[1] J.-M. Lehn, *Supramolecular Chemistry: Concept and Perspectives*, VCH, Weinheim, **1995**.

[2] a) V. Balzani, F. Scandola, *Supramolecular Photochemistry*, Harwood, Chichester, **1991**; b) V. Balzani, A. Juris, M. Venturi, S. Campagna, S. Serroni, *Chem. Rev.* **1996**, *96*, 759 – 833.

[3] P. J. Stang, B. Olenyuk, *Acc. Chem. Res.* **1997**, *30*, 502 – 518.

[4] a) R. V. Slone, K. D. Benkstein, S. Bélanger, J. T. Hupp, I. A. Guzei, A. L. Rheingold, *Coord. Chem. Rev.* **1998**, *171*, 221 – 243; b) S. M. Woessner, J. B. Helms, J. F. Houlis, B. P. Sullivan, *Inorg. Chem.* **1999**, *38*, 4380 – 4381; c) M. Fujita, J. Yazaki, K. Ogura, *J. Am. Chem. Soc.* **1990**, *112*, 5645 – 5647.

[5] a) A. Harriman, R. Ziessel, *Chem. Commun.* **1996**, 1707 – 1716; b) V. Grosshenny, A. Harriman, M. Hissler, R. Ziessel, *J. Chem. Soc. Faraday Trans.* **1996**, *92*, 2223 – 2238.

[6] a) B. Hong, J. V. Ortega, *Angew. Chem.* **1998**, *110*, 2210 – 2214; *Angew. Chem. Int. Ed.* **1998**, *37*, 2131 – 2134; b) B. Hong, *Comments Inorg. Chem.* **1999**, *20*, 177 – 207; c) J. V. Ortega, B. Hong, S. Ghosal, J. C. Hemminger, B. Breedlove, C. P. Kubiak, *Inorg. Chem.* **1999**, *38*, 5102 – 5112; d) D. Xu, H. J. Murfee, W. E. van der Veer, B. Hong, *J. Organomet. Chem.* **2000**, *596*, 53 – 63.

[7] P. D. Beer, F. Szemes, V. Balzani, C. M. Salá, M. G. B. Drew, S. W. Dent, M. Maestri, *J. Am. Chem. Soc.* **1997**, *119*, 11 864 – 11 875.

[8] **4** is prepared by combining 'C_4P_2' and $[RuCl_2(bpy)_2]$ (1/2.2, with excess NH_4PF_6) in THF/ethylene glycol (2/1, 30 mL). After refluxing the mixture for 48 h, removing the THF, and adding the residue into saturated aqueous KPF_6 solution (50 mL), the yellow solid is collected by filtration (yield 85 %, after column chromatography using basic alumina and acetonitrile/toluene as eluent). Analysis of this complex by CV and SWV shows one metal-based redox peak at + 1.06 V. D. Xu, B. Hong, unpublished results.

[9] a) D. E. Richardson, H. Taube, *Inorg. Chem.* **1981**, *20*, 1278 – 1285; b) T. Ito, T. Hamaguchi, H, Nagino, T. Yamaguchi, J. Washington, C. P. Kubiak, *Science* **1997**, *277*, 660 – 663.

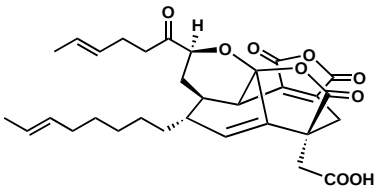
[10] a) C. Creutz, *Prog. Inorg. Chem.* **1983**, *30*, 1 – 73; b) M. B. Robin, P. Day, *Adv. Inorg. Chem. Radiochem.* **1967**, *10*, 247 – 270.

[11] a) V. Balzani, S. Campagna, G. Denti, A. Juris, S. Serroni, M. Venturi, *Acc. Chem. Res.* **1998**, *31*, 26 – 34; b) G. D. Storrier, K. Takada, H. D. Abruña, *Langmuir* **1999**, *15*, 872 – 884.

