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Optical Rotatory Dispersion Studies

XLII *. Disulfides and Diselenides **

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The rotatory dispersion of a number of disulfides and diselenides has been investigated and discussed. The steric relations of analogous disulfides and diselenides can be conveniently correlated by means of their dispersion curves, the same sign of the Cotton effects implying identical configuration.

Most of the optical rotatory dispersion work during the past five years (for reviews see Refs.[1–3]) has dealt with ketones and aldehydes. These compounds have their first ultraviolet absorption band in a readily accessible region of the spectrum (280—320 mμ) with such a low extinction ($\varepsilon < 100$) that it is usually possible to determine the optical rotation through this region and study the anomalous dispersion curves (for nomenclature see Refs.[3–4]). It has been clearly demonstrated that the shape of the anomalous dispersion curves can be correlated empirically to certain structural and steric features of the compounds, and in this way Cotton effect curves have found extensive use in the solution of various organic chemical problems [1–3]. It has also been shown [5,6] that the configurational relationship of some types of simple compounds, possessing only plain dispersion curves, can be deduced from the curves if the measurements are extended close to the anisotropic absorption region. It is evident, however, that plain curves cannot be as versatile as the more detailed Cotton effect curves, and the usefulness of optical rotatory dispersion in organic and theoretical chemistry lies principally in the area of Cotton effect curves.

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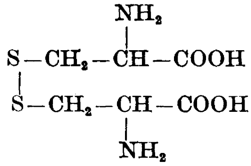
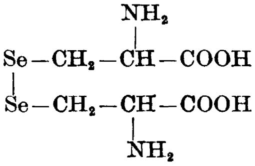
Some chromophores other than the carbonyl group may also give Cotton effects in a wavelength region currently accessible to spectropolarimetric work, and these chromophores have already been listed [3,7]. Because of the important biological functions of some organic disulfides, *e.g.* cystine and 6,8-thioctic acid, the disulfide group has recently attracted great interest, especially its energetics and spectral properties [8,9]. Despite this, however, prior to the present investigation the optical rotatory dispersion of disulfides has only been studied with cystine (I). This investigation [10] revealed a negative dispersion curve (Fig. 1) with a first extremum at 268 mμ, which seemed to be associated with a Cotton effect centered about the disulfide band at 255 mμ. Diselenides are closely analogous to disulfides in many respects and their ultraviolet absorption in particular is caused by similar electron excitations [11]. However, the diselenides absorb at longer wavelengths than the corresponding disulfides, hence it appeared likely that the optical rotatory dispersion curve of selenocystine (II) could be measured through the absorption region at 305 mμ. This proved to be the case and it was thus possible to demonstrate a Cotton effect centered about the low intensity absorption band (Fig. 1), showing that the diselenide band is optically active. These results suggest that the extremum in the dispersion curve of cystine is the through of a negative Cotton effect associated with the disulfide band. Similarly, (+)-*a*-dithio-*bis*propionic acid (III), (+)-dithio-*bis*phenylacetic acid (IV) and the corresponding diselenides (V and VII) exhibit very steep plain dispersion curves to the limit of the experimental measurements (Fig. 2), indicating imminent appearence of the first extrema of Cotton effects associated with the disulfide and diselenide absorption bands around 250 and 290 mμ, respectively. Although it was not possible to demonstrate any definite irregularities in the dispersion curves around the absorption bands of the diselenides V and VII, this may be due to the rather dilute solutions used and a weak positive Cotton effect may be hidden in a steep positive background curve.



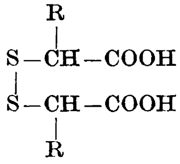
$$\begin{array}{l} \mathrm{S-CH_2-CH(NH_2)-COOH} \\ \mathrm{|} \\ \mathrm{S-CH_2-CH(NH_2)-COOH} \end{array}$$

I



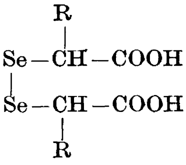
$$\begin{array}{l} \mathrm{Se-CH_2-CH(NH_2)-COOH} \\ \mathrm{|} \\ \mathrm{Se-CH_2-CH(NH_2)-COOH} \end{array}$$

II



$$\begin{array}{l} \mathrm{S-CH(R)-COOH} \\ \mathrm{|} \\ \mathrm{S-CH(R)-COOH} \end{array}$$

