

Work is underway to determine the scope of local conformational control in medium-ring alkene addition reactions.

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**Supplementary Material Available:** Spectral characterization of 1-3, 9, and 20 (2 pages). Ordering information is given on any current masthead page.

(12) Selected medium-large-ring  $\alpha$ -alkyl Z olefins. Dictiodiol: Finer, J.; Clardy, J.; Fenical, W.; Minale, L.; Riccio, R.; Battaile, J.; Kirkup, M.; More, R. E. *J. Org. Chem.* **1979**, *44*, 2044. Neolemanes: Izac, R. R.; Fenical, W.; Tagle, B.; Clardy, J. *Tetrahedron* **1981**, *37*, 2569. Rubradirin: Hoeksema, H.; Mizsak, S. A.; Baczynski, L. *J. Antibiot.* **1979**, *32*, 773. Macbecins: Muroi, M.; Haibara, K.; Asai, M.; Kamiya, K.; Kishi, T. *Tetrahedron* **1981**, *37*, 1123. Latrunculine A: Kashman, Y.; Groweiss, A.; Shmueli, U. *Tetrahedron Lett.* **1980**, *21*, 3629.

### Additivity Relation in the Amplitudes of Exciton-Split Circular Dichroism Curves Arising from Interactions between Different Chromophores and Its Application in Structural Studies

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Interaction of the electric transition moments of two or more chromophores within a chiral molecule constitutes a coupled oscillator.<sup>1</sup> This condition gives rise to Davydov split CD curves.<sup>2</sup> The closer the  $\lambda_{\max}$  of the interacting chromophores, the more efficient the coupling.<sup>3</sup> However, a split CD is observed when the  $\lambda_{\max}$  values differ by as much as 100 nm.<sup>3,4</sup> Valid analyses can also be obtained when only one of the Cotton effect extrema is discernable.<sup>4,5</sup>

The results of over 40 pyranose *p*-bromobenzoates showed that the amplitudes of split CD curves ("A values") can be approximated by the sum of dibenzoate interactions which are constants.<sup>6</sup> Herein we show that this additivity relation can be generalized as illustrated (Scheme I) by the interaction between enone (e.g., 1  $\lambda_{\max}$  244 nm ( $\epsilon$  12400), and 2  $\lambda_{\max}$  243 nm ( $\epsilon$  10300), in MeOH) and unsubstituted benzoate ( $\lambda_{\max}$  229.5 nm ( $\epsilon$  15300), in MeOH) chromophores. These results are then applied to a configurational problem involving complex natural product derivatives having benzoate and furan chromophores.

The phytocysteroids ponasterone A (PN-A, 1)<sup>7</sup> and ajugasterone C (AJG-C, 2)<sup>8</sup> can be converted into the 2,3-dibenzoate 3 and 2,3,11-tribenzoate 4 of the respective 6-hydroxy-20,22-

