Another possible explanation may be changes in the intracellular distribution of LDH.[10]

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Preparation of *cis*- and *trans*-*p*-Dithiane-2,3-dicarboxylic Acids and Optical Resolution of the Latter

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For certain steric correlations by the quasi-racemate method,[1] 2,3-disubstituted *p*-dithianes of known configuration were needed. Those reported in the literature were not suitable, either because all stereoisomers were not available, or because the absence of reactive groups prevented simple optical resolution. Moreover, their configurations are not known. An unsuccessful attempt to prepare the title acids (I) from the 2,3-dibromosuccinic acids and 1,2-ethanedithiol has been reported.[2]

The present paper describes the preparation of *cis*- and *trans*-I *via* their dimethyl-esters by the reaction of 1,2-dibromoethane with the disodium salts of dimethyl *meso*- and (±)-2,3-dimercaptosuccinate, respectively.

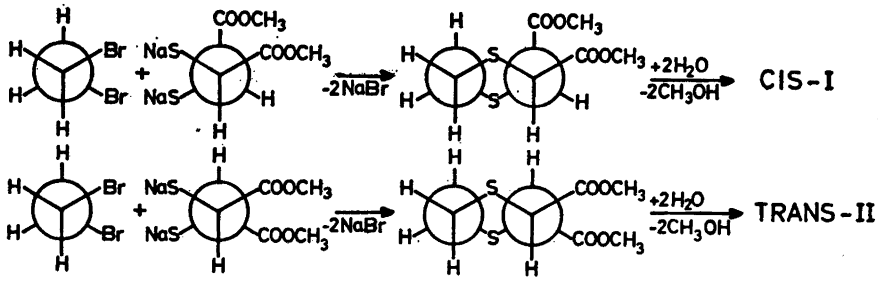
As the asymmetric carbon atoms are not affected, the firmly established configurations of the starting esters [3] are retained in the products. This conclusion is confirmed by optical resolution of *trans*-I *via* its brucine and cinchonidine salts. The infrared (IR) spectra of the antipodes were identical but differed from those of both *cis*- and *trans*-I, suggesting that the latter is a true racemate.

Thorough investigations by physical means indicate that the *p*-dithiane ring prefers the staggered chair conformation,[4a,b] where bulky substituents are known to occupy the equatorial rather than the axial positions. On this basis, *trans*-I should be more stable than *cis*-I, as both carboxyl groups in the former may be equatorial but only one in the latter. The reverse relation was, however, indicated by almost quantitative conversion of the dimethyl ester of *trans*-I into the corresponding ester of *cis*-I in alkaline media. In order to elucidate the reasons for this unusual behaviour, an X-ray investigation of *cis*-I has been undertaken.[5] The relatively high melting point of *cis*-I is also remarkable.

Experimental. Melting and boiling points are not corrected. The melting points of the acids were determined in a preheated apparatus to minimize anhydride formation.

Materials. Thioacetic acid was prepared from acetic anhydride,[6] b.p. 87°, n_D^{25} 1.4631.

Dimethyl cis-p-*dithiane-2,3-dicarboxylate.* Sodium (3.3 g, 142 mmol), dimethyl *meso*-2,3-dimercaptosuccinate (15.0 g, 71 mmol) and 1,2-dibromoethane (13.9 g, 71 mmol) were dissolved in 1000 ml abs. methanol in that order. The solution was left for 24 h at room temperature, then refluxed with stirring for another hour. The precipitate was filtered off. The methanol was removed from the filtrate by rotatory evaporation and the residue diluted with 200 ml of dry ether. The new precipitate, then the ether, were removed as before and the residual oil distilled *in vacuo*. The fraction boiling at 173–175°/9 mm was collected. It solidified within a few days and was recrystal-



lized from petroleum ether; yield 8.1 g (48 %), m.p. 60–61°. (Found: C 40.66; H 5.10; S 26.99. Calc. for $C_8H_{12}O_4S_2$: C 40.65; H 5.12; S 27.14).

cis-p-*Dithiane-2,3-dicarboxylic acid* (cis-*I*). The preceding compound was stirred for 3 h with a 50 % excess of 1 M sodium hydroxide. The resulting clear solution was strongly acidified and extracted with ether. The extract was dried and evaporated to dryness. The colourless residue was recrystallized from ethyl acetate; m.p. 202°. (Found: C 34.75; H 3.87; S 30.69; equiv. wt. (NaOH) 104.4. Calc. for $C_6H_8O_4S_2$: C 34.60; H 3.87; S 30.74; equiv. wt. 104.1).

Dimethyl (±)-trans-p-*dithiane-2,3-dicarboxylate* was prepared in the same manner as the *cis* isomer, except that the refluxing was omitted. The product was, however, not obtained in pure form by distillation as some isomerisation occurred during the reaction. The product did not solidify; yield 10.9 g (65 %), b.p. 141–143°/1 mm. In preparation of the (±)-acid distillation may be omitted and hydrolysis undertaken as described below.

(±)-trans-p-*Dithiane-2,3-dicarboxylate acid* ((±)-trans-*I*). The preceding compound was stirred for 1 h with 10 % excess of 0.2 M sodium hydroxide. The resulting clear solution was made acid to congo red and extracted with ether. The extract was dried and evaporated to dryness at room temperature. The residue was recrystallized twice from ethyl acetate-petroleum ether without heating above 45°; yield 6.7 g (45 %), m.p. 189°. (Found: C 34.67; H 3.87; S 30.69; equiv. wt. (NaOH) 104.5. Calc. for $C_6H_8O_4S_2$: C 34.60; H 3.87; S 30.79; equiv. wt. 104.1).

(+)-trans-p-*Dithiane-2,3-dicarboxylic acid.* Cinchonidine (11.3 g, 38.5 mmol) and (±)-*trans*-I (8.0 g, 38.5 mmol) were dissolved in boiling ethanol (200 and 100 ml, respectively) and the hot solutions mixed immediately. After cooling, the deposited salt (16 g) was collected and recrystallized four times from water (200 ml/g). As further recrystallization did not increase the specific rotation, the acid was liberated from the salt (5.7 g) by 1 M sulfuric acid and extracted with ether. The extract was dried and evaporated to dryness without heating. The residue was dissolved in ethyl acetate and petroleum ether added. The turbid solution was left at 0° for 3 h and the long slender needles of the pure acid (2 g) collected; m.p. 192°, $[\alpha]_D^{25}$ + 62.1° (in abs. ethanol).

(−)-trans-p-*Dithiane-2,3-dicarboxylic acid.* Brucine (15.1 g, 38.5 mmol) and (±)-*trans*-I (8.0 g, 38.5 mmol) were dissolved in boiling methanol (200 ml each) and the hot solutions mixed immediately. After cooling, the deposited salt (17.5 g) was collected and recrystallized four times from water (150 ml/g). Further treatment was as in the preceding paragraph. The yield of pure acid was 1.9 g; m.p. 192°, $[\alpha]_D^{25}$ −62.3° (in abs. ethanol).

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