of PD 116 740 in this system is 4.1 min.

Isolation of PD 116 740. Filtered fermentation broth (12 L) of culture WP 4669 was passed over 500 mL of Diaion HP-20 resin packed in water. After washing with methanol-water (2:8, 1 L), PD 116 740 was eluted with methanol-water (1:1). The eluates containing most of the PD 116 740 were combined and concentrated to dryness to give 3.2 g of crude concentrate. The residue was dissolved in methanol, filtered, diluted with water, and chromatographed over 900 g of C-18 silica gel (20 μm, Analytichem International). Elution with 3.5 L of water-methanol (9:1), followed by 2.5 L of water-methanol (85:15) and 3 L of water-methanol (3:1), resulted in the concentration of 1 in the 25% methanol eluates. After concentration to dryness, the residue (1.15 g) was crystallized from methanol and recrystallized from methanol-acetone to yield crystalline 1 (560 mg) as red plates: mp >300 °C; $[\alpha]_D$ +311° (*c* 0.44, MeOH); λ_{max} (MeOH) 255 nm (ϵ 14 500), 289 nm (ϵ 10 800) and 409 nm (ϵ 6 300); λ_{max} (MeOH + NaOH) 238 nm (ϵ 22 300), 321 nm (ϵ 7 000), 341 nm (ϵ 5 900), 389 nm (ϵ 4 970), 541 nm (ϵ 2 800); ν_{max} (KBr) 1645, 1620, 1590, 1270, and 1030 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 3.91 (3 H, s, OCH_3), 4.30 (1 H, dd, *J* = 2.0, 2.0, H-5), 4.44 (2 H, d, *J* = 5.8, H-13), 4.87 (1 H, dd, *J* = 2.0, 2.0, H-6), 5.21 (3 H, m, 3 × OH, signal disappears upon addition of D_2O), 6.78 and 6.79 (1 H each, s, H-2 and H-4), 7.47 and 7.49 (each 1 H, d, *J* = 7.5, H-9 and H-11), 7.76 (1 H, dd, *J* = 7.5, 7.5, H-10) and 9.7 (1 H, br s, OH); ^{13}C NMR (CD_3OD) δ 54.7, 62.4, 62.6, 70.7, 113.6, 115.0, 117.0, 118.1, 118.5, 119.3, 134.2, 135.4, 138.3, 140.1, 140.8, 145.4, 155.3, 158.6, 182.2, 185.1.

Anal. Calcd for $C_{20}H_{16}O_7$·1.39CH_3OH: C, 62.38; H, 5.22. Found: C, 62.39; H, 5.09.

Preparation of PD 116 740 Tetraacetate. PD 116 740 (10 mg) was treated with acetic anhydride (0.25 mL) in pyridine (0.75 mL) at room temperature for 2.5 h. The residue obtained after removal of excess reagents in vacuo was crystallized as yellow needles from methanol to yield 11.5 mg of **3**: mp 210–13 °C; ν_{max} ($CHCl_3$) 1746, 1677, 1656, 1589, 1371, 1282, 1114, 1035 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.91 (3 H, s), 1.92 (3 H, s), 2.14 (3 H, s), 2.21 (3 H, s), 4.02 (3 H, s, OCH_3), 5.13 (2 H, s, H-13), 6.00 (1 H, d, *J* = 2.6, H-5), 6.33 (1 H, d, *J* = 2.6, H-6), 7.28 (1 H, br s, H-2 or H-4), 7.32 (1 H, dd, *J* = 2.0, 7.0, H-11), 7.48 (1 H, br s, H-2 or H-4), and 7.7 (2 H, m, H-9 and H-10).

Single-Crystal X-ray Diffraction Analysis of PD 116 740 (1). Suitable crystals, in the form of dark red retangular solids, could be grown by slow evaporation of methanol-acetone solutions. A crystal of approximate dimensions 0.7 × 0.5 × 0.2 mm was selected for the analysis. Preliminary X-ray photographs displayed monoclinic symmetry, and accurate lattice constants of a = 9.157 (1) Å, b = 7.243 (1) Å, c = 14.064 (2) Å, and β = 82.78 (1)° were determined from a least-squares fit of 15 diffractometer-measured 2θ values. The systematic extinctions, crystal density, and optical rotation were uniquely accommodated by space group $P2_1$ with one molecule of composition $C_{20}H_{16}O_7$·CH_3OH forming the asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer-controlled four-circle diffractometer using variable speed, 1° ω scans and graphite-monochromated Cu K$\bar{\alpha}$ radiation (1.54178 Å).

