CD Exciton Chirality Method. New Red-Shifted Chromophores for Hydroxyl Groups

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Received March 31, 1993

Abstract: When hydroxyl groups are derivatized to apply the CD exciton chirality method, the absorption maxima of introduced chromophores should not overlap with that of the substrate, except for cases in which the coupling between the existing and the introduced chromophores are deliberately sought for. Thus, the availability of red-shifted chromophores that do not overlap with the substrate absorption would greatly expand the applicability of this versatile CD method. Four such red-shifted chromophores, chrom-II, -III, -IV, and -V, have been developed to convert hydroxyl groups into esters that absorb strongly in the range 360–410 nm. Using the chromophoric triazole amide, they can readily derivatize hydroxyl groups of the substrates on a microscale. The bischromophoric esters of 1(*R*),2(*R*)-cyclohexanediol (**14–18**) exhibited intense exciton-split CD curves with the signs correctly representing the absolute sense of twist between the two hydroxyl groups. The 1,2-diol moieties of taxinine (**2**) and chromomycin A_3 (**3**) derivatives, already having strong absorptions at 260–275 nm, were esterified with the new chromophores; this gave rise to strong couplets isolated from the CD Cotton effects of starting materials, the signs of which were in agreement with the absolute configurations of these two natural products. These O-acylating chromophores should be useful for determinations of absolute configurations and conformations of chiral substrates, including biopolymers; they could also be conveniently used in conjunction with the red-shifted chromophores developed recently for primary amino groups.

Introduction

The CD exciton chirality method is a versatile tool for determining the absolute configuration and/or conformation of molecules in solution.[1] The interactions between excited states of chromophores exhibit typical split CD Cotton effects, the signs of which are defined in a nonempirical manner by the chirality of the chromophores and an additivity relation.[1,2] Interpretations of the split CD curves are straightforward, the method being particularly useful when a sample is only available in submilligram quantities. However, the absorption maxima at 230–310 nm of the commonly introduced chromophores[1,2] frequently overlap with those of the substrates or of biopolymers, including nucleic acids and proteins. Unless one specifically utilizes the coupling between an existing chromophore and the introduced chromophore, the overlap of maxima leads to unnecessary complications in the interpretation of the data. Thus, availability of red-shifted chromophores that can be readily introduced into substrates should contribute greatly to further applications of the exciton chirality method.

Some red-shifted chromophores have already been made. We previously used the *p*-(dimethylamino)cinnamate chromophore (chrom-I, Figure 1), λ_{max} 362, ϵ 31 000, to study the absolute configuration of mitomycin C derivative, mitosene.[3] The chromophores were introduced by O,N-bisacylation of the substrate; however, the absorption maximum is not as red-shifted or as intense as those described below, and partial overlap with the substrate chromophore was still observed. We also studied the biscyanine derivative, which gave extremely strong UV and CD absorptions in the 480–550-nm region; however, the chromophore, although of great theoretical interest, is unstable and gave rise to split CD curves of signs opposite to those expected from the exciton chirality method.[4] Lightner recently reported that dipyrrinone carboxylic acid chromophores reacted with 1(*R*),2-(*R*)-cyclohexanediol to form the corresponding diester, which shows intense bisignate CD around 380 nm.[5]

For primary amino functions we have recently developed several red-shifted Schiff base and protonated Schiff base chromophores which are suited for selective microscale derivatizations and exhibit superior exciton chirality properties.[6] In this article we describe the preparations, spectral properties, and applications of four new red-shifted chromophores, chrom-II to -V (Figure 1), λ_{max} 360–410 nm, which can be used for microscale O- and probably N-derivatizations. Spectroscopic data for the bischromophoric derivatives of 1(*R*),2(*R*)-cyclohexanediol (**1**) are also given in Figure 1. To demonstrate the advantage of the red-shifted chromophores, derivatives of the natural products taxinine (**2**) and chromomycin A_3 (**3**), both with strong UV absorptions, were derivatized directly with one of the new chromophores, upon which exciton-split CD couplets separated from the substrate CD bands were obtained (Figures 4 and 5).

Synthesis of Red-Shifted Chromophores

Since chromophoric interactions in exciton coupling are *approximately* linearly proportional to the absorption coefficients of the chromophores,[1,7] we designed and synthesized a series of aromatic polyene chromophores (Figure 1, chrom-II to -V) having intense absorptions (ϵ 31 000–58 000) in the region 360–410 nm. Chrom-I is commercially available, while chrom-II was obtained by condensation of *p*-(dimethylamino)cinnamaldehyde (**5**) with triethyl phosphonoacetate (Scheme I). Scheme II outlines the

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(2) (a) Wiesler, W. T.; Vazquez, J. T.; Nakanishi, K. *J. Am. Chem. Soc.* **1987**, *109*, 5586–5592. (b) Wiesler, W. T.; Berova, N.; Ojika, M.; Meyers, H. V.; Chang, M.; Zhou, P.; Lo, L.-C.; Niwa, M.; Takeda, R.; Nakanishi, K. *Helv. Chim. Acta* **1990**, *73*, 509–551.

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(4) (a) Gargiulo, D.; Derguini, F.; Berova, N.; Nakanishi, K.; Harada, N. *J. Am. Chem. Soc.* **1991**, *113*, 7046–7047. (b) Berova, N.; Gargiulo, D.; Derguini, F.; Nakanishi, K.; Harada, N. *J. Am. Chem. Soc.* **1993**, *115*, 4769–4775.

(5) (a) Byun, S. Y.; Lightner, D. A. *Tetrahedron* **1991**, *47*, 9759–9772. (b) Byun, Y. S.; Lightner, D. A. *J. Org. Chem.* **1991**, *56*, 6027–6033.

(6) Gargiulo, D.; Cai, G.; Ikemoto, N.; Bozhkova, N.; Odingo, J.; Berova, N.; Nakanishi, K. *Angew. Chem.* **1993**, *105*, 913–915.

(7) The amplitudes of split Cotton effects are in fact proportional to the square of chromophoric ϵ's: Heyn, M. P. *J. Phys. Chem.* **1975**, *79*, 2424–2426.

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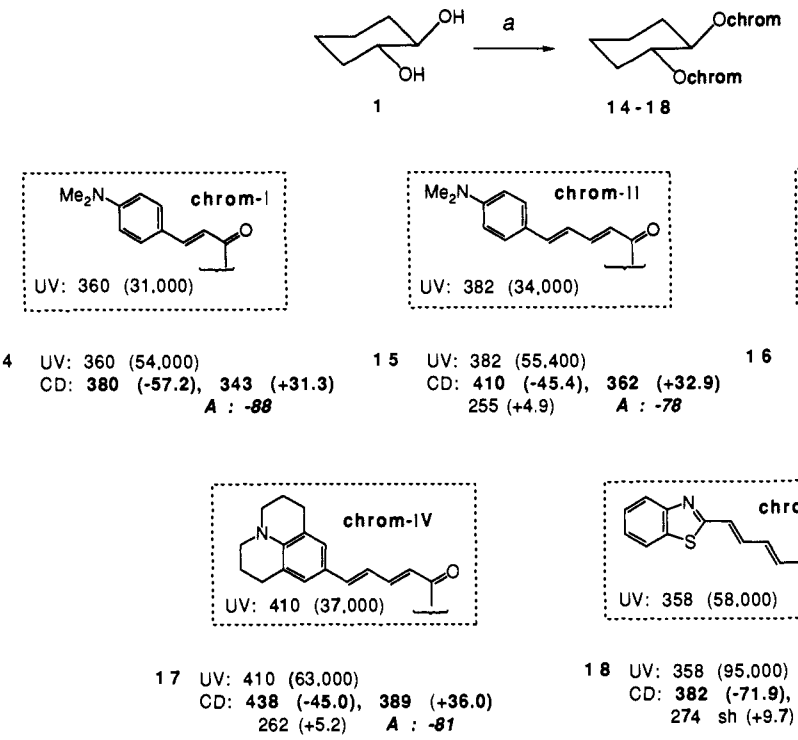
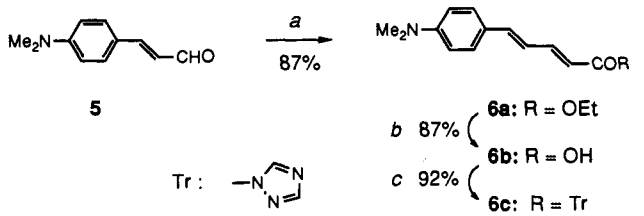


