a conjugated diene moiety (albeit part of a delocalized aromatic system in the case of 8) incorporated in a 4-carbon atom bridge, their behavior toward benzyne is quite different. Ketone **2** affords a 2 + 2 adduct, while hydrocarbon 8 yields a 4 + 2 adduct. The propensity of benzyne to give 2 + 2 cycloadducts with some conjugated dienes, notably 1,3-cycloheptadiene and 1,3,5-cycloheptatriene, is well documented.[7] In these cases the formation of 2 + 2 adducts has been attributed to deviation of the diene system from planarity, especially in the case of 1,3,5-cycloheptatriene, where no 4 + 2 cycloadduct is formed. The more rigid structures **2** and 8 possess essentially planar diene systems, and the failure of ketone **2** to provide any 4 + 2 cycloadduct is probably a consequence of an increased distance between C2 and C5 of the diene moiety in **2** relative to 8. The short span of the etheno bridge and the presence of the trigonal center at C9 in **2** imparts rigidity, which would maintain the original C2–C5 distance in the transition state of a hypothetical 4 + 2 cycloaddition with benzyne. In the case of 8 however, the C2–C5 distance is probably more suited to concerted 4 + 2 cycloaddition, particularly if the transition state possesses substantial bisnorcaradiene character, or if indeed 8 reacts via the bisnorcaradiene valence isomer.

The addition of benzyne **1** to **2** and 8 thus further illustrates the delicate balance that exists in the reaction of **1** with dienes: subtle structural differences in the diene can favor the 2 + 2 pathway with exclusion of the normal 4 + 2 addition mode.[8]

Experimental Section

NMR spectra were recorded with Bruker WP80 and Bruker AM300 instruments using $CDCl_3$ as solvent and TMS as internal standard. Mass spectra were obtained by using a Hewlett-Packard 5986 instrument, operating in the GC–MS mode. Benzenediazonium-2-carboxylate,[9] bicyclo[4.2.1]nona-2,4,7-trien-9-one,[10] and 1,6-methano[10]annulene[11] were prepared as described in the literature.

Addition of Benzyne to Bicyclo[4.2.1]nona-2,4,7-trien-9-one (2). Benzenediazonium-2-carboxylate derived from anthranilic acid (13.7 g, 0.1 mol) was decomposed during 2 h in a reluxing solution of ketone **2** (6.6 g, 0.05 mol) in 1,2-dichloroethane (120 mL). The solvent was evaporated, and the dark residue was chromatographed on neutral alumina (400 g). Elution with 5% ether–hexane gave unchanged **2** (2.45 g). Elution with 10% ether–hexane afforded 4b,5,8,10a-tetrahydro-5,8-methanobenzo-[3,4]cyclobuta[1,2]cycloocten-11-one (**3**) as a colorless solid (0.85 g, 8%), which crystallized from pentane as needles: mp 101–3 °C; MS, m/z 208 (M, 28), 207 (31), 180 (33), 179 (100), 178 (100), 176 (18), 166 (11), 165 (65), 152 (30), 151 (15), 128 (30), 115 (46), 102 (38), 89 (24), 76 (11); ^{13}C NMR (75.5 MHz, all d except where noted) δ 208.2 (s), 145.5 (s), 142.9 (s), 134.7, 131.0, 130.8, 128.0, 127.7, 124.8, 122.0, 121.0, 54.7, 52.5, 50.1, 48.1; ^1H NMR (300 MHz) δ 7.27–7.15 (m, 3 H, aryl), 7.02 (dd, J = 6.8, 1.0, 1 H, aryl), 6.29 (ddd, $J_{7,6}$ = 6.9, $J_{7,8}$ = 2.5, $J_{7,5}$ = 0.7, 1 H, H7), 6.24 (ddd, $J_{6,7}$ = 6.9, $J_{6,5}$ = 2.5, $J_{6,8}$ = 0.9, 1 H, H6), 5.95 (dd, $J_{10,9}$ = 11.0, $J_{10,10a}$ = 4.8, 1 H, H10), 5.82 (ddd, $J_{9,10}$ = 11.0, $J_{9,10a}$ = 2.0, $J_{9,8}$ = 8.9, 1 H, H9), 4.37 (ddd, $J_{10a,4b}$ = 4.8, $J_{10a,10}$ = 4.8, $J_{10a,9}$ = 2.0, 1 H, H10a), 3.95 (dd, $J_{4b,10a}$ = 4.8, $J_{4b,5}$ = 2.5, 1 H, H4b), 3.61 (ddd, $J_{5,4b}$ = 2.5, $J_{5,6}$ = 2.5, $J_{5,7}$ = 0.7, 1 H, H5), 3.33 (dd, $J_{8,9}$ = 8.9, $J_{8,7}$ = 2.5, 1 H, H8); ν_{max} ($CHCl_3$) 1770 cm^{-1}; λ_{max} (cyclohexane) 207 (log ϵ 4.48), 260 (3.51), 267 (3.66), 273 (3.66). Anal. Calcd for $C_{15}H_{12}O$: C, 86.51; H, 5.81. Found: C, 86.56; H, 5.95.