III R = CH_3
IV R = C_6H_5



$$\begin{array}{l} \mathrm{Se-CH(R)-COOH} \\ \mathrm{|} \\ \mathrm{Se-CH(R)-COOH} \end{array}$$

V R = CH_3
VI R = C_2H_5
VII R = C_6H_5

The location of the disulfide and diselenide absorption band varies considerably with the structure of the compounds [8,9], and a large bathochromic

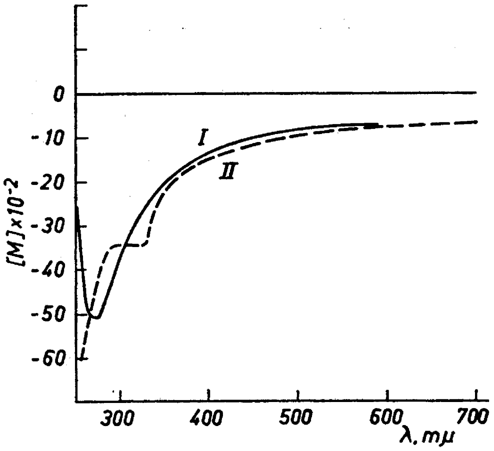


Fig. 1. Optical rotatory dispersion curves of (—)-cystine (I) and (—)-selenocystine (II).

shift is encountered when the disulfide or the diselenide group is incorporated in a six- and especially in a five-membered ring. The rotatory dispersion curves of (+)-1,2-dithiane-3,6-dicarboxylic acid (VIII) and (+)-1,2-diselenane-3,6-dicarboxylic acid (IX) are shown in Fig. 3. The disulfide shows an anomalous curve with a peak at 300 mμ, and the positive Cotton effect is definitely related to the absorption band, indicated by a shoulder at 280 mμ [12]. For the diselenide,

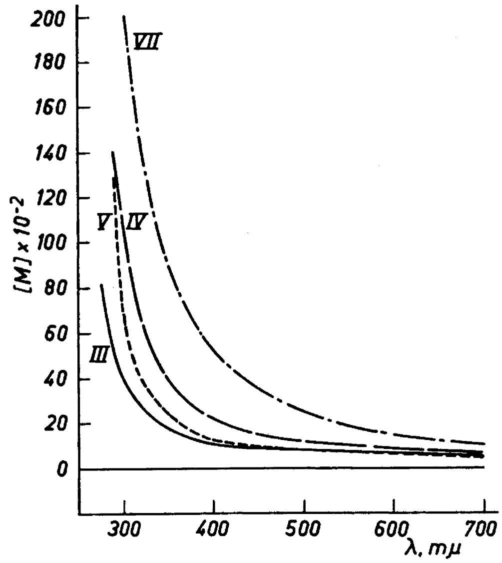
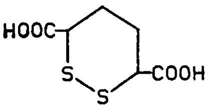


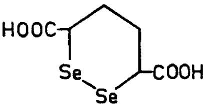
Fig. 2. Optical rotatory dispersion curves of (+)-α-dithio-*bis*propionic acid (III), (+)-dithio-*bis*phenylacetic acid (IV), (+)-α-diseleno-*bis*propionic acid (V) and (+)-diseleno-*bis*phenylacetic acid (VII).

which has its first absorption band at 341 mμ[11], it was possible to determine both the peak and the through of the Cotton effect.

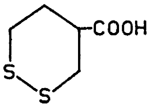
The effect of moving the disulfide group away from the asymmetric center can be seen by comparing the dispersion curves of 1,2-dithiane-3,6-dicarboxylic acid (VIII) and 1,2-dithiane-4-carboxylic acid (X). The latter acid, which has the disulfide group in the β-position to the asymmetric center, also shows a strong Cotton effect (Fig. 3) related to the ultraviolet absorption found at 298 mμ[13]. The disulfide and diselenide groups apparently give rise to Cotton effects when they are both adjacent to the asymmetric center (as for III—IX) or one carbon atom removed from it (as for I, II and X). Whether this will be generally true is as yet impossible to say, since only β-compounds with a carboxyl group attached to the assymmetric center have been studied. The vicinal action from the carboxyl group may be important with respect to the anisotropy of the disulfide and diselenide groups.