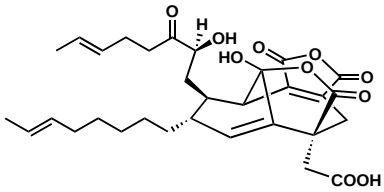
The Absolute Configuration and Asymmetric Total Synthesis of the CP Molecules (CP-263,114 and CP-225,917, Phomoidrides B and A)**

K. C. Nicolaou,* Jae-Kyu Jung, Won Hyung Yoon, Yun He, Yong-Li Zhong, and Phil S. Baran

The stunning molecular structures[1] coupled with the promising biological activities of the CP compounds (phomoidrides,[2] **1a** and **b**; Figure 1) have inspired numerous studies directed at their total synthesis.[3] In 1999 we reported the first total synthesis of these molecules in their racemic form.[4] Their absolute configuration, however, remained unknown despite the many attempts to prepare and analyze, through X-ray crystallography, a suitably crystalline derivative. After securing the overall structure and configuration at C7[5] of the CP molecules, admirably deduced by Kaneko and co-workers solely from NMR spectroscopic data, we were enticed by the challenge of establishing their absolute configuration. Such knowledge would provide an opportunity to explore modifications of our racemic synthesis and pave the way to optically active CP analogues and mimics, as well as guide future asymmetric total syntheses of these challenging target molecules. Here we report the absolute configuration of the CP molecules as unambiguously determined through chemical synthesis.



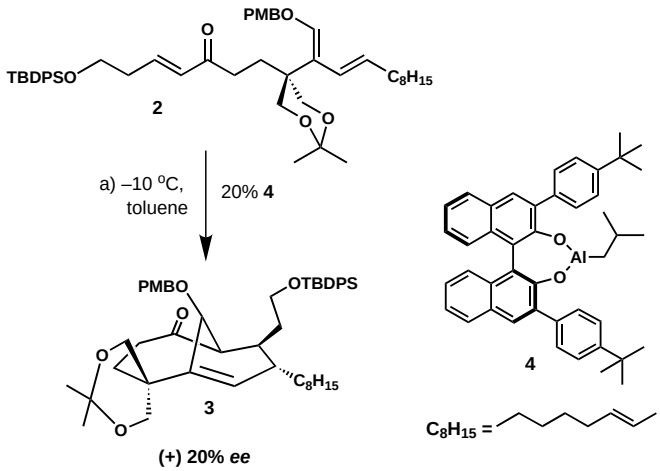
1a: (–)-CP-263,114 (phomoidride B)



1b: (+)-CP-225,917 (phomoidride A)

Figure 1. Absolute configuration of the CP compounds **1** and **2**.

Our reported total synthesis of the CP compounds[4] involved a type-II intramolecular Diels – Alder reaction[6] as a key step to generate the core skeleton of their molecules. Logic dictated that this step (Scheme 1), which converts the



Scheme 1. Enantioselective Diels – Alder reaction of prochiral triene **2** to form the known CP precursor **3** (20 % *ee*). PMB = *p*-methoxybenzyl; TBDPS = *tert*-butyldiphenylsilyl.

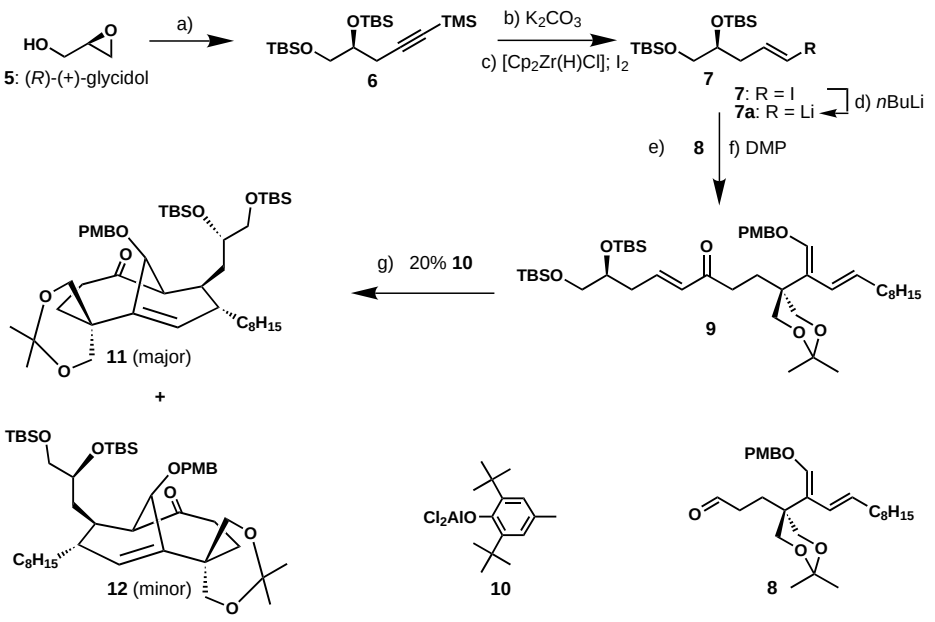
[*] Prof. Dr. K. C. Nicolaou, Dr. J.-K. Jung, W. H. Yoon, Y. He, Dr. Y.-L. Zhong, P. S. Baran
Department of Chemistry and
The Skaggs Institute for Chemical Biology
The Scripps Research Institute
10550 North Torrey Pines Road, La Jolla, CA 92037 (USA)
Fax: (+1) 858-784-2469
and
Department of Chemistry and Biochemistry
University of California San Diego
9500 Gilman Drive, La Jolla, CA 92093 (USA)
E-mail: kcn@scripps.edu