Photolysis of Ketone 3. A solution of **3** (300 mg) in deoxygenated 2-propanol (50 mL) was placed in a silica tube and irradiated for 12 h under a nitrogen atmosphere in a Rayonet photochemical reactor using 300-nm lamps. The solvent was evaporated, and the residue was filtered through a plug of alumina in pentane to remove polymeric material. Evaporation of the pentane gave 2,2a,5,9b-tetrahydro-1,2,5-metheno-1*H*-benzo[*a*]-cyclobuta[*c*]cycloheptene (**7**) as a colorless oil (170 mg, 65%). The GC trace in the GC–MS showed two peaks in the ratio 71:29, presumably reflecting rearrangement of **7** to **6**. The fragmentation patterns of the two components were virtually identical: m/z 180 (M, 69%), 179 (100), 178 (84), 177 (12), 176 (16), 165 (53), 152 (21), 151 (11), 89 (17); ^{13}C NMR (75.5 MHz, all d except where noted) δ 144.3 (s), 138.4 (s), 137.6, 127.4, 127.2, 126.5, 126.4, 125.3, 40.3, 36.2, 34.7, 19.9, 18.6, 17.5; ^1H NMR (300 MHz) δ 7.18 (dd, J = 7.0, 1.8, 1 H, aryl), 7.14 (ddd, J = 7.0, 7.0, 1.8, 1 H, aryl), 7.08 (ddd, J = 7.0, 7.0, 1.8, 1 H, aryl), 6.98 (dd, J = 7.0, 1.8, 1 H, aryl), 6.35 (ddd, 1 H, H4), 5.53 (dddd, 1 H, H3), 3.79 (dd, 1 H, H5), 3.74 (dddd, 1 H, H9b), 3.39 (ddddd, 1 H, H2a), 1.88 (ddd, 1 H, H2), 1.77 (dddd, 1 H, H1), 1.65 (ddddd, 1 H, H10); see also Table I.

In a separate experiment, ketone **3** (225 mg) in 2-propanol (90 mL) was irradiated as above, and the reaction was monitored by TLC. Only ketone **3** and hydrocarbon **7** were detected. After 6 h the photolysis was interrupted, and **7** (72 mg) and **3** (66 mg) were isolated by flash chromatography on silica gel.

Conversion of 7 into Phenanthrene. A solution of hydrocarbon **7** (61 mg, 0.34 mmol) and DDQ (80 mg, 0.35 mmol) in benzene (5 mL) was refluxed for 4 h. The mixture was filtered through silica gel in hexane, and the filtrate was evaporated to afford pure phenanthrene (42 mg, 70%), mp and mixed mp 99–100 °C.

