General Procedure for the Formation of the Diyne. Preparation of 12. To a stirred solution of **11** (0.5 g, 2.50 mmol) in 50 mL of dry THF under argon was added 1.0 M tetra-*n*-butylammonium fluoride in THF (6.26 mL, 6.26 mmol). The mixture was stirred for 20 h. The organic phase was washed with 20 mL of saturated ammonium chloride solution and 2 × 10 mL of brine and then dried over anhydrous sodium sulfate. The solvent was removed in vacuo and the residue purified by chromatography on Florisil (hexane elution) to yield 0.37 g (90.3%) of a clear oil: ^{1}H NMR ($CDCl_3$) δ 3.48 (2 H, s), 2.45 (4 H, t), 2.02 (1 H, s), 1.48 (4 H, m), 0.91 (6 H, t); IR (thin film) 3300, 2980, 2240, 1590, 1460, 1320, 1080, 720 cm^{-1}; MS (70 eV), *m/e* (relative intensity) 163 (M^+, 7), 134 (75), 111 (14), 109 (10), 99 (32), 85 (21), 69 (37), 63 (33), 57 (71), 43 (100), 39 (18).

(*Z*)-1-Chloro-1-nonen-3-yne (1): purified by Kugelrohr distillation, 85% yield; ^{1}H NMR ($CDCl_3$) δ 6.29 (1 H, d, J = 5.3 Hz), 5.86 (1 H, dd, J = 1.8, 5.3 Hz), 3.39 (2 H, dt, J = 1.8, 6.8 Hz), 1.61–1.30 (6 H, m), 0.91 (3 H, t); IR (thin film) 3080, 2960, 2210, 1460, 1330, 720 cm^{-1}; MS (70 eV), *m/e* 156 (M^+), 143, 119, 105, 91, 69, 55, 41.

1,3-Nonadiyne (2): purified by Kugelrohr distillation, 79% yield; ^{1}H NMR ($CDCl_3$) δ 2.27 (2 H, t), 1.97 (1 H, s), 1.58–1.34 (6 H, m), 0.91 (3 H, t); IR (thin film) 3300, 2940, 2220, 1460, 1240, 720 cm^{-1}; MS (70 eV), *m/e* 121 ($M^+ + 1$), 120 (M^+), 105, 91, 79, 77, 65, 56.

(*Z*)-1-Chloro-4-phenyl-1-buten-3-yne (3): purified by Kugelrohr distillation, 75% yield; ^{1}H NMR ($CDCl_3$) δ 7.53–7.35 (5 H, m), 6.46 (1 H, d, J = 7.4 Hz), 6.11 (1 H, d, J = 7.4 Hz); IR (thin film) 3080, 3020, 2200, 1600, 1460, 1440, 1340, 760 cm^{-1}; MS (70 eV), *m/e* 129, 96, 94, 39, 27.

4-Phenyl-1,3-butadiyne (4): purified by Kugelrohr distillation, 87% yield; ^{1}H NMR ($CDCl_3$) δ 7.53–7.28 (5 H, m), 2.49 (1 H, s); IR (thin film) 3300, 3060, 2200, 1590, 1485, 1440, 1220, 750, 690 cm^{-1}; MS (70 eV), *m/e* 126 (M^+), 125, 98, 74, 63, 49, 32.

(*Z*)-1-Chloro-6-hydroxy-1-hexen-3-yne (5): purified by Kugelrohr distillation, 99% yield; ^{1}H NMR ($CDCl_3$) δ 6.35 (1 H, d, J = 7.4 Hz), 5.88 (1 H, dd, J = 1.8, 7.4 Hz), 3.79 (2 H, d, J = 6.0 Hz), 2.67 (2 H, dt, J = 1.8, 6.0 Hz), 2.11 (1 H, bs); IR (thin film) 3600–3100, 3100, 2980, 2200, 1600, 1340, 1050, 850, 720 cm^{-1}; MS (70 eV), *m/e* 108 ($M^+ - 18$), 97, 92, 63, 61, 38, 31, 27.

3,5-Hexadiyn-1-ol (6): purified by chromatography on SiO_2 (75% hexane/25% ethyl acetate), 73% yield; ^{1}H NMR ($CDCl_3$) δ 6.19 (1 H, d), 5.89 (1 H, d), 3.77 (2 H, t), 2.55 (2 H, t), 2.05 (1 H, s), 2.01 (1 H, s); IR (thin film) 3600–3100, 3300, 2960, 2210, 1590, 1050, 740 cm^{-1}.