[**] We thank Drs. D. H. Huang, G. Siuzdak, and R. Chadha for assistance with NMR spectroscopy, mass spectrometry, and X-ray crystallography, respectively. This work was financially supported by the National Institutes of Health (USA), The Skaggs Institute for Chemical Biology, doctoral fellowships from the National Science Foundation (P.S.B.) and Boehringer Ingelheim (Y.H.), and grants from Array Biopharma, Boehringer Ingelheim, Schering Plough, Pfizer, Glaxo, Merck, Hoffmann-La Roche, DuPont, and Abbott Laboratories.

  0570-0833/00/3910-1829 $ 17.50+.50/0

prochiral triene **2** into the CP core **3**, would be a most appropriate stage for the introduction of asymmetry. Unfortunately, however, several reagent-based enantioselective approaches commencing with the known precursor **2**[4] failed to deliver appreciable levels of enantiocontrol. A study of this intramolecular process with a number of optically active catalysts led to Lewis acid **4**[7] as the optimum inducer of asymmetry, albeit delivering the CP core **3** in only 20% *ee*. We attributed the low levels of enantioselectivity in this reaction to the monodentate nature of the dienophile moiety and the flexibility of the aluminum–oxygen coordination bond of the initially formed complex between the substrate and the Lewis acid.

We then turned our attention to a strategy predicated on a substrate-based control of the diastereoselectivity of the intramolecular cycloaddition. Specifically, we envisaged modifying the triene **2** so as to introduce a bulky chiral moiety capable of influencing the facial selectivity of the intramolecular Diels–Alder reaction. Our goal was a smooth reentry into the previously chartered[4] path to the CP molecules to complete the asymmetric total synthesis without additional steps.

