Bis(trimethylsilyl)acetylene (1.7 g, 10 mmol) was then added, and the reaction became homogeneous and amber in color. The entire reaction was filtered through a 3-in. × 1-in. plug of chloroform-saturated silica gel and was eluted with 150 mL of chloroform; a vacuum aspirator was used to hasten the elution rate. The product was concentrated to 10 mL, treated with 1,3-cyclohexadiene (2 g, 25 mmol), and allowed to stand at room temperature overnight. The reaction mixture was then chromatographed over silica gel, eluting with 1:1 hexane/chloroform, collecting the R_f 0.5 material. Concentration of effluent in vacuo yielded 600 mg (27% overall from bis(trimethylsilyl)acetylene) of yellow crystals: mp 53–55 °C; IR (CCl_4 smear) 3085 (w vinyl CH), 2960 (m, CH), 1520 (s, NO_2), 1360 (s, NO_2) cm^{-1}; ^1H NMR ($CCl_4/CHCl_3$) δ 1.4 (m, 4 H, CH_2), 4.1 (m, 1 H, CH), 4.6 (m, 1 H CH), 6.3–6.6 (m, 2 H, CH). Anal. Calcd for $C_{11}H_{17}NO_2Si$: C 59.19; H, 7.62; N, 6.28. Found: C, 59.14, H, 7.45, N, 6.28.

2-Nitro-3-(trimethylsilyl)bicyclo[2.2.1]hepta-2,5-diene. The reaction of nitronium fluoroborate and bis(trimethylsilyl)acetylene was carried out exactly as described in the previous sequence involving cyclohexadiene. The resulting 10 mL of solution containing 1-nitro-2-(trimethylsilyl)acetylene was treated with 5 mL of cyclopentadiene and was stored under argon for 15 h. The reaction mixture was concentrated and chromatographed over silica gel and eluted with chloroform and the R_f = 0.7 material was collected. The effluent was concentrated and distilled in vacuo to give 1.0 g (50%) of yellow oil: bp 44 °C (0.1 Torr); IR (neat smear) 3080 (w, vinyl CH), 2960 (m, CH), 1505 (s, nitro), 1530 (s, nitro) cm^{-1}; ^1H NMR (CCl_4) δ 2.2 (m, 2 H, CH_2), 4.0 (m, 2 H, CH), 6.8 (m, 1 H, CH), 7.1 (m, 1 H, CH). Anal. Calcd for $C_{10}H_{15}NO_2Si$: C, 57.42; H, 7.18; N, 6.7. Found: C, 56.73; H, 7.43; N, 6.39.

X-ray Diffraction Analysis of 4-Nitro-5-(trimethylsilyl)pyrazole. $C_6H_{11}N_3O_2Si$, FW = 185.3, triclinic space group $P\bar{1}$, a = 6.573 (1) Å, b = 6.875 (1) Å, c = 12.138 (1) Å, α = 90.04 (1), β = 97.36 (1), γ = 116.63 (1)°, Vol. = 485.2 (1) Å^3, Z = 2, ρ_{calc} = 1.268 g/cm^3, λ(Cu kα) = 1.541 78 Å, μ = 19.1 cm^{-1}, $F(000)$ = 196, T = 295 K.

A clear colorless 0.15 × 0.17 × 0.32 mm crystal was used for data collection on an automated Nicolet R3m/V diffractometer with incident beam monochromator. Lattice parameters were determined from 25 centered reflections within $60 \le 2\theta \le 76°$. The data collection range of hkl was: $-7 \le h \le 6$, $0 \le k \le 7$, $-13 \le l \le 13$, $\sin(\theta)/\lambda)_{max}$ = 0.56 Å^{-1}. Three standards were monitored every 60 reflections and exhibited a maximum random variation of 3.5% during data collection. A total of 1659 reflections were measured in the $\theta/2\theta$ mode with a scan, width from $[2\theta(K_{\alpha 1}) - 1.0]$ to $[2\theta(K_{\alpha 2}) + 1.0]°$; scan rate was a function of count rate (8 deg/min minimum, 30 deg/min maximum). There were 1462 unique reflections, R_{int} = 0.024 from merging equivalent reflections, and 1394 were observed with $F_o > 3\sigma(F_o)$. Data corrected for Lorentz, polarization and absorption effects, max and min transmission 0.91 and 0.59.

The structure was solved by direct methods with the aid of program SHELXTL.[9] The minimized full-matrix least-squares function was $\sum w(|F_o| - |F_c|)^2$ where $w = 1/[\sigma^2(|F_o|) + g(F_o)^2]$. In this work g = 0.00025. The secondary extinction parameter was p = 0.036 (6) in $F_c^* = F_c/[1.0 + 0.002(p)F_o^2/\sin(2\theta)]^{0.25}$. There were 196 parameters refined: atom coordinates, anisotropic thermal parameters for all non-H atoms, and isotropic thermal parameters for the hydrogens, methyl hydrogens used riding model in SHELXTL, H riding on C, C–H = 0.96 Å, U(H) = 1.2 U_{eq}(C). The final residuals were R = 0.039 and R_w = 0.060 with an error for observations of unit weight of 2.90, N_o/N_v = 11.0. The largest shift to error ratio in the final refinement cycle was 0.076 and final difference Fourier excursions were 0.21 and −0.19 e Å^{-3}. Atomic scattering factors are from the *International Tables for X-ray Crystallography* (1974). Tables of atomic coordinates, bond distances and angles, and anisotropic thermal parameters are available as supplementary material.

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Registry No. $Si(CH_3)_3N_3$, 4648-54-8; 4-nitro-5-(trimethylsilyl)pyrazole, 36960-51-7; 4-nitro-5-(trimethylsilyl)-1,2,3-triazole, 122202-89-5; 2-nitro-3-(trimethylsilyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene, 125251-41-4; 2-nitro-3-(trimethylsilyl)bicyclo[2.2.1]-octa-2,5-diene, 107494-77-9; 2-nitro-3-(triisopropylsilyl)bicyclo-[2.2.1]hepta-2,5-diene, 107474-07-7; 2-nitro-3-(trimethylsilyl)bicyclo[2.2.1]hepta-2,5-diene, 107474-08-8; bis(trimethylsilyl)-acetylene, 14630-40-1; furan, 110-00-9; cyclopentadiene, 542-92-7; 1,3-cyclohexadiene, 592-57-4; *o*-(trimethylsilyl)nitrobenzene, 15290-22-9; 1-nitro-2-(triisopropylsilyl)acetylene, 107474-05-5; 1,4-bis(triisopropylsilyl)buta-1,3-diene, 125251-42-5.

Supplementary Material Available: X-ray crystal structure data for 4-nitro-5-(trimethylsilyl)pyrazole (2 pages); tables of structure factors for 4-nitro-5-(trimethylsilyl)pyrazole (6 pages). Ordering information is given on any current masthead page.

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Studies of the Total Synthesis of Fredericamycin A. Preparation of Key Partial Structures and Development of an Intermolecular Alkyne–Chromium Carbene Complex Benzannulation Cyclization Approach to the ABCD(E) Ring System

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A study illustrating factors effecting the cyclization mode and regioselectivity of the alkyne–chromium carbene complex benzannulation cyclization reaction is detailed in development of a synthetic approach to the fredericamycin A ABCD(E) ring system.

Fredericamycin A (1, NSC-305263), a quinone antitumor antibiotic[2] isolated from *Streptomyces griseus*[3] bearing a unique spiro[4.4]nonene central to its structure, has been shown to possess potent in vitro cytotoxic activity and

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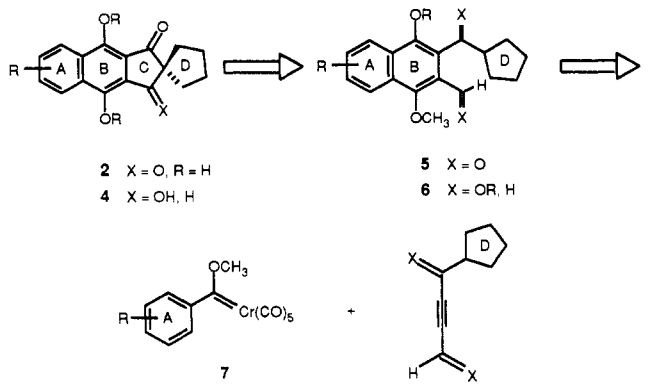
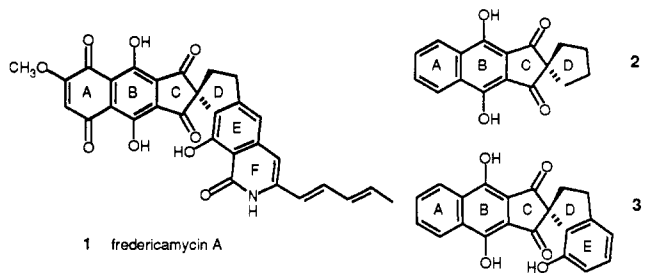
Scheme I



confirmed in vivo antitumor activity that may be derived from its inhibition of RNA and protein synthesis through nondiscriminant oxidative damage of DNA and/or the inhibition of DNA processing enzymes including topoisomerase II.[2,4,5] Consequently, since the unambiguous establishment of its structure through a single-crystal X-ray structure determination[6] after extensive spectroscopic studies failed to resolve tautomeric structures,[4] fredericamycin A has been the subject of continued biological[2,4,5] and extensive synthetic efforts[7] including one completed total synthesis.[8]

Herein, we provide full details of preliminary studies[9] on the development of a general approach to the construction of the fredericamycin A ABCD(E) ring system applicable to the total synthesis of fredericamycin A and structurally related analogues based on the implementation of a regiospecific, intermolecular alkyne–chromium carbene complex benzannulation cyclization.[10] The key to the potential development of this convergent approach to the fredericamycin A skeleton rests with the facility with which a simple aldol closure might provide for introduction of the spiro[4.4]nonene (CD ring system)[11] and the feasibility for implementation of a regioselective inter- or intramolecular alkyne–chromium carbene complex cyclization for construction of the fully substituted B ring hydroquinone, Scheme I. Herein, the preparation of **2** and **3** constituting key partial structures of the natural product is detailed in studies that establish this plan as a viable approach to the total synthesis of fredericamycin A.



