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Supplementary Material Available: Table S1 listing atomic coordinates and vibrational parameters (1 page). Ordering information is given on any current masthead page.

Synthesis of *dl*-Coriolin

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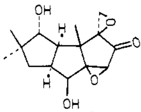
Interest in polycondensed cyclopentanoid natural products such as coriolin (**1**),[1a] hirsutic acid (**2**),[1b] hirsutene (**3**),[1c] and capnellane (**4**),[1d] among others, stems from their structural novelty and the antibacterial and/or antitumor activity that many possess.



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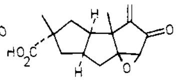

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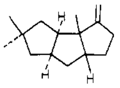

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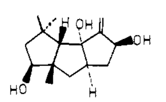
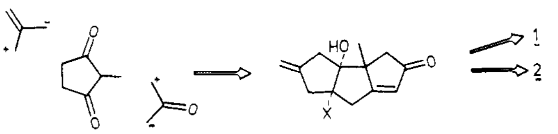


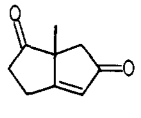
4

Although several elegant syntheses of hirsutane natural products have appeared, they are all targeted to a single member of this class from an early stage of synthesis.[2,3] We sought an approach which invoked a highly functionalized tricyclic intermediate that would provide flexibility of creating several members of this fascinating series of natural products and which would be available by two cyclopentane annulations (reaction 1)[4,5] via enedione **5**.[4,6]



(1)

In this communication, we wish to illustrate the first application of enedione **5** as a starting material in a synthesis of coriolin (**1**), the most complex member of the hirsutane class of natural products.



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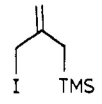

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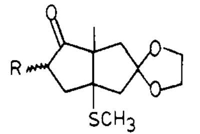
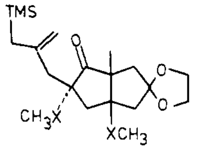
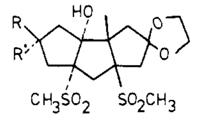


7 R=H
8 R=SCH_3

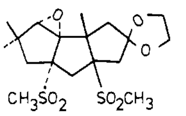
For the annulation of the third five-membered ring bearing appropriate functionality, we envisioned use of 2-(trimethylsilyl)methylallyl iodide (**6**)[7] as an electrophilic synthon for the 1,3-dipole, trimethylenemethane. While the kinetic enolate of enedione **5** reacted in reasonable yield with methylallyl iodide, it surprisingly gave unacceptable yields of alkylation product with **6**.[8] Assessing the poor results as due to the special reactivity of the strained enone, we converted the enone portion of **5** into a latent form by conjugate addition of methanethiol (catalytic $(C_2H_5)_3N$, 0 °C, CH_3OH, CH_2Cl_2, quantitative) and chemoselective ketalization to give **7**[9a,c] (0.95 equiv of $HOCH_2CH_2OH$, catalytic camphorsulfonic acid, PhH, Dean-Stark, 70% or 92% based upon recovered starting material).[10] A stereochemical anchor was introduced by clean monosulfenylation to **8**[9a,c] (2 equiv of KH, CH_3SSCH_3, DME, 40 °C, 79%). At this juncture, alkylation with **6** proceeded smoothly (KH, DME, room temperature) to give **9**[9] in 72% yield with the stereoselectivity estimated at >15:1.[11] The creation of the tricyclic nucleus was best performed by oxidation (4.0 equiv of MCPBA, CH_2Cl_2, aqueous $NaHCO_3$, room temperature, 63%) to the crystalline disulfone **10**[9,11b] (mp 116–117.5 °C) and fluoride-induced cyclization[5,12] [$(n\text{-}C_4H_9)_4NF$, THF, 50 °C, 87%] to give the key tricyclic intermediate **11**.[9,15] It is at this point that divergence into several families of compounds would appear feasible. For example, conversion of the methylene group into an α-methyl carboxylic acid should provide the structural change leading ultimately to hirsutic acid. Such a transformation has been previously used in hirsutic acid synthesis.[2]



9 X=S
10 X=SO_2



11 R,R'=CH_2
12 R=R'=CH_3



13

For coriolin, the geminal dimethyl group was efficiently introduced by cyclopropanation[13] [$(C_2H_5)_2Zn$, CH_2I_2, $PhCH_3$, catalytic O_2, 82%] followed by hydrogenolysis[14] (catalytic PtO_2, HOAc, NaOAc, 1 atm of H_2, 94%) to give **12**[9a,b,15] which results