Of the 1357 reflections measured in this fashion, 1250 (92%) were judged observed ($|F_o| \geq 3\sigma(F_o)$) after correction for Lorentz, polarization, and background effects.[7] A phasing model, consisting of all of the non-hydrogen atoms, was found uneventfully using direct methods. Hydrogens were located on a difference synthesis following partial refinement. Block-diagonal, least-squares refinements with anisotropic non-hydrogen atoms and isotropic hydrogens have converged to a standard crystallographic residual of 0.048 (R_w = 0.060) for the observed reflections. Additional crystallographic details are available and are described in the paragraph entitled Supplementary Material Available at the end of this paper.

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Registry No. 1, 98015-54-4; 3, 98015-55-5.

Supplementary Material Available: Tables of fractional coordinates, thermal parameters, bond distances, and bond angles for PD 116 740 (4 pages). Ordering information is given on any current masthead page.

(7) All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were REDUCE and UNIQUE, data reduction programs by M. E. Leonowicz, Cornell University, 1978; MULTAN 78, MULTAN 80, and RANTAN 80, systems of computer programs for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses) written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1978 and 1980; DIRDIF written by P. T. Beurskens et al., University of Nijmegen, Netherlands, 1981; MITHRIL, an automatic solution package written by C. J. Gilmore, University of Glasgow, Scotland, 1983; BLS78A, an anisotropic block-diagonal least-squares refinement written by K. Hirotsu, and E. Arnold, Cornell University, 1980; PLUTO78, a crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978; and BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu, Cornell University, 1978.

Communications

Nitrones by Heterolytic Fragmentation of γ-*N*-Hydroxyamino Sulfonates. Conversion of a Decahydroquinoline to a Perhydroazaazulene

Summary: (*E,Z*)-1-Azacyclodeca-1,6-diene 1-oxide (**4**) was generated by fragmentation of 1-hydroxy-*cis,cis*-5-[(*p*-tolylsulfonyl)oxy]decahydroquinoline (**3a**) under basic conditions. The nitrone **4** underwent in situ intramolecular cycloaddition to a 1-aza-11-oxatricyclo[5.3.1.0^{2,6}]undecane (**5**), and it could be trapped with styrene in an intermolecular dipolar cycloaddition to give **6**. This concerted fragmentation reaction represents a useful nitrone synthesis.

Sir: Heterolytic fragmentation reactions have come to be accepted as valuable stereospecific processes in the synthesis of many compounds, including natural products.[1] Grob and co-workers have demonstrated that the synchronous fragmentation of γ-amino alcohol derivatives requires an extended, anti-periplanar relationship between the C_α–X bond, the C_β–C_γ bond which is undergoing cleavage, and the nitrogen lone pair electrons.[2] Among the many systems with which this postulate has been

(1) For a review, see: Deslongchamps, P. "Stereoelectronic Effects in Organic Chemistry"; Pergamon Press: Oxford, England, 1983; pp 257-274.

(2) Grob, C. A. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 535-546.

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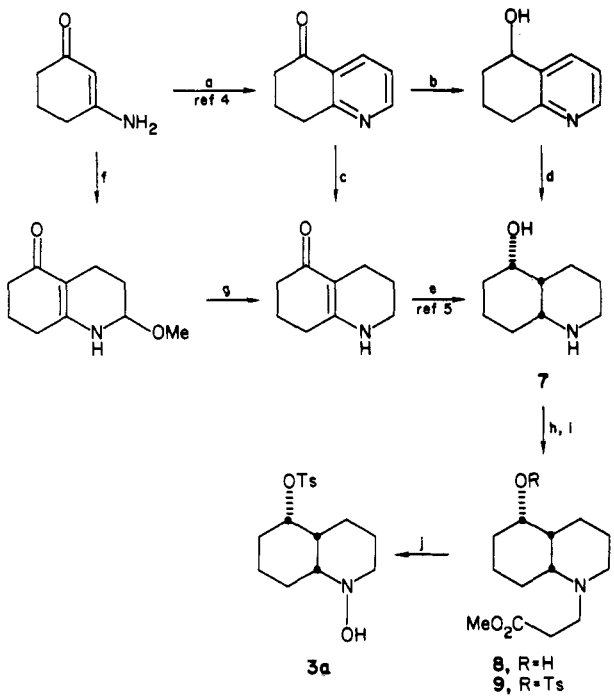
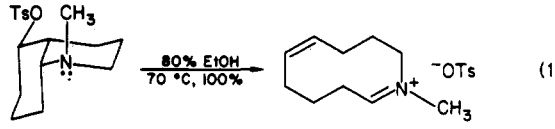
Scheme I. Synthesis of 3a[a]