(*Z*)-1-Chloro-5-hydroxy-1-hepten-3-yne (7): purified by chromatography on SiO_2 (75% hexane/25% ethyl acetate), 95% yield; ^{1}H NMR ($CDCl_3$) δ 6.40 (1 H, d), 5.91 (1 H, d), 4.53 (1 H, q), 2.07 (1 H, d), 1.80 (2 H, quin), 1.06 (3 H, t); IR (thin film) 3600–3100, 3080, 3000, 1600, 1340, 1140, 1040, 730 cm^{-1}; MS (70 eV), *m/e* 144 (M^+), 126, 111, 104, 88, 75, 49, 39.

5-Hydroxy-1,3-heptadiyne (8): purified by chromatography on Florisil (hexane elution), 77% yield; ^{1}H NMR ($CDCl_3$) δ 4.36 (1 H, t), 2.60 (1 H, bs), 2.20 (1 H, s), 1.75 (2 H, quin), 1.02 (3 H, t); IR (thin film) 3600–3100, 3300, 2980, 1450, 1380, 1250, 960 cm^{-1}; MS (70 eV), *m/e* 108 (M^+), 107, 91, 79, 55, 43, 32.

(*Z*)-1-Chloro-5,5-diethoxy-1-penten-3-yne (9): purified by chromatography on SiO_2 (hexane elution), 88% yield; ^{1}H NMR ($CDCl_3$) δ 6.46 (1 H, d), 5.94 (1 H, d), 5.40 (1 H, s), 3.80 (2 H, q), 3.64 (2 H, q), 1.26 (6 H, t); MS (70 eV), *m/e* 187 ($M^+ - 1$), 159, 143, 115, 87, 51, 39; IR (thin film) 3080, 2990, 2200, 1590, 1320, 1130, 1050, 720 cm^{-1}.

5,5-Diethoxy-1,3-pentadiyne (10): purified by chromatography on Florisil (70% hexane/30% ethyl acetate), 79% yield; ^{1}H NMR ($CDCl_3$) δ 5.30 (1 H, s), 3.75 (2 H, q), 3.61 (2 H, q), 2.23 (1 H, s), 1.25 (6 H, t); IR (thin film) 3300, 2990, 2220, 1440, 1220, 1140, 1040, 1010, 900 cm^{-1}; MS (70 eV), *m/e* 123 ($M^+ - 29$), 107, 79, 62, 51, 39.

(*Z*)-1-Chloro-1-undecene-3,5-diyne (13): purified by chromatography on Florisil (hexane elution), 67% yield; ^{1}H NMR ($CDCl_3$) δ 6.33 (1 H, d), 5.88 (1 H, d), 2.50 (2 H, t), 1.75–1.2 (6 H, m), 0.90 (3 H, t); IR (thin film) 3080, 2970, 2200, 1590, 1450, 720 cm^{-1}.

1,3,5-Undecatriyne (14): purified by chromatography on SiO_2 (hexane elution), 63% yield; ^{1}H NMR ($CDCl_3$) δ 2.39 (2 H, t), 1.99 (1 H, s), 1.71–1.20 (6 H, m), 0.91 (3 H, t); IR (thin film) 3300, 2980, 2210, 1590, 1460, 1380, 900, 730 cm^{-1}; UV (MeOH) 210, 222, 238, 273, 290, 311 nm.

(*Z*)-1-Carbomethoxy-6-chloro-5-hexen-3-yne (15): purified by chromatography on SiO_2 (80% hexane/20% ethyl acetate elution), 85% yield; ^{1}H NMR ($CDCl_3$) δ 6.32 (1 H, d), 5.83 (1 H, d), 3.71 (3 H, s), 2.72 (2 H, t), 2.60 (2 H, t); IR (thin film) 3080, 2970, 2210, 1700, 1590, 1460, 1370, 1200, 900, 730 cm^{-1}; MS (eV), *m/e* 172 (M^+), 141, 109, 99, 77, 51, 39.

4,6-Heptadiynoic acid methyl ester (16): purified by chromatography on SiO_2 (hexane elution), 64% yield; ^{1}H NMR ($CDCl_3$) δ 3.70 (3 H, s), 2.57 (4 H, s), 2.00 (1 H, s); IR (thin film) 3300, 3000, 2980, 2210, 1720, 1440, 1200, 1050, 620 cm^{-1}; MS (70 eV), *m/e* 136 (M^+), 121, 105, 77, 65, 51, 43.