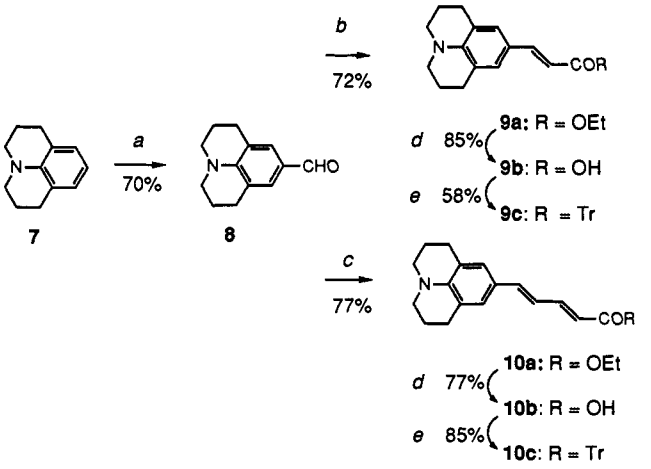
Figure 1. The λ_{max} (ϵ) in acetonitrile of chromophores chrom-I to -V and UV/vis and CD data for diesters **14–18** in acetonitrile. The *A* values indicate the differences in $\Delta\epsilon$ of the split CD curves. A negative sign shows that the first and second Cotton effects at longer and shorter wavelengths have negative and positive signs, respectively. Reagents and conditions: (a) for **14**, **4c**, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), CH_2Cl_2; for **15**, **6c**, DBU, CH_2Cl_2; for **16**, **9c**, DBU, CH_2Cl_2; for **17**, **10c**, DBU, CH_2Cl_2; for **18**, **13c**, DBU, CH_2Cl_2.

Scheme I[a]



[a] Reagents and conditions: (a) $(EtO)_2POCH_2CO_2Et$, $LiN(TMS)_2$, THF, room temperature. (b) LiOH, MeOH/H_2O/DME, room temperature. (c) 1,1′-carbonyldi(1,2,4-triazole), CH_2Cl_2. Tr, triazolyl.

Scheme II[a]



[a] Reagents and conditions: (a) $POCl_3$, DMF, 80–100 °C. (b) $(EtO)_2POCH_2CO_2Et$, NaH, benzene, room temperature. (c) $(EtO)_2POCH_2CH{=}CHCO_2Et$, $LiN(TMS)_2$, THF, room temperature. (d) LiOH, MeOH/H_2O/DME, room temperature. (e) 1,1′-carbonyldi(1,2,4-triazole), CH_2Cl_2. Tr, triazolyl.

sequences by which the julolidine type chromophores chrom-III and -IV were synthesized in a similar fashion in satisfactory yields. Julolidinyl aldehyde (**8**) was prepared by the formylation of julolidine (**7**) with DMF and phosphorus oxychloride in 72% yield and was then reacted with triethyl phosphonoacetate to furnish chrom-III (**9a**). Similarly, treatment of **8** with triethyl *trans*-4-phosphono-2-butenoate led to chrom-IV (**10a**). Employment of conditions described for olefination of phosphonate **11**[8] with aldehyde **12**[9] yielded **13a**, containing benzothiazole chromophore chrom-V (Scheme III). In all cases, the chromophoric acylating agents (**4c**, **6c**, **9c**, **10c**, and **13c**) were prepared by hydrolysis of the esters to acids with lithium hydroxide in excellent yield; the acids were then converted to their triazole amides as activated acylating reagents[10] (Schemes I-III).

Chromophoric Derivatives of 1(R),2(R)-Cyclohexanediol

The red-shifted chromophores were first tested with 1(*R*),2(*R*)-cyclohexanediol (**1**). 1(*R*),2(*R*)-Cyclohexanediol bischromophoric derivatives (**14–18**) were prepared as shown in Figure 1. The chromophores were initially introduced by acylation of the substrate with chromophoric acid chloride[3] or in the presence of DCC,[11] but these procedures were found to be difficult to work with in microgram scale. A search for improved conditions showed that the derivatizations could be performed on a microscale using the more active imidazole or triazole amide as acylating reagents, the latter being the more reactive (Figure 1). For example, the reaction of 1(*R*),2(*R*)-cyclohexanediol (**1**) with 3-[4-(dimethylamino)phenyl]-2-propenyl triazole (reaction time, 4 h) was faster than that of **1** with 3-[4-(dimethylamino)phenyl]-2-propenyl imidazole (18 h). Thus, the bischromophoric derivatives (**14–18**) were best prepared by treatment of **1** with an excess amount of triazole amide in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 43–89% yields. The advantages of using triazole

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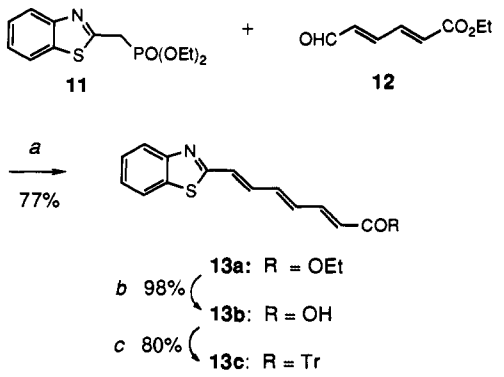
(10) Staab, H. A. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 351–367.
(11) Williams, A.; Ibrahim, I. T. *Chem. Rev.* **1981**, *81*, 589–636.

Scheme III[a]



[a] Reagents and conditions: (a) LiCl, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), CH_2Cl_2. (b) LiOH, $MeOH/H_2O/DME$, room temperature. (c) 1,1'-carbonyldi(1,2,4-triazole), CH_2Cl_2. Tr, triazolyl.

amides prepared in advance rather than *in situ* were that (i) the reactions can be conveniently performed on a microgram scale in high yield and (ii) the triazole amides can be stored and used whenever needed. In all cases, the bischromophoric derivatives of diol **1** with chrom-I to -V were also prepared on a 100–500-μg scale. In general, a small reaction vial was flame-dried and cooled under vacuum immediately prior to use. The reaction mixture of diol **1** and the triazole amide reagent was dried under vacuum for 2 h, and the solvent was added under argon. After concentration, the product was isolated through TLC and HPLC. If necessary, the yield was calculated from the UV/vis ϵ value. To avoid photoisomerization of the chromophore in the light, the reaction flasks were covered with aluminum foil, and the UV/vis and CD spectra were recorded immediately after preparation of the solution. It should be noted that, except for chrom-III, the UV and CD intensities of other chromophores are reduced from 40 to 60% when the dilute solutions used for measurements are left in the light for over 5 h. If for any reason experiments require the UV and CD solutions to be exposed to light for a long period, chrom-III should be employed, which according to sensitivity studies[12] was shown to be stable to light. The stability of chrom-III to light can be ascribed to the steric bulk of the julolidine moiety which disfavors the C=C double bond to adopt a cisoid structure.

UV and CD Spectral Data

The spectral properties of the diesters of 1(*R*),2(*R*)-cyclohexanediol (**14–18**) are listed in Figure 1. The exciton couplings of these bichromophoric derivatives give rise to bisignate CD curves with intense *A* values in the range −78 to −119 which correctly represent the absolute sense of twist between the two hydroxyl groups before derivatization.