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[1] (a) Takahashi, S.; Naganawa, H.; Iinuma, H.; Takita, T.; Maeda, K.; Umezawa, H. *Tetrahedron Lett.* **1971**, 1955. Nakamura, H.; Takita, T.; Umezawa, H.; Mamuru, K.; Yuga, N.; Iitaka, Y. *J. Antibiot.* **1974**, *27*, 301. (b) Comer, F. W.; McCapra, F.; Qureshi, I. H.; Scott, A. I. *Tetrahedron* **1967**, *23*, 4761. (c) Nozoe, S.; Furukawa, J.; Sankawa, U.; Shibata, S. *Tetrahedron Lett.* **1976**, 195. (d) Sheikh, Y. M.; Singy, G.; Kaisin, M.; Eggert, H.; Djerassi, C.; Tursch, B.; Dalzoe, D.; Braekman, J. C. *Tetrahedron* **1976**, *32*, 1172. Karlsson, R. *Acta Crystallogr., Sect. B* **1977**, *B33*, 1143. (e) Isocomene: Bohlmann, F.; LeVan, N.; Pickardt, J. *Chem. Ber.* **1977**, *110*, 3777. Zalkow, L. H.; Harris, R. N., III; VanDerveer, D.; Bertrand, J. A. *J. Chem. Soc., Chem. Commun.* **1977**, 456. Laurenene: Corbet, E. R.; Lauren, D. R.; Weavers, R. T. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1775. Modhephene: Zalkow, L. H.; Harris, R. N., III; VanDerveer, D. *J. Chem. Soc., Chem. Commun.* **1978**, 420.

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[3] (a) Tatsuta, K.; Akimoto, K.; Kinoshita, M. *J. Antibiot.* **1980**, *23*, 100. (b) Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1980**, *102*, 2097. Danishefsky, S.; Zamboni, R. *Tetrahedron Lett.* **1980**, 3439. Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3460. (c) Shibasaki, M.; Iseki, K.; Ikegami, S. *Tetrahedron Lett.* **1980**, 3587.

[4] Trost, B. M.; Curran, D. P. *J. Am. Chem. Soc.* **1980**, *102*, 5699.

[5] Trost, B. M.; Vincent, J. E. *J. Am. Chem. Soc.* **1980**, *102*, 5680.

[6] The absolute configuration of **5** produced with chiral phosphines has been determined. This, along with further asymmetric induction results, will be published shortly: Trost, B. M.; Curran, D. P. *Tetrahedron Lett.*, in press.

[7] Prepared by the action of sodium iodide (acetone) on the corresponding mesylate.[5]

[8] The source of this surprising difference in relative reactivity of **6** and methallyl iodide will be considered in detail in a forthcoming publication.

[9] (a) This compound has been characterized by IR and 270-MHz ^1H NMR spectroscopy. (b) This compound has been characterized by ^{13}C NMR spectroscopy. (c) Elemental composition has been established by high-resolution mass spectroscopy and/or combustion analysis.

[10] The byproducts were starting **6** and the diketal which was hydrolyzed (H_2O, $HClO_4$) to return **6** which could be easily recycled.

[11] (a) The use of the bis(phenylthio) compound gave greatly reduced stereoselectivities (2 or 3/1). (b) Selective oxidation of the bis(phenylthio) compound to the disulfone was not possible.

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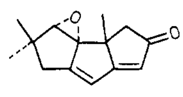
[14] Newham, J. *Chem. Rev.* **1963**, *63*, 127.

from selective cleavage of the least hindered bond of the cyclopropane. Elimination of water ($SOCl_2$, C_5H_5N, 0 °C, 92%) followed by epoxidation (MCPBA, CH_2Cl_2, room temperature, 87%) gave the crystalline epoxide **13**[9] (mp 189–189.5 °C dec) where the sulfone group at C(1) controls the stereochemistry of the epoxidation and subsequently of the hydroxyl group at C(9).