(*Z*)-1-Chloro-5-(ethylthio)-1-penten-3-yne (17): purified by chromatography on SiO_2 (80% hexane/20% ethyl acetate), 97% yield; ^{1}H NMR ($CDCl_3$) δ 6.38 (1 H, d), 5.90 (1 H, dd, J = 2.0, 7.4 Hz), 3.48 (2 H, d, J = 2.0 Hz), 2.74 (2 H, q), 1.31 (3 H, t); IR (thin film) 3080, 2980, 2200, 1600, 1240, 850, 720 cm^{-1}; MS (70 eV), *m/e* 160 (M^+), 131, 99, 73, 63, 45, 27.

1-(Ethylthio)-1,3-pentadiyne (18): purified by chromatography on SiO_2 (80% hexane/20% ethyl acetate solution), 78% yield; ^{1}H NMR ($CDCl_3$) δ 2.78 (2 H, q), 1.99 (3 H, s), 1.41 (3 H, t); ^{13}C NMR ($CDCl_3$) 81 (s), 78 (s), 65 (s), 64 (s), 30 (t), 15 (q), 6 (q); IR (thin film) 2980, 2100, 1450, 1250, 960, 760 cm^{-1}; MS (70 eV), *m/e* 124 (M^+), 96, 69, 57, 43.

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Consequences of Twofold Bridging of the [10]Annulene System as in *cis*-10,11-Dihydrodicyclopenta[*cd*,*gh*]pentalene

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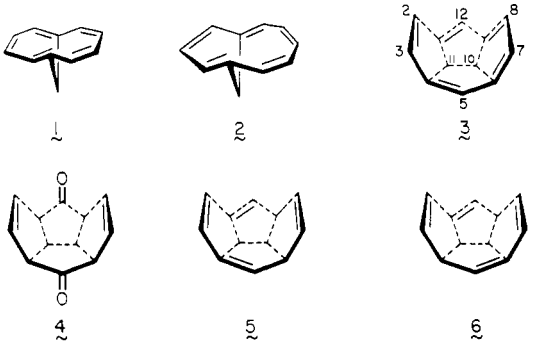
The concept of bridging a polyunsaturated macrocyclic hydrocarbon for the purpose of introducing conformational rigidity and maximizing $(4n + 2)\pi$ delocalization was first introduced by Vogel in 1964 for the [10]annulene core (see **1**).[3] In the intervening years, the concept has been extended to the 1,5-bridged isomer **2**,[4] but twofold bridging as in **3** has received only early theoretical attention.[5] As



1 2 3

4 5 6

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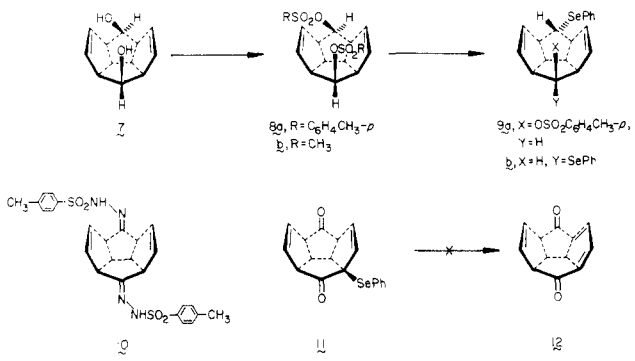
a consequence of our recently developed six-step synthesis of diketone **4**,[6] an intermediate prepared almost simultaneously in two other laboratories by fundamentally different routes,[7,8] we have given some attention to the possible conversion of **4** to **3**. A recent paper by Lannoye and Cooke[9] prompts us to report herein some of the complications associated with cumulative introduction of additional unsaturated centers into this carbocyclic framework. The obvious difficulties we have encountered are addressed by computational analysis of the strain energies inherent in **3**, **5**, and **6**.

The first of two strategies to be developed for arrival at **3** was based on the initial conversion of **4** to either or both of the tetraenes **5** and **6**. The cup-shaped topology of the diketone guaranteed that reduction with diisobutylaluminum hydride would proceed with complete stereoselectivity to give **7**. Recrystallization of this product from methanol delivered a 1:1 complex with the solvent, heating of which to 100 °C at 0.1 Torr for 3 h provided the desolvated product. Despite the sterically congested nature of the endo hydroxyl groups in **7**, ditosylation and dimesylation could be accomplished straightforwardly.

