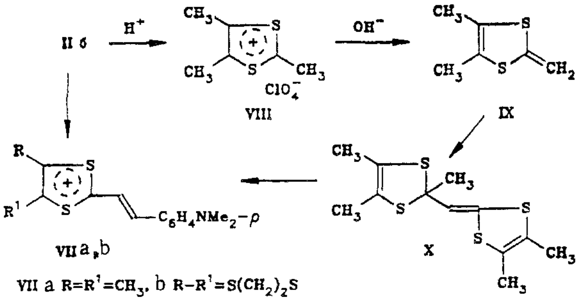
*Compounds IIIa-c were recrystallized from ethanol; IIId was reprecipitated from benzene—hexane.

TABLE 3. Characteristics of Ethyl 1,3-Dithiol-2-ylideneacetates IVa-d

Compound	Empirical formula	mp, °C (from hexane)	IR spectrum, cm^{-1}	PMR spectrum, ppm	Yield, %
IVa	$C_7H_8O_2S_2$	34...36	1547, 1655	1,23 (t, 3H); 4,14 (q, 2H); 6,06 (s, 1H); 6,50 (s, 1H); 6,64 (s, 1H)	68
IVb	$C_9H_{12}O_2S_2$	47..,48	1578, 1653	1,24 (t, 3H); 4,16 (q, 2H); 2,01 (s, 6H); 5,91 (s, 1H)	75
IVc	$C_9H_{12}O_2S_4$	48...49	1520, 1655	1,23 (t, 3H); 4,15 (q, 2H); 2,37 (s, 3H); 2,43 (s, 3H); 5,95 (s, 1H)	75
IVd	$C_9H_{10}O_2S_4$	92...93	1551, 1659	1,21 (t, 3H); 3,26 (s, 4H); 4,14 (q, 2H); 5,95 (s,1H)	61

We investigated the cleavage of isopropylidene malonates IIb, d by acids in order to develop a method for obtaining 2-methyl-1,3-dithiolium salts that is an alternative to the known cyclization of β-ketodithioacetic acid esters with acids [7]. 2-Methyl-1,3-dithiolium salts react with aromatic aldehydes to give strongly colored 2-arylvinylenedithiolium salts [7]. Hemicyanines VIIa, b, which were isolated in the form of violet (VIIa) and blue (VIIb) crystals, were obtained by heating IIb, d in acetonitrile with perchloric acid in the presence of p-dimethylaminobenzaldehyde.

An aqueous solution of trimethyl-1,3-dithiolium perchlorate (VIII), which was obtained by heating isopropylidene malonate IIb in perchloric acid, is deprotonated by sodium carbonate to give dimethyl-1,3-dithiole-2-methylidene (IX), which was isolated from the reaction mixture in the form of dimer X. The PMR spectra of IX and X in trifluoroacetic acid coincide and correspond to the spectrum of trimethyl-1,3-dithiolium trifluoroacetate. Dimer X reacts with p-dimethylaminobenzaldehyde in glacial acetic acid to give salt VIIa.



EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil were recorded with a Specord 75 IR spectrometer. The UV spectra were obtained with a Specord UV-vis spectrophotometer. The PMR spectra of solutions in $CDCl_3$ were recorded with a Perkin—Elmer R-12A spectrometer (80 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The results of elementary analysis for C, H, and S were in agreement with the calculated values.

2-Alkylthio-1,3-dithiolium salts were obtained by the method in [8].

1,3-Dithiol-2-ylideneisopropylidene Malonates IIa-f. A 0.01 mole sample of pyridine was added dropwise to a suspension of 0.01 mole of alkylthiodithiolium salt Ia-f and 0.01 mole of isopropylidene malonate in 30 ml of acetonitrile, and the mixture was heated on a water bath for 2 h. It was then cooled, and the precipitate was filtered, washed with acetonitrile, and recrystallized. The characteristics of IIa-f are presented in Table 1.

Monoethyl 1,3-dithiol-2-ylidenemalonates IIIa-d. A solution of 0.012 mole of sodium ethoxide in ethanol was added to a solution or suspension of 0.01 mole of IIa-d in 100 ml of refluxing ethanol, and the mixture was refluxed with stirring for 30 min. The precipitated sodium salt of IIIa-d was removed by filtration, washed with ether, and dried. The salt was dissolved in the minimum amount of water (in 75% ethanol in the preparation of IIId), and IIIa-d were precipitated with hydrochloric acid, washed with water, and recrystallized. The characteristics of IIIa-d are given in Table 2.