Studies on the Intermolecular Alkyne–Chromium Carbene Complex Benzannulation Cyclization. In initial efforts it was anticipated that the electronic nature of the alkyne might prove to be a useful and perhaps predominant element by which the regioselectivity of an intermolecular alkyne–chromium carbene complex benzannulation cyclization could be controlled. However, a study of the electronic and steric features of the alkyne that control the alkyne–chromium carbene complex cyclization mode[10] and regioselectivity[10,12–14] revealed that the benzannulation chemical conversions were optimal with neutral alkynes (neutral alkynes > electron-deficient alkynes) and that modest steric differences in the substitution pattern at the alkyne α-carbons proved sufficient to permit complete regiocontrol in the intermolecular cyclization reactions, eq 1–2 (Table I, supplementary material) and Table I. As detailed by Dötz and Wulff, the regioselectivity of the benzannulation cyclization is derived from destabilizing steric interactions generated enroute to the initial chromium metallocyclobutane intermediate preferentially placing the alkyne large substituent ortho to the free phenol of the reaction product. More recently,

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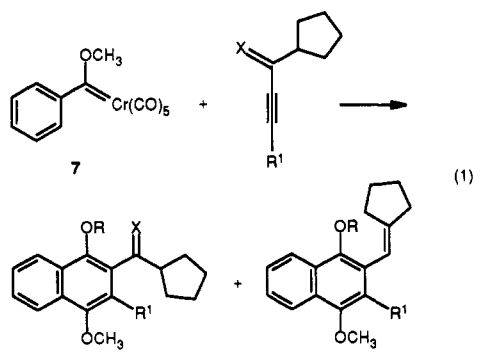
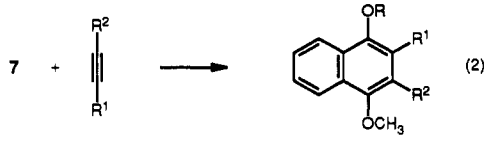


(1)

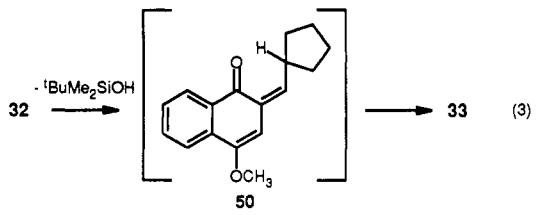
	X	R^1	R	Product(s)	
8	$OSiMe_2{}^tBu$, H	H	$COCH_3$	26 : 27	
9	$OSiPh_2{}^tBu$, H	H	$COCH_3$	28 : 27	
10	$OSiMe_2{}^tBu$, H	CO_2CH_3	H	29 : 30	(R = H)
11	$OSiPh_2{}^tBu$, H	CO_2CH_3	H	31 : 30	(R = $COCH_3$)
12	$OSiMe_2{}^tBu$, H	$CH_2OSiMe_2{}^tBu$	H	32 : 33	
13	O	$CH_2OSiMe_2{}^tBu$	H	34 : -	
14	O	CO_2CH_3	H	35 : -	
15	O	H	H	36 : -	
16	O	$SiMe_3$	H	37 : -	
17	O	$CH{=}CHOCH_3$	H	38 : -	



(2)

	R^1	R^2	R	Product(s)
18	CO_2CH_3	H	H	39
19	$COCH_3$	H	H	40
20	$CH(OSiMe_2{}^tBu)CH_3$	H	H	41
			$COCH_3$	42
21	CO_2CH_3	CO_2CH_3	H	43
22	$CH{=}CHOCH_3$	H	H	44
			$COCH_3$	45
23	$CH{=}CHOCH_3$	$SiMe_3$	H	46
			$COCH_3$	47
24	$SnBu_3$	H	H	48
25	$SnBu_3$	$CH_2OSiMe_2{}^tBu$	H	49

Yamashita has detailed studies that indicate that these observations are not altered with the introduction of alkyne electron-donating or electron-withdrawing substituents.[10,12-14] In agreement with the recent efforts of Wulff,[10c] the benzannulation reactions proved to be conducted optimally in heptane versus ethereal solvents (Et_2O, THF)[15] at chromium carbene complex concentrations of 0.3 M in the presence of a slight excess of alkyne (1.0–1.5 equiv). Under such conditions, the product of the reaction of alkyne **12** with the Fisher chromium carbene complex **7** proved to be **33** (Table I, entry 6) derived from the in situ elimination of *tert*-butyldimethylsilanol from the primary reaction product **32** and subsequent 1,4-hydrogen migration of the unstable ortho quinomethide **50** to provide **33**, eq 3.[16] The elimination reaction was suppressed when the reaction was conducted under the Yamashita benzannulation reaction conditions (1.5 equiv of Ac_2O, 1.5 equiv of Et_3N,[14] Table I, entry 3). Contrary to expectations, this was attributed exclusively to the inclusion of acetic anhydride in the reaction mixture under conditions that do *not* acylate the product phenol *and that accelerate the rate of the benzannulation reaction* (Table I, entries 4–5).[17] Thus, **32** and **33** may be obtained cleanly from the reaction of **7** with **12**, depending on the reaction conditions selected.



(3)

In addition to the rate acceleration due to the inclusion of acetic anhydride, the benzannulation reactions proved much cleaner, providing fewer or no minor byproducts. In selected instances, no benzannulation reaction product was detected under the standard reaction conditions (heptane 80 °C or THF, 65 °C) while the reactions conducted with the inclusion of acetic anhydride (1–1.5 equiv) permitted the clean conversion to the expected benzannulation reaction product (Table I, entries 1, 2, 10 vs 9, and **67** → **68**). This effect of acetic anhydride proved to be presently unique since the inclusion of trifluoroacetic anhydride ($(CF_3CO)_2O$), di-*tert*-butyl dicarbonate ($(tBuOCO)_2O$), or succinic anhydride in the benzannulation reaction mixture failed to productively accelerate the reaction of **7** with **12**. The rate-determining step of the reactions of the Fischer carbene complexes with alkynes is loss of carbon monoxide to provide a coordinately unsaturated carbene complex then accessible for alkyne ligation.[10] Thus, although the origin of the rate acceleration of the benzannulation reactions due to the inclusion of acetic anhydride in the reaction mixture is not yet well defined, it is due to an accelerated loss of carbon monoxide from the initial carbene complex. Experimentally it was determined that the added acetic anhydride is not consumed in the process of conducting the benzannulation reaction,[18] and this observation suggests that acetic anhydride may serve as an effective, readily displaced bidentate ligand for a coordinately unsaturated chromium carbene complex. Alternatively, in the presence of sterically hindered or poor π-donor alkynes and a poor ligating solvent (heptane vs THF or ether), the coordinately unsaturated chromium carbene complex may form unreactive dimeric or oligomeric chromium carbene complexes. In poor donor solvents, the redissociation of a dimeric chromium carbene complex, e.g., $[ArC(OCH_3)]_2Cr_2(CO)_9$, to provide the coordinately unsaturated complex may become the rate-determining step in the alkyne–chromium carbene complex cyclization. The inclusion of acetic anhydride in the reaction mixture of the benzannulation reactions may prevent the dimerization of the chromium carbene complex or may facilitate the redissociation of a dimeric chromium carbene complex to provide the reactive, coordinately unsaturated complex. Further efforts to delineate the role of acetic anhydride

(15) Other solvents examined include *N,N*-dimethylformamide, methylene chloride, and acetonitrile and the attempted benzannulation reactions provided no recognizable products or multiple products.

(16) Warming a solution of **33** in heptane (80 °C, 24 h) provided **34**, confirming the in situ conversion of **33** to **34** under the benzannulation reaction conditions.

(17) Acetylation of **32** (1.5 equiv of Ac_2O, 1.5 equiv of Et_3N, cat. DMAP, CH_2Cl_2, 4 days, 61%) provided **54**, R = $COCH_3$: ^1H NMR ($CDCl_3$, 200 MHz, ppm) δ 8.16 (1 H, m, aromatic), 7.74–7.51 (3 H, m, aromatic), 5.03 (1 H, d, J = 9.5 Hz, OCHTBDMS), 4.94 (2 H, m, OCH_2TBDMS), 4.09 (3 H, s, OCH_3), 2.91 (1 H, m, CHC_4H_8), 2.53 (3 H, s, $OCOCH_3$), 2.12–1.27 (8 H, m, C_4H_8), 0.96 (9 H, s, $OSiC(CH_3)_3$), 0.87 (9 H, s, $OSiC(CH_3)_3$), 0.23 (6 H, s, $OSiCH_3$), 0.12 (3 H, s, $OSiCH_3$), 0.10 (3 H, s, $OSiCH_3$).

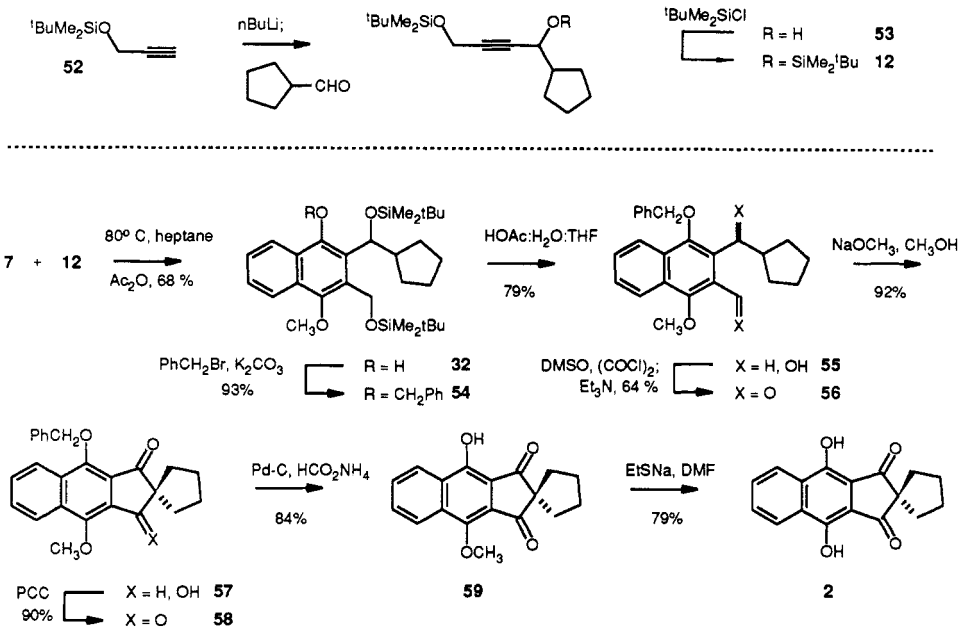
(18) The benzannulation reaction of **7** with **12** conducted in C_6D_6 and followed by ^1H NMR spectroscopy showed no evidence for partial or full consumption of acetic anhydride and use of 2.5 vs 1.0 equiv of acetic anhydride did not have an additional discernable effect on the course of the benzannulation reaction.

Table I. Intermolecular Alkyne–Chromium Carbene Complex Benzannulation Studies

entry	alkyne	X	R^1	equiv	conditions	product(s)[a] yield, %	R	yield, %	R
1	8	$OSiMe_2tBu$, H	H	1.4	Ac_2O–Et_3N (1.5:1.5 equiv), 80 °C, heptane, 1 h, 0.3 M	**26**, 47	$COCH_3$	**27**, –	$COCH_3$
2	9	$OSiPh_2tBu$, H	H	1.5	Ac_2O–Et_3N (1.5:1.5 equiv), 80 °C, heptane, 3 h, 0.1 M	**28**, 32	$COCH_3$	**27**, –	$COCH_3$
3	12	$OSiMe_2tBu$, H	CH_2OSiMe_2tBu	1.1	Ac_2O–Et_3N (1.0:1.0 equiv), 80 °C, heptane, 4 h, 0.3 M	**32**, 68	H	**33**, –	H
4	12			0.8	Et_2N (1.0 equiv), 80 °C, heptane, 16 h, 0.3 M	**32**, 30	H	**33**, 17	H
5	12			1.0	Ac_2O (1.0 equiv), 80 °C, heptane, 3 h, 0.3 M	**32**, 66	H	**33**, –	H
6	12			1.0	80 °C, heptane, 17 h, 0.3 M	**32**, –	H	**33**, 74	H
		R^1	R^2						
7	18	CO_2CH_3	H	1.5	65 °C, THF, 6 h, 0.08 M	**39**, 32	H		
8	19	$COCH_3$	H	1.5	65 °C, THF, 5 h, 0.03 M	**40**, 28	H		
9	20	$CH(OSiMe_2tBu)CH_3$	H	1.5	80 °C, heptane, 43 h, 0.3 M	**41**, 0	H		
10	20			1.5	Ac_2O–Et_3N (1.5:1.5 equiv), 80 °C, heptane, 1 h, 0.3 M	**42**, 74	$COCH_3$		

[a] All yields are based on pure product isolated by chromatography (SiO_2) and all new products provided the expected ^1H NMR, IR, EI/CIMS, and satisfactory HRMS. Compounds **39** and **40** proved identical with authentic materials.