Addition of Benzyne to 1,6-Methano[10]annulene (8). Benzenediazonium-2-carboxylate, prepared from anthranilic acid (1.40 g, 10.2 mmol), was added to a solution of 8 (1.45 g, 10.2 mmol) in 1,2-dichloroethane (30 mL). The mixture was stirred under reflux until gas evolution ceased and all the solid had decomposed (30 min). The solvent was evaporated, and the residue was adsorbed onto silica gel and submitted to flash chromatography. Elution with 5% dichloromethane–hexane gave 8 (720 mg) in the early fractions. This was followed by 4a,9,9a,10-tetrahydro-9,10-etheno-4a,9a-methanoanthracene (**9**) as pale yellow crystals (401 mg, 18%): mp 118.5–119.5 °C; MS m/z 217 (M – 1, 26), 202 (100), 191 (13), 102 (52); ^{13}C NMR (20.1 MHz) δ 147.2 (s), 133.3 (d), 129.7 (d), 124.4 (d), 123.7 (d), 120.7 (d), 47.2 (d), 35.6 (s), 19.2 (dd); ^1H NMR (80 MHz) δ 7.10–6.83 (m, 4 H, aryl), 6.32 (AA′ part of AA′XX′, 2 H, vinyl H11 and H12), 6.05–5.52 (AA′BB′, 4 H, H1-H4), 3.99 (XX′ part of AA′XX′, 2 H, bridgehead H9 and H10), 2.39 (d, J = 4.7, 1 H, H13), –0.09 (d, J = 4.7, 1 H, H13). Anal. Calcd for $C_{17}H_{14}$: C, 93.54; H, 6.46. Found: C, 93.51; H, 6.40.

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Supplementary Material Available: The observed and simulated 300-MHz ^1H NMR spectrum of hydrocarbon **7** (2 pages). Ordering information is given on any current masthead page.

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Stereochemical Aspects of the Reaction of Lithio(1-methyl-2-propenyl)diphenylphosphine Oxide with β-Substituted Aldehydes. Short Syntheses of (-)-α-Selinene and (+)-α-Helmiscapene[1]

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Yamamoto and co-workers have reported that the reaction of the Wittig–Horner reagent, lithio(1-methyl-2-

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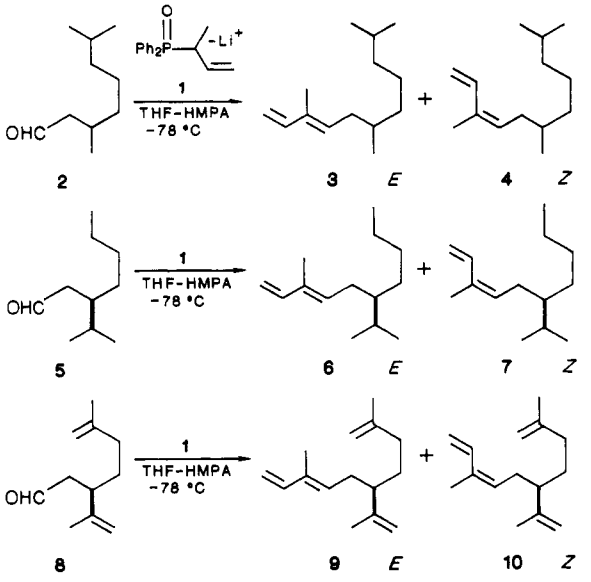
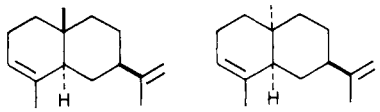
propenyl)diphenylphosphine oxide (1), with simple aldehydes in THF–HMPA at low temperatures provides a useful route to the corresponding *E*-3-methyl 1,3-dienes with greater than 90% stereoselectivity.[2] No examples of reactions of reagent 1 with β-substituted aldehydes were included in this study. We wish to report the reaction of 1 with β-substituted aldehydes **2**,[3] **5**, and **8**[4] in THF–HMPA at −78 °C. The reaction of 1 with the chiral aldehyde **8**, obtainable in three steps from (*R*)-(+)-limonene, provided a mixture of conjugated dienes which upon intramolecular Diels–Alder reaction yielded a mixture of decalin derivatives containing the eudesmane sesquiterpenes (−)-α-selinene (**11**) and (+)-α-helmiscapene (**12**).