However, all attempts to date to effect double elimination of the sulfonate ester groups in **8a** or **8b** have not yielded a characterizable product. To exemplify the problematic nature of this transformation, specific attention is called to the action of excess potassium *tert*-butoxide on **8a** in a dimethyl sulfoxide–tetrahydrofuran solvent system at room temperature. After 30 min, 31% of **8a** could be recovered, but no less polar product of any type was observed. Highly activated alumina[10] was similarly uneffective.

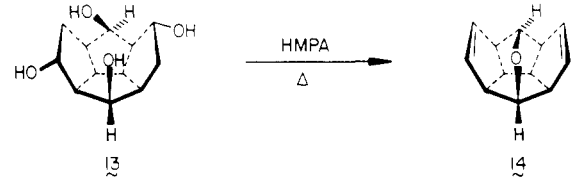


To test whether a cis elimination might provide more optimal conditions, ditosylate **8a** was treated with phenyl selenide anion. Adjustment of stoichiometry, reaction time, and temperature made possible the isolation of **9a** or direct conversion to **9b**. Oxidation of **9b** with sodium metaperiodate required overnight to proceed to completion. Subsequent warming (up to the boiling point of carbon tetrachloride) in the presence of diisopropylamine as acid scavenger produced small amounts of multicomponent mixtures; except for diphenyl diselenide, the other components were not successfully identified.

Further transformation of the diketone led to the bis(tosylhydrazone) **10** in order to make possible an opportunity to utilize the Bamford–Stevens reaction. However, heating of **10** with sodium in ethylene glycol with provision for removal of volatile products gave no **5** or **6**. While the possibility cannot be ruled out that these hydrocarbons had been formed in the above reactions, rapid autoxidation would prohibit their direct spectroscopic observation.

The absence of a viable double elimination process led us to examine alternatively the introduction of a single additional double bond first. The plan also called for retention of both carbonyl groups to enable simplified chemical manipulation subsequently. It proved a relatively easy matter to transform **4** into **11**. However, conditions for the successful base-promoted conversion of the derived selenoxide to **12** (or a tautomer thereof) could never be found.

The previously reported inability to dehydrate **13** beyond the diene stage in hot HMPA[9] provides further indication that introduction of more than two bonds into this framework is not easily achieved.



In order to assess the heats of formation and strain energies of **3**, **5**, **6**, and **15**, theoretical calculations were carried out. The four structures were first minimized by

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using MODEL (version KS 2.91)[11] to obtain Allinger MM2 steric energies. The minimized structures from MODEL were then reminimized by means of MMX,[12] which considers the effect of conjugation and provides an estimation of the values contained in Table I. The conjugated atoms were tagged as "π-atoms" prior to minimization. All of the minimized structures were found to be shaped like a tortoise shell.

Table I. Results of Theoretical Calculations[a]

compd	ΔH_f[b]	strain energy[b]	total energy[b]	steric energy[c]
15	36.12	26.50	31.80	31.32
5	103.99	47.56	49.38	52.19
6	109.79	49.04	50.86	52.31
3	181.11	97.45	98.11	103.71

[a] All energies in kcal/mol. [b] MMX. [c] MODEL.

If **15** is considered as the point of reference, its conversion to either **5** or **6** by formal loss of two molecules of hydrogen is seen to be accompanied by an approximate doubling of the strain energy. An additional, more acute increase in energy content takes place upon introduction of the fifth double bond to arrive at **3**. Noteworthy as they are, these substantive differences in relative energy may actually be underestimated. During the calculations, the

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(12) MM2 with MMP1 π subroutines incorporated for localized π electron systems (written by Yuh, Y. H.; Allinger, N. L.).

individual π bonds are maintained as strictly planar structural subunits. However, molecular models denote a marked tendency for those unsaturated linkages located in the two central rings to be somewhat torsionally twisted, particularly in **3**. The superpositioning of these forces would, of course, result in further increases in the energy gaps separating these molecules.

Although the values presented in Table I do not appear to be prohibitive, they are strongly suspected to be too low for the reasons discussed above. Whatever the actual state of affairs, the thermodynamic disadvantage is appreciable. This conclusion is supported by the inability of more obvious synthetic processes to deliver these unsaturated systems even in token amounts.

Experimental Section

Diketone 4 was prepared in the predescribed manner[6] and obtained as colorless cubes, mp 222–223 °C (from ethyl acetate).