Of the chromophores listed in Figure 1, *p*-(dimethylamino)-cinnamate (chrom-I)[3] is convenient in the sense that it is commercially available; however, it is the least red-shifted. Although milligram quantities of the substrate are required when its acid chloride is used, this can be scaled down to the microgram scale upon usage of the triazole amide. Extension of the conjugation by one double bond leading to chrom-II results in a 20–30-nm bathochromic shift; this chromophore has been used in derivatizing the taxinine and chromomycin derivatives. The julolidine type chromophores (chrom-III and -IV) are similar to the *N,N*-dimethylaniline type chromophores (chrom-I and -II). However, the nitrogen atom is more in-plane with the aromatic

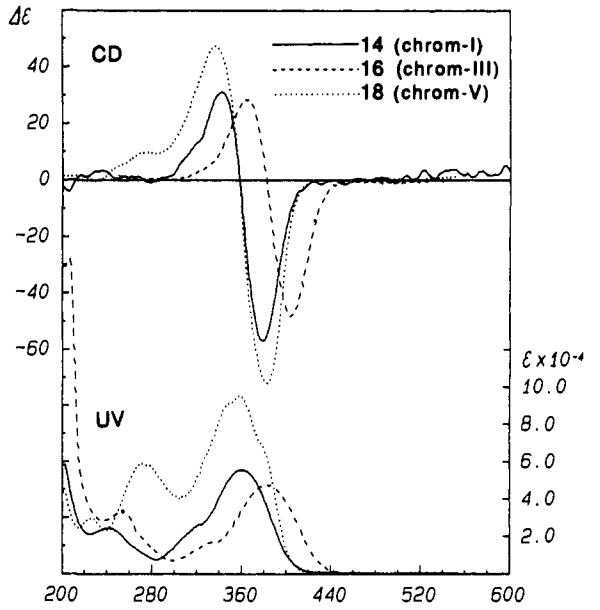


Figure 2. UV/vis and CD in acetonitrile of **14** (solid), **16** (dashed), and **18** (dotted).

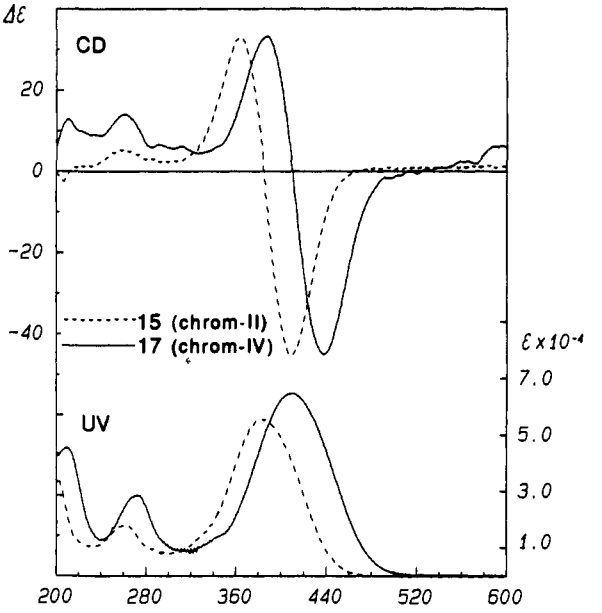


Figure 3. UV/vis and CD in acetonitrile of **15** (dashed) and **17** (solid).

ring in julolidine than in *N,N*-dimethylaniline,[13] and this increase in hybridization results in the bathochromic and hyperchromic shifts in the former type of chromophore. Thus, the λ_{max} positions of these two types of chromophores are in the order chrom-III > chrom-I (Figure 2) and chrom-IV > chrom-II (Figure 3), chrom-IV being the most red-shifted.

Benzothiazole chromophore (chrom-V) is another red-shifted chromophore with a strong CT band at 358 nm (ϵ 58 000).[14] As can be seen in Figure 2, the *A* value of diester **18** is the largest of the chromophores shown in Figure 1; since an approximately linear relation exists between the *A* value and the UV ϵ and since the *A* value is inversely proportional to the square of the

(12) Exposure to light of an NMR solution of bis(dimethylamino)cinnamate **14** for a long period, i.e., 24 h, led to partial double bond isomerization as evidenced by the appearance of cis coupling (J = 12.8 Hz) in addition to the trans coupling (J = 16.0 Hz) of the olefinic protons. The same isomerization was observed for the higher homologue **15** upon UV irradiation (see Experimental Section).

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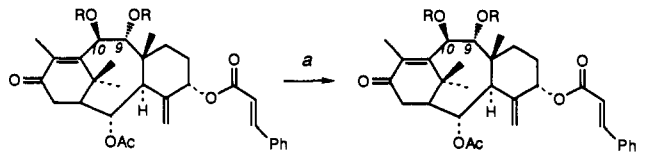
(14) Koning, H. D.; Mallo, G. N.; Springer-Fidder, A.; Subramanian-Erhart, K. E. C.; Huisman, H. O. *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 683–688.

Scheme IV[a]



2: R = Ac (Taxinine)
2a: R = H

22a: R = chrom-I
22b: R = chrom-II
22c: R = chrom-IV

[a] Reagents and conditions: (a) Reference 16. (b) For **22a**, **4c** (excess), DBU (excess), MeCN, 12 h; for **22b**, **6c** (excess), DBU (excess), MeCN, 24 h; for **22c**, **10c** (excess), DBU (excess), MeCN, 24 h.

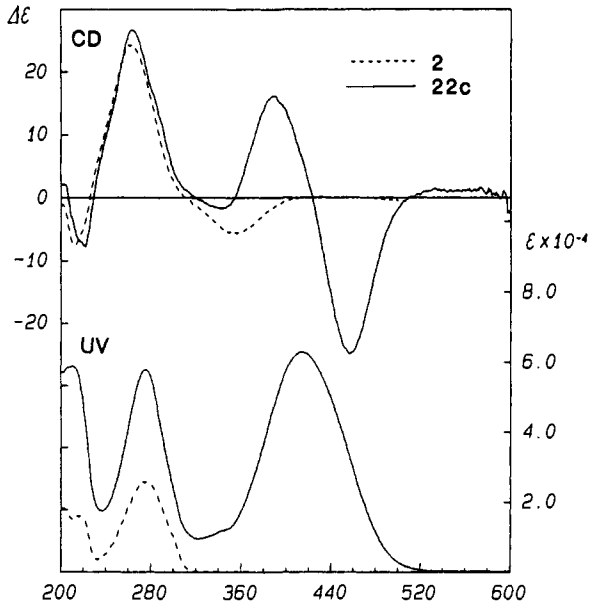


Figure 4. UV/vis and CD in acetonitrile of taxinine (**2**) (dashed) and bischromophoric derivative **22c** (solid).

interchromophoric distance, chromophores such as chrom-V could be useful in derivatizing hydroxyl groups which are remote.[1]

Application of Red-Shifted Chromophores to Taxinine and Chromomycin A_3

A demonstration of the utility of these red-shifted chromophores is provided by derivatives of taxinine (**2**) and chromomycin A_3 (**3**). Taxinine (**2**) (Scheme IV), the major component of the Japanese yew tree,[15] belongs to the taxoid group of diterpenes,[15] where taxol[16a] and taxotere[16b] are prominent members attracting great interest because of their antitumor activities. The highly strained enone moiety of taxinine shows a strong Cotton effect at 262 nm arising from a π–π^* transition, and a weaker Cotton effect at 354 nm from an n–π^* transition (Table I, Figure 4), the 262-nm Cotton effect overlapping with the bands of conventional chromophores. Chromomycin A_3 (**3**), which was previously used as a clinical antitumor antibiotic, contains a naphthalene moiety absorbing at 270 nm.[17] If one were to determine the absolute configuration by the exciton chirality method, again derivatization with a nonoverlapping red-shifted chromophore would lead to straightforward results.