Deprotection of the epoxide **13** was accomplished by sequential acid (10% $HClO_4$, acetone, 35 °C) and base (DBU, CH_2Cl_2) treatment to give the unusual dienone **14**[9] in 91% yield. Hydrogenolysis of the allylic epoxide with sodium naphthalenide (DME, −45 °C) produces a mixture of olefin isomers after protonation which isomerize (catalytic DBU, CH_2Cl_2, room temperature, 52% overall yield) to a single crystalline dienone alcohol **15**[9,15] (mp 127–128 °C). The 11-Hz coupling constant between H(8) and H(9) supports the assigned stereochemistry.[3]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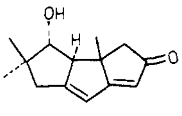
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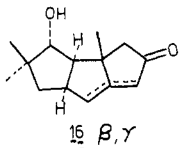
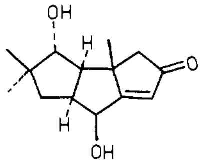
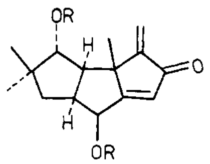

16 β,γ
17 α,β

The dienone **15** offers a splendid opportunity to introduce the remaining hydroxyl group since dissolving metal reduction and kinetic protonation will produce directly the β,γ-unsaturated enone **16** that is required. Indeed, lithium in liquid ammonia reduction followed by quenching into a pH 5.8 buffer gave an 80:20 ratio of **16** and **17**. Without manipulation, this mixture was chemoselectively epoxidized[16] (MCPBA, CH_2Cl_2) and the crude epoxide directly isomerized (DBU, CH_2Cl_2) to the allylic alcohol **18**,[9,15] mp 156–158 °C, in overall 63% yield and recovered α,β-enone **17** in overall 19% yield. The latter exhibited spectral properties identical with those of an authentic sample.[3c] Since **17** in principle can be deconjugated to reform **16** by a procedure similar to that employed in the other syntheses of coriolin,[3] this minor byproduct is also useful along the synthetic route. Crystalline diol **18**, available in 15 steps from enedione **5** in an overall yield of 5.3%, requires only α-methylenation and epoxidation to be converted into coriolin (**1**).


18


19 R = TMS
20 R = H

Formation of the kinetic enol silyl ether (LDA, THF–HMPA, then Me_3SiCl) of the bis(trimethylsilyl) ether of **18** (*O*,*N*-bis(trimethylsilyl)trifluoroacetamide, DMF, 40 °C) followed directly by reaction with dimethylmethyleneammonium iodide (Eschenmoser's salt)[17] in refluxing chloroform gave the corresponding Mannich base. Quaternization of the crude product (CH_3I, ether, room temperature) and elimination (DBU, CH_2Cl_2, room temperature) delivered the bis(trimethylsilyl) ether of the methylenated product **19** (46% overall yield from **18**). While standard desilylation methods tended to destroy the molecule, pyridine–polyhydrogen fluoride[18] in THF smoothly accomplished the final unmasking to give dienone **20** (>85% yield), the penultimate intermediate in all of the previous syntheses of coriolin and identical in all respects to an authentic sample.[19] The completion of the synthesis of **20** then constitutes a completion of the synthesis of coriolin since Danishefsky and his group successfully epoxidized **20** either in a one-step nonstereoselective or four-step stereoselective procedure to produce **1**.

The synthesis of coriolin clearly demonstrates the utility of the enedione **5** and methylenecyclopentane annulation in the total synthesis of polycondensed cyclopentanoid natural products. Its success provides impetus to convert the key tricycle **11** to other members of the family.

Acknowledgment. We thank the National Science Foundation and the National Cancer Institute of the National Institutes of Health for their generous financial support of our programs and the latter for a postdoctoral fellowship award to D.P.C. We thank Dr. S. Ikegami for spectral data for **18** and especially express our gratitude to Professor S. Danishefsky for not only providing comparison spectra but also a sample of **20** and a preprint of his full paper.