To a mixture of **4** (0.30 g, 1.61 mmol) and tosylhydrazide (0.75 g, 4.03 mmol) in 95% ethanol (8 mL) was added one drop of concentrated hydrochloric acid. This mixture was heated at reflux for 12 h, cooled, and filtered to remove the precipitated product. The bis(tosylhydrazone) was washed thoroughly with ether and dried in vacuo over phosphorus pentoxide. There was obtained 0.82 g (97%) of **10**, mp >300 °C dec, which was used without further purification: IR (KBr, cm^{-1}) 3230, 3070, 2970, 2920, 1645, 1600, 1495, 1405, 1350, 1310, 1170, 1100, 1030, 1000, 930, 890, 850, 820, 805, 755, 715, 670; ^1H NMR (300 MHz, DMSO-d_6) δ 10.40 (s, 2 H), 7.72 (d, J = 8.1 Hz, 4 H), 7.38 (d, J = 8.1 Hz, 4 H), 5.60–5.50 (m, 2 H), 5.40–5.30 (m, 2 H), 4.05–3.90 (m, 2 H), 3.65–3.5 (m, 2 H), 3.50–3.35 (m, 2 H), 2.36 (s, 6 H); ^{13}C NMR (75 MHz, DMSO-d_6) 164.88, 143.09, 136.35, 134.30, 130.72, 129.43, 127.25, 57.03, 52.90, 46.84, 20.99 ppm.

Hydride Reduction of 4. A hexane solution of diisobutylaluminum hydride (1.5 mL of 1 M, 1.5 mmol) was added dropwise during 1 min to a cold (0 °C), magnetically stirred solution of **4** (93.1 mg, 0.50 mmol) in 20 mL of dry tetrahydrofuran under nitrogen. The reaction mixture was stirred at 0 °C for 40 min, treated with saturated ammonium chloride solution (10 mL), and kept stirring for an additional 1.5 h. This solution was added to 10% hydrochloric acid (5 mL) and extracted with ethyl acetate (3 × 25 mL). The combined organic phases were washed with water (10 mL) and brine (10 mL), dried, and evaporated. Recrystallization of the solid residue from methanol gave 771 mg (69.4%) of the 1:1 methanol complex of **7** as colorless prisms, mp 186–188 °C (with loss of MeOH): IR (KBr, cm^{-1}) 3400, 3080, 3060; ^1H NMR (300 MHz, CD_3OD) δ 7.07 (br s, 4 H), 5.17 (t, J = 7.7 Hz, 2 H), 4.8–4.6 (m, 4 H), 4.55–4.45 (m, 2 H); ^{13}C NMR (75 MHz, CD_3OD) 134.05, 75.19, 57.89, 47.23 ppm.

Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.54; H, 7.36.

Tosylation of 7. A solution of **7** (460 mg, 2.42 mmol) and *p*-toluenesulfonyl chloride (1.84 g, 9.65 mmol) in dry pyridine (18.4 mL) was stirred at room temperature for 51 h, poured into ice-water (300 mL), and acidified with 10% hydrochloric acid (100 mL). This solution was extracted with dichloromethane (3 × 200 mL), and the combined organic layers were washed with water and brine prior to drying. Solvent evaporation left a residue, which was separated into its components by preparative TLC on silica gel (elution with 66% petroleum ether in ethyl acetate). The less polar major product (797 mg, 66.1%) proved to be **8a**, while the minor component proved to be the monotosylate (182 mg, 21.9%).

For **8a**: colorless solid, mp 175.5–176.5 °C (from dichloromethane–petroleum ether); ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 4 H), 7.32 (d, J = 8.2 Hz, 4 H), 5.47 (s, 4 H), 4.82 (t, J = 7.9 Hz, 2 H), 3.40–3.20 (m, 4 H), 3.00–2.85 (m, 2 H), 2.41 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) 144.82, 134.16, 132.88, 129.44, 127.83, 81.45, 54.75, 44.92, 21.66 ppm.

Anal. Calcd for $C_{26}H_{26}O_6S_2$: C, 62.63; H, 5.26. Found: C, 62.52; H, 5.39.

For the monotosylate: ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 2 H), 7.31 (d, J = 8.2 Hz, 2 H), 5.63 (dd, J = 3.6, 2.3 Hz, 2 H), 5.46 (dd, J = 5.6, 2.7 Hz, 2 H), 4.82 (t, J = 8.1 Hz, 1 H), 4.27 (t, J = 7.9 Hz, 1 H), 3.35–3.15 (m, 4 H), 3.05–2.85 (m, 2 H), 2.56 (br s, 1 H), 2.39 (s, 3 H); MS, m/z (M^+) calcd 344.1682, obsd 344.1080.