The β-methyl aldehyde **2** was prepared by chromic acid oxidation of tetrahydrogeraniol.[3] The β-isopropyl aldehyde **5** was prepared by ozonolysis of (*R*)-(+)-dihydrolimonene in methanol followed by reductive workup with dimethyl sulfide and a trace of *p*-toluenesulfonic acid to give 1,1-dimethoxy-3-isopropyl-6-heptanone,[5] Wolff-Kishner reduction of the carbonyl group and hydrolysis of the acetal function with aqueous perchloric acid. This product showed the same spectral properties as those reported previously for **5**.[6] Aldehyde **8** was prepared by the procedure of Sonnet and co-workers[4] which involved conversion of (*R*)-(+)-limonene into 1,1-dimethoxy-3-isopropenyl-6-heptanone by ozonolysis as described above, methylenation of the ketone with methylenetriphenylphosphorane, and hydrolysis of the acetal.

The reactions of **2**, **5**, and **8** were conducted with an excess of reagent **1** under the conditions described by Yamamoto and co-workers.[2] The mixtures of *E* and *Z* conjugated dienes produced were not separable by chromatography, but the *Z*/*E* ratios were easily determined by integration of the ^{1}H NMR signals for the respective C-2 protons of these isomers. The literature precedent[2,7,8] has shown that the C-2 protons of the *Z* dienes of the type **4**, **7**, and **10** normally absorb ca. 0.4 ppm downfield from the C-2 protons of *E* dienes such as **3**, **6**, and **9**. For each of the three β-substituted aldehydes the *E*/*Z* ratio was found to be approximately 4:1. Thus, although the preference for the formation of the *E* dienes was not as great for these compounds as for the aldehydes studied by Yamamoto and co-workers,[2] the *E* isomers were the predominant products in each case.

Intramolecular Diels–Alder reactions of appropriate trienes and trienones provide useful methods of synthesis of a variety of fused-ring systems including the eudesmane sesquiterpenes.[7,9,10] For example, Taber and Saleh have used the intramolecular Diels–Alder reaction of an acyclic triene containing a 6-hydroxyisopropyl group for a stereoselective synthesis of racemic α-eudesmol.[9] The mixture of the chiral tetraenes **9** and **10** appeared to be useful for the synthesis of optically active eudesmane sesquiterpenes containing isopropenyl side chains. Thus, heating of this mixture in a toluene solution containing a trace of hydroquinone in a sealed tube at 240 °C for 36 h gave a mixture of decalins in 70% yield, which according to gas chromatographic analysis, contained ca. 65% (−)-α-selinene (**11**), ca. 20% of the cis-fused eudesmane (+)-α-helmiscapene[11] (**12**), ca. 10% of a third component, and several minor components which made up a total ca. 5% of the mixture. Samples of **11**, **12**, and the third component were



11 12

collected by preparative gas chromatography. Compound **11** exhibited identical IR and ^{1}H NMR spectral properties to those previously reported[12] for the natural product. The spectral properties of compound **12** were identical with those that we reported previously[7] and were nearly identical with those reported for (−)-α-helmiscapene, the naturally occurring enantiomer of **12**.[11] The conversion of the mixture of tetraenes largely into (−)-α-selinene is consistent with the results of Taber and Saleh[9] who proposed that bulky C-6 substituents on the acyclic chains of 1,3,9-decatriene derivatives cause substantial 1,3- and 1,4-chiral induction to produce trans-fused decalin systems with the C-6 substituents equatorial. The optical rotation of the sample (−)-α-selinene, which was obtained in five steps from (*R*)-(+)-limonene, was $[\alpha]^{25}_D$ −13.1° ($CHCl_3$, 0.5%) [reported[12] $[\alpha]^{25}_D$ −14.5° ($CHCl_3$, 1.0%)], and the optical rotation of (+)-α-helmiscapene was $[\alpha]^{25}_D$ +102° ($CHCl_3$, 0.7%) [reported for (−)-α-helmiscapene[11] $[\alpha]_D$

(1) This research was supported by a grant (ACS-PRF 18245-ACl-C) and an Undergraduate Summer Research Fellowship to S.F. from the donors of the Petroleum Research Fund, administered by the American Chemical Society, for which we are grateful.