Table I. UV/Vis and CD in Acetonitrile for Taxinine (**2**), Taxinine Derivatives (**22a–c**), and Isochromomycinone Derivatives (**3a**, **23a–d**)[a]

compd	UV: λ_{max} (ϵ)	CD: λ ($\Delta\epsilon$)	*A*
2	274 (26 000)	354 (–5.6), 262 (+24.4), 212 (–7.5)	
22a	364 (54 000)	388 (–29.2), 347 (+12.9), 268 (+20.9), 219 (–8.2)	–42
22b	382 (55 400)	418 (–25.8), 370 (+17.6), 271 (+30.0), 216 (–8.9)	–43
22c	413 (63 000)	455 (–24.9), 389 (+16.2), 341 (–1.7), 263 (+24.5), 218 (–1.7)	–41
3a	267 (54 000)	370 (–0.3), 335 (+0.8), 269 (–3.5), 223 (+4.5)	
23a	387 (34 000)	365 (–4.0), 323 (+1.5), 274 (–13.0), 256 (+21.0), 225 (+4.9)	
23b	392 (34 000)	387 (+1.6), 264 (–7.6), 223 (+7.3)	
23c	385 (55 400)	426 (+16.5), 357 (–8.5), 277 (–3.1), 225 (+3.7)	+25
23d	357 (53 600)	390 (+47.2), 334 (–24.6), 252 (+3.5), 230 (+3.5), 227 (–12.4), 209 (+4.8)	+72

[a] The *A* values indicate the differences in $\Delta\epsilon$ between the two extrema of the split CD curves. A negative sign shows that the first and second Cotton effects at longer and shorter wavelengths have negative and positive signs, respectively, and *vice versa*. For **2** and **3a**, only the main absorption bands before derivatization are given, whereas for the rest (**22** and **23**), the maxima of the introduced chromophores are given.

In order to determine the absolute configuration of the taxane skeleton, the exciton chirality method was applied to 9,10-desacetyltetrahydrotaxinine by converting the 9,10-glycol moiety into the bis(benzoate).[18] However, interpretation of the CD data was not necessarily straightforward because of the interaction between the enone of the substrate (λ_{max} 274 nm) and benzoate chromophores (λ_{max} 230 nm); a conclusion from the CD interpretation was subsequently confirmed by X-ray crystallography.[19] To obtain the bischromophoric derivatives of taxinine (**22a–c**), 9,10-dihydroxy taxinine **2a** was first prepared by hydrolysis of taxinine (**2**),[20] and then acylated with red-shifted chromophores chrom-I (**22a**), -II (**22b**), and -IV (**22c**). Their UV and CD data are listed in Table I. All derivatizations were carried out on a microgram scale with triazole amide as the acylating agent in the presence of DBU. From the nonoverlapping negative CD coupling at the longer wavelengths, the stereochemistry at C-9 and C-10 of the diol can be unambiguously assigned as *R* (Figure 4), in agreement with previous results.

The absolute configuration of chromomycin A_3 was determined in 1979.[17b] Because of the difficulties in introducing two benzoate chromophores at C-1′ and C-2′ of a chromomycin derivative by conventional methods, the skeletal absolute configuration was determined by the exciton chirality method where the exciton coupling between the naphthalenoid absorption and a *p*-methoxybenzoate chromophore introduced at C-1′ of isochromomycinone derivative **3a**[21] (Scheme V) was interpreted. In the present case, it was possible to derivatize both C-1′ and C-2′ of **3a** with the triazole amides of chrom-II and chrom-V in microscale under very mild conditions. The UV and positively split CD curves, given in Table I and Figure 5, clearly show that the chirality between the 1′/2′ substituents is positive. The monoderivative **23a**, resulting from a short acylation period of **3a**, showed an

(15) (a) Lythgoe, B. In *The Alkaloids*; Manske, R. H. E., Ed.; Academic Press: New York, 1968; Vol. X, p 597. (b) *Natural Products Chemistry*; Nakanishi, K., Goto, T., Ito, S., Natori, S., Nozoe, S., Eds.; Kodansha: Tokyo/Academic Press: New York, 1974; Vol. 1, pp 281–284.

(16) (a) Wani, M. C.; Taylor, H. L.; Wall, M. E.; Coggon, P.; Mcphail, A. T. *J. Am. Chem. Soc.* **1971**, *93*, 2325–2327. (b) Lavelle, F.; Fizames, C.; Guéritte-Voegelein, G.; Guénard, D.; Potier, P. *Proc. Am. Assoc. Cancer Res.* **1989**, *30*, 2254.

(17) (a) Miyamoto, M.; Morita, K.; Kawamatsu, Y.; Noguchi, S.; Marumoto, R.; Sasai, M.; Nohara, A.; Hakadaira, Y.; Lin, Y. Y.; Nakanishi, K. *Tetrahedron* **1966**, *22*, 2761–2783. (b) See also: Thiem, J.; Meyer, B. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1331–1336.

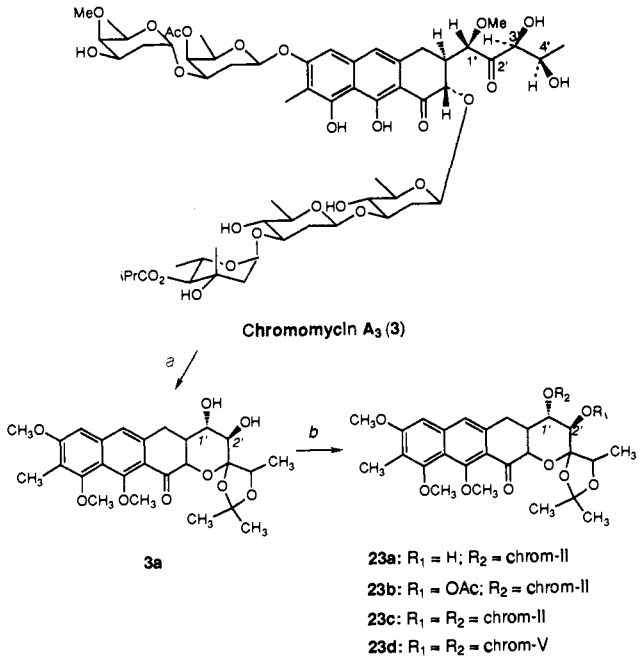
(18) (a) Harada, N.; Nakanishi, K. *J. Am. Chem. Soc.* **1969**, *91*, 3989–3991. (b) Reference 1, p 104.

(19) Shiro, M.; Koyama, H. *J. Chem. Soc. B* **1971**, 1342–1346.

(20) Harada, N. Ph.D. Thesis, Tohoku University, Sendai, 1969.

(21) (a) Harada, N.; Nakanishi, K.; Tatsuoka, S. *J. Am. Chem. Soc.* **1969**, *91*, 5896–5898. (b) Reference 1, pp 223–227.

Scheme V[a]



[a] Reagents and conditions: (a) Reference 17a. (b) For **23a**, **6c** (1 equiv), DBU, CH_2Cl_2, 0.5 h; for **22b**, **23a**, AcOH, 1,1′-carbonyldi(1,2,4-triazole), DBU; for **23c**, **6c** (excess), DBU (excess), CH_2Cl_2, 7 days; for **23d**, **13c** (excess), DBU (excess), CH_2Cl_2, 4 days.

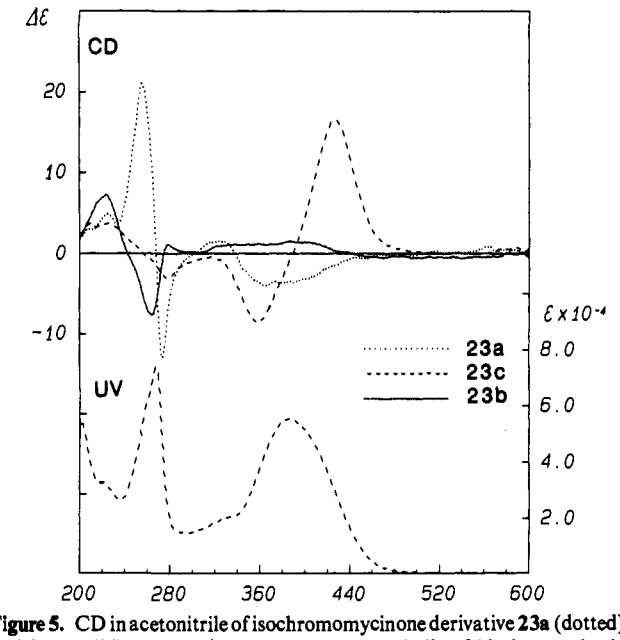


Figure 5. CD in acetonitrile of isochromomycinone derivative **23a** (dotted) and **23b** (solid) and UV/vis and CD in acetonitrile of bischromophoric isochromomycinone derivative **23c** (dashed).

unexpected CD couplet at 274 nm (−13) and 256 nm (+21) (Figure 5). This negative couplet at a position corresponding to the naphthalene ^1B_b band, λ_{max} 267 nm, could tentatively be assigned to an *intermolecular* coupling between two naphthalene rings due to strong hydrogen bonds involving the 2′-OH groups; upon further acetylation of 2′-OH, this characteristic couplet disappears (Figure 5). However, other interpretations are possible, and additional studies would be necessary to clarify the origin of this "couplet".