Ethyl 4,5-Dimethyl-1,3-dithiol-2-ylideneacetate (IVb) and 2-(2-Ethoxycarbonylmethyl-4,5-dimethyl-1,3-dithiol-2-yl)ethoxycarbonylmethyl-4,5-dimethyl-1,3-dithiole (V, $C_{18}H_{24}O_4S_4$). A 1-g sample of IIIb was refluxed in 10 ml of diglyme for 45 min, after which 100 ml of water was added, and the mixture was extracted with ether. The ether extract was washed with $NaHCO_3$ and water and dried, and the solvent was evaporated. The residue was refluxed with 10 ml of hexane. The 0.18 g (18%) of a yellowish substance that did not dissolve in hexane was identified as V and had mp 157-159°C. It was recrystallized from 100 ml of hexane to give a product with mp 163-165°C. IR spectrum: 1565 (C=C), 1668 (=C—COOEt), 1703 cm^{-1} (CH_2COOEt). PMR spectrum: 1.22 (t, 6H), 1.98 (s, 12H), 3.53 (s, 2H), 4.16 (q, 2H); (in CF_3COOH): 1.45 (t, 3H), 2.83 (s, 6H), 4.48 (q, 2H), 4.77 (s, 2H).

The hexane solution after separation of V was evaporated, the residue was dissolved in 3-5 ml of hexane, and the solution was cooled to −5°C and filtered. The yield of IVb was 0.65 g (75%); its characteristics are presented in Table 3.

Compounds IVa, c were similarly obtained and separated from the accompanying dimers. The formation of dimer IVd was not observed.

2-(p-Dimethylaminostyryl)-1,3-dithiolium Perchlorates VIIa ($C_{15}H_{18}ClNO_4S_2$) and VIIb ($C_{15}H_{16}ClNO_4S$). Perchloric acid (5 ml) and 5 mmoles of p-dimethylaminobenzaldehyde were added to a suspension of 5 mmoles of IIb, d in 30 ml of acetonitrile, and the mixture was refluxed for 30 min. It was then cooled, and VIIa, b were precipitated by means of ether and recrystallized. Compound VIIa was obtained in 60% yield and had mp 255-256°C (dec., from ethanol–ethyl acetate). UV spectrum (in CH_3CN): λ_{max} 295, 365, 620 nm; log ε 3.79, 3.08, 4.85. Compound VIIb was obtained in 68% yield and had mp 260°C (dec., from CH_3CN). UV spectrum (in CH_3CN): λ_{max} 310, 355, 455, 675 nm; log ε 3.75, 3.75, 3.58, 5.04.

2-(2,4,5-Trimethyl-1,3-dithiol-2-yl)methylidene-4,5-dimethyl-1,3-dithiole (X, $C_{12}H_{16}S_4$). A 0.5-g sample of IIb was dissolved by heating in 5 ml of perchloric acid, and the solution was refluxed for 10 min, cooled, and poured over a mixture of ice and water. The aqueous mixture was extracted with ether, and the ether layer was washed with water, dried, and evaporated. The residue was recrystallized from hexane (~5 ml) to give 0.15 g (58%) of colorless crystals with mp 91-92°C. PMR spectrum: 1.8 (s, 6H), 1.85 (s, 6H), 1.93 (s, 3H), 5.18 (s, 1H); (in CF_3COOH): 2.78 (s, 6H), 3.32 (s, 3H).

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PORPHYRAZINES AS MULTICENTER BASES

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UDC 547.979.733

A critical analysis is made of the existing work on the acid-base properties of porphyrazines.

In [1], the acid-base properties of porphyrazine (tetraazaporphine, H_2TAP) were studied. A series of assertions of the authors as well as an examination of the results of the investigation of the acid-base equilibria of H_2TAP, provoke a reply. It is known that if the special technique of photoexcitation [2] is not used, a spectrophotometric method [3] can serve to determine the equilibrium constant K_a (K_{BH^+}) or K_b of molecules in the ground state. On the other hand, the idea itself of singly protonated phthalocyanines, developed in the work of Berezin (see the literature in [4]), is a simplication of the acid-base behavior of phthalocyanines, assuming only one meso atom of nitrogen participates in the protonation, although there are four such atoms having unshared electron pairs in phthalocyanine molecules, MPc (Pc is the $C_{32}H_{16}N_8$ fragment). This simplification came about because they only studied the acid-base properties in concentrated H_2SO_4 [4] without first studying the behavior in mediums of lower acidity.

The spectrophotometric method is compared in [1] with the thermodynamic method, by which is understood the study of the equilibria of H_2Pc and MPc in concentrated H_2SO_4 under isothermal conditions [4]. The inadequacy of using this lies in the fact that the dissolu-

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Ivanovo Chemical Technological Institute, Ivanovo 153460. Ivanovo State University, Ivanovo 153377. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1625-1630, December, 1988. Original article submitted July 16, 1987; revision submitted April 1, 1988.

0009-3122/88/2412-1342$12.50