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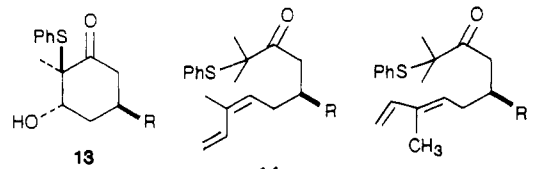
−100°]. Our recent previous synthesis of **11** from carvone[7] and the synthesis reported by Kutney and Singh[13] from a thujone-derived intermediate are less efficient than that described above.

The minor component of the thermal reaction, although not completely identified, appeared from its ^{1}H NMR spectrum to contain an internal conjugated diene system. This possibly could result from a thermal 1,5-sigmatropic hydrogen rearrangement of the *Z* diene **10**, which would not be expected to readily undergo an intramolecular Diels–Alder reaction.[9,10]

The *E* dienes formed in the above Wittig–Horner reactions presumably arise via threo adducts derived from the anion **1** and the aldehyde. Yamamoto and co-workers[2] have suggested that the *E* dienes are favored as a result of thermodynamic control. Recently, we found that the reaction of 2 equiv of reagent **1** with the β-ketol **13a** in THF–HMPA at −78 °C gave a 9:1 mixture of *Z* and *E* dienes **14a** and **15a**.[7] The first equivalent of **1** presumably



13 **14** **15**

a, R = isopropenyl; **b**, R = H

acts as a base to deprotonate the hydroxyl group of **13a** and cause retroaldol cleavage of the ring to an open chain aldehydo enolate intermediate. The *Z* diene, which is ultimately formed, must arise from a diastereomeric mixture of erythro adducts of this intermediate and reagent **1**. When β-ketol **13a** was reacted with **1**, as described above, but at 0 °C rather than −78 °C, a 3:2 mixture of *Z* and *E* isomers **14a** and **15a** was isolated. This suggests that there may be a kinetic preference for the formation of the erythro adducts in this system. In contrast to **13a**, β-ketol **13b** gave a ca. 1:3 mixture of *Z* and *E* dienes **14b** and **15b** upon reaction with 2 equiv of **1** at −78 °C.

The open chain aldehydo enolates derived from retroaldol cleavage of β-ketols **13a** and **13b** differ only by the presence of the β-isopropenyl group in the former. Therefore, the possibility existed that the β-substituent might be responsible for the fact that a large proportion of the *Z* diene was obtained in the reaction of **13a** and **1**. However, since reactions of β-substituted aldehydes **2**, **5**, and **8** with **1** gave diene mixtures containing largely the corresponding *E* isomers, this is apparently not the case. Possibly, subtle factors involving the presence of both the enolate moiety and the β-isopropenyl substituent in the aldehydo intermediate account for the unusual stereochemical results observed in the reaction of **13a** and **1**.

Experimental Section

All reactions were carried out under a nitrogen atmosphere unless otherwise stated. Solvents and reagents were purified and dried by standard techniques. ^{1}H NMR spectra were measured in $CDCl_3$ solutions at 200 MHz. Optical rotations were measured on a Perkin-Elmer 241 polarimeter in $CHCl_3$.

Flash column chromatography was carried out with E. Merck 60 silica gel (230–400 mesh). Gas chromatographic purification was carried out on a Varian Aerograph 90-P using a 10 ft × 0.25 in. stainless steel column containing 20% silicone SE-30 on 80/100 mesh Chromosorb W.

3-Isopropylheptanal (5). To 12.5 g (0.057 mol) of 1,1-dimethoxy-3-isopropyl-6-heptanone, produced by the procedure of Kitahara et al.,[5] dissolved in 77.5 mL of ethylene glycol were added 5.6 g (0.1 mol) of potassium hydroxide and 5.6 g (0.175 mol) of hydrazine. This mixture was refluxed for 1.5 h and distillation was carried out until the temperature reached 195–200 °C. Then, the mixture was refluxed an additional 4 h. After cooling, the mixture was poured into cold water (70 mL) with stirring. The organic layer was separated and the aqueous layer washed with two 50-mL portions of ether. The combined organic layer and washings were washed with 6 N hydrochloric acid (50 mL) and brine, dried, and concentrated in vacuo to produce 3.3 g (0.016 mol, ca. 30%) of 1,1-dimethoxy-3-isopropylheptane. Cleavage of the acetal was affected by stirring a solution of 3.3 g (0.016 mol) of the acetal in 30 mL of a saturated aqueous solution of THF containing 0.41 mL of perchloric acid for 4.0 h at room temperature. The mixture was poured into ether (20 mL) and the aqueous layer washed with two 30-mL portions of ether. The combined organic layer and washings were washed with brine, dried, and concentrated in vacuo. Distillation provided 1.0 g (ca. 40%) of **5**, bp 64–67 °C (4.6 mm), which exhibited identical spectral properties with those previously reported.[6]