Conclusion

Intense bisignate CD curves are seen for bischromophoric esters of 1(*R*),2(*R*)-cyclohexanediol (**14–18**) with the red-shifted chromophores chrom-I-V in the region 360–410 nm. The derivatization can be performed on a microscale with chromophoric triazole amide as acylation agent. These chromophores have been introduced into the taxinine and chromomycin skeletons, both of which have strong absorptions which would interact with those of conventional chromophores used in the exciton chirality method; the red-shifted chromophores give clear-cut couplets unperturbed by the substrate absorptions, and thus lead to unambiguous assignment of absolute configurations. The chromophores described above should also prove to be useful when used in conjunction with the red-shifted chromophores recently developed for the microscale derivatization of primary amino groups.[6] Further applications of these chromophores in the field of biopolymers are under study.

Experimental Section

General Procedures. Solvents employed were reagent grade. Anhydrous solvents were dried and distilled (THF and benzene from Na/benzophenone; CH_2Cl_2 from CaH_2). Acetonitrile was dried over molecular sieves (4 Å). Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. Moisture-sensitive reactions were performed in flame-dried glassware under argon. Reactions were followed by thin-layer chromatography (TLC) using Analtech silica gel GHLF (250 nm thick).

Chromatography solvents were HPLC grade. Flash chromatography was performed using ICN silica gel (32-63 mesh). HPLC purifications were performed using a Rainin HPLC system equipped with a Rainin Dynamax Model UV-D detector.

^1H NMR spectra were obtained on a Varian VXR400, VXR300, or VXR200 and are reported in parts per million (δ) relative to $CHCl_3$ (7.24 ppm) as an internal reference, with coupling constants (*J*) reported in hertz (Hz). Low-resolution and high-resolution FAB mass spectra were measured on a JEOL JMS-DX303 HF mass spectrometer using glycerol matrix and Xe ionizing gas. CI mass spectra were measured on a NERMAG R10-10 spectrometer with CH_4 or NH_3 as ionizing gas. UV/vis and CD spectra were recorded as acetonitrile solutions on a Perkin-Elmer Lambda 4B UV/vis spectrophotometer and JASCO J-720 spectropolarimeter driven by a JASCO DP700N data processor, respectively. Smoothing and other manipulation of spectra were carried out with software developed in house: DFT (discrete Fourier transform) procedure for smoothing. The concentration of natural product derivatives (**22a–c** and **23a–d**) in acetonitrile used for the measurements of UV/vis and CD spectra was determined from the experimental ε value.

Representative Procedure for the Preparation of Chromophoric Triazole Amide (Method A): 1-[1-Oxo-3-[4-(dimethylamino)phenyl]-2-propenyl]-1*H*-1,2,4-triazole (4c). A solution of (dimethylamino)cinnamic acid **4** (500 mg, 2.6 mmol) and 1,1′-carbonyldi(1,2,4-triazole) (480 mg, 2.9 mmol) in CH_2Cl_2 (50 mL) and acetone (10 mL) was stirred at room temperature for 4 h. The solution was then washed with saturated aqueous $NaHCO_3$ (3 × 20 mL) and brine (20 mL) and dried (Na_2SO_4). The organic layer was concentrated under reduced pressure to give **4c** as a yellow solid (484 mg, 81%): ^1H NMR (400 MHz, $CDCl_3$) δ 3.08 (s, 6 H, $N(CH_3)_2$), 6.69 (d, *J* = 8.9 Hz, 2 H, Ar), 7.42 (d, *J* = 16.0 Hz, 1 H, H-2), 7.60 (d, *J* = 8.9 Hz, 2 H, Ar), 8.07 (d, *J* = 16.0 Hz, 1 H, H-3), 8.06 (s, 1 H, triazole), 9.01 (s, 1 H, triazole).

5-[4-(Dimethylamino)phenyl]-2,4-pentadienoic Acid, Ethyl Ester (6a).[22] To a solution of triethyl phosphonoacetate (1.012 g, 4.50 mmol) in anhydrous (9 mL) under argon was added dropwise a solution of lithium bis(trimethylsilyl)amide (4.32 mL, 1 M in THF) over 30 min at −78 °C. The mixture was stirred at this temperature for 1 h, and a solution of (dimethylamino)cinnamaldehyde (0.525 g, 3.00 mmol) in anhydrous THF (3 mL) was added. The reaction mixture was stirred at −78 °C under argon for *ca.* 4 h and was allowed to warm to room temperature. The reaction was quenched with acetic acid at *ca.* 0 °C adjusting to pH 7. The mixture was extracted with ether (3 × 20 mL), and the organic layers were combined, washed with brine, dried (Na_2SO_4), and purified by flash chromatography (silica gel, 20%–30% ethyl acetate/hexane) to afford the ester **6a** (0.638 g, 87%) as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, *J* = 7.2 Hz, 3 H, OEt), 2.99 (s, 6 H, $N(CH_3)_2$), 4.20 (q, *J* = 7.2 Hz, 2 H, OEt), 5.86 (d, *J* = 15.2 Hz, 1 H, H-2), 6.66 (d, *J* = 8.8 Hz, 2 H, *m*-Ar), 6.68 (dd, *J* = 11.2, 15.6 Hz, 1 H, H-4), 6.82 (d, *J* = 15.6 Hz, 1 H, H-5), 7.35 (d, *J* = 8.8 Hz, 2 H, *o*-Ar), 7.43 (dd, *J*

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= 11.2, 15.2 Hz, H-3); CI-MS (CH_4) m/z 246 (100) $(M + 1)^+$, 200 (12); FAB-HRMS for $C_{15}H_{19}NO_2$, calcd 245.1416, found 245.1408.

1-[1-Oxo-5-[4-(dimethylamino)phenyl]-2,4-pentadienyl]-1*H*-1,2,4-triazole (6c). Method A was used to prepare **6c** (92%) from the corresponding acid: ^1H NMR (400 MHz, $CDCl_3$) δ 3.03 (s, 6 H, $N(CH_3)_2$), 6.67 (d, J = 8.9 Hz, 2 H, *m*-Ar), 6.88 (dd, J = 11.3, 15.2 Hz, 1 H, H-4), 7.06 (d, J = 15.2 Hz, 1 H, H-5), 7.08 (d, J = 15.0 Hz, 1 H, H-2), 7.41 (d, J = 8.9 Hz, 2 H, *o*-Ar), 7.88 (dd, J = 11.3, 15.0 Hz, 1 H, H-3), 8.03 (s, 1 H, triazole), 8.97 (s, 1 H, triazole).

9-Formyl-2,3,6,7-tetrahydro-1*H*,5*H*-benzo[*ij*]quinolizine (8). Dry dimethylformamide (3.4 mL) was treated with $POCl_3$ (0.79 mL, 8.5 mmol) dropwise at 0 °C. A solution of 2,3,6,7-tetrahydro-1*H*,5*H*-benzo[*ij*]-quinolizine (julolidine) (**7**) (1.47 g, 8.5 mmol) in DMF (1.36 mL) was then added, and the resulting mixture was heated at 80–100 °C for 2 h. The solution was allowed to cool to room temperature and was poured into ice water. The solution was neutralized to pH 6–8 by addition of saturated sodium acetate. The desired aldehyde precipitated out of solution as a greenish-yellow solid. The solid was filtered, washed with water (25 mL) and hexanes (5 mL), and dried over P_2O_5 to afford pure aldehyde **8** (1.19 g, 70%): ^1H NMR (200 MHz, $CDCl_3$) δ 1.98 (m, 4 H, CH_2), 2.75 (t, J = 6.3 Hz, 4 H, CH_2Ar), 3.28 (t, J = 5.8 Hz, 4 H, CH_2N), 7.21 (s, 2 H, Ar), 9.60 (s, 1 H, CHO); CI-MS (CH_4) m/z 202 $(M + 1)^+$.