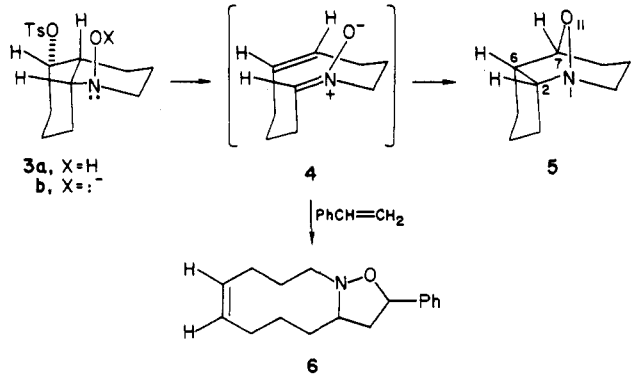
[a] (a) HC≡CCHO, DMF, 110 °C, 48%; (b) $NaBH_4$, MeOH, 94%; (c) H_2, PtO_2, HOAc, MeOH, 65 psig, 65%; (d) same as c, 36% recrystallized; (e) H_2, PtO_2, HOAc, 500 psig, 30% recrystallized; (f) CH=CHCHO, MeOH, 95%; (g) $NaBH_3CN$, pH 4, 93%; (h) CH_2=CHCOOCH$_3$, 95%; (i) TsCl, DMAP, CH_2Cl_2, 99%; (j) MCPBA, CH_2Cl_2, then 1 M NH_4OH, 84%.

tested is *N*-methyl-*cis*,*cis*-5-[(*p*-tolylsulfonyl)oxy]decahydroquinoline (1), which afforded the immonium salt **2** in quantitative yield upon solvolysis (eq 1).[3] We reasoned



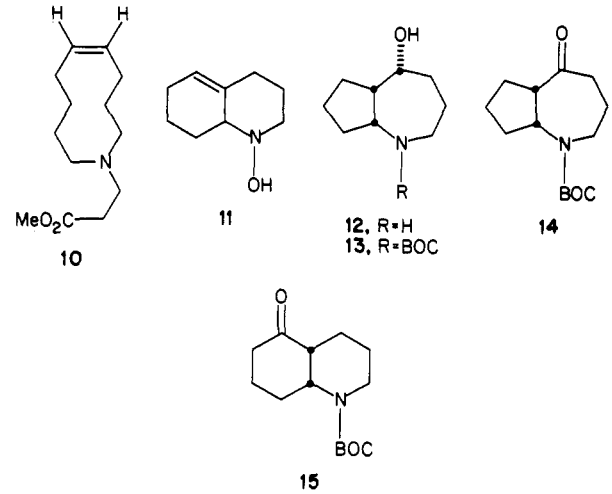
(1)

that a similar pathway applied to the *N*-hydroxy analogue **3** of **1** might afford the olefinic nitrone **4**, which could be trapped either by intramolecular cycloaddition to give isoxazolidine **5** or by external dipolarophiles to give adducts such as **6**. This report outlines our successful achievement of this strategy.



Although there are several reported routes to *cis*,*cis*-decahydroquinolin-5-ol (**7**),[4-7] we found it convenient to use the sequences outlined in Scheme I. Michael addition of **7** to methyl acrylate gave the tertiary amino alcohol **8**, which was tosylated to produce **9**. Oxidation with MCPBA followed by shaking with cold, 1 M ammonium hydroxide and flash chromatography gave **3a** in good yield.[8,9]

In order to verify the structure and stereochemistry of **9** (and, therefore, **7** and **8**), it was heated in 2,2,2-trifluoroethanol for 30 min to give the expected immonium salt by fragmentation. Sodium cyanoborohydride reduction led to the *cis*-olefinic γ-aminopropanoate **10** in 78% yield (from **9**). The ^{13}C NMR spectrum of **10** showed 13 carbon resonance lines with the olefinic carbons appearing at 132.3 and 128.4 ppm. The IR spectrum showed strong absorption at 690 cm^{-1} consistent with cis double bond stereochemistry.



