

ELECTROPHILIC SUBSTITUTION REACTIONS OF ESTERS OF
4,5-SUBSTITUTED 1,3-DITHIOL-2-YLIDENEACETIC AND
1,3-DITHIOL-2-YLIDENEMALONIC ACIDS

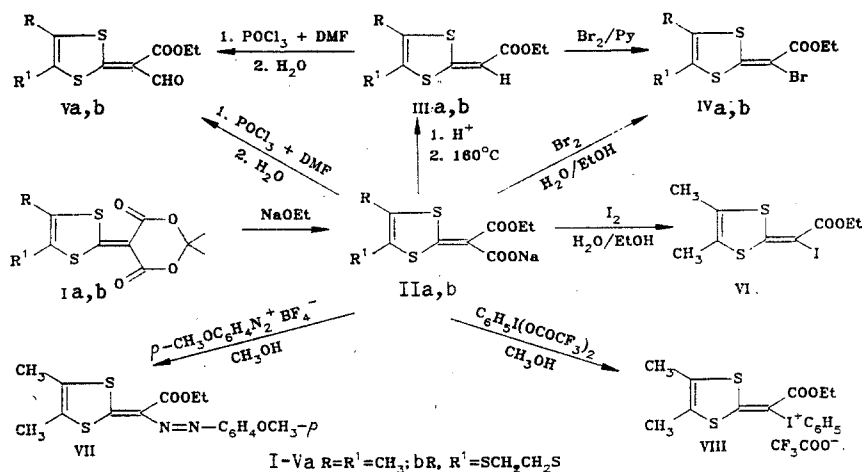
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UDC 547.461.3'738

The electrophilic substitution reactions (with halogens, POCl_3 + DMF, diazonium salts, iodoso compounds) of both esters of 4,5-substituted 1,3-dithiol-2-ylideneacetic acids and sodium salts of monoethyl esters of the corresponding malonic acids can be used for the synthesis of 2-methylene-1,3-dithiole derivatives.

It is known that 2-methylene-1,3-dithiole derivatives have biological activity [1] and are intermediates in the preparation of dyes [2]. We recently obtained isopropylidene 1,3-dithiol-2-ylidene malonates I, by cleavage of which with sodium ethoxide 1,3-dithiol-2-ylidenemalonic acid monoethyl ester sodium salts II were synthesized in high yields. Heating of the 1,3-dithiol-2-ylidenemalonic acid monoethyl esters at 150-160°C led to ethyl 1,3-dithiol-2-ylideneacetates III [3].

Several possibilities for the use of the previously obtained II and III as starting compounds for the synthesis of 2-methylene-1,3-dithiole derivatives have been demonstrated in the present research.

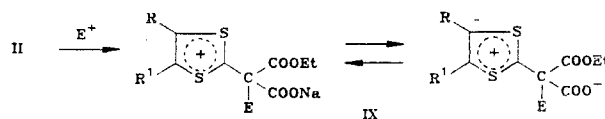


As we assumed, III readily undergoes electrophilic substitution reactions. Ethyl esters (IVa, b) of the corresponding 1,3-dithiol-2-ylidenebromoacetic acids are formed in the reaction of IIIa, b with bromine in the presence of pyridine. Compounds III undergo Vilsmeier formylation, and aldehydes are obtained after hydrolysis of the intermediately formed dimethylimmonium salts.

We have observed that malonic acid monoethyl ester sodium salts II can be used as the starting compounds with the same success for the synthesis of IV and V. Compounds II react with bromine and undergo Vilsmeier formylation at room temperature to give IV and V, respectively. Splitting out of carbon dioxide occurs at room temperature, in contrast to the decarboxylation of 1,3-dithiol-2-ylidenemalonic acid monoethyl esters, for which heating to 150-160°C is required. This can be explained by the formation of intermediate IX, which is inclined to undergo facile decarboxylation.

TABLE 1. Characteristics of 2-Methylene-1,3-dithiol Derivatives IV-VIII

Compound	Empirical formula	T _{mp} , °C	IR spectrum, cm ⁻¹	PMR spectrum (in CDCl ₃), δ, ppm
IVa	C ₉ H ₁₁ BrO ₂ S ₂	82...83	1642	1.3 (t, 3H); 2.04 (s, 6H); 4.24 (q, 2H)
IVb	C ₉ H ₉ BrO ₂ S ₂	89...90	1641	1.3 (t, 3H); 3.3 (s, 4H); 4.25 (q, 2H)
Va	C ₁₀ H ₁₂ O ₃ S ₂	89...91	1620, 1672, 2889, 2969	1.36 (t, 3H); 2.3 (s, 6H); 4.35 (q, 2H); 9.96 (s, 1H)
Vb	C ₁₀ H ₁₀ O ₃ S ₂	139...140	1618, 1672, 2854, 2914	1.27 (t, 3H); 3.28 (s, 4H); 4.27 (q, 2H); 9.9 (s, 1H)
VI	C ₉ H ₁₁ IO ₂ S ₂	120...121	1634	1.28 (t, 3H); 1.98 (s, 3H); 2.04 (s, 3H); 4.2 (q, 2H)
VII	C ₁₆ H ₁₈ N ₂ O ₃ S ₂	138...139	1602, 1656	1.41 (t, 3H); 2.18 (s, 3H); 2.24 (s, 3H); 3.89 (s, 3H); 4.45 (q, 2H); 6.94 (d.d, 2H); 7.81 (d.d, 2H)
VIII	C ₁₇ H ₁₆ F ₃ IO ₄ S ₂	110...113	1658	1.26 (t, 3H); 2.08 (s, 3H); 2.15 (s, 3H); 4.28 (q, 2H); 7.3...7.61 (m, 3H); 7.98 (d.d, 2H)