Scheme II



in accelerating the rate of the chromium carbene complex benzannulation reaction are in progress.

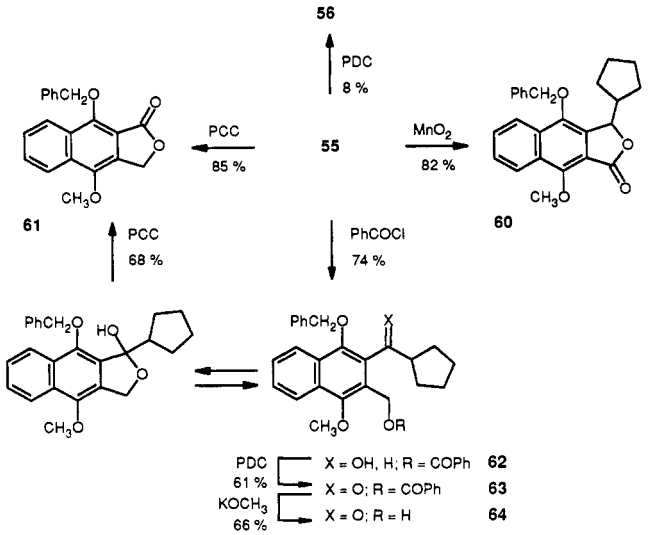
Fredericamycin A ABCD(E) Ring System. The implementation of the regiospecific benzannulation reaction of **7** with **12** in the construction of the fredericamycin A ABCD carbon framework is detailed in Scheme II. Protection of the free phenol of the benzannulation product **32** as its benzyl ether **54** was accomplished cleanly under mild basic conditions (78%) without competitive elimination of *tert*-butyldimethylsilanol. Subsequent deprotection of the primary and secondary benzylic alcohols under aqueous acid hydrolysis conditions (HOAc–H_2O–THF, 79%) followed by direct oxidation of diol **55** provided keto aldehyde **56** (64%) cleanly only under the conditions of Swern oxidation.[19] The success of the Swern oxidation of **55** proved critically dependent upon the reaction conditions in which the activation of both alcohols through formation of the bisalkoxysulfonium salt preceded base-catalyzed elimination of dimethyl sulfide with formal oxidation of the primary and secondary benzylic alcohols. As may be anticipated, the use of alternative reagents for oxidation of diol **55** led to the preferential generation of products derived from oxidation of the hemiacetal or hemiketal monoxidation products, Scheme III.[20-22] Keto aldehyde **56** cleanly closed the spirocyclic keto alcohol **57** (92%) upon exposure to sodium methoxide, thus providing the functionalized spiro[4.4]nonene subunit of fredericamycin A and establishing the viability of this approach to the fredericamycin A ABCD ring system. Oxidation[20] of **57** provided dione **58** (90%) without detection of a competitive retro aldol reaction, and the subsequent sequential deprotection of **58** provided **2**.[23,24]

The extension of these observations to the preparation of the fredericamycin A ABCDE ring system is detailed

(19) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.

(20) PCC: Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.
(21) PDC: Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.
(22) NaOCl: Stevens, R. V.; Chapman, K. T. *Tetrahedron Lett.* **1982**, *23*, 4647.
(23) Ram, S.; Spicer, L. D. *Synth. Commun.* **1987**, *17*, 415.
(24) Feutrill, G. I.; Mirrington, R. N. *Aust. J. Chem.* **1972**, *25*, 1719.

Scheme III



in Scheme IV and required the use of the more highly functionalized alkyne **67** in a sequence that employed substrates representative of those required for incorporation into the total synthesis of the natural product. Alkyne **67** was prepared from 7-hydroxyindanone (**65a**)[25] as detailed in Scheme IV without event with the exception that the Wittig methoxymethylenation of 7-benzyloxyindanone (**65a**) and the subsequent acid-catalyzed hydrolysis of **65b** proceeded smoothly under the conditions detailed by Novák and Salemink[26] and more modestly under standard reaction conditions ($CH_3SO_2CH_2Na$ base, $Ph_3PCHOCH_3$, DMSO; *n*-BuLi base, $Ph_3PCHOCH_3$, THF). Regiospecific benzannulation cyclization of **67** with **7** under the conditions detailed herein (0.3 M **7**, 1.0 equiv of **67**, 80 °C, heptane, 1.0 equiv of Ac_2O, 3 h) cleanly provided **68** (85%) as the exclusive benzannulation product (≥95%) without the detection of subsequent products derived from the elimination of *tert*-butyldimethylsilanol. In sharp contrast, the benzannulation cyclization of **7** with **67** under the standard reaction conditions (65 °C, THF; 80 °C, heptane; 18–24 h) provided no major identifiable products. Protection of the free phenol as its benzyl ether **69** (80%), fluoride-promoted deprotection of the primary and secondary benzylic alcohols (68%),[27,28] and subsequent Swern oxidation[19] of diol **70** provided keto aldehyde **71** (66%) cleanly. Base-catalyzed aldol closure of **71** smoothly provided the spirocyclic keto alcohol **72** as a 1:1.5 mixture of two diastereomers thus affording the key, functionalized fredericamycin A spiro[4.4]nonene subunit (>90%). Subsequent oxidation[20] of the benzylic alcohols **72** provided dione **73** (85% overall from **71**). Exhaustive deprotection of **73** was accomplished in a single operation upon treatment with boron tribromide (90%) to provide **3**.[29] Partial and sequential deprotection of the benzyl ethers of **73** afforded **74** and **75** and ultimately provided an alternative preparation of **3** from **73**.[23,24]

The facility with which an alkyne–chromium carbene complex benzannulation cyclization reaction may be conducted under the modified reaction conditions detailed herein with incorporation of sensitive alkynes, its implementation in a regiospecific cyclization applicable to fredericamycin A B-ring preparation (**67** → **68**), and the apparent ease with which a simple aldol cyclization may be employed in the formation of a functionalized spiro[4.4]nonene characteristic of fredericamycin A (**71** → **72**) establish the viability of this synthetic approach to fredericamycin A. The application of these observations in the total syntheses of fredericamycin A and structural analogues is in progress and will be reported in due course.[30]

Experimental Section[31]

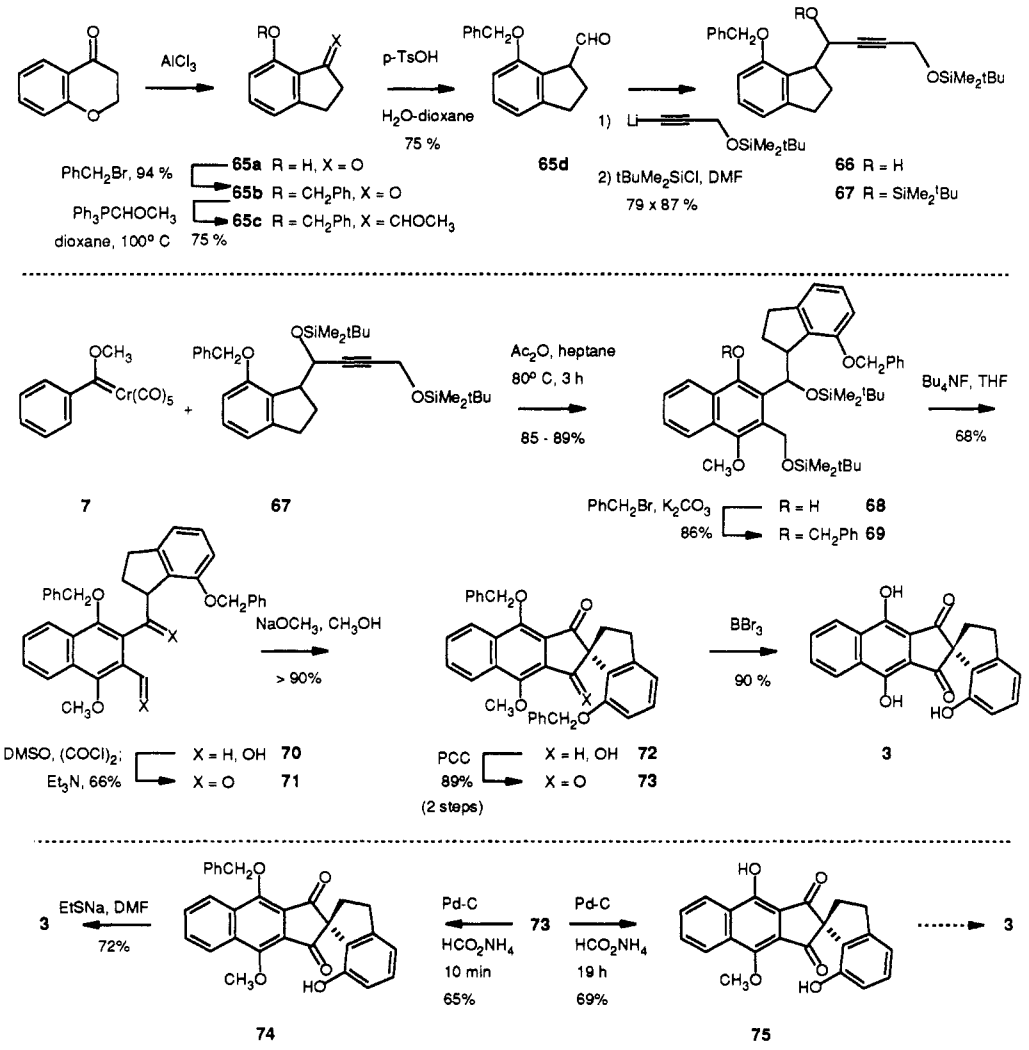
1,4-Bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-cyclopentyl-2-butyne (12). A solution of 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-propyne[32] (**52**, 2.74 g, 16.1 mmol) in tetrahydrofuran (50 mL) at −78 °C was treated with *n*-butyllithium (2.30 M, 7.00 mL, 16.1 mmol). The solution was warmed to 0 °C over 0.5 h, recooled to −78 °C, and treated with cyclopentylmethanal (Wiley Organics, 1.58 g, 16.1 mmol). The reaction mixture was stirred at −78 °C for 15 min and treated with water. The mixture was diluted with water (300 mL) and neutralized with the addition of 10% aqueous hydrochloric acid, and the aqueous phase was extracted with ether (2 × 15 mL). The combined ether extracts were dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (SiO_2, 17 cm × 10 cm, 10% EtOAc–hexane eluant) afforded 2.10 g (4.34 g theoretical, 49%) of **53** as a colorless oil: ^1H NMR ($CDCl_3$, 300 MHz) δ 4.35 (2 H, m, $CH_2OTBDMS$), 4.28 (1 H, m, $CHOH$), 2.20 (1 H, m, CHC_4H_8), 2.05 (1 H, br s, OH), 1.60 (8 H, m, C_4H_8), 0.91 (9 H, s, $OSiC(CH_3)_3$), 0.12 (6 H, s, $OSi(CH_3)_2$).