(*E*)- and (*Z*)-3,6,10-Trimethyl-1,3-undecadiene (3 and 4). To a solution of 4.06 g (0.016 mol) of (1-methyl-2-propenyl)diphenylphosphine oxide (**1**) in 50 mL of anhydrous THF at −78 °C was added dropwise with stirring 6.4 mL of a 2.5 M solution of *n*-butyllithium in hexanes. The mixture was stirred for 20 min at −78 °C and 5.6 mL (0.032 mol) of anhydrous HMPA was added. A solution of 1.91 g (0.012 mol) of 3,7-dimethyloctanal (**2**)[3] in 5.0 mL of anhydrous THF was then added dropwise with stirring over 15 min while the temperature was kept below −72 °C. Stirring was continued at −78 °C for 10 min, and the mixture was poured into 30 mL of cold water. The organic layer was separated, and the aqueous layer was washed with two 30-mL portions of ether. The combined organic layer and etheral washings were washed with two 15-mL portions of a saturated aqueous solution of lithium bromide, the organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed in vacuo. Flash chromatography of the residue on silica gel using 1:19 ethyl acetate/hexane as the elutant gave 0.98 g (47%) of a 4:1 mixture (based upon integration of the C-2 proton region of the ^{1}H NMR spectrum) of dienes **3** and **4** as a colorless oil. The mixture showed the following spectral properties: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.80–0.95 (m, 9 H, 3 CH_3's), 1.05–1.69 (m, 8 H), 1.73 (s, 3 H, vinyl CH_3), 1.88–2.22 (m, 2 H), 4.88–5.16 (m, 2 H), 5.43–5.58 (t, *J* = 8 Hz, 1 H), 6.39 (dd, *J* = 17, 11 Hz, 0.8 H), and 6.78 (dd, *J* = 17, 10 Hz, 0.2 H); IR (neat) 3110, 2985, 2940, 2890, 1615, 1470, 1395, 1370, 990, and 890 cm^{-1}. Anal. Calcd for $C_{14}H_{26}$: C, 86.52; H, 13.48. Found: C, 86.33; H, 13.27.

(*E*)- and (*Z*)-3-Methyl-6-isopropyl-1,3-decadiene (6 and 7). By use of 2.46 g (0.0096 mol) of reagent **1** and 0.80 g (0.0051 mol) of 3-isopropylheptanal (**5**) in a procedure similar to that described above, 0.79 g (80%) of a 4:1 mixture of dienes **6** and **7** was obtained as a colorless oil. The mixture showed the following: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.80–0.96 (m, 9 H, 3 CH_3's), 1.10–1.41 (m, 8 H), 1.74 (s, 3 H, vinyl CH_3), 1.96–2.19 (m, 2 H), 4.82–5.25 (m, 2 H), 5.49 (t, *J* = 8 Hz, 1 H), 6.39 (dd, *J* = 17, 11 Hz, 0.8 H), and 6.79 (dd, *J* = 17, 11 Hz, 0.2 H); IR (neat) 3100, 2985, 2940, 2890, 1650, 1610, 1470, 1395, 1370, 1090, 990, and 890 cm^{-1}. Anal. Calcd for $C_{14}H_{26}$: C, 86.52; H, 13.48. Found: C, 86.47; H, 13.47.