VIII

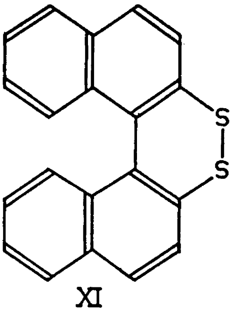


IX



X

A considerable bathochromic shift can be expected if the disulfide groups are conjugated with an aromatic system. The ultraviolet spectrum of 1,1'-dinaphthylene-2,2'-disulfide (XI)[14] is rather complex, with absorption bands at 238, 262, 318, 348 and 400 mμ (shoulder). It is likely that the low intensity, 400 mμ, band is related to an excitation at the conjugated system extended over the disulfide group, and a negative Cotton effect is also found in this wavelength region (Fig. 4).



XI

The five-membered cyclic disulfide 6,8-thioctic acid (XII) has an important function in the decarboxylation of α-keto acids[15] and possibly also in photosynthesis[16]. It is therefore natural that special emphasis has been placed on studies of the chemistry of 1,2-dithiolane compounds[15,17]. Disulfides with a five-membered ring absorb at longer wavelengths than those with a six-membered ring, the values for 1,2-dithiolane and 1,2-dithiane being 334 and 295 mμ, respectively[18]; 1,2-dithiolane compounds should therefore be very suitable for spectropolarimetric studies. It was also found (Fig. 5) that the dispersion

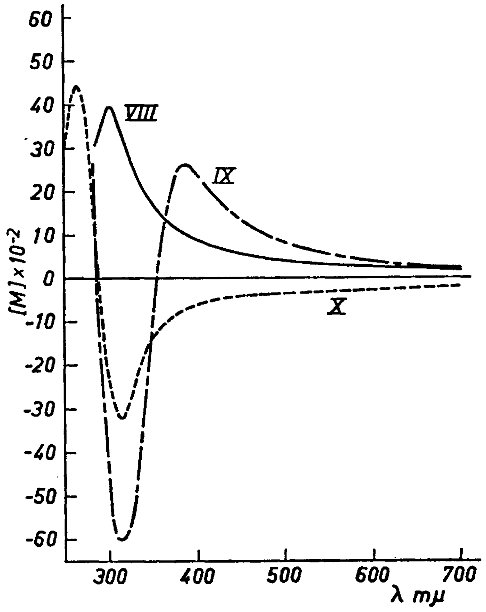
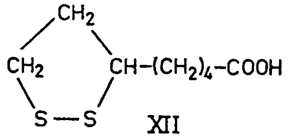


Fig. 3. Optical rotatory dispersion curves of (+)-1,2-dithiane-3,6-dicarboxylic acid (VIII), (—)-1,2-diselenane-3,6-dicarboxylic acid (IX) (—)-1,2-dithiane-4-carboxylic acid (X).

curve of 6,8-thioctic acid (XII) has a Cotton effect which is clearly related to the disulfide absorption band.



XII

The anisotropy of the disulfide group is even more strikingly demonstrated with some epidithio steroids. In Fig. 6 is shown the dispersion curve of 1α,5α-epidithioandrostane-3,17-dione (XIII). The curve has a negative Cotton effect with a trough at 405 mμ and a peak at 340 mμ superimposed on the strongly rotating positive Cotton effect [20] of androstane-3,17-dione. Selective reduction of the keto groups of XIII to 1α,5α-epidithioandrostane-3α,17β-diol (XIV) causes no appreciable changes in the negative Cotton effect, but the positive Cotton effect typical for androstane-3,17-dione disappears. Further reduction to 3α,17β-dihydroxyandrostane-1α,5α-dithiol (XV) affords a plain dispersion curve. The ultraviolet absorption of these three steroids has been investigated in detail [21], and a comparison between the absorption and dispersion curves shows an almost exact correspondence of the negative Cotton effect with the absorption maximum of the disulfide group. The very small irregularities in

