

$M^{-1} \text{ sec}^{-1}$, or some 10 times the value for quinuclidine, our best amine catalyst. Tetraethylammonium thiophenoxide has a catalytic constant of $4.2 M^{-1} \text{ sec}^{-1}$ toward **1** and is also a potent catalyst for racemization of 1,2-diphenyl-1-propanone, $k = 1.6 \times 10^{-3} M^{-1} \text{ sec}^{-1}$ at 25° . With amines this reaction has to be studied at temperatures above 100° to get a reasonable rate.

Apparently, the strong catalytic effect of thiol anions toward proton removal has not been noted before. This effect may be of considerable importance in connection with several enzyme systems. For example β -aspartate ammonia lyase has been postulated to use a cysteinyl-S⁻ group to remove the β -proton in the elimination of the groups H...NH₃⁺, a step which previously did not have strong support.¹⁶ It turns out that many enzymes which catalyze a reaction that formally requires removal of a proton from carbon such as aldol-type condensations and β elimination do in fact have -SH groups at the active site. Specific examples are rabbit muscle aldolase¹⁷ and thiolase¹⁸ where alternative roles have been suggested for the thiol group at the active site. We have no intention to suggest that a -S- group must participate in all enzymes of these classes. Since the substrate is often actually enclosed in a relatively hydrophobic region,¹⁹ our example in propionitrile may have direct bearing on an important aspect of these mechanisms.

1-Nitro-1-phenylethane was prepared by oxidation of α -methylbenzylamine by peracetic acid²⁰ and purified from acetophenone by a combination of distillation and treatment with 2,4-dinitrophenylhydrazine. We obtained crystalline product in 10% yield, mp $28\text{--}31^\circ$, $[\alpha]_D^{25}$ ₄₄₆ -32 (*c* 4, propionitrile). The 1,2-diphenyl-1-propanone was a sample prepared by J. LeBlanc.^{21,22}

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Circular Dichroism of Disulfides with Dihedral Angles of 0, 30, and 60° in the 400–185 nm Spectral Region¹

Sir:

In efforts to understand the dependence of the optical activity of disulfide-containing biological molecules on the CSSC dihedral angle ϕ , we have measured the CD spectra of (9*S*,10*S*)(-)-*trans*-2,3-dithiadecalin (**1a**),^{2,3} (4*R*,5*R*)(+)-4,5-isopropylidenedioxy-1,2-dithiane (**1b**),^{2,4} (4*R*,5*R*)(+)-4,5-dihydroxy-1,2-dithiane (**1c**)^{2,4} and

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the 4,5-*O,O*-diacetate of **1c** (**1d**),⁵ $\phi \simeq 60^\circ$,^{6,7} methyl 4,6-dideoxy-4,6-epidithio- α -D-galactoside (**2a**)⁸ and the 2,3-*O,O*-diacetate of **2a** (**2b**), $\phi \simeq 30^\circ$,⁶ and 1 α ,5 α -epidithioandrostand-3 α ,17 β -diol (**3**),¹⁰ $\phi \simeq 0^\circ$.¹⁰ The disulfide chirality in **1a**, **2a**, and **2b** is *M* (left-handed helix) and *P* in **1b**, **1c**, and **1d**.

Previous studies have demonstrated the blue shift (370–250 nm) of the first transition as ϕ is opened from 0 to 90° ¹¹ and correlated the sign of the CD band (negative) for this transition with the disulfide chirality (*M*)^{2,12}. Various theoretical treatments¹³ are in substantial agreement as to the nature of this transition, which is in Boyd's notation^{13b} $n_a \rightarrow \sigma^*_{ss}$. While CD bands at ~ 240 ^{2,3,12a} and 200 nm^{2,14} have been observed for 1,2-dithianes, the chiroptical properties of the higher energy transitions remain in general little understood. Of particular interest is a CD band ($n_b \rightarrow \sigma^*_{ss}$)^{13b} of opposite sign to $n_a \rightarrow \sigma^*_{ss}$ which is predicted to shift toward the red as ϕ is opened, becoming nearly degenerate with $n_a \rightarrow \sigma^*_{ss}$ at $\phi \simeq 90^\circ$.¹⁵