When **3a** was refluxed in absolute ethanol for 8 h followed by flash chromatography, the *N*-hydroxy-$\Delta^{4a,5}$-octahydroquinoline **11** was isolated in 27% yield, together with minor amounts of ethyl ethers (detected by NMR). This result suggested that the *N*-hydroxyamino nitrogen was too weakly basic to participate in a concerted fragmentation and that a competing E_1 pathway dominated.

To increase the basicity we resorted to salt formation. Heating **3a** in tetrahydrofuran in the presence of sodium hydride and an excess of styrene for 24 h allowed isolation of the intermolecular cycloadduct **6** in 59% yield. Analytical and spectral data were fully consistent with structure **6**, and the IR spectrum has a strong absorption at 699 cm^{-1} (cis-CH=CH-). Apparently smooth fragmentation of **3a** to **4** took place via anion **3b**. We did not establish the stereochemistry of **6**, but we assume it has a trans orientation at C_{10} and C_{12} arising from an exo transition state with the *E* isomer of nitrone **4**.[10]

The predicted fragmentation–intramolecular cycloaddition was achieved by heating **3a** in refluxing tetrahydrofuran containing 1.05 equiv of potassium *tert*-butoxide for 24 h. The crude yield of **5** was 96%, and **5** was

(3) Grob, C. A.; Kiefer, H. R.; Lutz, H. J.; Wilkens, H. J. *Helv. Chim. Acta* **1967**, *50*, 416–431.

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(5) Grob, C. A.; Kiefer, H. R. *Helv. Chim. Acta* **1965**, *48*, 799–808.
(6) Johnson, R. A.; Murray, H. C.; Reineke, L. M.; Fonken, G. S. *J. Org. Chem.* **1968**, *33*, 3207–3217.
(7) Comins, D. L.; Abdullah A. H. *Tetrahedron Lett.* **1985**, *26*, 43–46.
(8) This sequence is a modification of a general method for preparation of *N*,*N*-dialkylhydroxylamines: Rogers, M. A. T. *J. Chem. Soc.* **1955**, 769–772.
(9) All new compounds gave 300-MHz ^1H NMR, 50-MHz ^{13}C NMR, IR, high-resolution mass spectrometry, and/or satisfactory C, H, N analyses consistent with the assigned structures.
(10) 300-MHz NMR indicated the presence of 6–8% of the C_{12} stereoisomer: ^1H NMR ($CDCl_3$) δ 7.3 (m, 5 H), 5.4 (m, 2 H), 4.9 (t, 1 H, *J* = 7.3 Hz), 3.3–2.3 (m, 5 H), 2.2–0.7 (10 H); ^{13}C NMR ($CDCl_3$) 131.7, 128.7, 128.3, 127.5, 126.7, 78.2, 65.6, 50.9, 40.0, 29.7, 26.2, 24.9, 24.7, 23.3, 22.5 ppm; **6**-HCl, mp 130–132 °C.

isolated as its hydrochloride in 84%. Pure **5** was a colorless liquid which showed the expected 9-line ^{13}C NMR spectrum.[11] High-resolution mass spectrometry confirmed the formula $C_9H_{15}NO$.

That **5** did indeed possess the rearranged perhydroazaazulene skeleton[12] was demonstrated by hydrogenolysis (Zn dust, 80% aqueous acetic acid, 70 °C, 77%, mp 128–130 °C) to amino alcohol **12**, which was different from the educt **7**. Protection of the amine with the *t*-BOC group (di-*tert*-butyl carbonate, THF, H_2O, NaOH, 75%), followed by oxidation (PDC, CH_2Cl_2, 99%, mp 47–48 °C) gave the protected amino ketone **14**. The IR spectrum of **14** showed the ketone C=O stretching frequency at 1700 cm^{-1}. A similar protection–oxidation sequence applied to **7** gave the amido ketone **15** (oil, 92% from **7**), which showed the ketone C=O stretch at 1715 cm^{-1}.

We have established that nitrones can be prepared by heterolytic fragmentation of γ-*N*-hydroxyamino sulfonates under basic conditions and that these can be transformed into useful intra- and intermolecular 1,3-dipolar cycloadducts. We are continuing our examination of other suitable systems.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work.