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(15) **11**: ^1H NMR ($CDCl_3$, 270 MHz) δ 1.54 (3 H, s), 1.75 (1 H, br d), 2.31 (1 H, br d), 2.53 (1 H, d), 2.63 (1 H, d), 2.8–3.2 (4 H, m), 2.93 (3 H, s), 3.06 (3 H, s), 3.34 (1 H, s, exchanges with D_2O), 3.39 (1 H, br d), 3.50 (1 H, br d), 3.90 (4 H, m), 4.94 (1 H, br s), 4.97 (1 H, br s); ^{13}C NMR ($CDCl_3$, 19 MHz) δ 146.5, 113.9, 107.8, 94.6, 78.3, 76.6, 64.1 (two carbons), 59.9, 48.9, 46.2, 45.4, 44.2, 40.4, 39.7, 39.0, 19.0; IR ($CHCl_3$) 3500 br, 1670 cm^{-1}, no carbonyl; MS, *m/e* calcd for $C_{17}H_{26}O_7S_2$ 406.1113; found 406.1120. Anal. Calcd for C, H. **12**: ^1H NMR ($CDCl_3$, 270 MHz) δ 1.19 (3 H, s), 1.33 (3 H, s), 1.52 (3 H, s), 1.5–3.0 (10 H, m), 3.00 (3 H, s), 3.08 (3 H, s), 3.64 (1 H, s, exchanges w/D_2O), 3.92 (4 H, m); ^{13}C NMR ($CDCl_3$, 50.1 MHz) 114.8, 98.5, 78.4; 76.7, 64.4, 64.2, 58.5, 52.7, 51.6, 47.7, 45.9, 43.5, 40.3, 39.5, 37.4, 32.0, 31.8, 20.4; IR ($CHCl_3$) 3500 cm^{-1} br. **15**: ^1H NMR ($CDCl_3$, 270 MHz) 1.07 (3 H, s), 1.17 (3 H, s), 1.24 (3 H, s), 2.13 (1 H, br s), 2.1–2.6 (4 H, m), 3.03 (1 H, br d, $J = 11$ Hz), 3.80 (1 H, d, $J = 11$ Hz), 5.61 (1 H, s), 6.15 (1 H, br d, $J = 2$ Hz); ^{13}C NMR ($CDCl_3$, 50.1 MHz), 210.0 (s), 197.1 (s), 167.9 (s), 117.2 (d), 115.4 (d) 76.9 (d), 64.1 (d), 55.1 (s), 49.8 (t), 44.7 (s), 40.0 (t), 27.8, (q) 24.9 (q), 22.5 (q); IR ($CHCl_3$) 3600, 3500 br, 1685, 1600 cm;$^{-1}$ MS, *m/e* calcd for $C_{14}H_{18}O_2$, 218.1302; found 218.1306. Anal. Calcd for $C_{14}H_{18}O_2$: C, H. **18**: ^1H NMR ($CDCl_3$, 270 MHz) δ 0.95 (3 H, s), 1.10 (3 H, s), 1.45 (3 H, s), 1.48 (1 H, dd, $J = 13$, 9 Hz), 1.85 (1 H, dd, $J = 13$, 10 Hz), 2.22 (1 H, dd, $J = 12$, 9 Hz), 2.38 (1 H, d, $J = 17$ Hz), 2.52 (1 H, d, $J = 17$ Hz), 2.73 (1 H, m), 3.81 (1 H, d, $J = 9$ Hz), 4.65 (1 H, d, $J = 6$ Hz), 5.84 (1 H, s); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 210.8 (s), 190.9 (s), 123.8 (d), 81.2 (d), 68.7 (d), 56.6 (d), 56.1 (t), 47.8 (s), 45.0 (d), 44.3 (s), 35.2 (t), 26.6 (q), 24.9 (q), 20.4 (q); IR ($CHCl_3$) 3600, 3500 br, 1708, 640 cm^{-1}; MS, *m/e* calcd for $C_{14}H_{20}O_3$, 236.1407; found 236.1412. Anal. Calcd for $C_{14}H_{20}O_3$: C, H.

(16) Enone **17** was not epoxidized under these conditions. See ref 3b,c.

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(19) Compound **20** was identical (analytical TLC, IR, 270-MHz NMR, MS) to a sample kindly provided by Professor S. Danishefsky.

Hopping and Delocalized Electrons in Class II Mixed-Valence Oxovanadates

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Mixed-valence compounds that can be described in terms of partially trapped discrete valence states (class II in the Robin–Day scheme[1]) attract considerable current interest in view of the insight they can provide for electron transfer and exchange processes.[2] Theoretical models[1,3] for mixed-valence compounds distinguish between "delocalized" and "trapped" descriptions, the former implying a ground-state or resonance averaging of valences and the latter implying the possibility of thermally activated intramolecular electron hopping. Although it has been presumed that all trapped valence state compounds are delocalized to some extent in order to account for the observation of intervalence charge transfer (IT) transitions in their optical spectra, the complexes reported here are the first examples of mixed-valence compounds

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(2) Meyer, T. J. "Mixed Valence Compounds"; Brown, D. B., ed.; D. Reidel Publishing Co.: Dordrecht, The Netherlands, 1980; p 75.

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