The CD spectrum of **1a** in hexane (294 (-5.5),¹⁶ 243.5 (+5.0), 205 (-33), shortest wavelength recorded 182 (+42)) is shown in Figure 1. Better insight into the origin of optical activity in the far-uv region is provided by CD spectra of **1a** in vapor (negative bands at 216 and 206 nm, positive bands at 196 sh and 188 nm),¹⁷ **1a** in methanol (210 sh (-18), 202 (-24)), **1c** in

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(15) It has been suggested^{13a,b,d} that the $n_b \rightarrow \sigma^*_{ss}$ transition is responsible for the 240-nm band in 1,2-dithiane and that overlap of the $n_a \rightarrow \sigma^*_{ss}$ and $n_b \rightarrow \sigma^*_{ss}$ CD bands causes the apparent low rotational strength of the 250-nm region where $\phi \simeq 90^\circ$.

(16) Measurements were made with a Durrum/JASCO Model ORD/UV CD-5 incorporating the SS-10 modification. CD data are represented as $\lambda_{\text{max}} (\Delta\epsilon)$ where $\Delta\epsilon = [\theta]/3300$. Shoulders are designated by sh.

(17) Absorption bands at 211, 202, ~ 191 , and ~ 188 nm have been observed in vapor spectra of 1,2-dithiane by V. Ramakrishnan, S. D. Thompson, and S. P. McGlynn, *Photochem. Photobiol.*, **4**, 907 (1965).

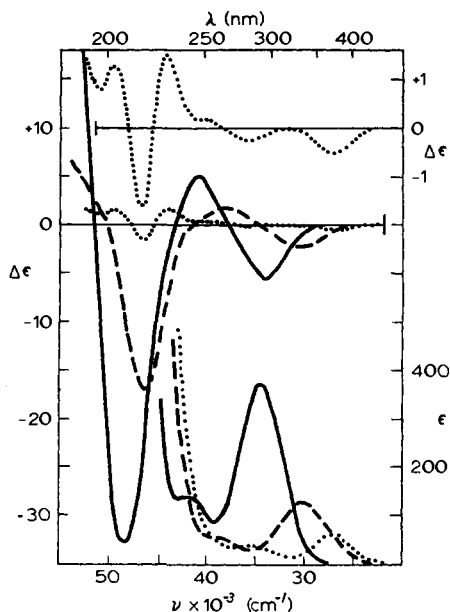


Figure 1. Absorption (lower curves) and CD spectra of **1a** (—), **2b** (---), and **3** (····) in *n*-hexane, excepting the uv spectrum of **3**, which is in methanol.

methanol (220 sh (+3.6), 205 sh (+16), 195 (+23)), and **1d** in hexane (218 sh (+2.4), 200 sh (+20), 193 (+23)). From these and additional data¹⁸ we can characterize the optical activity of *M* chiral disulfides where $\phi \approx 60^\circ$ as resulting from negative bands at ~ 290 (band 1), 220 (band 3), 208 (band 4), and 198 nm (band 5), with positive bands at ~ 240 (band 2), and $\lesssim 182$ nm (two bands collectively designated as band 6). The intensity of bands 2, 4, and 5 progressively decreases while that of band 3 increases in changing from hexane to methanol to water solvent.

The CD curve of **2b** in hexane (Figure 1) (330 (−2.5), 262 (+1.5), 214.5 (−17), 193 sh (+2.6), ca. 184 (+6.4)) is very similar to the curve of **1a** in hexane. Closing ϕ from 60 to 30° causes the first three extrema to shift to longer wavelength and decrease in intensity by about one-half while maintaining the relationship between disulfide chirality and the sign of each CD band observed for **1a–1d**. Solvent studies of **2a** and **2b** failed to resolve the intense band at 214.5 nm into two bands as in **1a–1d**. Band intensity variation as a function of solvent, however, parallels that observed for **1a–1d** with the appearance of a shoulder at ~ 230 nm for **2a** in water.

The comparatively very low intensity of the CD bands of **3** in hexane (Figure 1) (370 (−0.52),¹⁹ 280 (−0.27), 245 sh (+0.18), 226.5 (+1.6), 214 (−1.7), 201.5 (+1.2)) and the loss of the characteristic pattern of signed bands observed when $60^\circ \gtrsim \phi \gtrsim 30^\circ$ is consistent with our expectations for a *cis* planar disulfide which, while no longer an inherently dissymmetric chromophore, derives optical activity from interaction of the now symmetric chromophore with the dissymmetric environment.