Mesylation of 7. A magnetically stirred solution of **7** (2.0 g, 10.5 mmol) in dichloromethane (50 mL) was treated with freshly distilled triethylamine (6 mL, 43 mmol) and cooled to −5 °C. Freshly distilled methanesulfonyl chloride (2.4 mL, 31 mmol) was added dropwise at 0 °C, and the reaction mixture was stirred for an additional hour at this temperature before being transferred to a separatory funnel with another 50 mL of dichloromethane. This mixture was treated successively with ice–water (50 mL), cold 10% hydrochloric acid (50 mL), saturated sodium bicarbonate solution (50 mL), and brine (50 mL). Drying and evaporation gave 3.45 g (95%) of **8b** as colorless crystals, mp 186 °C (from dichloromethane–ether): IR (KBr, cm^{-1}) 1360, 1350, 1340, 1330, 1185, 1175, 1060, 1005, 1000, 990, 980, 970, 895, 850, 760; ^1H NMR (300 MHz, $CDCl_3$) δ 5.67 (s, 4 H), 5.08 (t, J = 7.9 Hz, 2 H), 3.61–3.56 (m, 4 H), 3.15–3.10 (m, 2 H), 3.09 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) 132.86, 80.61, 54.92, 44.99, 38.21 ppm; MS, m/z (M^+) calcd 346.0544, obsd 346.0545.

S_N2 Displacement by Phenyl Selenide Anion of 8a. Degassed ethanol (4 mL, dried over CaH_2) was carefully added dropwise during 5 min to a mixture of diphenyl diselenide (270 mg, 0.902 mmol) and sodium borohydride (70 mg, 1.83 mmol) under nitrogen at room temperature. The resulting solution was stirred for 10 min, treated with a solution of **8a** (199 mg, 0.4 mmol) in anhydrous tetrahydrofuran (1.5 mL), and stirred for 46 h at the reflux temperature. After being cooled to room temperature, the reaction mixture was treated with saturated ammonium chloride solution (10 mL), added to water (30 mL), and extracted with dichloromethane (4 × 20 mL). The combined organic layers were dried and evaporated to leave a yellow solid, which was separated into its components by preparative TLC (silica gel, elution with 60% petroleum ether in dichloromethane). There were isolated 150 mg (79.8%) of **9b** and 15 mg (8%) of **9a**.

For **9a**: IR (KBr, cm^{-1}) 3065, 3050, 1600, 1580, 1475, 1355, 1190, 1175, 895, 740; ^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 8.3 Hz, 2 H), 7.55–7.45 (m, 2 H), 7.32 (d, J = 8.3 Hz, 2 H), 7.3–7.2 (m, 3 H), 5.50–5.35 (m, 4 H), 4.85 (t, J = 7.5 Hz, 1 H), 3.83 (s, 1 H), 3.45–3.35 (m, 2 H), 3.35–3.2 (m, 4 H), 2.41 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 144.6, 137.3, 133.9, 130.8, 130.3, 129.8, 129.0, 127.7, 127.4, 82.5, 60.6, 53.7, 48.7, 47.9, 21.6 ppm; MS, m/z (M^+) calcd 484.0611, obsd 484.0620.

For **9b**: mp 157–158 °C (from dichloromethane–petroleum ether); IR (KBr, cm^{-1}), 3060, 1580, 1455, 1435, 1290, 1145, 1025, 885, 740, 730, 690; ^1H NMR (300 MHz, $CDCl_3$) δ 7.56–7.51 (m, 4 H), 7.29–7.24 (m, 6 H), 5.34 (s, 4 H), 3.89 (s, 2 H), 3.81–3.76 (m, 2 H), 3.34–3.32 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) 135.63, 133.86, 130.70, 129.02, 127.24, 59.55, 52.90, 46.69 ppm; MS, m/z (M^+) calcd 470.0052, obsd 470.0018.

Anal. Calcd for $C_{24}H_{22}Se_2$: C, 61.55; H, 4.74. Found: C, 61.69; H, 4.92.