(*E*)- and (*Z*)-3,9-Dimethyl-11-(methylethenyl)-1,3,9-decatriene (9 and 10). By use of 2.61 g (0.010 mol) of reagent **1** and 1.0 g (0.0060 mol) of (*R*)-(+)-6-methyl-3-(1-methylethenyl)-6-heptenal (**8**)[4] under conditions similar to those described for the preparation of the mixture of dienes **3** and **4**, 1.0 g (82%) of a 4:1 mixture (based on integration of the C-2 proton region of the ^{1}H NMR spectrum) of dienes **9** and **10** was obtained as a colorless oil. The mixture showed the following: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.39–2.32 (m, 16 H, including three vinyl methyl singlets at δ 1.62, 1.71, and 1.74), 4.61–5.57 (m, 7 H), 6.37 (dd, *J* = 18, 10 Hz, 0.8 H), and 6.78 (dd, *J* = 18, 10 Hz, 0.2 H); IR (neat) 3100, 2998, 1665, 1622, 1460, 1390, 1140, 1115, 1000, 905 cm^{-1}. Anal. Calcd for $C_{15}H_{24}$: C, 88.16, H, 11.84. Found: C, 88.10; H, 11.84.

Intramolecular Diels–Alder Reaction of the 4:1 Mixture of Tetraenes 9 and 10. A solution of 0.9 g (0.0044 mol) of the 4:1 mixture of tetraenes **9** and **10** in 25 mL of toluene containing 20 mg of hydroquinone was heated in a sealed tube at 240 °C for

(13) Kutney, J. P.; Singh, A. K. *Can. J. Chem.* **1984**, *62*, 1407.

36 h. The mixture was allowed to cool to room temperature and poured into 50 mL of ether. The organic phase was washed with two 30-mL portions of water and dried over anhydrous magnesium sulfate, and the solvent was removed in vacuo to give 0.63 g (70%) of an oil. Gas chromatographic analysis of the mixture showed that it contained three major components which made up ~65%, ~20%, and ~10% of the mixture and several minor components whose concentrations totaled 5% of the mixture. The three major components were collected separately by preparative gas chromatography. The major product exhibited identical IR and ^{1}H NMR spectral properties with those reported for (-)-α-selinene (**11**).[7,12] It showed $[\alpha]^{25}_D$ -13.1° ($CHCl_3$, 0.5%) [reported[12] $[\alpha]^{25}_D$ -14.5° ($CHCl_3$, 1.0%)]. The second component showed identical spectral properties with those of the cis-fused eudesmane **12**,[11] which we reported previously.[7] It also showed essentially the same spectral properties as those reported for its naturally occurring enantiomer[11] and $[\alpha]^{25}_D$ 102° ($CHCl_3$, 0.7%) [reported[11] for (-)-enantiomer $[\alpha]_D$ 100°]. The third component was not conclusively identified, but its ^{1}H NMR spectrum indicated that four vinyl methyl groups were present. This suggested that it contained an internal conjugated diene system which possibly formed via a 1,5-sigmatropic hydrogen shift in the *Z* diene **10**.

Discorhabdin D, an Antitumor Alkaloid from the Sponges *Latrunculia brevis* and *Prianos* sp.

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Discorhabdins C (**1**), A (**2**), and B (**3**) have been isolated as the major pigments from three sponge species of the genus *Latrunculia* du Bocage (family Latrunculiidae, order Hadromerida) from New Zealand.[1,2] Discorhabdin A (**2**) has also been isolated independently (and named prianosin A) from an Okinawan sponge, *Prianos melanos*[3,4] (family Hymeniacidonidae, order Halichondrida), and its structure and absolute configuration demonstrated by X-ray crystallography. These compounds, representatives of a new class of alkaloid, were strongly cytotoxic and antimicrobial but did not show in vivo antitumor activity. A related compound with significant in vivo antitumor activity has now been found to cooccur with discorhabdin A (**2**) in a New Zealand collection of *L. brevis* Ridley and Dendy. Discorhabdin A (**2**) and this new compound, discorhabdin D (**4**), have also been isolated from a Japanese sponge of the genus *Prianos*.[3,5] The structure of discorhabdin D (**4**) is reported here, based on spectral comparisons with the known discorhabdins.[2] This structure, although based on