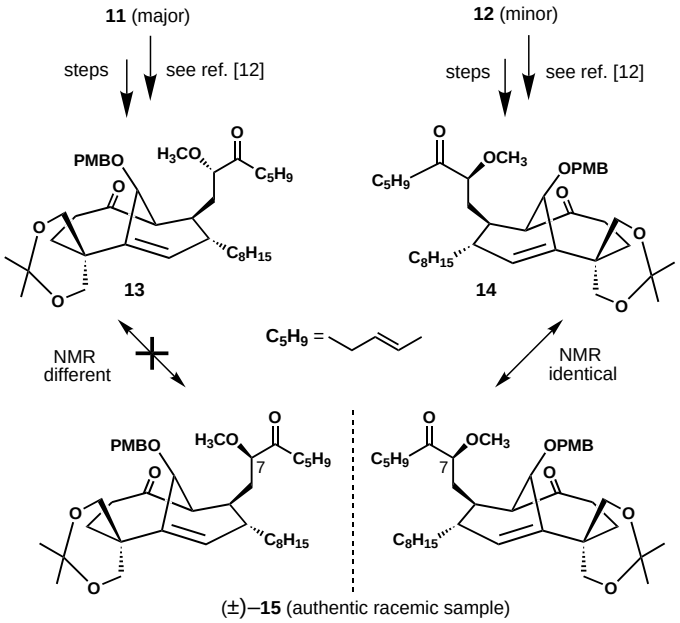


Scheme 2. Diastereoselective Diels–Alder reaction of triene **9** to form the CP precursors **11** and **12**. a) 1. TMSC≡CH (1.5 equiv), *n*BuLi (1.4 equiv), THF, −78 °C, added to a solution of (*R*)-glycidol (**5**; 1.0 equiv), *n*BuLi (1.1 equiv), THF, −78→25 °C, 12 h; 2. TBSOTf (3.0 equiv), 2,6-lutidine (1.0 equiv), 0→25 °C; b) K_2CO_3 (2.0 equiv), MeOH, 25 °C, 12 h; c) [$Cp_2Zr(H)Cl$] (1.2 equiv), benzene, 25 °C, then I_2 (1.0 equiv), CCl_4, 25 °C, 54% overall yield (from **5**); d) **7** (1.5 equiv), *n*BuLi (1.5 equiv), THF, −78 °C, 30 min; e) **7a** added to **8** in THF, −78 °C, 30 min, 90%; f) DMP (1.3 equiv), $NaHCO_3$ (5.0 equiv), CH_2Cl_2, 25 °C, 10 min, 70%; g) **10** (0.2 equiv), toluene, −80 °C, 1 h, 88% (**11**:**12** = 5.7:1). DMP = Dess–Martin periodinane; TBS = *tert*-butyldimethylsilyl; Tf = trifluoromethanesulfonyl; TMS = *tert*-butyltrimethylsilyl.

The construction of the designed asymmetric Diels–Alder precursor **9** is outlined in Scheme 2. Thus, the *R* enantiomer of glycidol (**5**) was arbitrarily chosen and converted, in one step (epoxide opening with TMS-acetylide, followed by quenching with TBSOTf) to the *tri*-silyl acetylene **6**. Selective removal of the pendant TMS group, followed by exposure to the Schwartz reagent [$Cp_2Zr(H)Cl$][8] and addition of I_2 led to the vinyl iodide **7** in 54% overall yield from **5**. Metal–halogen exchange (*n*BuLi) facilitated the union of the vinyl iodide **7** with the aldehyde **8**[4] furnishing, after oxidation with DMP,[9] enone **9** via the lithio derivative **7a**.

Initial Lewis acid induced cyclizations with **9** led to dissapointingly low diastereomeric excesses. For instance, exposure of **9** to 20 mol% Et_2AlCl in CH_2Cl_2 at −10 °C afforded **11** and **12** as a 2:1 mixture (Scheme 2). Extensive experimentation, whose details will have to await the full account of this work, led us to catalyst **10**[10] (Scheme 2). Thus, in the presence of 20 mol% of **10** at −80 °C in toluene, cycloaddition ensued to produce a 5.7:1 mixture (70% *de*) of **11** and **12** in 88% combined yield.

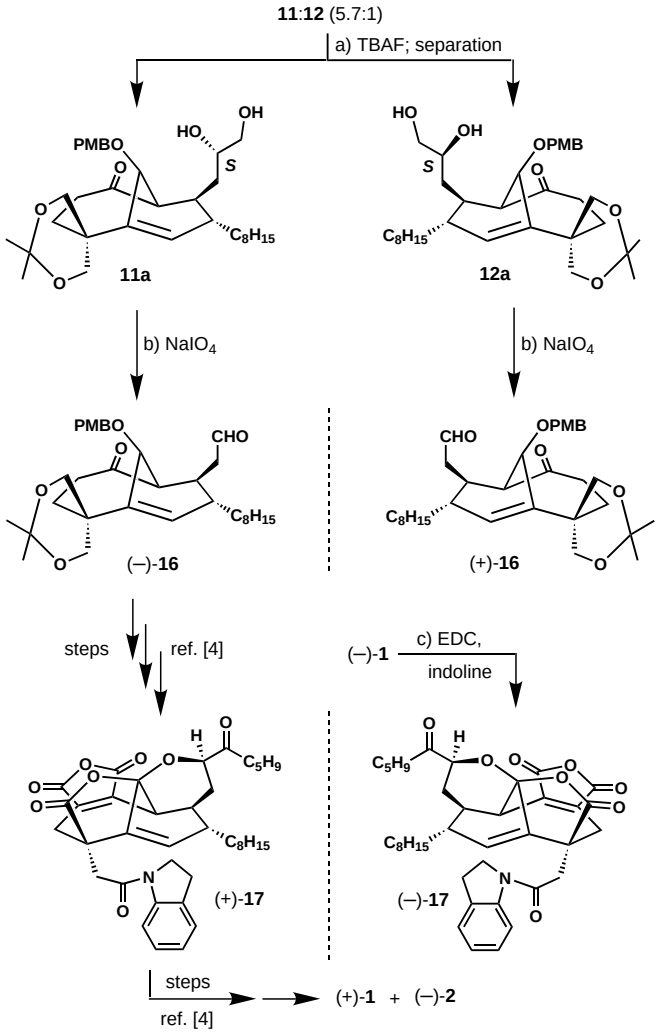
The relative configuration of these two diastereomers (**11** and **12**) was deduced by NMR correlation of downstream intermediates **13** and **14** with an authentic racemic sample **15**[11] (Scheme 3).[12]