A solution of **53** (3.45 g, 12.8 mmol) in *N,N*-dimethylformamide (50 mL) was treated with imidazole (2.18 g, 32.1 mmol) and *tert*-butyldimethylsilyl chloride (2.90 g, 19.2 mmol). The reaction mixture was stirred at ambient temperature for 29 h before it was diluted with water (500 mL) and extracted with ether (2 × 200 mL). The ether extracts were dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, 18 cm × 10 cm, petroleum ether–ether–methylene chloride (3:1:1) eluant) afforded 3.71 g (4.93 g theoretical, 75%) of **12** as a colorless oil: ^1H NMR ($CDCl_3$, 300 MHz) δ 4.33 (2 H, m, $CH_2OTBDMS$), 4.21 (1 H, d, J = 6.7 Hz, CHOTBDMS), 2.14 (1 H, m, CHC_4H_8), 1.56 (8 H, m, C_4H_8), 0.91 (9 H, s, $OSiC(CH_3)_3$), 0.90 (9 H, s, $OSiC(CH_3)_3$), 0.13 (3 H, s, $OSiCH_3$), 0.12 (6 H, s, $OSi(CH_3)_2$), 0.09 (3 H, s, $OSiCH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 86.49 (e), 82.66 (e), 66.86 (o, $OCHC_5H_9$), 52.05 (e, OCH_2TBDMS), 47.23 (o, CHC_4H_8), 29.07 (e), 28.78 (e), 26.08 (o, 6 C, $OSiC(CH_3)_3$), 26.00 (e), 18.52 (e, 2 C, $OSiC(CH_3)_3$), −4.06 (o, $OSiCH_3$), −4.82 (o, $OSiCH_3$), −4.86 (o, 2 C, $OSiCH_3$); IR (film) ν_{max} 2956, 2930, 2858, 1254, 1094, 836 cm^{-1}; EIMS *m/e* (relative intensity) 381 (M^+ − H, 1), 367 (10, $M^+ - CH_3$), 325 (33, $M^+ - C_4H_9$), 251 (17, M^+ − OTBDMS), 147 (base), 119 (19), 73 (23); CIMS (2-methylpropane) *m/e* 383 (10, M^+ + H), 251 (base, M^+ + H − HOTBDMS); EIHRMS *m/e* calc for $C_{21}H_{42}O_2Si_2$ 382.2723, found 382.2719.

3-[1-Cyclopentyl-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-2-[1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-

(25) Loewenthal, H. J. E.; Schatzmiller, S. *J. Chem. Soc., Perkin Trans. 1* **1975**, *21*, 2149.
(26) Novák, J.; Salemink, C. A. *Tetrahedron Lett.* **1981**, *22*, 1063.
(27) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
(28) Mild aqueous acid hydrolysis of **69** (HOAc–H_2O–THF, 3:2:2, 60–65 °C) proved much less effective.
(29) BBr_3: Vickery, E. H.; Dahler, L. F.; Eisenbrawn, E. J. *J. Org. Chem.* **1979**, *24*, 4444. Sodium ethanethiolate (DMF, 150 °C, 3 h) proved less successful in providing **3** directly from **73**.
(30) Preliminary attempts to productively incorporate **33** into a preparation of the fredericamycin A ABCD ring system through phenol functionalization [**54**, R = CO_2tBu: ^1H NMR ($CDCl_3$, 300 MHz) δ 8.11 (1 H, d, J = 9.6 Hz, C8-H), 7.93 (1 H, d, J = 9.5 Hz, C5-H), 7.50 (2 H, m, C6 and C7-H), 6.30 (1 H, br s, $CH{=}C_5H_8$), 4.81 (2 H, s, $CH_2OTBDMS$), 4.01 (3 H, s, OCH_3), 2.47 (2 H, m, $CH{=}CCH_2$), 2.14 (2 H, m, $CH{=}CCH_2$), 1.65 (4 H, m, CH_2CH_2), 1.53 (9 H, s, $CO_2C(CH_3)_3$), 0.90 (9 H, s, $OSiC(CH_3)_3$), 0.12 (6 H, s, $OSi(CH_3)_2$); IR (film) ν_{max} 2954, 2886, 2856, 1762, 1472, 1370, 1248, 1148, 1120, 1106, 1066, 836, 776 cm^{-1}; EIMS *m/e* (relative intensity) 498 (M^+, 0.2), 441 (1, $M^+ - C(CH_3)_3$), 398 (5), 326 (26), 237 (1), 165 (1), 91 (2), 77 (1), 75 (8), 57 (base); CIMS (2-methylpropane) *m/e* 398 (5, $M^+ + H - CO_2C_4H_9$), 267 (base); EIHRMS *m/e* calc for $C_{29}H_{42}O_5Si$ 498.2836, found 498.2806. Anal. Calcd for $C_{29}H_{42}O_5Si$: C, 69.88; H, 8.43; Si, 5.62. Found: C, 69.73; H, 8.80; Si, 5.23]. Subsequent intramolecular bromo- or iodolactonization have not proven successful.
(31) General experimental procedures may be found in the supplementary material.
(32) Logue, M. W.; Teng, K. *J. Org. Chem.* **1982**, *47*, 2549.

Scheme IV



methyl]-1-methoxy-4-naphthalenol (32). (a) A solution of 7[33] (69 mg, 0.22 mmol), 1,4-bis[[(1,1-dimethylethyl)dimethylsilyl]-oxy]-1-cyclopentyl-2-butyne (**12**, 89 mg, 0.23 mmol), acetic anhydride (0.02 mL, 0.22 mmol), and triethylamine (0.03 mL, 0.22 mmol) in heptane (0.7 mL) was warmed at 80 °C for 3.75 h. The cooled reaction mixture was concentrated in vacuo. Flash chromatography (SiO_2, 16 cm × 6 cm, petroleum ether–ether–methylene chloride (20:1:1) eluant) afforded 79 mg (120 mg theoretical, 68%) of pure **32** as a white crystalline solid. The conversion of **12** (0.17–7.10 mmol) to **32** was routinely achieved in 66–69% yield: mp 62–64 °C (white prisms, hexane); ^1H NMR ($CDCl_3$, 200 MHz) δ 9.17 (1 H, s, OH), 8.24 (1 H, m, aromatic), 8.02 (1 H, m, aromatic), 7.46 (2 H, m, C6- and C7-H), 5.28 (1 H, d, J = 6.0 Hz, CHOTBDMS), 4.91 (1 H, d, J = 10.8 Hz, C*H*HOTBDMS), 4.82 (1 H, d, J = 10.9 Hz, CH*H*OTBDMS), 3.90 (3 H, s, OCH_3), 2.42 (1 H, m, C*H*C_4H_8), 1.80–1.43 (8 H, m, C_4H_8), 0.94 (9 H, s, $OSiC(CH_3)_3$), 0.91 (9 H, s, $OSiC(CH_3)_3$), 0.19 (3 H, s, $OSiCH_3$), 0.18 (3 H, s, $OSiCH_3$), 0.16 (3 H, s, $OSiCH_3$), −0.11 (3 H, s, $OSiCH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 149.20 (e, C1), 148.04 (e, C4), 127.89 (e, C9), 126.71 (e, C10), 126.51 (o, C8), 126.21 (e, C3), 125.71 (o, C5), 123.09 (o, C7), 122.46 (o, C8), 121.07 (e, C2), 76.37 (o, CHOTBDMS), 63.89 (o, OCH_3), 57.16 (e, CH_2OTBDMS), 48.24 (o, CHC_4H_8), 29.34 (e, CH_2), 28.94 (e, CH_2),

Table II. Benzannulation Reaction of 7 with 12

alkyne (equiv)	conditions	product(s) (% yield)
12 (1.0)	1.0 equiv of Ac_2O, heptane, 80 °C, 3 h, 0.3 M	**32** (66)
12 (1.1)	1.0 equiv of Ac_2O, 1.0 equiv of Et_3N, heptane, 80 °C, 4 h, 0.3 M	**32** (68)
12 (1.2)	1.0 equiv of Ac_2O, 1.0 equiv of Et_3N, heptane, 80 °C, 3 h, 0.3 M	**32** (67)
12 (1.05)	1.0 equiv of Ac_2O, 1.0 equiv of Et_3N, heptane, 80 °C, 3 h, 0.3 M	**32** (63)
12 (0.95)	1.0 equiv of Ac_2O, 1.0 equiv of Et_3N, heptane, 80 °C, 3 h, 0.3 M	**32** (65)[a]
12 (0.90)	1.0 equiv of Ac_2O, 1.0 equiv of Et_3N, heptane, 80 °C, 3 h, 0.3 M	**32** (62)[a]
12 (0.75)	1.0 equiv of Ac_2O, 1.0 equiv of Et_3N, heptane, 80 °C, 3 h, 0.3 M	**32** (67)[a]
12 (0.90)	1.5 equiv of Ac_2O, 1.5 equiv of Et_3N, heptane, 54 °C, 11 h, 0.3 M[b]	**32** (44)[a]
12 (0.8)	1.0 equiv of Et_3N, heptane, 80 °C, 16 h, 0.3 M	**32** (30), **33** (17)
12 (1.0)	1.0 equiv of Ac_2O, THF, 65 °C, 3 h, 0.3 M	**32** (29)
12 (1.0)	heptane, 80 °C, 17 h, 0.3 M	**33** (74)
12 (1.0)	heptane, 40 °C, 20 h, 0.3 M	**32** (48)
12 (1.0)	acetone, 55 °C, 4.5 h, 0.3 M	**32** (24)
12 (3.0)	heptane, 56 °C, 24 h, 0.3 M[b]	**32** (51), **33** (26)

[a] Yield based on alkyne **12** as limiting agent. [b] Under sonication.

(33) Chromium carbene complex **7** is commercially available from Aldrich Chemical Co. For its preparation, see: (a) Peterson, G. A.; Kunng, F. A.; McCallum, J. S.; Wulff, W. D. *Tetrahedron Lett.* **1987**, *28*, 1381. (b) Chan, K.-S.; Wulff, W. D. *J. Am. Chem. Soc.* **1986**, *108*, 5229. (c) Yamashita, A. *J. Am. Chem. Soc.* **1985**, *107*, 5823. (d) Semmelhack, M. F.; Bozell, J. J.; Keller, L.; Sato, T.; Spiess, E. J.; Wulff, W.; Zask, A. *Tetrahedron* **1985**, *41*, 5803. (e) Dötz, K. H.; Popall, M. *Tetrahedron* **1985**, *41*, 5797. (f) Wulff, W. D.; Yang, D. C. *J. Am. Chem. Soc.* **1984**, *106*, 7565. (g) Wulff, W. D.; Chang, K.-S.; Tang, P.-C. *J. Org. Chem.* **1984**, *49*, 2293. (h) Wulff, W. D.; Tang, P.-C. *J. Am. Chem. Soc.* **1984**, *106*, 434. (i) Dötz, K. H.; Kuhn, W. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 732. (j) Dötz, K. H.; Pruskil, I.; Mühlemeier, J. *Chem. Ber.* **1982**, *115*, 1278.

26.40 (o, 3 C, $OSiC(CH_3)_3$), 25.96 (o, 3 C, $-OSiC(CH_3)_3$), 25.08 (e, CH_2), 24.88 (e, CH_2), 18.72 (e, $OSiC(CH_3)_3$), 18.20 (e, $OSiC(CH_3)_3$), -4.90 (o, $OSiCH_3$), -5.00 (o, 2 C, $OSiCH_3$), -5.25 (o, $OSiCH_3$); IR (film) ν_{max} 3314, 2956, 2858, 1472, 1388, 1254, 1058, 1002, 836, 780 cm^{-1}; EIMS *m/e* (relative intensity), 530 (M^+, 3), 398 (34), 326 (base), 267 (34), 251 (36), 147 (11), 75 (45), 73 (52), 57 (12); CIMS (2-methylpropane) *m/e* 531 ($M^+ + 1$, 0.4), 267 (base); EIHRMS *m/e* calc. for $C_{30}H_{50}O_4Si_2$ 530.3248, found 530.3247.