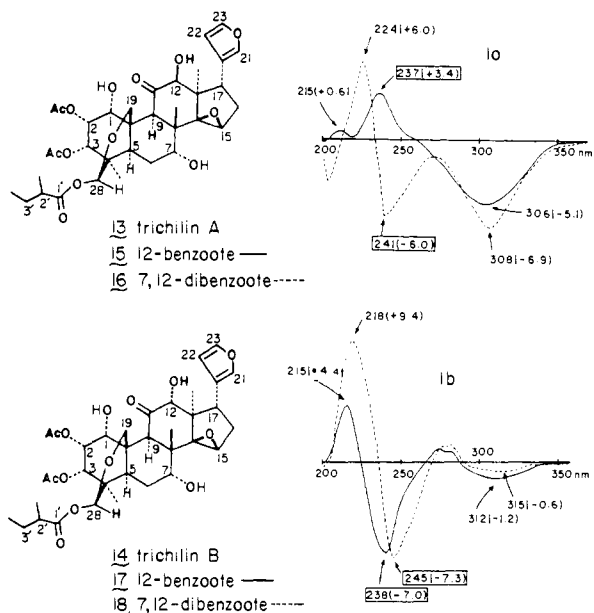
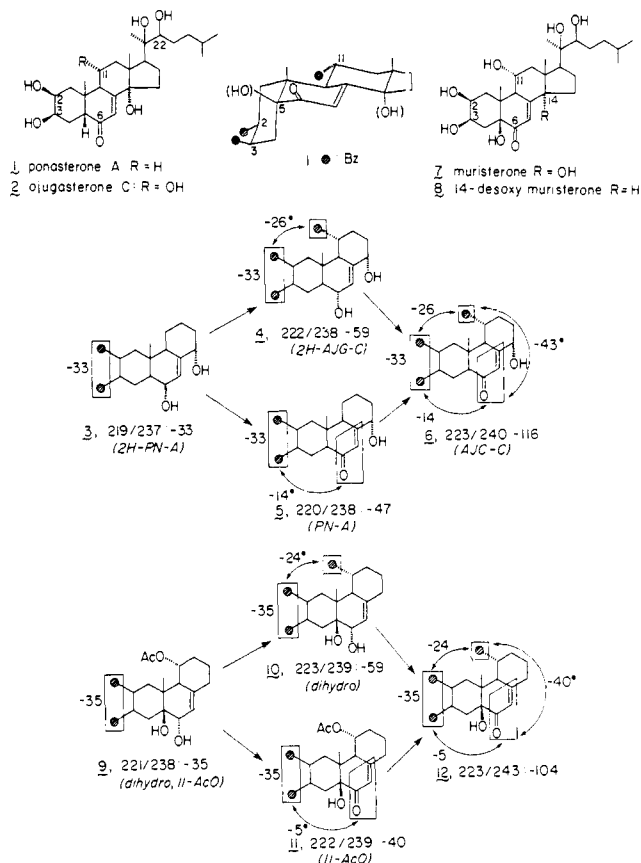


Figure 1. CD of 12-benzoates and 7,12-dibenzoates of trichilins A and B, in MeOH.

#### Scheme I



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acetone, by acid hydrolysis of the 2,3,20,22-diacetonide to the 20,22-acetonide, benzylation, and NaBH<sub>4</sub> reduction.<sup>9</sup> Dibenzoate 3 displays a split CD (all data in MeOH) with negative/positive Cotton effects at 237 nm/219 nm, *A* -33, arising from the negatively coupled oscillator (see conformational structure I). In tribenzoate 4 the *A* value is -59. In view of the additivity relation,<sup>6</sup> the 2,3-dibenzoate and 11-benzoate interaction can then be assigned an *A* value of -26\* (calculated values indicated by

(9) All derivatives were purified by HPLC and fully characterized by spectroscopic methods.

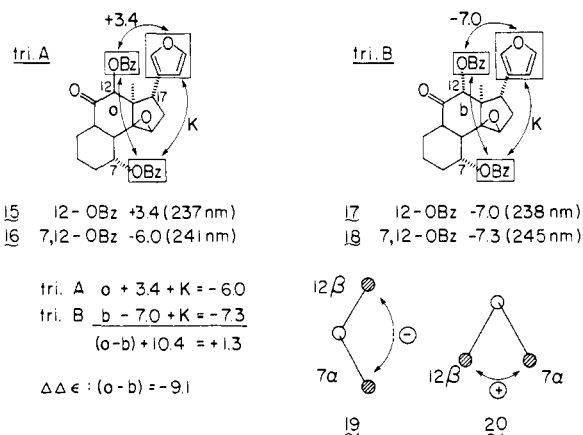


Figure 2. Deduction of 12-benzoate configurations.

an asterisk). Similarly, in **5**, the interaction value for the 2,3-dibenzoate and -7-en-6-one moieties can be estimated to be  $-14^*$  from the  $A$  values of  $-33$  for **3** and  $-47$  for **5**. The interaction value between the 11-benzoate and enone in **6** is thus  $-116 - (-14) - (33) - (-26) = -43^*$ .

Treatment of muristerone (**7**)<sup>10</sup> with  $\text{Me}_3\text{SiCl}/\text{NaI}$  gave 14-deoxymuristerone (**8**), which when assayed on *Drosophila* Kc-H cells exhibited 80-fold increased activity relative to 20-hydroxyecdysone.<sup>11</sup> A similar set of derivatives (**9–12**, all 20,22-acetonides) of **8** gave interaction values very close to those of the set **3–6**.