Scheme 3. Determination of the relative configuration of intermediates **11** and **12** by NMR spectroscopic correlation with the authentic racemic sample **15** (relative configuration at C7 as depicted).

In preparation for reentry into the previously developed route for the synthesis of the CP compounds, **11** and **12** were converted to the enantiomeric aldehydes (−)-**16** and (+)-**16**, respectively, (Scheme 4). Desilylation with TBAF followed by flash column chromatography (silica gel, hexanes/EtOAc (2:1)) of the diol mixture **11a**/**12a** allowed almost complete separation of the two diastereomers **11a** (major) and **12a** (minor) (Table 1). Sodium periodate induced oxidative cleav-

  0570-0833/00/3910-1830 $ 17.50+.50/0 *Angew. Chem. Int. Ed.* **2000**, *39*, No. 10



Scheme 4. Unambiguous proof of the absolute configuration of the CP compounds (−)-**1** and (+)-**2** and of the indoline derivative (−)-**17** by asymmetric total synthesis of (+)-**17**, (+)-**1**, and (−)-**2** from intermediate **11**. a) TBAF (4.0 equiv), THF, 0 → 25 °C, 2 h, > 95 %; c) EDC (3.0 equiv), DMAP (3.0 equiv), indoline (1.5 equiv), CH_2Cl_2, 25 °C, 2.5 h; then 1N HCl, 25 °C, 5 min, 92 %. EDC = 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride; DMAP = 4-(dimethylamino)pyridine; TBAF = tetra-*n*-butylammonium fluoride.

age of diols **11a** and **12a** resulted in the formation of aldehydes (−)-**16** and (+)-**16**, respectively. Based on the diastereomeric enrichment of **11a** (ca. 15:1), the enantiomeric excess of (−)-**16** was calculated to be ca. 87 %.

The optically enriched aldehyde (−)-**16**, whose racemic form is a known intermediate in the total synthesis of racemic **1** and **2**, was then efficiently converted to the indoline (+)-**17** as previously described[4] (Scheme 4). Due to the ease of purification and handling and the amplified optical rotation of the indoline derivatives, we made comparisons at this stage, and therefore, the naturally derived indoline (−)-**17** was obtained by coupling **1**[13] with indoline in the presence of EDC (92 %). Synthetic **17**, derived from the major Diels–Alder product **11**, was found to be identical to natural **17** according to NMR spectroscopy, TLC (three different solvent systems), HPLC, and IR spectroscopy. The optical rotation, however, was opposite in magnitude ($[\alpha]_D^{23} = +56.2$; $c = 0.08$; CH_2Cl_2) to that of the naturally derived **17** ($[\alpha]_D^{23} = -80.0$; $c = 0.1$; CH_2Cl_2). Circular dichroism (CD) spectroscopy verified the identity of synthetic **17** as the enantiomer of natural **17** by virtue of the pronounced antipodal Cotton effect observed (Figure 2).[14] Synthetic **17** was also processed to give *ent*-**1** and *ent*-**2**. Therefore, the absolute configuration of the CP molecules can be confidently assigned as depicted in Figure 1. The asymmetric synthesis of *ent*-**1** and *ent*-**2** can obviously be employed to procure the natural enantiomers of the the CP molecules simply by utilizing (*S*)-glycidol.