Anal. Calc for $C_{30}H_{50}O_4Si_2$: C, 67.93; H, 9.43. Found: C, 67.90; H, 9.79.

(b) A solution of **7**[33] (37 mg, 0.12 mmol), **12** (43 mg, 0.11 mmol), and acetic anhydride (0.01 mL, 0.12 mmol) in heptane (0.4 mL) was warmed at 80 °C for 3 h. The cooled reaction mixture was concentrated in vacuo. Radial chromatography (1-mm plate, petroleum ether–ether–methylene chloride (20:1:1) eluant) afforded 40 mg (60 mg theoretical, 66%) of **32**.

3-(1-Cyclopentylidene)-2-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1-methoxy-4-naphthol (33). A solution of **7**[33] (0.69 g, 2.2 mmol) and **12** (1.02 g, 2.67 mmol) in heptane (7.5 mL) was warmed at 80 °C for 18 h. The reaction mixture was cooled to room temperature and solvent was removed in vacuo. Flash chromatography (SiO_2, 25 cm × 7.5 cm, petroleum ether–ether–methylene chloride (20:1:1) eluant) afforded 0.49 g (0.90 g theoretical, 56%) of **33** as a colorless oil. The conversion of **12** (0.20–2.67 mmol) to **33** was routinely achieved in 52–74% yield: ^1H NMR ($CDCl_3$, 300 MHz) δ 8.20 (1 H, d, *J* = 9.1 Hz, C8-H), 8.06 (1 H, d, *J* = 9.1 Hz, C5-H), 7.48 (2 H, m, C6 and C7-H), 6.42 (1 H, s, $CH{=}C_5H_8$), 5.71 (1 H, s, OH), 4.77 (2 H, s, $CH_2OTBDMS$), 3.99 (3 H, s, OCH_3), 2.55 (2 H, m, $CH{=}CCH_2$), 2.14 (2 H, m, $CH{=}CCH_2$), 1.74 (4 H, m, CH_2CH_2), 0.92 (9 H, s, $OSiC(CH_3)_3$), 0.14 (6 H, s, $OSi(CH_3)_2$); IR (film) ν_{max} 3512, 2956, 2930, 2884, 2856, 1654, 1628, 1594, 1472, 1456, 1436, 1384, 1288, 1254, 1116, 1046, 838 cm^{-1}; EIMS *m/e* (relative intensity), 398 (M^+, 5), 326 (23), 251 (11), 171 (28), 163 (11), 105 (22), 91 (6), 77 (18), 75 (base, HOTBDMS), 57 (56); CIMS (2-methylpropane) *m/e* 397 ($M^+ + H$, 70), 267 ($M^+ + H$ – HOTBDMS, base); EIHRMS *m/e* calc for $C_{24}H_{34}O_3Si$ 398.2277, found 398.2280.

7-(Phenylmethoxy)indan-1-one (65b). A solution of 7-hydroxyindan-1-one[25] (3.22 g, 21.7 mmol) in *N,N*-dimethylformamide (50 mL) was treated with potassium carbonate (30.06 g, 217.4 mmol), tetrabutylammonium iodide (0.80 g, 2.2 mmol), and benzyl bromide (3.88 g, 32.6 mmol). The reaction mixture was stirred for 10 h at ambient temperature before being diluted with water (500 mL) and extracted with ethyl acetate–ether (1:1, 2 × 200 mL). The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (SiO_2, 15 cm × 8 cm, 10–20% EtOAc–hexane eluant) afforded 4.84 g (5.17 g theoretical, 94%) of **65b** as a white crystalline solid: mp 59–60 °C (white prisms, hexane–EtOAc, 1:1); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.48 (2 H, m, aromatic), 7.31 (4 H, m, aromatic), 6.94 (1 H, d, *J* = 7.5 Hz, C4-H), 6.73 (1 H, d, *J* = 8.1 Hz, C6-H), 5.22 (2 H, s, OCH_2Ph), 3.01 (2 H, t, *J* = 5.6 Hz, CH_2Ar), 2.62 (2 H, t, *J* = 6.2 Hz, CH_2CH_2Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 204.31 (e, CO), 157.85 (e), 156.92 (e), 136.60 (e), 136.12 (o), 128.54 (o), 127.66 (o), 126.54 (o), 125.66 (e), 118.70 (o), 110.65 (o), 69.88 (e, OCH_2Ph), 36.80 (e, CH_2Ar), 25.50 (e, CH_2CH_2Ar); IR (KBr) ν_{max} 3034, 2928, 1695, 1597, 1500, 1478, 1468, 1454, 1303, 1279, 1232, 1196, 1089, 1066, 1022, 776, 730 cm^{-1}; EIMS *m/e* (relative intensity) 238 (M^+, 10), 220 (1, $M^+ - H_2O$), 209 (1, M^+ – CHO), 91 (base), 77 (4), 65 (21), 55 (1); CIMS (2-methylpropane) *m/e* 239 ($M^+ + H$, base); EIHRMS *m/e* calc for $C_{16}H_{14}O_2$ 238.0993, found 238.0990.

Anal. Calc for $C_{16}H_{14}O_2$: C, 80.67; H, 5.88. Found: C, 80.78; H, 6.14.

2,3-Dihydro-1-(methoxymethylene)-7-(phenylmethoxy)-1*H*-indene (65c). A suspension of (methoxymethyl)triphenylphosphonium chloride (1.44 g, 4.20 mmol) in dioxane (12 mL) was treated with potassium *tert*-butoxide (0.47 g, 4.2 mmol) in one portion at 0 °C.[26] The resulting red reaction mixture was stirred at ambient temperature for 0.8 h before it was treated with **65b** (0.20 g, 0.84 mmol) in dioxane (2 mL). The resulting reaction mixture was stirred at ambient temperature for 2 h followed by warming at reflux for 2 h. The mixture was cooled to ambient temperature, diluted with water (100 mL), and extracted with ether (2 × 150 mL). The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Radial chromatography (PCTLC, 2-mm plate, 1% EtOAc–hexane eluant) afforded 0.17 g (0.22 g theoretical, 75%) of **65c** predominantly as the *E* isomer. Recrystallization from methanol provided pure ***E*-65c** as a white crystalline solid: mp 78–80 °C (white needles, MeOH); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.47 (2 H, m, aromatic), 7.38 (3 H, m, aromatic), 7.10 (1 H, m, CH=C), 7.01 (1 H, t, *J* = 7.7 Hz, C5-H), 6.84 (1 H, d, *J* = 7.6 Hz, C4-H), 6.72 (1 H, d, *J* = 8.1 Hz, C6-H), 5.15 (2 H, s, OCH_2Ph), 3.63 (3 H, s, OCH_3), 2.99 (2 H, m, CH_2Ar), 2.78 (2 H, m, CH_2CH_2Ar); IR (KBr) ν_{max} 3060, 2932, 1660, 1582, 1480, 1452, 1266, 1228, 1128, 1064, 756 cm^{-1}; EIMS *m/e* (relative intensity), 266 (M^+, 12), 175 (9, $M^+ - C_7H_7$), 160 (29), 91 (base), 77 (3), 65 (5); CIMS (2-methylpropane) *m/e* 267 ($M^+ + H$, base); EIHRMS *m/e* calc for $C_{18}H_{18}O_2$ 266.1306, found 266.1304.

1-Formyl-7-(phenylmethoxy)indane (65d). A solution of **65c** (0.99 g, 3.70 mmol) in aqueous dioxane (1:3, 20 mL) was treated with *p*-toluenesulfonic acid and warmed at reflux for 16 h.[26] The reaction mixture was cooled, diluted with water (300 mL), and extracted with ethyl acetate (300 mL). The organic extract was dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (Florisil 200–300, 15 cm × 5 cm, 5% EtOAc–hexane eluant) afforded 0.70 g (0.93 g theoretical, 75%) of **65d** as white flakes: mp 49–50 °C (white needles, hexane); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.80 (1 H, d, *J* = 2.4 Hz, CHO), 7.34 (5 H, m, Ph), 7.20 (1 H, t, *J* = 7.8 Hz, C5-H), 6.90 (1 H, d, *J* = 7.5 Hz, C4-H), 6.77 (1 H, d, *J* = 8.1 Hz, C6-H), 5.10 (2 H, s, OCH_2Ph), 4.15 (1 H, m, CHCHO), 2.99 (2 H, m, CH_2Ar), 2.44 (1 H, m, $CHHCH_2Ar$), 2.22 (1 H, m, $CHHCH_2Ar$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200.61 (o, CHO), 155.70 (e), 147.21 (e), 136.97 (e), 129.72 (o), 128.74 (o), 128.06 (o), 127.23 (o), 117.78 (o), 109.61 (o), 69.93 (e, OCH_2Ph), 55.99 (o, CHCHO), 32.36 (e, CH_2Ar), 25.33 (e, $CHCH_2Ar$); IR (KBr) ν_{max} 1718 (CHO), 1588, 1478, 1450, 1390, 1300, 1264, 1088, 1066, 772 cm^{-1}; EIMS *m/e* (relative intensity), 252 (M^+, 2), 223 (15, M^+ – CHO), 133 (5), 91 (base), 77 (2), 65 (6); CIMS (2-methylpropane) *m/e* 253 ($M^+ + H$, base); EIHRMS *m/e* calc. for $C_{17}H_{16}O_2$ 252.1150, found 252.1150.

Anal. Calc for $C_{17}H_{16}O_2$: C, 80.95; H, 6.35. Found: C, 80.62; H, 6.44.

1,4-Bis[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-1-[7′-(phenylmethoxy)-1′-indanyl]-2-butyne (67). A solution of 3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-propyne[32] (**52**, 0.92 g, 5.4 mmol) in tetrahydrofuran (50 mL) was treated with *n*-butyllithium (2.50 M, 2.17 mL, 5.4 mmol) at −78 °C. The reaction mixture stirred at 0 °C for 0.5 h and recooled to −78 °C, and **65d** (1.24 g, 4.9 mmol) in tetrahydrofuran (5 mL) was added. The resulting reaction mixture was stirred at 0 °C for 2 h before being quenched with the addition of water (10 mL). The mixture was neutralized with 10% aqueous hydrochloric acid, diluted with water (300 mL), and extracted with ether (2 × 200 mL). The combined ether extracts were dried ($MgSO_4$) and concentrated in vacuo to give 1.64 g of crude **66**. Due to partial decomposition of **66** upon attempted chromatographic purification (SiO_2 or Florisil) it was carried crude into the next step.