14-Deoxymuristerone 11-benzoate-2,3,20,22-diacetonide exhibited CD extrema at 223 nm/234 nm with an  $A$  value of  $-41$  arising from the interaction between the 11-OBz and enone chromophores. The excellent agreement between this value and the estimated values of  $-43^*$  (**6**) and  $-40^*$  (**12**) indicates that the additivity relation noted among identical benzoate chromophores<sup>6</sup> can be generalized to include other chromophores.

An application of this is provided by the following example. The root bark of the East African plant *Trichilia roka* (Meliaceae) contains the two major potent antifeedants trichilin A (**13**) and B (**14**), the structures of which differ only at C-12. The configuration at this center was inferred from chemical shift comparisons of the aromatic H's of their *p*-bromobenzoates.<sup>12</sup> CD data provide a more direct means of analysis.

In the CD of trichilin A 12-benzoate (**15**, Figure 1) the positive Cotton effect at 237 nm is one of the two extrema of a split benzoate CD, the interacting counterpart being the furan chromophore ( $\lambda_{\text{max}}$  200 nm  $\epsilon$  4500). The negative branch of this split CD is masked by the Cotton effects of the ester groups on ring A. However, the discernment of one branch suffices for data analysis.<sup>4,5</sup> In dibenzoate **16**, the observed branch appears as a negative Cotton effect at 241 nm.

The  $\Delta\epsilon = -6.0$  value observed for **16** is a summation of the interactions: 12-OBz/furan (+3.4), furan/ $7\alpha$ -OBz (=K) and  $7\alpha$ -OBz/12-OBz (=a) (Figure 2). The  $\Delta\epsilon = -7.3$  value for trichilin B dibenzoate **18** is likewise a summation of three such interactions. As shown in Figure 2, the difference in the  $\Delta\epsilon$  values of the two interactions  $a$  and  $b$  can be estimated to be  $-9.1^*$ . Namely, chirality  $a$  between  $7\alpha$ -OBz and 12-OBz in **16** is more negative than the corresponding chirality  $b$  in **18**. This leads to the  $12\beta$ -OH configuration for trichilin A and  $12\alpha$ -OH configuration for trichilin B as indicated in projections **19** and **20**.<sup>13</sup>

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(13) It should be noted that the CD of trichilin dibenzoates (Figure 1a,b) are both negatively split. Therefore, if interactions with the furan chromophore were not considered, one would conclude that the chirality between the 7- and 12-benzoate groups in **16** and **18** are both negative, which is clearly not the case.

Various attempts to analyze optical rotation  $[M]_D$  on the basis of additivity of pairwise interaction have met with varying degrees of success;<sup>14</sup> one practical drawback in these approaches has been the numerous empirically derived parameters that have had to be considered. We believe that the additivity relation found in the split CD of interacting dissimilar chromophores will be of great value in facilitating the interpretation of CD curves in configurational and related studies.<sup>15</sup>

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### Crown Thiaether Chemistry. Crystal Structure of 1,4,7,10,13,16-Hexathiacyclooctadecane, the Hexathia Analogue of 18-Crown-6

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The chemistry of crown thiaethers<sup>2-5</sup> has not developed in parallel with the extensive chemistry of crown ethers.<sup>6-10</sup> In particular, only a few crown thiaethers have been characterized structurally,<sup>11-13</sup> even though thiaether coordination chemistry<sup>14</sup> has recently assumed new significance since discovery of thiaether coordination to copper in the blue copper protein plastocyanin.<sup>15</sup> As part of our current interest in the coordination chemistry of crown thiaethers we have determined the X-ray structure of the prototypical ligand of this class, hexathia-18-crown-6. Our results show that hexathia-18-crown-6 belongs to a new class of macrocyclic thiaethers: it is the first macrocyclic sulfur ligand to have both endo- and exodentate sulfur atoms, thereby proving that endodentate sulfur atoms can occur in large, unstrained rings. Moreover, we can now rationalize the markedly different conformational preferences observed for crown ethers and crown thiaethers.

Hexathia-18-crown-6 was prepared by a modification of the procedure of Ochrymowycz et al.<sup>16</sup> and purified by column chromatography. Recrystallization from 4:1 hexane/acetone (v/v) afforded needles suitable for diffraction measurements. Anal.

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