(11) A stereochemical designation of **5** is (2*RS*,6*SR*,7*SR*)-1-aza-11-oxatricyclo[5.3.1.$0^{2,6}$]undecane: ^1H NMR ($CDCl_3$) δ 4.18 (dt, H_7, J_1 = 11.3 Hz, J_2 = 8.5 Hz), 4.1 (br t, H_2, J = 5.5 Hz), 3.6 (m, $H_{10\beta}$), 3.15 (m, H_6), 3.0 (dd, $H_{10\alpha}$, J_1 and $J_2 \simeq$ 6–7 Hz), 2.25 (m, H_3), 2.15 (m, H_3), 2.05–1.6 (m, 7 H), 1.35 (m, $H_{9\alpha}$); ^{13}C NMR ($CDCl_3$) 75.5, 72.0, 53.4, 49.8, 32.1, 25.53, 25.48, 24.4, 15.6 ppm; **5**-HCl, mp 204–206 °C dec.

(12) An examination of molecular models indicates that intramolecular cycloaddition of **4** in the other regiosense, i.e., to give 1-aza-11-oxatricyclo[4.4.1.$0^{2,7}$]undecane, is sterically constrained.

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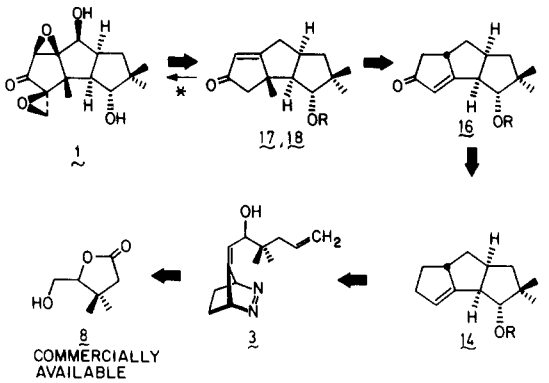
Intramolecular 1,3-Diyl Trapping Reactions. A Formal Total Synthesis of (±)-Coriolin

Summary: A formal total synthesis of racemic coriolin (**1**) from furanone **8** is described. An intramolecular 1,3-diyl trapping reaction served as the key step in the construction of the linearly fused tricyclopentanoid alcohol **14**.

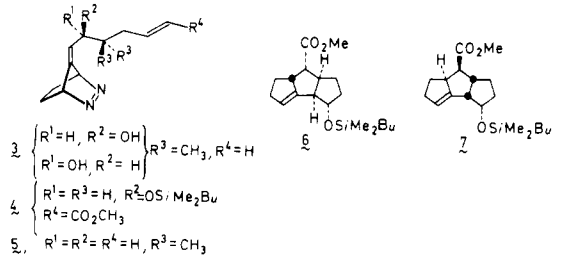
Sir: Coriolin (**1**) was first isolated in 1969 from fermentation broths of the Basidiomycete *Coriolus consors*.[2] By 1974, its structure had been firmly established through both chemical and X-ray crystallographic studies.[3] Attracted by reports of the antibiotic and antitumor activity of coriolin and diketocoriolin B (**2**), researchers have devised a number of elegant syntheses of coriolin, the first of which appeared in 1980.[4]

Scheme I. Retrosynthetic Analysis[a]



[a] * = convergent point.

We now report a stereo- and regiocontrolled formal total synthesis of coriolin which further illustrates the versatility and synthetic utility of the intramolecular 1,3-diyl trapping reaction (note Schemes I and II). The selection of diazene **3** rather than any of several reasonable alternative diyl precursors was guided by our knowledge of the following principles. First, the intramolecular diyl trapping reaction is stereoselective and favors the formation of cis,anti ring-fused tricyclopentanoids.[5] It is reasonable to assume that this preference will again be observed, thereby leading to the establishment of the proper relative stereochemistries at C_1, C_6, and C_8 (coriolin numbering).[6] Second, photodeazetation (at 7 °C) of optically active diazene **4**



leads to the *cis,anti*-tricyclopentanoids **6** and **7** in a ratio of 26:1,[7] thereby suggesting that deazetation of **3** should lead to a large preference for the formation of the required

(1) Senior Research Assistant of the National Fund for Scientific Research (Belgium).

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(6) The numbering system shown in structure **1** is used throughout.

(7) Stone, K. J.; Little, R. D. *J. Am. Chem. Soc.* **1985**, *107*, 2495.

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