A solution of crude **66** (1.64 g, 3.9 mmol) in *N,N*-dimethylformamide (10 mL) was treated with imidazole (0.66 g, 9.7 mmol) and *tert*-butyldimethylsilyl chloride (0.88 g, 5.8 mmol). The reaction mixture was stirred at ambient temperature for 29 h, diluted with water (300 mL), and extracted with ether (3 × 100 mL). The combined ether extracts were dried ($MgSO_4$) and concentrated in vacuo. Radial chromatography (PCTLC, 4-mm plate, 5% EtOAc–hexane eluant) afforded 1.77 g (2.64 g theoretical, 67% (two steps)) of pure **67** as a colorless oil: ^1H NMR ($CDCl_3$, 300 MHz) δ 7.38 (5 H, m, Ph), 7.13 (1 H, t, *J* = 7.6 Hz, C5-H), 6.83 (1 H, d, *J* = 7.5 Hz, C4-H), 6.71 (1 H, d, *J* = 7.8 Hz, C6-H), 5.09 (2 H, s, OCH_2Ph), 5.05 (1 H, m, CHOTBDMS), 4.40 (2 H, s, OCH_2TBDMS), 3.63 (1 H, m, CHAr), 3.09 (1 H, m, $CHHAr$), 2.82 (1 H, m, $CHHAr$), 2.53 (1 H, m, $CHHCH_2Ar$), 2.18 (1 H, m, $CHHCH_2Ar$), 0.95 (9 H, s, $OSiC(CH_3)_3$), 0.68 (9 H, s, $OSiC(CH_3)_3$), 0.17 (6 H, s, $OSi(CH_3)_2$), −0.07 (3 H, s, $OSiCH_3$), −0.32 (3 H, s, $OSiCH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) 155.68 (e), 148.56 (e), 137.64 (e), 131.06 (e), 128.82 (o), 128.67 (o), 128.01 (o), 127.35 (o), 117.49 (o), 108.79 (o), 87.26 (e), 82.19 (e), 69.73 (e, OCH_2Ph), 64.52 (o, CHOTBDMS), 52.13 (e, $CH_2OTBDMS$), 50.37 (o, CHAr), 33.33 (e, CH_2Ar), 26.43 (e, CH_2CH_2Ar), 26.10 (o, 3 C, $OSiC(CH_3)_3$), 25.74 (o, 3 C, $OSiC(CH_3)_3$), 18.56 (e, $OSiC(CH_3)_3$), 18.10 (e, $OSiC(CH_3)_3$), −4.81 (o, $OSiCH_3$), −4.90 (o, $OSiCH_3$), −5.06 (o, $OSiCH_3$), −5.64 (o, $OSiCH_3$); IR (film) ν_{max} 2956, 2930, 2858, 1472, 1464, 1258, 1128, 1086 cm^{-1}; EIMS *m/e* (relative intensity),

Table III. Benzannulation Reaction of 7 with 67

alkyne (equiv)	conditions	product(s) (% yield)
67 (1.0)	1.0 equiv of Ac_2O, 80 °C, heptane, 3 h, 0.3 M	68 (85)
67 (1.0)	80 °C, heptane, 20 h, 0.3 M	68 (–)[a]

[a] No major products isolated.

536 (M^+, 1), 479 (1, $M^+ - C(CH_3)_3$), 445 (17, $M^+ - C_7H_7$), 223 (42), 91 (base, $C_7H_7^+$), 75 (22), 73 (56, $Si(CH_3)_3^+$), 57 (23); CIMS (2-methylpropane) *m/e* 537 (3, M^+), 405 (base, $M^+ + H$ – HOTBDMS); CIHRMS *m/e* calc for $C_{32}H_{48}O_3Si_2$ 537.3220, found 537.3210.

2-[1-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-1-methoxy-3-[1-[7′-(phenylmethoxy)-1′-indanyl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-naphthalenol (68). A solution of 7[33] (0.84 g, 2.69 mmol), **67** (1.58 g, 2.96 mmol), and acetic anhydride (0.25 mL, 2.7 mmol) in heptane (10 mL) was warmed at 80 °C for 3 h. The cooled reaction mixture was diluted with ether (25 mL) and filtered through Celite. The filtrate was concentrated in vacuo. Radial chromatography (PCTLC, 4-mm plate, 5% EtOAc–hexane eluant) afforded 1.57 g (1.84 g theoretical, 85%) of **68** as a white crystalline solid. The conversion of **67** (2.7–5.5 mmol) to **68** was routinely achieved in 85–88% yield: mp 122–123 °C (white plates, hexane); ^1H NMR ($CDCl_3$, 200 MHz) δ 9.67 (1 H, s, OH), 8.16 (1 H, m, C8-H), 8.00 (1 H, m, C5-H), 7.42 (2 H, m, C6 and C7-H), 7.25–7.05 (11 H, m, aromatic), 6.87 (1 H, d, *J* = 7.3 Hz, C4′-H), 6.51 (1 H, d, *J* = 8.1 Hz, C6′-H), 5.65 (1 H, d, *J* = 5.8 Hz, CHOTBDMS), 4.79 (1 H, d, *J* = 12.8 Hz, OC*H*HPh), 4.70 (1 H, d, *J* = 11.2 Hz, C*H*HOTBDMS), 4.51 (1 H, d, *J* = 12.8 Hz, OCH*H*Ph), 4.00 (1 H, d, *J* = 11.2 Hz, CH*H*OTBDMS), 3.94 (1 H, m, CHAr), 3.84 (3 H, s, OCH_3), 3.19 (1 H, m, C*H*HAr), 2.84 (1 H, m, CH*H*Ar), 2.55 (1 H, m, C*H*HCH_2Ar), 2.08 (1 H, m, CH*H*CH_2Ar), 0.84 (9 H, s, OSiC$(CH_3)_3$), 0.83 (9 H, s, OSiC$(CH_3)_3$), 0.06 (3 H, s, $OSiCH_3$), –0.06 (3 H, s, $OSiCH_3$), –0.07 (3 H, s, $OSiCH_3$), –0.19 (3 H, s, $OSiCH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz) 156.29 (e), 150.07 (e), 148.01 (e), 147.43 (e), 137.82 (e), 132.08 (e), 129.06 (o), 128.71 (o), 127.90 (e), 127.74 (o), 127.02 (e), 126.98 (o), 126.76 (e), 126.36 (o), 125.46 (o), 123.25 (o), 122.23 (o), 119.86 (e), 117.78 (o), 109.91 (o), 75.82 (o, CHOTBDMS), 69.89 (e, OCH_2Ph), 63.52 (o, OCH_3), 56.17 (e, $CH_2OTBDMS$), 50.31 (o, CHAr), 32.28 (e, CH_2Ar), 28.32 (e, CH_2CH_2Ar), 26.39 (o, 3 C, OSiC$(CH_3)_3$), 26.37 (o, 3 C, OSiC$(CH_3)_3$), 18.57 (e, OSi*C*$(CH_3)_3$), 17.93 (e, OSi*C*$(CH_3)_3$), –4.87 (o, $OSiCH_3$), –5.21 (o, $OSiCH_3$), –5.32 (o, $OSiCH_3$), –5.84 (o, $OSiCH_3$); IR (KBr) ν_{max} 3302, 2956, 2928, 2856, 1592, 1462, 1264, 1056, 1042, 996, 838, 786, 766 cm^{-1}; EIMS *m/e* (relative intensity), 684 (M^+, 1), 552 (6, M^+ – HOTBDMS), 461 (41), 223 (15), 91 (base), 77 (5), 75 (92), 57 (14); CIMS (2-methylpropane) *m/e* 552 (base, $M^+ + H$ – HOTBDMS); EIHRMS *m/e* calc for $C_{41}H_{56}O_5Si_2$ 684.3666, found 684.3664.

Anal. Calc for $C_{41}H_{56}O_5Si_2$: C, 71.93; H, 8.19. Found: C, 71.71; H, 8.56.

3-[1-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]methyl]-4-methoxy-1-(phenylmethoxy)-2-[1-[7′-(phenylmethoxy)-1′-indanyl]-1-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-methyl]naphthalene (69). A solution of **68** (0.62 g, 0.90 mmol), potassium carbonate (1.24 g, 8.9 mmol), and tetra-*n*-butylammonium iodide (0.03 g, 0.1 mmol) in *N,N*-dimethylformamide (10 mL) was treated with benzyl bromide (0.16 mL, 1.3 mmol), and the resulting reaction mixture was stirred at ambient temperature for 48 h. The solution was diluted with water (200 mL) and extracted with ether (2 × 200 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. Radial chromatography (PCTLC, 2-mm plate, 5% EtOAc–hexane eluant) afforded 0.55 g (0.69 g theoretical, 80%) of pure **69** as a white crystalline solid. The conversion of **68** (0.9–4.8 mmol) to **69** was routinely achieved in 80–86% yield: mp 135 °C, sharp (white prisms, hexane); ^1H NMR ($CDCl_3$, 200 MHz) δ 8.04 (1 H, m, aromatic), 7.96 (1 H, m, aromatic), 7.54–6.70 (12 H, m, aromatic), 6.43 (2 H, m, aromatic), 6.17 (1 H, d, *J* = 8.1 Hz, aromatic), 5.77 (1 H, d, *J* = 10.2 Hz, OC*H*HPh), 5.45 (1 H, d, *J* = 10.2 Hz, OCH*H*Ph), 5.10 (1 H, d, *J* = 10.1 Hz, OC*H*HPh), 4.64 (1 H, d, *J* = 14.7 Hz, C*H*HOTBDMS), 4.60 (1 H, m, CHOTBDMS), 4.36 (1 H, d, *J* = 10.0 Hz, OCH*H*Ph), 4.35 (1 H, d, *J* = 14.6 Hz, CH*H*OTBDMS), 3.91 (3 H, s, OCH_3), 3.09 (2 H, m), 2.73 (2 H, m), 2.17 (1 H, m), 1.00 (9 H, s, OSiC$(CH_3)_3$), 0.85 (9 H, s, OSiC$(CH_3)_3$), 0.26 (3 H, s, $OSiCH_3$), 0.24 (3 H, s, $OSiCH_3$), 0.07 (3 H, s, $OSiCH_3$), –0.51 (3 H, s, $OSiCH_3$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 157.39 (e), 154.48 (e), 148.39 (e), 147.97 (e), 138.82 (e), 134.12 (e), 133.76 (e), 131.23 (e), 129.27 (e), 128.64 (o), 128.53 (o), 128.46 (o), 128.43 (o), 127.66 (o), 127.15 (o), 126.82 (o), 126.46 (o), 126.26 (o), 125.82 (o), 125.80 (o), 123.37 (o), 123.20 (o), 117.82 (o), 110.95 (o), 75.28 (e, OCH_2Ph), 69.90 (e, OCH_2Ph), 69.95 (o, OCH_3), 63.93 (o, CHOTBDMS), 57.51 (e, $CH_2OTBDMS$), 49.53 (o, CHAr), 30.85 (e, CH_2Ar), 30.33 (e, CH_2CH_2Ar), 26.33 (o, 3 C, OSiC$(CH_3)_3$), 25.99 (o, 3 C, OSiC$(CH_3)_3$), 18.75 (e, OSi*C*$(CH_3)_3$), 18.14 (e, OSi*C*$(CH_3)_3$), –5.00 (o, $OSiCH_3$), –5.11 (o, $OSiCH_3$), –5.26 (o, $OSiCH_3$), –5.49 (o, $OSiCH_3$); IR (film) ν_{max} 3066, 3032, 2956, 2928, 2894, 2856, 1586, 1474, 1352, 1338 cm^{-1}; EIMS *m/e* (relative intensity), 551 (32), 303 (24), 221 (18), 91 (base, $C_7H_7^+$), 73 (53), 57 (14); CIMS (2-methylpropane) *m/e* 511 (base, $M^+ + H$ – HOTBDMS, – HOTBDMS); CIHRMS *m/e* calc for $C_{48}H_{62}O_5Si_2$ 643.3243, found 643.3245 ($M^+ + H$ – HOTBDMS).

Anal. Calc for $C_{48}H_{62}O_3Si_2$: C, 74.42; H, 8.01. Found: C, 74.51; H, 8.42.