Table 1. Selected physical and spectroscopic data of compounds **11a** and **12a**.

11a: $[\alpha]_D^{23} = -50.6$ ($c = 1.3$, $CHCl_3$); IR (neat): $\tilde{\nu} = 3388$, 2991, 2928, 2857, 1692, 1613, 1514, 1452, 1376, 1303, 1252, 1199, 1160, 1094, 1035, 968, 875, 840 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 7.19$ (d, $J = 8.8$ Hz, 2H), 6.85 (d, $J = 8.8$ Hz, 2H), 5.44–5.35 (m, 3H), 4.49 (d, $J = 11.0$ Hz, 1H), 4.37 (d, $J = 11.0$ Hz, 1H), 4.30 (dd, $J = 11.4$, 1.1 Hz, 1H), 4.14 (q, $J = 2.2$ Hz, 1H), 4.06 (d, $J = 11.8$ Hz, 1H), 4.02 (d, $J = 11.4$ Hz, 1H), 3.90–3.85 (m, 1H), 3.79 (s, 3H), 3.56 (dd, $J = 11.4$, 3.3 Hz, 1H), 3.51 (dd, $J = 11.4$, 1.5 Hz, 1H), 3.44 (dd, $J = 11.4$, 7.3 Hz, 1H), 3.03 (s, 1H), 2.81 (s, 1H), 2.59 (s, 1H), 2.39 (q, $J = 7.3$ Hz, 1H), 2.33 (t, $J = 13.2$ Hz, 1H), 2.21 (td, $J = 13.2$, 1.9 Hz, 1H), 2.02–1.93 (m, 3H), 1.69–1.54 (m, 6H), 1.43 (s, 3H), 1.39 (s, 3H), 1.48–1.11 (m, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 216.4$, 159.4, 142.3, 131.4, 129.7, 129.5, 129.4, 124.8, 114.0, 97.9, 77.3, 71.6, 69.4, 67.3, 67.1, 64.5, 58.3, 55.3, 41.9, 41.8, 40.6, 38.9, 36.4, 32.7, 32.6, 29.6, 29.3, 28.7, 27.9, 27.0, 20.5, 18.0; HR-MS (MALDI): calcd for $C_{34}H_{50}O_7Na^+$ [M+Na^+]: 593.3449, found: 593.3457

12a: $[\alpha]_D^{23} = +43.4$ ($c = 2.0$, $CHCl_3$); IR (neat): $\tilde{\nu} = 3413$, 2991, 2928, 2857, 1685, 1613, 1514, 1452, 1375, 1303, 1251, 1199, 1165, 1092, 1035, 968, 875, 839 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): $\delta = 7.20$ (d, $J = 8.4$ Hz, 2H), 6.87 (d, $J = 8.8$ Hz, 2H), 5.45–5.38 (m, 2H), 5.37–5.33 (m, 1H), 4.54 (d, $J = 11.0$ Hz, 1H), 4.36 (d, $J = 11.0$ Hz, 1H), 4.31 (dd, $J = 11.4$, 1.4 Hz, 1H), 4.13 (q, $J = 1.9$ Hz, 1H), 4.07 (d, $J = 11.8$ Hz, 1H), 4.03 (d, $J = 11.8$ Hz, 1H), 3.80 (s, 3H), 3.78–3.72 (m, 2H), 3.61–3.56 (m, 1H), 3.51 (dd, $J = 11.4$, 1.5 Hz, 1H), 3.46–3.40 (m, 1H), 3.30 (s, 1H), 2.43 (q, $J = 7.0$ Hz, 1H), 2.38 (t, $J = 13.6$ Hz, 1H), 2.24–2.18 (m, 2H), 2.03–1.94 (m, 3H), 1.71–1.52 (m, 6H), 1.43 (s, 3H), 1.40 (s, 3H), 1.48–1.13 (m, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 217.3$, 159.4, 142.3, 131.4, 129.6, 129.4, 128.7, 124.9, 114.0, 97.9, 77.1, 72.4, 71.5, 67.4, 66.5, 64.9, 58.5, 55.3, 45.2, 41.8, 40.6, 38.9, 37.0, 32.9, 32.6, 29.6, 29.3, 28.4, 27.9, 26.9, 20.6, 18.0; HR-MS (MALDI): calcd for $C_{34}H_{50}O_7Na^+$ [M+Na^+]: 593.3449, found: 593.3471