3-(2,3,6,7-Tetrahydro-1*H*,5*H*-benzo[*ij*]quinolizin-9-yl)-2-propenoic Acid, Ethyl Ester (9a). To a suspension of NaH (39.6 mg, 0.99 mmol) in benzene (4 mL) was added triethyl phosphonoacetate (0.2 mL, 0.99 mmol) dropwise at room temperature under argon. The cloudy mixture was stirred at room temperature until clear. A solution of aldehyde **8** (200 mg, 0.99 mmol) in benzene (2.0 mL) was then added dropwise and the mixture stirred for 16 h. The solution was filtered and concentrated under reduced pressure, and the residue was purified by flash chromatography (20% ethyl acetate/hexane) to afford the ester **9a** (193 mg, 72%) as a bright yellow solid: ^1H NMR (200 MHz, $CDCl_3$) δ 1.34 (t, J = 7.2 Hz, 3 H, OEt), 1.96 (m, 4 H, CH_2), 2.75 (t, J = 6.2 Hz, 4 H, CH_2Ar), 3.24 (t, J = 5.7 Hz, 4 H, CH_2N), 4.24 (q, J = 7.2 Hz, 2 H, OEt), 6.17 (d, J = 15.8 Hz, 1 H, H-2), 7.00 (s, 2 H, Ar), 7.55 (d, J = 15.8 Hz, 1 H, H-3).

Representative Procedure for the Conversion of Ester to Acid (Method B): 3-(2,3,6,7-Tetrahydro-1*H*,5*H*-benzo[*ij*]quinolizin-9-yl)-2-propenoic Acid (9b). A solution of ester **9a** (177 mg, 0.653 mmol) in MeOH (2 mL) and dimethyl ether (2 mL) was treated with a solution of lithium hydroxide (82.2 mg, 1.959 mmol) in water (1 mL). The solution was stirred at room temperature for 24 h, concentrated under reduced pressure, diluted with H_2O (3 mL), and extracted with ether (4 mL) to remove any remaining ester. The aqueous phase was adjusted to pH 5 with acetic acid and extracted with ether (3 × 10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to afford the acid **9b** (135 mg, 85%) as a bright yellow solid: ^1H NMR (200 MHz, $CDCl_3$) δ 1.93 (m, 4 H, CH_2), 2.70 (t, J = 6.4 Hz, 4 H, CH_2Ar), 3.19 (t, J = 5.8 Hz, 4 H, CH_2N), 6.09 (d, J = 15.6 Hz, 1 H, H-3), 6.96 (s, 2 H, Ar), 7.56 (d, J = 15.6 Hz, 1 H, H-3); EI-MS m/z 243 (M^+).

1-[1-Oxo-3-(2,3,6,7-tetrahydro-1*H*,5*H*-benzo[*ij*]quinolizin-9-yl)-2-propenyl]-1*H*-1,2,4-triazole (9c). Method A was used to prepare the reddish-orange triazole amide **9c** in 58% yield: ^1H NMR (200 MHz, $CDCl_3$) δ 1.97 (m, 4 H, CH_2), 2.76 (t, J = 5.9 Hz, 4 H, CH_2Ar), 3.29 (t, J = 5.1 Hz, 4 H, CH_2N), 7.18 (s, 2 H, Ar), 7.35 (d, J = 16.8 Hz, 1 H, H-2), 7.98 (d, J = 16.8 Hz, 1 H, H-3), 8.06 (s, 1 H, triazole), 9.01 (s, 1 H, triazole); EI-MS m/z 294 (M^+).

5-(2,3,6,7-Tetrahydro-1*H*,5*H*-benzo[*ij*]quinolizin-9-yl)-2,4-pentadienoic Acid, Ethyl Ester (10a). To a solution of triethyl *trans*-4-phosphono-2-butenoate (0.9 mL, 3.94 mmol) in THF (10 mL) at –70 °C under argon atmosphere was added lithium bis(trimethylsilyl)amide (3.94 mL, 1 M in THF), and the mixture was stirred at –70 to –40 °C for 1 h. A solution of aldehyde **8** (400 mg, 1.97 mmol) in THF (5 mL) was then added at –70 °C, and the resulting solution was allowed to warm to room temperature and was stirred for 24 h. The reaction was quenched with aqueous acetic acid (2 mL, 1.0 M) at 0 °C, and the cloudy mixture was stirred for 30 min at 0 °C. It was then extracted with ether (3 × 10 mL), and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography (20% ethyl acetate/hexane) to give the ester **10a** (448 mg, 77%) as an orange-yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 1.62 (t, J = 7.2 Hz, 3 H, OEt), 2.26 (m, 4 H, CH_2), 3.05 (dd, J = 6.4, 6.0 Hz, 4 H, CH_2Ar), 3.52 (dd, J = 5.2, 6.0 Hz, 4 H, CH_2N), 4.52 (q, J = 7.2 Hz, 2 H, OEt), 6.14 (d, J = 15.2 Hz, 1 H, H-2), 6.94 (dd, J = 15.2, 10.8 Hz, 1 H, H-4), 7.05 (d, J = 15.2 Hz, 1 H, H-5), 7.58 (s, 2 H, Ar), 7.74 (dd, J = 10.8, 15.2 Hz, 1 H, H-3).

5-(2,3,6,7-Tetrahydro-1*H*,5*H*-benzo[*ij*]quinolizin-9-yl)-2,4-pentadienoic Acid (10b). Method B provided 140 mg (77%) of acid **10b** as a red-orange solid: ^1H NMR (400 MHz, DMSO-d_6) δ 1.84 (dd, J = 5.4, 5.2 Hz, 4 H, CH_2), 2.65 (t, J = 6.0 Hz, 4 H, CH_2Ar), 3.15 (dd, J = 5.2, 5.8 Hz, 4 H, CH_2N), 5.77 (d, J = 15.0 Hz, 1 H, H-2), 6.73 (m, 2 H, H-4, H-5), 6.91 (s, 2 H, Ar), 7.24 (dd, J = 10.2, 15.0 Hz, 1 H, H-3).

1-[1-Oxo-5-(2,3,6,7-tetrahydro-1*H*,5*H*-benzo[*ij*]quinolizin-9-yl)-2,4-pentadienyl]-1*H*-1,2,4-triazole (10c). Method A provided triazole amide **10c** (85%) as a red-orange solid: ^1H NMR (400 MHz, $CDCl_3$) δ 1.96 (m, 4 H, CH_2), 2.75 (dd, J = 6.4 Hz, 4.0 H, CH_2Ar), 3.25 (t, J = 5.6 Hz, 4 H, CH_2N), 6.84 (dd, J = 11.2, 14.5 Hz, 1 H, H-4), 6.97 (d, J = 14.5 Hz, 1 H, H-2), 6.99 (s, 2 H, Ar), 7.03 (d, J = 14.5 Hz, 1 H, H-5), 7.88 (dd, J = 11.6, 14.5 Hz, 1 H, H-3), 8.05 (s, 1 H, triazole), 8.99 (s, 1 H, triazole); FAB-MS m/z 321 $(M + 1)^+$.

Diethyl (2-Benzothiazolylmethyl)phosphonate (11). To a solution of lithium diisopropylamide (35 mL, 2.0 M in heptane/THF/ethylbenzene) in THF (35 mL) was added a solution of 2-methylbenzothiazole (2.09 g, 14 mmol) in THF (20 mL) at –78 °C. After being stirred for 1 h under argon, the solution was warmed to 0 °C and quenched with saturated ammonium chloride. The mixture was poured into water, extracted with ether (3 × 20 mL), dried (Na_2SO_4), and concentrated under reduced pressure to afford the crude phosphonate as a yellow oil. The residue was purified by flash chromatography (1:1 ethyl acetate/hexane) to afford **11** (3.55 g, 89%) as a yellow solid: ^1H NMR (200 MHz, $CDCl_3$) δ 1.31 (t, J = 7.0 Hz, 6 H, CH_3), 3.68 (s, 1 H, CH_2), 3.79 (s, 1 H, CH_2), 4.15 (m, 4 H, OCH_2), 7.41 (m, 2 H, Ar), 7.84 (d, J = 8.0 Hz, 1 H, Ar), 8.00 (d, J = 8.0 Hz, 1 H, Ar); CI-MS (CH_4) m/z 286 (M^+).