3-(1-Hydroxymethyl)-2-[1-hydroxy-1-[7′-(phenylmethoxy)-1′-indanyl]methyl]-4-methoxy-1-(phenylmethoxy)-naphthalene (70). A solution of **69** (0.55 g, 0.71 mmol) in tetrahydrofuran (10 mL) was treated with a solution of tetra-*n*-butylammonium fluoride in tetrahydrofuran (1 M, 3.58 mL, 3.6 mmol). The resulting reaction mixture was stirred at ambient temperature for 72 h. The solvent was removed in vacuo. Radial chromatography (PCTLC, 2-mm plate, 20% EtOAc–hexane eluant) afforded 0.27 g (0.39 g theoretical, 68%) of **70** as a light yellow foam and 0.09 g (16%) of recovered starting material (**69**): ^1H NMR ($CDCl_3$, 300 MHz) δ 8.10 (1 H, d, *J* = 8.0 Hz, aromatic), 7.89 (1 H, d, *J* = 8.4 Hz, aromatic), 7.47 (2 H, m, aromatic), 7.35 (5 H, m, aromatic), 7.16 (1 H, m, aromatic), 7.05 (4 H, m, aromatic), 6.84 (1 H, d, *J* = 7.4 Hz, aromatic), 6.77 (2 H, d, *J* = 7.3 Hz, aromatic), 6.47 (1 H, d, *J* = 8.1 Hz, OC*H*HPh), 5.55 (1 H, d, *J* = 8.5 Hz, OCH*H*Ph), 4.71 (2 H, dd, *J* = 10.3, 10.3 Hz, OCH_2Ph), 4.59 (1 H, d, *J* = 12.1 Hz, C*H*HOH), 4.41 (1 H, d, *J* = 11.9 Hz, CH*H*OH), 4.16 (1 H, d, *J* = 4.8 Hz, C*H*OH), 4.08 (1 H, m, CHAr), 3.88 (3 H, s, OCH_3), 2.94 (1 H, m, C*H*HAr), 2.73 (1 H, m, CH*H*Ar), 2.52 (1 H, m, C*H*HCH_2Ar), 2.11 (1 H, m, CH*H*CH_2Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.67 (e), 151.74 (e), 149.20 (e), 147.68 (e), 137.60 (e), 136.61 (e), 131.79 (e), 131.15 (e), 129.81 (e), 128.85 (o), 128.56 (o), 128.41 (o), 128.35 (e), 127.85 (o), 127.68 (o), 127.11 (o), 126.88 (o), 126.48 (o), 126.29 (o), 123.07 (o), 122.84 (o), 117.75 (o), 109.39 (o), 75.74 (e, OCH_2Ph), 71.09 (o, OCH_3), 69.70 (e, OCH_2Ph), 63.39 (o, CHOH), 56.66 (e, CH_2OH), 49.73 (o, CH_2Ar), 30.98 (o, CH_2Ar), 29.85 (e, CH_2CH_2Ar); IR (film) ν_{max} 3332, 3066, 3032, 2972, 2936, 2870, 1586, 1496, 1476, 1454, 1382, 1352, 1308, 1266, 1238, 1104, 1058, 1026, 1010, 910 cm^{-1}; EIMS *m/e* (relative intensity), 442 (1), 322 (1), 305 (8), 215 (6), 91 (base), 77 (2); CIMS (2-methylpropane) *m/e* 529 (29, $M^+ + H - H_2O$), 253 (base); CIHRMS *m/e* calc for $C_{36}H_{33}O_4$ ($M^+ + H - H_2O$) 529.2379, found 529.2372.

2-[1-Oxo-1-[7′-(phenylmethoxy)-1′-indanyl]methyl]-4-methoxy-1-(phenylmethoxy)naphthalene-3-carboxaldehyde (71). A solution of oxalyl chloride (0.09 mL, 1.0 mmol) in methylene chloride (20 mL) at –67 °C was treated with dimethyl sulfoxide (0.16 mL, 2.2 mmol). The resulting solution was stirred for 15 min, treated with **70** (0.25 g, 0.46 mmol) in methylene chloride (3 mL), and further stirred at –67 °C for an additional 1 h. Addition of triethylamine (0.63 mL, 4.6 mmol) was followed by removal of the cooling bath, and the solution was allowed to warm over a period of 20 min. The mixture was quenched with the addition of water, further diluted with water (200 mL), and extracted with ether (3 × 100 mL). The combined ether extracts were dried ($MgSO_4$) and concentrated in vacuo. Radial chromatography (PCTLC, 2-mm plate, 5–15% EtOAc–hexane eluant) afforded 0.16 g (0.25 g theoretical, 66%) of pure **71** as yellow foam: mp 53–55 °C (EtOAc–hexane, 1:1); ^1H NMR ($CDCl_3$, 300 MHz) δ 10.30 (1 H, s, CHO), 8.10 (1 H, m, aromatic), 7.91 (1 H, m, aromatic), 7.56 (2 H, m, aromatic), 7.28 (4 H, m, aromatic), 7.13 (1 H, t, *J* = 7.7 Hz, aromatic), 7.05 (2 H, m, aromatic), 6.96 (2 H, m, aromatic), 6.92 (1 H, m, aromatic), 6.73 (2 H, d, *J* = 7.3 Hz, aromatic), 6.52 (1 H, d, *J* = 8.1 Hz, aromatic), 4.90 (1 H, d, *J* = 11.1 Hz, OC*H*HPh), 4.76 (1 H, d, *J* = 11.2 Hz, OCH*H*Ph),

4.71 (1 H, d, J = 8.4 Hz, CHAr), 4.66 (1 H, d, J = 11.9 Hz, OC*H*HPh), 4.26 (1 H, d, J = 11.9 Hz, OCH*H*Ph), 3.93 (3 H, s, OCH_3), 3.40 (1 H, m), 2.92 (2 H, m), 2.29 (1 H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 205.16 (e, CO), 189.08 (o, CHO), 159.22 (e), 155.94 (e), 148.27 (e), 148.11 (e), 137.26 (e), 136.81 (e), 132.65 (e), 131.13 (e), 129.92 (o), 129.09 (o), 128.99 (e), 128.41 (o), 128.12 (o), 127.86 (o), 127.62 (o), 127.48 (o), 127.23 (o), 126.45 (o), 123.85 (o), 123.75 (e), 123.45 (o), 117.62 (o), 108.93 (o), 78.35 (e, OCH_2Ph), 69.19 (e, OCH_2Ph), 65.87 (o, OCH_3), 56.49 (o, CHAr), 32.85 (e, CH_2Ar), 30.14 (e, CH_2CH_2Ar); IR (KBr) ν_{max} 3032, 2938, 1698, 1678, 1588, 1454, 1410, 1348, 1268, 1064 cm^{-1}; EIMS m/e (relative intensity), 542 (M^+, 1), 451 (1, $M^+ - C_7H_7$), 313 (3), 223 (37), 91 (base), 65 (5); CIMS (2-methylpropane) m/e 543 (base, $M^+ + H$); CIHRMS m/e calc for $C_{36}H_{30}O_5$ 543.2171, found 543.2162.

Anal. Calc for $C_{36}H_{30}O_5$: C, 79.68; H, 5.57. Found: C, 79.38; H, 5.47.

2,3-Dihydro-7-(phenylmethoxy)-1*H*-indene-1-spiro-2′-[4′-methoxy-9′-(phenylmethoxy)-2′*H*-benz[*f*]indene]-1′,3′-dione (73). A solution of **71** (0.31 g, 0.57 mmol) in methanol (10 mL) was treated with sodium methoxide (25% solution in methanol, 13 μL, 0.1 mmol). The reaction mixture was warmed to 65 °C and stirred for 3 h. The cooled reaction mixture was concentrated in vacuo to afford pure **72** as a mixture of two diastereomers (1.5:1) that was carried to the next step without purification. A pure sample of **72** was secured by flash chromatography (SiO_2, 15% EtOAc–hexane eluant): ^1H NMR ($CDCl_3$, 300 MHz) δ 8.34 (2 H, t, J = 5.4 Hz, aromatic), 8.22 (1 H, d, J = 8.4 Hz, aromatic), 8.12 (1 H, d, J = 8.2 Hz, aromatic), 7.72–6.61 (13 H, m, aromatic), 5.85 (1 H, d, J = 3.4 Hz, C*H*OH), 5.50 and 5.30 (1 H, 2 d, J = 10.0 Hz and J = 10.6 Hz, 1:1.5 respectively), 4.93–4.70 (3 H, m), 4.13 and 3.92 (3 H, 2 s, diastereomeric OCH_3, 1:1.5), 3.17 (2 H, m), 2.99 (1 H, d, J = 2.9 Hz, CHO*H*), 2.87–2.33 (2 H, m); ^{13}C NMR ($CDCl_3$, 50 MHz) 205.04 and 204.89 (e, CO), 155.46 (e), 154.76 (e), 151.16 (e), 150.96 (e), 149.93 (e), 148.85 (e), 148.47 (e), 137.78 (e), 137.74 (e), 137.49 (e), 136.74 (e), 136.31 (e), 136.23 (e), 136.22 (e), 133.83 (e), 133.65 (e), 133.27 (e), 130.64 (e), 130.50 (e), 130.31 (o), 129.90 (o), 129.41 (o), 129.35 (o), 129.12 (o), 128.80 (o), 128.51 (o), 128.26 (o), 128.05 (o), 127.72 (o), 127.46 (o), 127.08 (o), 126.83 (o), 125.86 (o), 125.62 (o), 123.03 (e), 122.86 (o), 122.16 (o), 118.63 (o), 118.01 (o), 110.21 (o), 109.59 (o), 77.92 and 77.62 (e, OCH_2Ph), 75.40 and 75.06 (o, CHOH), 70.47 and 69.80 (e, OCH_2Ph), 67.92 and 66.99 (e, C2 spirocarbon), 62.49 and 61.67 (o, OCH_3), 39.34 and 32.85 (e, CH_2Ar), 32.18 and 31.97 (e, CH_2CH_2Ar); IR (film) ν_{max} 3504, 3032, 2936, 1708, 1618, 1590, 1498, 1476, 1456, 1348 cm^{-1}; EIMS m/e (relative intensity) 542 (M^+, 10), 451 (10, $M^+ - C_7H_7$), 91 (base, $C_7H_7^+$), 77 (1), 65 (4); CIMS (2-methylpropane) m/e 543 ($M^+ + H$, 82), 435 (base, $M^+ + H - H_2O - C_7H_6$); EIHRMS m/e calc for $C_{36}H_{30}O_5$ 542.2093, found 542.2098.

A solution of crude **72** in methylene chloride (20 mL) was treated with pyridinium chlorochromate (0.37 g, 1.7 mmol). The resulting reaction mixture was stirred at ambient temperature for 14 h, diluted with ether (10 mL), and filtered through Celite. Radial chromatography (PCTLC, 2-mm plate, 15% EtOAc–hexane eluant) afforded 0.27 g (0.31 g theoretical, 89% for two steps) of pure **73** as a white crystalline solid: mp 153 °C, sharp (white needles, EtOH); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.37 (2 H, m, aromatic), 7.74 (2 H, m, aromatic), 7.54 (2 H, d, J = 6.9 Hz, aromatic), 7.36 (2 H, m, aromatic), 7.25 (2 H, m, aromatic), 6.99 (1 H, d, J = 7.5 Hz, aromatic), 6.68 (4 H, m, aromatic), 6.49 (2 H, t, J = 7.5 Hz, aromatic), 5.30 (1 H, d, J = 10.6 Hz, OC*H*HPh), 4.81 (1 H, d, J = 10.6 Hz, OCH*H*Ph), 4.72 (2 H, s, OCH_2Ph), 3.98 (3 H, s, OCH_3), 3.33 (2 H, t, J = 7.3 Hz, CH_2Ar), 2.56 (2 H, t, J = 7.5 Hz, CH_2CH_2Ar); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200.86 (e, 2 C, CO), 154.13 (e), 151.44 (e), 149.88 (e), 148.70 (e), 137.11 (e), 135.87 (e), 133.72 (e), 133.58 (e), 130.41 (o), 130.29 (o), 129.67 (o), 128.88 (o), 128.69 (o), 128.46 (o), 127.82 (o), 127.50 (o), 127.13 (o), 125.32 (o), 125.02 (o), 124.94 (e), 117.88 (o), 109.02 (o), 77.69 (e, OCH_2Ph), 69.93 (e, OCH_2Ph), 66.75 (e, C2 spirocarbon), 63.10 (o, OCH_3), 35.39 (e, CH_2Ar), 32.89 (e, CH_2CH_2Ar); IR (KBr) ν_{max} 3068, 2942, 1730, 1700, 1590, 1454, 1396, 1384, 1346, 1272, 1218, 1026 cm^{-1}; EIMS m/e (relative intensity) 540 (M^+, 3), 449 (3), 343 (1), 201 (2), 91 (base), 65 (5); CIMS (2-methylpropane) m/e 541 (base, $M^+ + H$); CIHRMS m/e calc for $C_{36}H_{28}O_5$ 541.2015, found 541.2007.