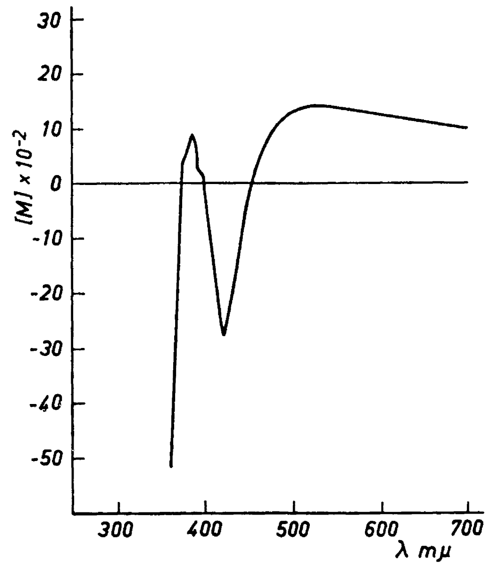
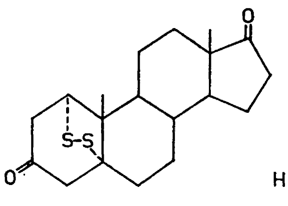
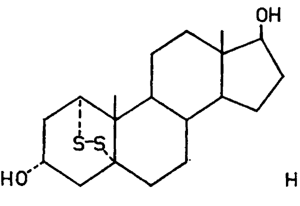


Fig. 4. Optical rotatory dispersion curve of (+)-1,1'-dinaphthylene-2,2'-disulfide (XI).

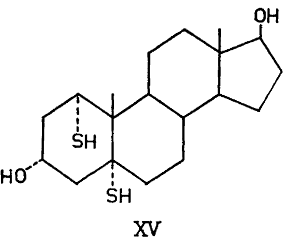
the rotatory dispersion curve of the dithiol XV at 340 and 405 mμ is most probably due to the presence of a trace of the disulfide XIV which can also be seen in the absorption curves [21] (Fig. 7).



XIII



XIV



XV

Optically active selenocystine (II) has been prepared [22] from L-(—)-serine in a reaction sequence that did not involve the asymmetric center. The analogous configuration of cystine and selenocystine of the same sign of rotation (at the D-line) could in addition to this also be determined [22] by use of the quasi-racemate method [23]. As can be seen in Fig. 1 these two amino acids have both negative Cotton effect curves.

(+)-*a*-Dithio-*bis*propionic acid (III) and (+)-*a*-diseleno-*bis*propionic acid (V) have similar rotatory dispersion curves (Fig. 2), and the configuration of these two acids has also been shown to be the same [24]. The similarity in the rotational shifts of dithio-*bis*phenylacetic acid (IV) and diseleno-*bis*phenylacetic acid (VII) in different solvents at the D-line has been presented as evidence for the identical configuration of the acids with the same sign of rota-

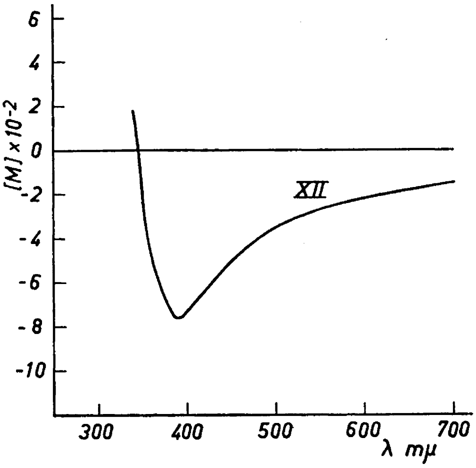


Fig. 5. Optical rotatory dispersion curve of (—)-6,8-thioctic acid (XII).

tion [25], and here too the dispersion curves are very similar (Fig. 2), the main difference being that the rotatory dispersion curves of the diselenides are relatively displaced towards higher wavelengths, due to the diselenides absorb-

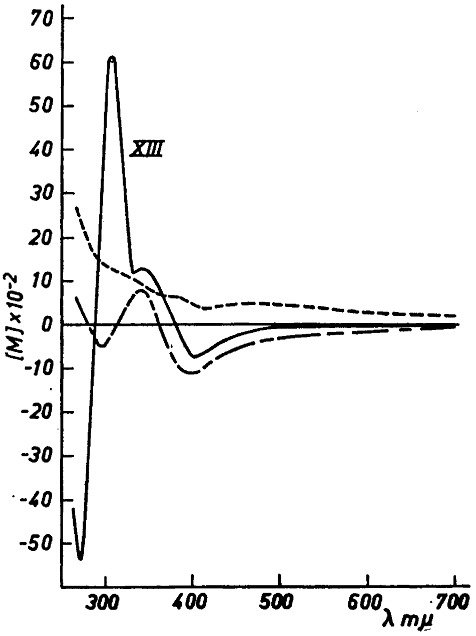


Fig. 6. Optical rotatory dispersion curves of 1α,5α-epidithioandrostane-3,17-dione (XIII), 1α,5α-epidithioandrostane-3α,17β-diol (XIV) — — — and 3α,17β-dihydroxyandrostane-1α,5α-dithiol (XV) - - - -.