Compound IIa reacts with iodine to give 2-iodomethylene-1,3-dithiole derivative VI and undergoes diazo coupling with diazonium salts. A new type of phenyliodonium salt VIII (which is stable at temperatures near 0°C) is formed in the reaction of IIa with phenyliodoso-trifluoroacetate.

The structures of IV-VIII are confirmed by data from the IR and PMR spectra (see the experimental section).

EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil were recorded with a Specord 75 IR spectrometer. The PMR spectra of solutions of the compounds in CDCl₃ were obtained with a Perkin-Elmer R-12A spectrometer (80 MHz) with hexamethyldisiloxane (HMDS) as the internal standard (Table 1).

The results of elementary analysis of all of the compounds obtained were correct.

The monoethyl esters of 4,5-dimethyl- and 4,5-ethylenedithio-1,3-dithiol-2-ylidene-malonic acid and ethyl esters (IIIa,b) of 4,5-dimethyl- and 4,5-ethylenedithio-1,3-dithiol-2-ylideneacetic acid were synthesized in accordance with [3]. Sodium salts IIa,b were obtained from stoichiometric amounts of the corresponding acids and sodium ethoxide in ethanol.

Ethyl 4,5-Dimethyl-1,3-dithiol-2-ylidenebromoacetate (IVa). A 0.4-ml sample of pyridine and (dropwise) 0.25 ml (5 mmole) of bromine were added to a solution of 1 g (5 mmole) of IIIa in 10 ml of acetonitrile, and the mixture was allowed to stand at room temperature for 1 h. The solvent was then evaporated, the residue was extracted with ether, and the extract was washed with water, dried, and evaporated. The residue was recrystallized from hexane to give 1.1 g (85%) of colorless crystals that darkened in light.

Ethyl 4,5-Ethylenedithio-1,3-dithiol-2-ylidenebromoacetate (IVb). This compound was similarly obtained in 74% yield.

Ethyl 4,5-Ethylenedithio-1,3-dithiol-2-ylideneformyl-acetate (Vb). A 0.25-ml (5 mmole) sample of POCl₃ was added dropwise with stirring to a solution of 0.8 ml of DMF in 5 ml of absolute methylene chloride, after which 0.5 g (1 mmole) of IIb was added in the course of 10 min. The mixture was then allowed to stand at room temperature for 2 h, after which it was refluxed for 30 min and cooled. Approximately 10 g of silica gel, 0.5 ml of water, and 100 ml of benzene were added and the mixture was stirred and allowed to stand for ~20 h at room temperature. The mixture was filtered, and the silica gel on the filter was washed with benzene. The filtrate was evaporated, and the precipitate was washed with hexane and reprecipitated from benzene by means of hexane. The yield was 0.53 g (96%).

Ethyl 4,5-Dimethyl-1,3-dithiol-2-ylideneformylacetate (Va). This compound was similarly obtained from 0.6 g of IIa, 2.3 ml of DMF, and 0.45 ml of POCl₃ in 10 ml of methylene chloride. The yield was 0.4 g (76%).

Ethyl 4,5-Dimethyl-1,3-dithiol-2-ylideneiodoacetate (VI). A solution of 0.7 g (3 mmole) of iodine in 10 ml of ethanol was added dropwise with stirring to a solution of 0.8 g (3 mmole) of IIa in 50 ml of water. The reaction mixture became turbid, and a colorless precipitate formed. The precipitate was removed by filtration, air dried in the dark, and recrystallized from hexane. The yield was 0.8 g (80%).

Ethyl 4,5-Dimethyl-1,3-dithiol-2-ylidene(p-methoxyphenylazo)acetate (VII). A 0.5-g (2 mmoles) sample of IIa was dissolved in 30 ml of methanol, and 0.4 g (2 mmole) of p-methoxybenzenediazonium tetrafluoroborate was added in several portions. After 30 min, the precipitate was removed by filtration and recrystallized from hexane. The yield of orange-red crystals was 0.5 g (80%).

Ethyl 4,5-Dimethyl-1,3-dithiol-2-ylidene(phenyliodonio)acetate Trifluoroacetate (VIII C₁₇H₁₆F₃IO₄S₂). A 0.76-g (2 mmole) sample of phenyliodoso trifluoroacetate was added to a solution of 0.5 g (2 mmole) of IIa in 30 ml of methanol, and the mixture was allowed to stand at room temperature for 2 h. It was then evaporated to 5 ml, and VIII was precipitated in the form of light-yellow crystals by means of ether. The yield was 0.8 g (85%). The product was reprecipitated from chloroform by means of hexane and was stored in the dark at no higher than 5°C.

LITERATURE CITED

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