The transition energies (λ_{\max}) of the observed CD bands for **1–3** are summarized as a function of ϕ in

(18) Spectra of **1b** and **1c** in hexane, **1b** and **1d** in methanol, **1b**, **1c**, and **1d** in water.

(19) Consistent with the long-wavelength ORD of **3** reported by C. Djerassi, A. Fredga, and B. Sjöberg, *Acta Chem. Scand.*, **15**, 417 (1961).

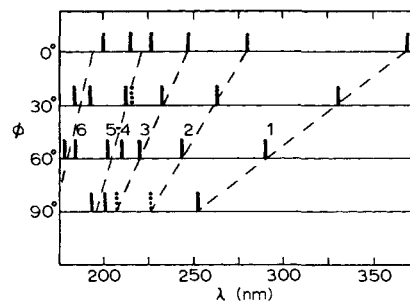


Figure 2. Dihedral angle, ϕ , dependence of electronic transitions of disulfides represented as λ_{\max} of absorption or CD bands. Transitions represented by dots are postulated but have not been observed. Bands which appear more or less to keep their identity upon changing the dihedral angle are interconnected by broken lines.

Figure 2. Absorption bands at ~ 250 , 208–200 sh, and 195 nm, observed for CH_3SSCH_3 ^{18e} and characteristic of related acyclic disulfides²⁰ where $\phi \approx 90^\circ$,²¹ are included. Extrapolation of bands 2 and 3 to 90° places them in the 210–230-nm region while the far-uv bands correlate with bands 4 and 5 in **1a**. Bands 2 and 3 have a constant apparent²² separation of ~ 0.6 eV, and their energy shift as ϕ is opened nearly parallels that of $n_a \rightarrow \sigma^*_{ss}$ (band 1), the gap between bands 1 and 2 decreasing very slightly from 1.1 eV at $\phi \approx 0^\circ$ to 1.0 eV at 30° to 0.9 eV at 60°. The characteristics of bands 2 and 3 are consistent with their assignment to transitions having $n_a \rightarrow \sigma^*_{cs}$ character where the two excited states result from splitting of the doubly degenerate C–S σ^* configurations.^{13g,17} The similarities between bands 2 and 3 of disulfides and the first two bands of simple sulfides which also have been described as resulting from $n \rightarrow \sigma^*$ transitions²³ support this hypothesis.

The CD curves of *M* chiral disulfides where $\phi \approx 90^\circ$ should, by analogy with the results for $60^\circ \gtrsim \phi \gtrsim 0^\circ$, contain contributions from six transitions leading to negative extrema at ~ 250 (band 1) and 210–190 nm (bands 3–5) and positive extrema at ca. 225 (band 2) and < 190 nm (band 6) with intensities ~ 1.5 times those observed for dithianes. Observation of these chiroptical properties will depend upon: (1) the extent of overlap of the various oppositely signed bands resulting in their mutual cancellation and (2) the lack of significant contributions from additional transitions such as $n_b \rightarrow \sigma^*_{ss}$ ¹⁵ and $n_b \rightarrow \sigma^*_{cs}$. It is interesting to note that the temperature-dependent CD curves of L-cysteine reported by Takagi and Ito²⁴ have negative bands at 255, 200, and ca. 190 nm which are consistent in sign, relative intensity, and wavelength with bands 1 and 4–5 expected for *M* chiral disulfides.

While it is clear that all of the observed bands of the compounds studied appear to reflect both the sense and magnitude of the disulfide chirality, a comparison of the

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curves with those obtained from 3-carboxy- and 3,5-dicarboxy-substituted 1,2-dithiolanes,^{12c} disulfide-bridged diketopiperazines,^{12b,25} and various cystine derivatives such as *cyclo*-L-cystine^{14,26} and [2,7-cystine]-gramicidin S²⁷ makes clear that the interaction of the disulfide with peripheral groups can lead to chiroptical features significantly different from those expected for the "isolated" disulfide.