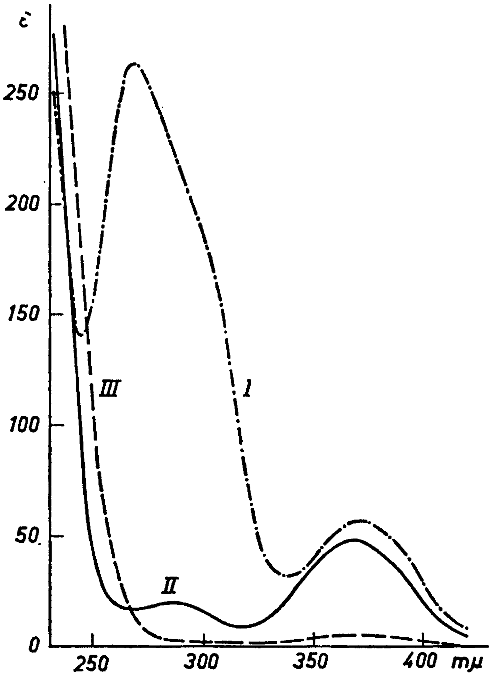


Fig. 7. Ultraviolet absorption spectra of 1α,5α-epidithioandrostane-3,17-dione (XIII) (curve I), 1α,5α-epidithioandrostane-3α,17β-diol (XIV) (curve II) and 3α,17β-dihydroxyandrostane-1α,5α-dithiol (XV) (curve III).

ing at higher wavelengths than the corresponding disulfides. The configurational identity of (+)-1,2-dithiane-3,6-dicarboxylic acid (VIII) and (+)-1,2-diselenane-3,6-dicarboxylic acid (IX) has been established by careful studies of the two-component mixtures of these acids [26,27]. It can be seen in Fig. 3 that the optical rotatory dispersion curves in this case also will give direct information about the steric relationship between the compounds.

The use of optical rotatory dispersion curves for the stereochemical correlations of disulfides and diselenides is well illustrated by the results outlined above. From these examples it is evident that the sterochemistry of analogous disulfides and diselenides can be correlated conveniently by means of their dispersion curves, the same sign of the Cotton effects implying identical configuration.

EXPERIMENTAL *

(−)-Cystine (I) R.D. (Fig. 1) in 0.1 N hydrochloric acid. The dispersion curve is reproduced from J. A. Schellman [10].

(−)-Selenocystine (II) [22] R.D. (Fig. 1) in 0.1 N hydrochloric acid (c 0.105): $[M]_{700}$ −650°, $[M]_{589}$ −770°, $[M]_{320}$ −3 460°, $[M]_{290}$ −3 450°, $[M]_{260}$ −6 060°.

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* Several of the dispersion curves were measured by Mrs. T. Nakano to whom we express our thanks.

(+)-a-Dithio-bispropionic acid (III)[28] R.D. (Fig. 2) in methanol (*c* 0.150), temp 31°: $[M]_{700}$ + 480°, $[M]_{589}$ + 750°, $[M]_{400}$ + 1 040°, $[M]_{350}$ + 1 820°, $[M]_{300}$ + 4 230°, $[M]_{275}$ +8 120°.

(+)-Dithio-bisphenylacetic acid (IV)[29] R.D. (Fig. 2) in methanol (*c* 0.149), temp. 31°: $[M]_{700}$ + 690°, $[M]_{589}$ + 920°, $[M]_{400}$ + 2 200°, $[M]_{350}$ + 3 890°, $[M]_{300}$ + 10 100°, $[M]_{287.5}$ + 13 900°.

(+)-a-Diseleno-bispropionic acid (V)[25] R.D. (Fig. 2) in methanol (*c* 0.142), temp. 29°: $[M]_{700}$ + 380°, $[M]_{589}$ + 450°, $[M]_{400}$ + 880°, $[M]_{350}$ + 1 330°, $[M]_{300}$ + 4 050°; (*c* 0.028): $[M]_{270}$ + 9 780°.