Selenenylation of 4. A hexane solution of *n*-butyllithium (0.72 mL of 1.48 M, 1.06 mmol) was added dropwise to a cold (0 °C) solution of diisopropylamine (112 mg, 1.11 mmol) in dry tetrahydrofuran (10 mL). After 30 min of stirring, the solution was cooled to −78 °C and added to a solution of **4** (155 mg, 0.833 mmol) in the same solvent (8 mL) at −78 °C. After 1 h, a solution of benzeneselenenyl chloride (152 mg, 0.833 mmol) in dry tetrahydrofuran (5 mL) was added dropwise during 2 min. The reaction mixture was stirred at −78 °C for 3 h, warmed to room temperature, and stirred for an additional 60 min before being acidified with saturated ammonium chloride solution (5 mL) and poured into water. The product was extracted into dichloromethane (3 × 50 mL), and the combined organic layers were dried and evaporated. The residual greenish oil was purified by preparative TLC on silica gel to give 117 mg (41%, 68% based on recovered **4**) of **11** as colorless prisms: mp 144–145 °C (from dichloromethane–hexane); IR ($CHCl_3$, cm^{-1}) 1730; ^1H NMR (300 MHz, $CDCl_3$) δ 7.6–7.1 (m, 5 H), 5.8–5.45 (m, 4 H), 3.85–3.55 (m, 3 H), 3.55–3.4 (m, 1 H), 3.1–2.9 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) 212.96, 211.21, 137.28, 137.21, 126.93, 133.58, 133.42, 133.29, 129.15, 128.93, 126.75, 71.27, 62.30, 62.11, 52.04, 41.30 ppm.

Anal. Calcd for $C_{18}H_{14}O_2Se$: C, 63.35; H, 4.14. Found: C, 63.32; H, 4.01.

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Communications

Structure and Biosynthesis of Novel Antibiotics, Aurantinins A and B Produced by *Bacillus aurantinus*

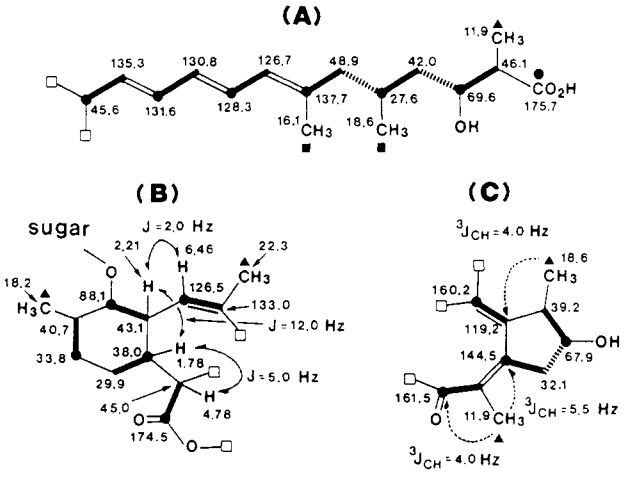
Summary: Structures of aurantinins A (1) and B (2), novel antibacterial antibiotics isolated from bacterium, have been determined in part by biosynthetic means using ^{13}C-labeled precursors.

Sir: The aurantinins A (1) and B (2)[1] comprise a novel polyketide antibiotic complex produced by *Bacillus aurantinus* Masuma and Ōmura sp. nov. which show antimicrobial activity against Gram-positive bacteria, especially anaerobes. In the present report, we describe structure elucidation of the antibiotics based on NMR analysis and biosynthetic means using ^{13}C-labeled precursors.

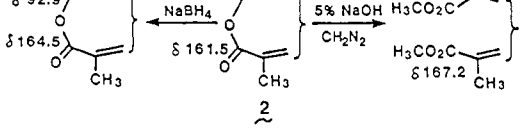
Antibiotics 1 and 2 were isolated from the ethyl acetate extract of the cultured broth by Sephadex LH-20 followed by centrifugal liquid chromatography, preparative silica gel thin-layer chromatography, and then Sephadex LH-20. Antibiotics 1 and 2 possess the following physicochemical properties. 1: mp 139 °C; $[\alpha]^{25}_D$ +126° (*c* 1.0, MeOH); FD-MS, *m/z* 636 (M^+); $C_{38}H_{52}O_8$.[2] 2: mp 98 °C; $[\alpha]^{25}_D$ +124° (*c* 0.33, MeOH); FD-MS, *m/z* 780 (M^+); $C_{44}H_{60}O_{12}$. The UV absorption (λ_{max}^{EtOH} 268, 278, 287, and 320 nm) of the aurantinins suggested the presence of a triene chromophore.