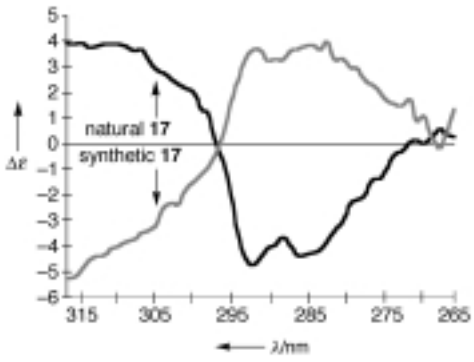


Figure 2. CD spectra (CH_2Cl_2, 25 °C, ca. 0.5 mM) of synthetic **17** (grey line) and natural **17** (black line).

Received: March 20, 2000 [Z 14868]

[1] T. T. Dabrah, T. Kaneko, W. Massefski, Jr., E. B. Whipple, *J. Am. Chem. Soc.* **1997**, *119*, 1594; T. T. Dabrah, H. J. Harwood, Jr., L. H. Huang, N. D. Jankovich, T. Kaneko, J.-C. Li, S. Lindsey, P. M. Moshier, T. A. Subashi, M. Therrien, P. C. Watts, *J. Antibiot.* **1997**, *50*, 1.

[2] D. Hepworth, *Chem. Ind. (London)* **2000**, *2*, 59.
[3] a) K. C. Nicolaou, M. W. Härter, L. Boulton, B. Jandeleit, *Angew. Chem.* **1997**, *109*, 1243; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1194; b) K. C. Nicolaou, M. H. D. Postema, N. D. Miller, G. Yang, *Angew. Chem*. **1997**, *109*, 2922; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2821; c) H. M. L. Davies, R. Calvo, G. Ahmed, *Tetrahedron Lett*. **1997**, *38*, 1737; d) P. W. M. Sgarbi, D. L. J. Clive, *Chem. Commun.* **1997**, 2157; e) A. Armstrong, T. J. Critchley, A. A. Mortlock, *Synlett* **1998**, 552; f) O. Kwon, D.-S. Su, D. Meng, W. Deng, D. C. D'Amico, S. J. Danishefsky, *Angew. Chem.* **1998**, *110*, 1978; *Angew. Chem. Int. Ed.* **1998**, *37*, 1877; g) O. Kwon, D.-S. Su, D. Meng, W. Deng, D. C. D'Amico, S. J. Danishefsky, *Angew. Chem.* **1998**, *110*, 1981; *Angew. Chem. Int. Ed.* **1998**, *37*, 1880; h) N. Waizumi, T. Itoh, T. Fukuyama, *Tetrahedron Lett.* **1998**, *39*, 6015; i) C. Chen, M. E. Layton, M. D. Shair, *J. Am. Chem. Soc.* **1998**, *120*, 10784; j) A. J. Frontier, S. J. Danishefsky, G. A. Koppel, D. Meng, *Tetrahedron* **1998**, *54*, 12721; k) M. M. Bio, J. L. Leighton, *J. Am. Chem. Soc.* **1999**, *121*, 890; l) K. C. Nicolaou, P. S. Baran, R. Jautelat, Y. He, K. C. Fong, H.-S. Choi, W. H. Yoon, Y.-L. Zhong, *Angew. Chem.* **1999**, *111*, 532; *Angew. Chem. Int. Ed.* **1999**, *38*, 549; m) D. L. J. Clive, S. Sun, X. He, J. Zhang, V. Gagliardini, *Tetrahedron Lett*. **1999**, *40*, 4605; n) D. Meng, S. J. Danishefsky, *Angew. Chem*. **1999**, *111*, 1582; *Angew. Chem. Int. Ed.* **1999**, *38*, 1485; o) T. Yoshimitsu, M. Yanagiya, H. Nagaoka, *Tetrahedron Lett.* **1999**, *40*, 5215; p) D. Meng, Q. Tan, S. J. Danishefsky, *Angew. Chem*. **1999**, *111*, 3393; *Angew. Chem. Int. Ed.* **1999**, *38*, 3197; q) G. A. Sulikowski, F. Agnelli, R. M. Corbett, *J. Org. Chem*. **2000**, *65*, 337; r) For biosynthetic explorations, see: P. Spencer, F. Agnelli, H. J. Williams, N. P. Keller, G. A. Sulikowski, *J. Am. Chem. Soc.* **2000**, *122*, 420; s) For reviews, see ref. [2] and U. Diederichsen, *Nachr. Chem. Tech. Lab.* **1999**, *47*, 1423 and E. M. Carreira, *Angew. Chem.* **2000**, *112*, 1473; *Angew. Chem. Int. Ed.* **2000**, *39*, 1415.