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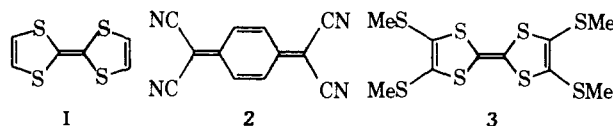
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Tetrathiomethoxytetrathiofulvalene. Electrochemical Synthesis and Characterization

Sir:

The recent discovery^{1,2} of highly conductive organic charge transfer complexes which are formed from derivatives of tetrathiofulvalene (**1**) and the acceptor



molecule, tetracyano-*p*-quinodimethane (TCNQ) (**2**), has stirred interest in the discovery of new electron donors and acceptors which exhibit similar conductivity.³ We wish to report the synthesis, *via* electrochemical methods, of both **1** and tetrathiomethoxytetrathiofulvalene (**3**).

The procedure reported here involves alkylation of 1,3-dithiole-2-thiones⁴ to form 2-thioethoxy-1,3-dithiolium ions, followed by electrochemical reduction to the 2,2' dimer, an orthothiooxalate. The orthothiooxalate is isolated and pyrolyzed to the tetrathiofulvalene.⁵ Good to nearly quantitative yields are obtained for each step, and, in our hands, the method has

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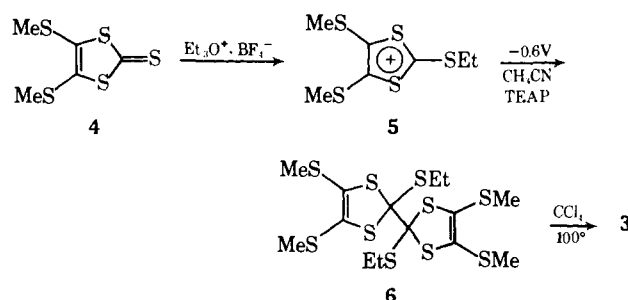
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proven to be superior to the base catalyzed dimerization of 1,3-dithiolium ion, the method used by Coffen⁶ initially to synthesize **1**. The method also appears to be a more general preparation of tetrathioethylenes from trithiocarbonates than desulfurization by trivalent phosphorus compounds.^{7,8}

The preparation of **3** illustrates the procedure. The trithiocarbonate **4** was prepared by the method of Wawzonek and Heilman.⁹ An excess of CS₂ was cathodically reduced (Pt, DMF, 0.4 M TBAI¹⁰) at -2.00 V *vs.* sce. After 0.16 F was passed, the electrolysis was stopped, excess CS₂ was removed by nitrogen purging, and 10 g of CH₃I was added. After 2 hr at room temperature, the excess CH₃I was removed, and the products were extracted with ether. The product **4** was recrystallized from ligroine as long reddish needles: mp 100–101°; nmr (δ) 2.51 (s); current yield 75%. Meerwein's reagent ethylated **4** at room temperature in CH₂Cl₂ to yield **5** which was cathodically reduced (Pt, CH₃CN, 0.2 M TEAP¹⁰) at -0.6 V *vs.* sce (1.0 F/mol). The orthothiooxalate **6** was recovered by chloroform



extraction; crude yield: 99.5%; mp 77–79°; nmr (δ) 1.37 (t) 6 H, 2.40 (s) 6 H, 3.0 (q) 4 H; uv (CH₃CN) 307 nm, log ε 4.19. Finally, **6** was pyrolyzed in a sealed tube for 4 hr to yield **3** as a red oil in a total yield of 75% (coulometric analysis). On standing in acetonitrile, pale yellow needles formed: mp 94.5–96.0°; nmr (δ) 2.46 (s); mass spectrum (*m/e*) 388 (p), 373 (-CH₃), 341 (-SCH₃), 194 (p/2); uv see Table I. The distinctive

Table I. Spectral Data for Tetrathiomethoxytetrathiofulvalene, Its Radical Cation and Dication in Acetonitrile

3		3 ^{•+}		3 ²⁺	
λ, nm	log ε	λ, nm	log ε	λ, nm	log ε
370(s)	3.23	461	3.25	710	3.51
329	3.89	366	3.25	488	2.7
309	3.94	329	3.75	456	2.7
260	3.89	262	4.04		

electrochemical behavior of **3** easily permitted its analysis in the presence of other products (probably diethyl disulfide).

Cyclic voltammograms of **3** in CH₃CN at a platinum working electrode (Figure 1) exhibit two reversible one-electron couples at 0.47 and 0.71 V *vs.* sce which cor-

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