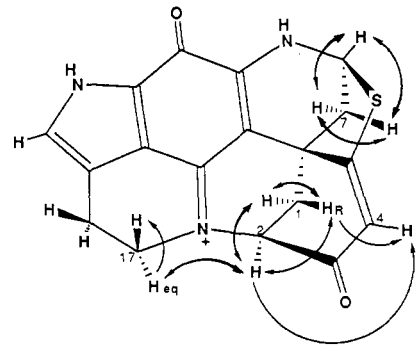
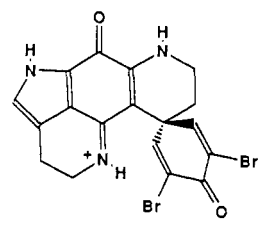
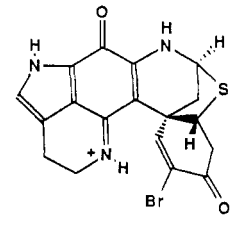


Figure 1. Enhancements observed in difference NOE spectra of discorhabdin D (**4**).

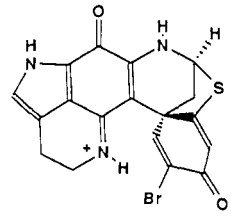
the same ring system as discorhabdin C, possesses two further heterocyclic rings to give a total of seven interlocking rings (four heterocyclic and one spiro) and seven double bonds, which is remarkable in a compound of this molecular weight.



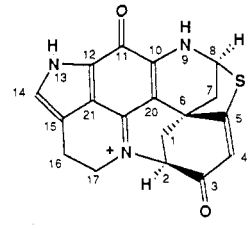
1



2



3



4

Discorhabdin D (**4**) was separated from discorhabdin A (**2**) by either reverse-phase or centrifugal counter current chromatography and characterized as the dark-green hydrochloride. The UV and IR spectra of these two compounds were similar, as were their molecular formulae. High-resolution FABMS established a composition of $C_{18}H_{14}N_3O_2S$ for MH^+ of discorhabdin D (MH^+ of **2** was $C_{18}H_{15}BrN_3O_2S$). This led to the initial hypothesis that the basic C, N, O, and S framework of the new compound was closely related to that in discorhabdin A (**2**), although discorhabdin D (**4**) has one more degree of unsaturation. This similarity was confirmed by homo- and heteronuclear correlation and specific decoupling NMR experiments, which revealed the substructures CCH_2CHNH and $CNH\text{-}CH{=}CCH_2CH_2N$ with chemical shifts (^{1}H and ^{13}C) and coupling constants (J_{HH} and J_{CH}) similar to those of C7 to NH9 and NH13 to C17 respectively in discorhabdin A (**2**) (and B (**3**)).[2]

Since there were the same number of sp^2 carbons in the ^{13}C NMR spectra of discorhabdins A (**2**) and D (**4**) the extra degree of unsaturation in **4** could be ascribed to an additional ring. As there was no signal corresponding to N*H*18 and the C17 signal was some 6 ppm downfield from the C17 signals in discorhabdins A and B (suggesting an additional carbon substituent on N18[6]), it was concluded that this additional ring was formed by a bond between

(1) Perry, N. B.; Blunt, J. W.; McCombs, J. D.; Munro, M. H. G. *J. Org. Chem.* **1986**, *51*, 5476.
(2) Perry, N. B.; Blunt, J. W.; Munro, M. H. G. *Tetrahedron* **1988**, *44*, 1727.
(3) Kobayashi, J.; Cheng, J.; Ishibashi, M.; Nakamura, H.; Ohizumi, Y.; Hirata, Y.; Sasaki, T.; Lu, H.; Clardy, J. *Tetrahedron Lett.* **1987**, *28*, 4939.
(4) The late Dr. Hoshino examined both Japanese collections and considered that they were the same species.
(5) Previous reports of compounds from *Prianos* sp.: Kashman, Y.; Rotem, M. *Tetrahedron Lett.* **1979**, 1707. Sokoloff, S.; Halevy, S.; Usieli, V.; Colorni, A.; Sarel, S. *Experientia* **1982**, *38*, 337. Manes, L. V.; Bakus, G. J.; Crews, P. *Tetrahedron Lett.* **1984**, *25*, 931.
(6) Stothers, J. B. *Carbon-13 NMR Spectroscopy*; Academic Press: New York, 1972; pp 269-277.

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