7-(2-Benzothiazolyl)-2,4,6-heptatrienoic Acid, Ethyl Ester (13a).[14] To a solution of phosphonate **11** (500 mg, 1.75 mmol), LiCl (89 mg, 2.10 mmol), and DBU (287 μL, 1.92 mmol) in CH_2Cl_2 (20 mL) was added ethyl 6-oxo-2(*E*),4(*E*)-hexadienoate[9] (**12**) (324 mg, 2.1 mmol) dropwise under argon at room temperature. The reaction mixture was stirred at room temperature for 16 h, quenched with H_2O (25 mL), and extracted with CH_2Cl_2 (3 × 25 mL). The combined extracts were dried ($MgSO_4$), concentrated under reduced pressure, and purified by flash chromatography (10–20% ethyl acetate/hexane) to afford **13a** (385 mg, 77%) as an orange solid: ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (t, J = 7.1 Hz, 3 H, OEt), 4.23 (q, J = 7.1 Hz, 2 H, OEt), 6.01 (d, $J_{2,3}$ = 15.0 Hz, 1 H, H-2), 6.61 (dd, $J_{3,4}$ = 10.8, $J_{4,5}$ = 15.0 Hz, 1 H, H-4), 6.75 (dd, $J_{5,6}$ = 10.8, $J_{4,5}$ = 15.0 Hz, 1 H, H-5), 6.99 (d, $J_{6,7}$ = 15.4 Hz, 1 H, H-7), 7.26 (dd, $J_{5,6}$ = 10.8, $J_{6,7}$ = 15.4 Hz, 1 H, H-6), 7.35 (dd, $J_{2,3}$ = 15.0, $J_{3,4}$ = 10.8 Hz, 1 H, H-3), 7.44 (m, 2 H, Ar), 7.85 (d, J = 8.0 Hz, 1 H, Ar), 7.99 (d, J = 8.0 Hz, 1 H, Ar); CI-MS (NH_3) m/z 286 (M^+).

7-(2-Benzothiazolyl)-2,4,6-heptatrienoic Acid (13b). Method B provided acid **13b** (98%) as a yellow powder: ^1H NMR (200 MHz, acetone-d_6) δ 6.08 (d, J = 15.0 Hz, 1 H, H-2), 6.86 (dd, $J_{4,5}$ = 15.0, $J_{3,4}$ = 10.8 Hz, 1 H, H-4), 6.99 (dd, $J_{4,5}$ = 15.0, $J_{5,6}$ = 10.8 Hz, 1 H, H-5), 7.1 (d, J = 15.4 Hz, 1 H, H-7), 7.40 (m, 2 H, H-3, H-6), 7.5 (m, 2 H, Ar), 7.95 (d, J = 7.8 Hz, 1 H, Ar), 8.03 (d, J = 7.8 Hz, 1 H, Ar); CI-MS (NH_3) m/z 258 $(M + 1)^+$.

1-[1-Oxo-7-(2-benzothiazolyl)-2,4,6-heptatrienyl]-1*H*-1,2,4-triazole (13c). Method A provided pure triazole **13c** (80%) as a bright orange solid: ^1H NMR (300 MHz, $CDCl_3$) δ 6.80 (dd, $J_{4,5}$ = 15.0, $J_{3,4}$ = 10.8 Hz, 1 H, H-4), 6.97 (dd, $J_{4,5}$ = 15.0, $J_{5,6}$ = 10.8 Hz, 1 H, H-5), 7.11 (d, J = 15.1 Hz, 1 H, H-7), 7.30 (m, 2 H, H-2, H-6), 7.47 (m, 2 H, Ar), 7.81 (dd, $J_{2,3}$ = 15.3, $J_{3,4}$ = 10.8 Hz, 1 H, H-3), 7.86 (d, J = 7.4 Hz, 1 H, Ar), 8.02 (d, J = 8.0 Hz, 1 H, Ar), 8.07 (s, 1 H, triazole), 9.00 (s, 1 H, triazole); CI-MS (CH_4) m/z 309 $(M + 1)^+$.

1(*R*),2(*R*)-*trans*-Cyclobexanediol Bis[3-[4-(dimethylamino)phenyl]-2-propenoate] (14). To a solution of 1(*R*),2(*R*)-*trans*-cyclohexanediol (3.0 mg, 0.026 mmol) and *p*-(dimethylamino)cinnamoyl triazole (22 mg, 0.1 mmol) in CH_2Cl_2 (2 mL) was added a solution of DBU (*ca.* 0.04 mL, 0.01 M in CH_2Cl_2). The solution was then stirred at room temperature for 6 h, and it was then concentrated under reduced pressure. The product was isolated by preparative TLC (silica gel, 33% ethyl acetate/hexane) to give **14** (10.1 mg, 84%) as a yellow solid: ^1H NMR ($CDCl_3$) δ 1.75 (m, 2 H, cyclohexyl), 2.98 (s, 12 H, $N(CH_3)_2$), 4.97 (t, J = 4.2 Hz, 2 H, cyclohexyl), 6.14 (d, J = 16.0 Hz, 2 H), 6.61 (d, J = 8.9 Hz, 4 H), 7.36 (d, J = 8.9 Hz, 4 H), 7.55 (d, J = 16.0 Hz, 2 H); FAB-MS 462 (M^+); FAB-HRMS for $C_{28}H_{34}N_2O_4$, calcd 462.2519, found, 462.2514.

Diesters of cyclohexanediol (**15–18**) were prepared from 1(*R*),2(*R*)-*trans*-cyclohexanediol (**1**) using the corresponding chromophoric triazole amides (**6c–13c**) following the general procedure given for diester **14**.

1(*R*),2(*R*)-*trans*-Cyclobexanediol Bis[5-[4-(dimethylamino)phenyl]-2,4-pentadienoate] (15) (88%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (m, 4 H, cyclohexyl), 1.73 (m, 2 H, cyclohexyl), 2.09 (m, 2 H, cyclohexyl), 2.97 (s, 12 H, $N(CH_3)_2$), 4.94 (m, 2 H, cyclohexyl), 5.81 (d, J = 15.1 Hz, 2 H, H-2), 6.62 (d, J = 8.7 Hz, 4 H, *m*-Ar), 6.63 (dd, J = 11.0, 15.5 Hz, 2 H, H-4), 6.79 (d, J = 15.5 Hz, 2 H, H-5), 7.31 (d, J = 8.7 Hz, 4 H, *o*-Ar), 7.38 (dd, J = 11.0, 15.1 Hz, 2 H, H-3); CI-MS (NH_3) m/z 515 (M + 1)$^+$; FAB-HRMS (for $C_{32}H_{38}N_2O_4$, calcd 514.2832, found 514.2867.

1(*R*),2(*R*)-*trans*-Cyclohexanediol Bis[3-(2,3,6,7-tetrahydro-1*H*,5*H*-benzo[*ij*]quinolizin-9-yl)-2-propenoate] (16) (60%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (m, 4 H), 1.26 (m, 4 H), 1.60 (m, 8 H), 1.93 (m, 8 H, CH_2), 2.70 (t, J = 6.4 Hz, 8 H, CH_2Ar), 3.20 (t, J = 5.6 Hz, 8 H, CH_2N), 5.00 (m, 2 H, cyclohexyl), 6.10 (d, J = 16.0 Hz, 2 H, H-2), 6.94 (s, 4 H, Ar), 7.49 (d, J = 16.0 Hz, 2 H, H-3); FAB-MS m/z 566 (M$^+$), FAB-HRMS m/z for $C_{36}H_{42}N_2O_4$, calcd 566.3145, found 566.3154.