[4] Part 1: K. C. Nicolaou, P. S. Baran, Y.-L. Zhong, H.-S. Choi, W. H. Yoon, Y. He, K. C. Fong, *Angew. Chem*. **1999**, *111*, 1774; *Angew. Chem. Int. Ed.* **1999**, *38*, 1669; Part 2: K. C. Nicolaou, P. S. Baran, Y.-L. Zhong, K. C. Fong, Y. He, W. H. Yoon, H.-S. Choi, *Angew. Chem*. **1999**, *111*, 1781; *Angew. Chem. Int. Ed.* **1999**, *38*, 1676.
[5] A synthesis of an epimer of **1** at C7 has been reported by Danishefsky and coworkers, see ref. [3p].
[6] T. G. Lease, K. J. Shea, *J. Am. Chem. Soc.* **1993**, *115*, 2248.
[7] Catalyst **4** was prepared from the corresponding (*S*)-diol and Al(*i*Bu_3) (1.0 equiv, 1.0 M in hexanes) by stirring the two compounds in toluene at ambient temperature for 30 min. The diol was prepared according to the methods of K. B. Simonsen, K. V. Gothelf, K. A. Jørgensen, *J. Org. Chem.* **1998**, *63*, 7536 and P. Wipf and J.-K. Jung (see J.-K. Jung, Ph. D. Thesis, University of Pittsburgh, **1999**).
[8] J. Schwartz, J. Labinger, *Angew. Chem*. **1976**, *88*, 402 – 409; *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 333 – 340.
[9] a) D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155 – 4156; b) D. B. Dess, J. C. Martin, *J. Am. Chem. Soc.* **1991**, *113*, 7277 – 7278; c) S. D. Meyer, S. L. Schreiber, *J. Org. Chem.* **1994**, *59*, 7549 – 7552.
[10] Catalyst **10** was prepared by adding $EtAlCl_2$ (1 M in hexanes) to a solution of the corresponding phenol (1.1 equiv) in toluene at 0 °C and stirring the mixture at ambient temperature for 30 min.
[11] Racemic **15** was prepared from the corresponding α-hydroxy dithiane[4] by stirring with NaH (1.1 equiv) and MeI (1.1 equiv) at 0 °C (80 % yield) followed by dithiane deprotection with PhI(O-$COCF_3)_2$, in aqueous methanol (71 %).
[12] Compounds **13** and **14** were prepared from **11** and **12** in 29 and 22 % overall yield, respectively, by the following seven-step sequence: 1) TBAF (3.0 equiv), THF, 0 → 25 °C; 2) TBSCl (1 equiv), imidazole (1 equiv), CH_2Cl_2, 0 → 25 °C; 3) NaH (1.1 equiv), MeI (1.1 equiv), THF, 0 °C; 4) TBAF (1.5 equiv), THF, 25 °C; 5) DMP (1.2 equiv), CH_2Cl_2, 25 °C; 6) C_5H_9MgBr (1.1 equiv), THF, 0 °C; 7) DMP (1.2 equiv), CH_2Cl_2, 25 °C.
[13] A sample of natural **1** was kindly provided to us by Dr. T. Kaneko, Pfizer (Groton, CT).
[14] A similar effect was observed for (−)-**16** and (+)-**16**.

  0570-0833/00/3910-1832 $ 17.50+.50/0