Anal. Calc for $C_{36}H_{28}O_5$: C, 79.85; H, 5.18. Found: C, 79.79; H, 5.06.

2,3-Dihydro-7-hydroxy-1*H*-indene-1-spiro-2′-(4′,9′-dihydroxy-2′*H*-benz[*f*]indene)-1′,3′-dione (3). A solution of **73** (43 mg, 0.08 mmol) in methylene chloride (4 mL) at −78 °C was treated with a solution of boron tribromide in methylene chloride (Aldrich, 1 M, 0.29 mL, 0.29 mmol).[29] The cooling bath was removed, and the resulting solution was allowed to warm to ambient temperature over 19 h. The mixture was diluted with water (10 mL) and extracted with ether (2 × 10 mL). The combined ether extracts were dried ($MgSO_4$) and concentrated in vacuo. Radial chromatography (PCTLC, 1-mm plate, EtOAc–hexane–methanol (3:6.5:0.5) eluant) afforded 24.9 mg (27.6 mg theoretical, 90%) of **3** as a yellow crystalline solid: mp 257–259 °C (dec, yellow needles, EtOAc–hexane, 1:1); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.03 (2 H, br s, OH), 8.46 (2 H, m, C8 and C5-H), 7.78 (2 H, m, C6 and C7-H), 7.16 (1 H, t, J = 7.6 Hz, C5′-H), 6.96 (1 H, d, J = 7.4 Hz, C4′-H), 6.50 (1 H, d, J = 7.7 Hz, C6′-H), 4.43 (1 H, br s, OH), 3.30 (2 H, m, CH_2Ar), 2.57 (2 H, m, CH_2CH_2Ar); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 203.05 (e, 2 C, CO), 153.32 (e), 148.48 (e), 146.11 (e), 130.19 (e), 129.97 (o), 129.83 (o), 128.62 (e), 124.61 (o), 116.09 (e), 115.57 (o), 112.96 (o), 66.01 (e, C2 spirocarbon), 34.84 (e, CH_2), 32.11 (e, CH_2); IR (KBr) ν_{max} 3416, 1698, 1680, 1612, 1592, 1522, 1470, 1318, 1288 cm^{-1}; EIMS m/e (relative intensity), 346 (M^+, 66), 328 (24, $M^+ - H_2O$), 300 (11), 133 (49), 91 (base, $C_7H_7^+$), 77 (37), 55 (30); CIMS (2-methylpropane) m/e 347 ($M^+ + H$, base); EIHRMS m/e calc for $C_{21}H_{14}O_5$ 346.0841, found 346.0842.

Anal. Calc for $C_{21}H_{14}O_5$: C, 72.83; H, 4.05. Found: C, 72.43; H, 4.10.

2,3-Dihydro-7-hydroxy-1*H*-indene-1-spiro-2′-[4′-methoxy-9′-(phenylmethoxy)-2′*H*-benz[*f*]indene]-1′,3′-dione (74). A solution of **73** (30 mg, 0.056 mmol) in methanol (5 mL) was treated with ammonium formate (35 mg, 0.6 mmol) and Pd–C (10%, 6 mg, 0.2 wt equiv).[23] The resulting mixture was warmed at 65 °C for 10 min. The solution was cooled to ambient temperature and filtered through a plug of Florisil. Flash chromatography (SiO_2, 10 cm × 3.5 cm, 10% EtOAc–hexane eluant) afforded 16.3 mg (25 mg theoretical, 65%) of **74** as a pale yellow oil: ^1H NMR ($CDCl_3$, 300 MHz) δ 10.10 (1 H, OH), 8.39 (1 H, m, aromatic), 8.32 (1 H, m, aromatic), 7.75 (2 H, m, aromatic), 7.25 (2 H, m, aromatic), 6.98 (1 H, d, J = 7.4 Hz, aromatic), 6.69 (3 H, m, aromatic), 6.59 (2 H, m, aromatic), 4.74 (1 H, d, J = 10.7 Hz, OC*H*HPh), 4.67 (1 H, d, J = 10.6 Hz, OCH*H*Ph), 3.93 (3 H, s, OCH_3), 3.31 (2 H, m, CH_2Ar), 2.55 (2 H, m, CH_2CH_2Ar); IR (film) ν_{max} 3332, 3032, 2938, 1718, 1676, 1618, 1598, 1364, 1340, 1268 cm^{-1}; EIMS m/e (relative intensity) 450 (M^+, 26), 359 (29, $M^+ - C_7H_7$), 91 (base, $C_7H_7^+$), 77 (4); CIMS (2-methylpropane) m/e 451 ($M^+ + H$, base); EIHRMS m/e calc for $C_{29}H_{22}O_5$ 450.1467, found 450.1460.

2,3-Dihydro-7-hydroxy-1*H*-indene-1-spiro-2′-(9′-hydroxy-4′-methoxy-2′*H*-benz[*f*]indene)-1′,3′-dione (75). A solution of **73** (39.9 mg, 0.74 mmol) in methanol (3 mL) was treated with ammonium formate (47 mg, 0.7 mmol) and Pd–C (10%, 79 mg 2 wt equiv).[23] The resulting mixture was stirred at ambient temperature for 19 h and filtered through a plug of Florisil. Flash chromatography (SiO_2, 11 cm × 3.5 cm, 15–50% EtOAc–hexane gradient elution) afforded 18.3 mg (26.6 mg theoretical, 69%) of **75** and 5.1 mg (15%) of **74**. For **75**: ^1H NMR ($CDCl_3$, 300 MHz) δ 10.18 (1 H, br s, OH), 8.45 (2 H, m, C8 and C5-H), 7.76 (2 H, m, C6 and C7-H), 7.09 (1 H, t, J = 7.7 Hz, C5′-H), 6.90 (1 H, d, J = 7.5 Hz, C4′-H), 6.43 (1 H, d, J = 7.9 Hz, C6′-H), 5.00 (1 H, br s, OH), 4.24 (3 H, s, OCH_3), 3.26 (2 H, m, CH_2Ar), 2.54 (2 H, m, CH_2CH_2Ar); ^{13}C NMR ($CDCl_3$, 50 MHz) 200.27 (e, 2 C, CO), 152.04 (e), 151.54 (e), 149.39 (e), 148.80 (e), 134.27 (e), 130.70 (o), 129.54 (o), 129.22 (e), 128.06 (e), 125.65 (o), 124.70 (o), 121.44 (e), 117.88 (o), 116.95 (e), 113.44 (o), 66.70 (e, C2 spirocarbon), 63.47 (o, OCH_3), 35.71 (e, CH_2Ar), 32.65 (e, CH_2CH_2Ar); IR (film) ν_{max} 3332, 2976, 2936, 1720, 1678, 1618, 1594, 1468, 1364, 1338, 1294, 1028 cm^{-1}; EIMS m/e (relative intensity) 360 (M^+, base), 345 (56, $M^+ - CH_3$), 327 (16), 77 (16), 55 (6); CIMS (2-methylpropane) m/e 361 ($M^+ + H$, base); EIHRMS m/e calc for $C_{22}H_{16}O_5$ 360.0997, found 360.0995.

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Supplementary Material Available: A summary table of the results of the benzannulation reaction study (eqs 1-2), full experimental for **2**, **8-9**, **20**, **54-64**, characterization of **26**, **28-31**, **33**, **39-40**, **42-43**, and **45**, and ^{1}H NMR spectra of **12**, **33**, **65c**, **70**, **74**, and **75** (24 pages). Ordering information is given on any current masthead page.

Efficient Oxidation of Phenyl Groups to Carboxylic Acids with Ruthenium Tetraoxide. A Simple Synthesis of (*R*)-γ-Caprolactone, the Pheromone of *Trogoderma granarium*

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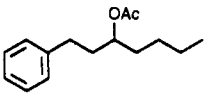
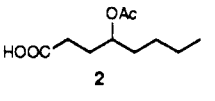
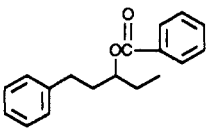
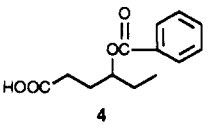
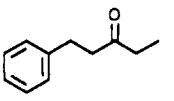
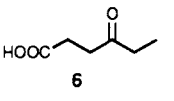
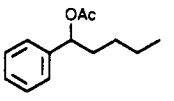
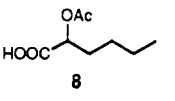
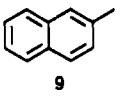
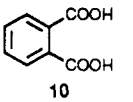
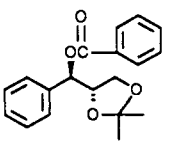
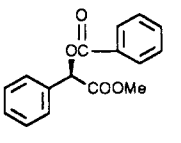
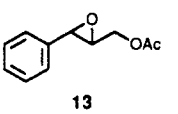
The oxidation of aromatic rings to carboxylic acids with ruthenium tetraoxide is shown to be a very efficient and simple reaction using periodic acid as the stoichiometric oxidant in a biphasic solvent system (CCl_4, CH_3CN, H_2O). The reaction can be very sensitive to the nature of the ring substituents when more than one aromatic ring is present. The procedure is compatible with other functional groups except for those that are quite acid sensitive. A simple synthesis of (*R*)-γ-caprolactone employs Sharpless asymmetric epoxidation and the presented oxidation procedure as key steps.

The utility of ruthenium tetraoxide as an organic oxidant has been widely recognized.[1] Catalytic procedures using stoichiometric oxidants such as periodate,[1,2] hypochlorite,[1,3] bromate,[4] permanganate,[4] cerium sulfate,[4] and electrochemically generated $Cl_2[Cl^+]$[5] have been reported. In 1981, Sharpless et al.[6] reported an improved procedure to oxidize a wide range of organic functions based on the use of a biphasic system containing acetonitrile, as a special additive to prevent catalyst inactivation, and sodium periodate as the stoichiometric oxidant. This method has since become almost a standard procedure for the oxidative cleavage of olefins,[7] diols,[8] cyclic allylic alcohols, and α,β-unsaturated ketones[9] and oxidation of primary alcohols to carboxylic acid,[10] ethers to esters,[11] acetylenes to 1,2-diketones,[12] furan[13,14] and thiophene[13] rings to carboxylic acids, and cyclic sulfites to cyclic sulfates.[15]

Table I

compd	product	yield, %
 1	 2	76
 3	 4	80
 5	 6	65
 7	 8	60
 9	 10	62
 11	 12	84[a]
 13	irresolvable mixture	

[a] Isolated as methyl ester.

Although two cases of oxidation of an aromatic ring to a carboxylic acid, with good yields, are reported in the

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