1(*R*),2(*R*)-*trans*-Cyclohexanediol Bis[5-(2,3,6,7-tetrahydro-1*H*,5*H*-benzo[*ij*]quinolizin-9-yl)-2,4-pentadienoate] (17) (68%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (m, 4 H, cyclohexyl), 1.75 (m, 2 H, cyclohexyl), 1.95 (m, 8 H, CH_2 julolidine), 2.11 (m, 2 H, CH_2, cyclohexyl), 2.72 (t, J = 6.4 Hz, 8 H, CH_2Ar), 3.19 (t, J = 5.6 Hz, 8 H, CH_2N), 4.94 (m, 2 H, cyclohexyl), 5.78 (d, J = 15.4 Hz, 2 H, H-2), 6.59 (dd, J = 11.0, 15.4 Hz, 2 H, H-4), 6.71 (d, J = 15.4 Hz, 2 H, H-5), 6.90 (s, 4 H, Ar), 7.38 (dd, J = 11.0, 15.4 Hz, 2 H, H-3); CI-MS (CH_4) m/z 618 (M$^+$), 619 (M + 1)$^+$; FAB-HRMS m/z for $C_{40}H_{46}N_2O_4$, calcd 618.3458, found 618.3463.

1(*R*),2(*R*)-*trans*-Cyclohexanediol Bis[7-(2-benzothiazolyl)-2,4,6-heptatrienoate] (18) (43%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.43 (m, 4 H), 1.65 (m, 2 H), 2.10 (m, 2 H), 4.97 (m, 2 H), 5.96 (d, J = 15.4 Hz, 2 H, H-2), 6.50 (dd, $J_{4,5}$ = 14.8, $J_{3,4}$ = 10.6 Hz, 2 H, H-4), 6.75 (dd, $J_{4,5}$ = 14.7, $J_{5,6}$ = 10.0 Hz, 2 H, H-5), 6.98 (d, J = 15.2 Hz, 2 H, H-7), 7.27 (m, 4 H, H-3, H-6), 7.44 (m, 4 H, Ar), 7.82 (d, J = 7.8 Hz, 2 H, Ar), 7.97 (d, J = 7.8 Hz, 2 H, Ar); EI-MS m/z 595 (M$^+$); FAB-HRMS for $C_{34}H_{31}N_2O_4S_2$, calcd 595.1725, found 595.1729.

The following compounds were prepared on a microscale. The products were purified by HPLC and analyzed by MS, UV, and CD spectra.

Representative Procedure for the Preparation of Bischromophoric Derivatives of Dihydroxy Taxinine (22b). To a solution of dihydroxy taxinine (**2a**) (10 μg, 0.04 μmol) and triazole amide **6c** (0.5 mg, 2.2 μmol) in acetonitrile (0.5 mL) was added DBU (*ca.* 0.08 mL, 0.1 M in acetonitrile). The resulting mixture was stirred at room temperature overnight. It was then diluted with water (0.5 mL) and extracted with ether (3 × 0.5 mL), and the ether layers were combined, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was dissolved in methanol and passed through a column of aluminum oxide (basic) to remove the excess triazole amide **6c**. The product was purified by TLC (silica gel, 30% ethyl acetate/hexane) and HPLC (3-μm YMC silica gel, 40% ethyl acetate/hexane): CI-MS 921 (M + 1)$^+$; FAB-HRMS for $C_{57}H_{64}N_2O_9$, calcd 920.4612, found 920.4596.

Bischromophoric derivatives **22a** and **22c** were prepared from dihydroxy taxinine **2a** using the corresponding chromophoric triazole amides **4c** and **10c** following the general procedure given for **22b**.

22a: HPLC (3-μm YMC silica gel, 40% ethyl acetate/hexane); FAB-MS 869 (M$^+$); FAB-HRMS for $C_{53}H_{61}N_2O_9$, calcd 869.4377, found 869.4418.

22c: HPLC (3-μm YMC silica gel, 30% ethyl acetate/hexane); FAB-MS 1024 (M$^+$); FAB-HRMS for $C_{65}H_{72}N_2O_9$, calcd 1024.5240, found 1024.5270.

Isochromomycinone Monoderivative 23a. A solution of the isochromomycinone derivative **3a**[17a] (0.80 mg, 1.6 μmol), triazole amide **6c** (0.43 mg, 1.6 μmol), and DBU (0.3 mL 0.01 M solution in acetonitrile) in anhydrous acetonitrile was left to stand at room temperature in the dark for 30 min. TLC (1:1:2 ethyl acetate/dichloromethane/hexane) of the reaction mixture showed the presence of one main product and only traces of the starting material **3a**. The main product was isolated by preparative TLC (silica gel, 1:1:2 ethyl acetate/dichloromethane/hexane) and additionally purified by HPLC (5-μm YMC silica gel, 1:20:80 methanol/dichloromethane/hexane): CI-MS (NH_3) m/z 688 (100) (M + 1)$^+$; FAB-MS for $C_{39}H_{45}NO_{10}$, calcd 687.3043, found 687.3054.

Isochromomycinone Monoderivative 23b. A solution of acetic acid (1.0 mg, 0.017 mmol) and 1,1′-carbonyldi(1,2,4-triazole) (3.0 mg, 0.018 mmol) in anhydrous acetonitrile (0.5 mL) was stirred for 20 min at room temperature.[5a] A solution of the monoderivative **23a** (0.30 mg, 0.4 μmol) and DBU (0.4 mL from 0.01 M in acetonitrile) in anhydrous acetonitrile (0.5 mL) was then added. Molecular sieves (4 Å) were added, and the mixture was allowed to stand overnight in the dark at room temperature. After evaporation of the solvent, the main product of the reaction, less polar than the starting material, was isolated by preparative TLC (silica gel, 1:1:2 ethyl acetate/dichloromethane/hexane) and additionally purified by HPLC (5-μm YMC silica gel, 25% ethyl acetate/hexane): CI-MS (NH_3) m/z 730 (100) (M + 1)$^+$; FAB-HRMS for $C_{41}H_{74}NO_{11}$, calcd 729.3149, found 729.3163.

Isochromomycinone Bis Derivative 23c. A solution of **3a** (0.30 mg, 0.6 μmol), triazole amide **6c** (12.0 mg, 0.045 mmol), and DBU (10 drops, 0.1 M solution in acetonitrile) in anhydrous acetonitrile (1 mL) was stirred for 7 days at room temperature in the dark. After evaporation of the solvent, the product was purified by preparative TLC (silica gel, 1:1:2 ethyl acetate/dichloromethane/hexane) and by HPLC (5-μm YMC silica gel, 3% methanol/dichloromethane): CI-MS (NH_3) m/z 887 (100) (M + 1)$^+$; FAB-HRMS for $C_{52}H_{58}N_2O_{11}$, calcd 886.4041, found 886.4028.

Isochromomycinone Bis Derivative 23d. A solution of **3a** (0.1 mg, 0.2 μmol), triazole amide **6c** (1.0 mg, 3.75 μmol), and DBU (1 drop, 0.01 M solution in acetonitrile) in anhydrous acetonitrile (0.2 mL) was stirred for 4 days at room temperature in the dark. After evaporation of the solvent, the product was purified by preparative TLC (silica gel, 40% ethyl acetate/hexane) and by HPLC (3-μm YMC silica gel, 40% ethyl acetate/hexane): FAB-MS 967 (M$^+$); FAB-HRMS for $C_{54}H_{51}N_2O_{11}S_2$, calcd 967.2935, found 967.2964.

Irradiation of 15. A solution of **15** (3.00 mg, 0.006 mmol) in acetonitrile (3 mL) was irradiated for 40 min with 1000-W high-pressure mercury lamp behind a Pyrex glass. HPLC analysis (5-μm YMC silica gel, 4:3:20 ethyl acetate/dichloromethane/hexane) of the reaction mixture showed the presence of the starting material and two new products. The new products were separated from the starting material as a mixture by HPLC (the same conditions as above). The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of this mixture shows the presence of an isomer with a cis double bond between C-4 and C-5 (dd at 6.12 ppm, J = 11.0 Hz for H-4) as well as an isomer with a cis double bond between C-2 and C-3 (d at 5.53 ppm, J = 11.2 Hz for H-2).

Acknowledgment. We are grateful to Dr. P. Zhou for developing the CD/UV software. The studies were supported by NIH Grant 34509 (to K.N.) and NSF Grant INTG 90-15531 (to K.N. and N. Berova).