Methanolysis of 2 afforded the same monomethyl ester 3 [mp 94–96 °C; $[\alpha]^{25}_D$ +148° (*c* 0.35, MeOH); FD-MS, *m/z* 650 (M^+)] as a product obtained by methylation of 1 with CH_2N_2, indicating that the aglycon part of 2 is identical with that of 1. Comparative ^{13}C NMR spectral data for 1 and 2 suggested the existence of a novel ulose (a ketone carbonyl at δ 206.5, an anomeric carbon at δ 105.1, three oxygenated carbons at δ 78.0, 77.8, and 72.8, and a methyl at δ 18.4) in 2. $^1H/^1H$ and $^1H/^{13}C$ COSY spectral analyses assigned 6-deoxy-β-*ribo*-hexopyranos-3-ulose as the sugar. The ^{13}C spectrum of 2 indicated the presence of eight methyls, five methylenes, eight methines, six oxygenated methines, six double bonds, and four carbonyls.

In order to elucidate the C–C connectivity of the aglycon part of 2, biosynthetic studies were performed with ^{13}C labeled precursors. The feeding experiments[3] using ^{13}C-labeled acetate and L-methionine clearly indicated an alternating labeling pattern typical of a polyketide. The ^{13}C spectrum of aurantinin B labeled with [1-^{13}C]acetate showed strong enrichment for 16 carbon signals (δ 175.7, 174.5, 161.5, 160.2, 144.5, 137.7, 131.6, 128.3, 126.5, 88.1, 69.6, 67.9, 45.6, 38.0, 33.8, and 27.6). In the feeding experiment with [2-^{13}C]acetate, 17 carbon signals (δ 135.3, 133.0, 130.8, 126.7, 119.2, 118.5, 48.9, 46.1, 45.0, 43.1, 42.0, 40.7, 39.2, 32.1, 29.9, 18.6, and 16.1) including two methyl carbons were enriched. The ^{13}C spectrum of [1,2-^{13}C]-acetate labeled aurantinin B exhibited additional satellite peaks for all carbon signals except for the carbons arising from methionine as the biosynthetic precursor and the sugar moiety. The observation of intra- and intermolecular ^{13}C–^{13}C coupling patterns of acetate units in the 2D INADEQUATE spectrum[4] and LSPD (^1H and ^{13}C long-range selective decoupling) experiment permitted derivation of partial structures A, B, and C. Regarding the connectivity



between structures B and C, the existence of an acid anhydride moiety in 2 was derived from the ^{13}C NMR data[5] of dihydroaurantinin B obtained by $NaBH_4$ reduction of



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(1) (a) Ōmura, S.; Nishikiori, T., Ōiwa, R., Iwai, Y.; Masuma, R.; Katagiri, M., *J. Antibiot.* **1976**, *29*, 477–478. (b) Nishikiori, T.; Masuma, R.; Ōiwa, R.; Katagiri, M.; Awaya, J.; Iwai, Y.; Ōmura, S. *J. Antibiot.* **1978**, *31*, 525–532. (c) Konda, Y.; Nakagawa, A.; Harigaya, Y.; Onda, M.; Masuma, R.; Ōmura, S. *J. Antibiot.* **1988**, *41*, 268–270.

(2) The molecular formula, $C_{35}H_{54}O_9$ for aurantinin A reported in ref 1 should be revised to $C_{38}H_{52}O_8$ from FD mass and ^{13}C NMR spectral data of its triacetae and monomethyl ester.

(3) The ^{13}C precursors (0.2%, w/v), 98% enriched [1-^{13}C]acetate, [2-^{13}C]acetate, [1,2-^{13}C]acetate, [1-^{13}C]propionate, and [*methyl*-^{13}C]L-methionine were added to a 6-h fermentation broth (media: glycerol, 0.8%; starch, 0.9%; soybean meal, 2.0%; dry yeast, 0.3%; NaCl, 0.5%; $(NH_4)_2SO_4$, 0.2%; K_2HPO_4, 0.1%; $CaCO_3$ 0.3%; pH 7.0) and the cultivation continued at 27 °C for 42 h. ^{13}C labeled aurantinins (2–4 mg) were isolated from the cultured broth (1-2 L) by the isolation procedure described in this paper. ^1H and ^{13}C NMR spectra were measured with a Varian XL-400 in deuterioacetone.

(4) 2D-INADEQUATE spectrum of [1,2-$^{13}C_2$]acetate labeled aurantinin B was taken under the following conditions: number of accumulations, 2050; J_{CC} = 60 Hz; number of increments, 64; delay time, D_1 = 3 s; total acquisition time, 122 h.

(5) The existence of the anhydride moiety in 2 was confirmed by the following ^{13}C NMR data:

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