(+)-a-Diseleno-bis-n-butyric acid (VI)[25] R.D. in methanol (*c* 0.095), temp. 29°: $[M]_{700}$ + 370°, $[M]_{589}$ + 510°, $[M]_{400}$ + 1 190°, $[M]_{350}$ + 2 600°, $[M]_{300}$ + 6 740°, $[M]_{390}$ + 12 900°.

(+)-Diseleno-bisphenylacetic acid (VII)[25] R.D. (Fig. 2) in methanol (*c* 0.190), temp. 26°: $[M]_{700}$ + 990°, $[M]_{589}$ + 1 510°, $[M]_{400}$ + 5 180°, $[M]_{350}$ + 9 540°; (*c* 0.038): $[M]_{300}$ + 19 700°, $[M]_{290}$ + 23 800°.

(+)-1,2-Dithiane-3,6-dicarboxylic acid (VIII)[26] R.D. (Fig. 3) in methanol (*c* 0.092), temp. 27°: $[M]_{700}$ + 190°, $[M]_{589}$ + 260°, $[M]_{400}$ + 920°; (*c* 0.018): $[M]_{305}$ + 3 920°, $[M]_{285}$ + 3 060°.

(+)-1,2-Diselenane-3,6-dicarboxylic acid (IX)[25] R.D. (Fig. 3) in methanol (*c* 0.091), temp. 28°: $[M]_{700}$ + 210°, $[M]_{589}$ + 400°, $[M]_{400}$ + 2 420°; (*c* 0.018): $[M]_{387.5}$ + 2 620°, $[M]_{315}$ −6 010°, $[M]_{282.5}$ + 2 660°.

(−)-1,2-Dithiane-4-carboxylic acid (X)[13] R.D. (Fig. 3) in methanol (*c* 0.148), temp. 25°: $[M]_{700}$ −230°, $[M]_{589}$ −280°, $[M]_{400}$ −590°, $[M]_{315}$ −3 200°, $[M]_{265}$ + 4 420°, $[M]_{250}$ + 2 920°.

(+)-1,1′-Dinaphthylene-2,2′-disulfide (XI)[14] R.D. (Fig. 4) in dioxane (*c* 0.090), temp. 25°: $[M]_{700}$ + 980°, $[M]_{589}$ + 1 270°, $[M]_{525}$ + 1 390°, (*c* 0.014): $[M]_{422.5}$ −2 750°, $[M]_{387.5}$ + 880°, $[M]_{360}$ −5 150°.

(−)-6,8-Thioctic acid (XII)[30] R.D. (Fig. 5) in methanol (*c* 0.136), temp. 27°: $[M]_{700}$−150°, $[M]_{589}$ −220°, $[M]_{390}$ −760°; (*c* 0.034): $[M]_{340}$ +180°.

1a,5a-Epidithioandrostane-3,17-dione (XIII)[19] R.D. (Fig. 6) in methanol (*c* 0.095), temp. 24°: $[M]_{700}$ −30°, $[M]_{589}$ −30°, $[M]_{402.5}$ −730°, $[M]_{342.5}$ + 1 270°, $[M]_{332.5}$ + 1 190°; (*c* 0.019): $[M]_{307.5}$ + 6 110°, $[M]_{270}$ −5 360°, $[M]_{262.5}$ −4 220.

1a,5a-Epidithioandrostane-3a,17β-diol (XIV)[19] R.D. (Fig. 6) in methanol (*c* 0.100), temp. 23°: $[M]_{700}$ −60°, $[M]_{589}$ −170°, $[M]_{400}$ −1 120°, $[M]_{342.5}$ + 760°, $[M]_{295}$ −510°, $[M]_{265}$ + 600°.

3a,17β-Dihydroxyandrostane-1a,5a-dithiol (XV)[19] R.D. (Fig. 6) in methanol (*c* 0.095), temp. 25°: $[M]_{700}$ + 200°, $[M]_{589}$ + 230°, $[M]_{450}$ + 460°, $[M]_{415}$ + 330°, $[M]_{370}$ + 630° (infl.), $[M]_{300}$ + 1 350°, $[M]_{265}$ + 2 780°.

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