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Protecting Group Improvement by Isotopic Substitution: Synthesis of the Quinone System of Fredericamycin A

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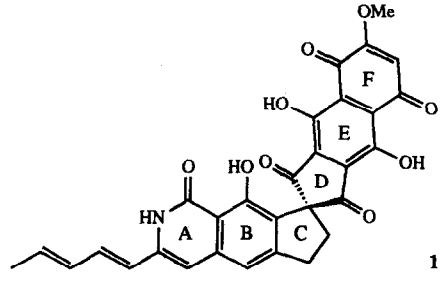
This paper is dedicated to Professor Sir Derek Barton, FRS on the occasion of his seventy-fifth birthday

Abstract Use of a trideuteriomethyl group for protection of phenolic oxygen (as in **29**, Scheme 4), instead of the classical methyl group, serves to suppress an unwanted intramolecular hydrogen transfer (**12**→**14**, Scheme 2) during radical cyclization. The resulting spiro compound (**31**, Scheme 5) can be converted, by selective demethylation and oxidation, into a substance (**35**, Scheme 6) that represents the spirodiketone-quinone system of the antitumor agent Fredericamycin A.

In synthetic work[1] on the antitumor agent fredericamycin A (**1**) we approached the CD subunit by the



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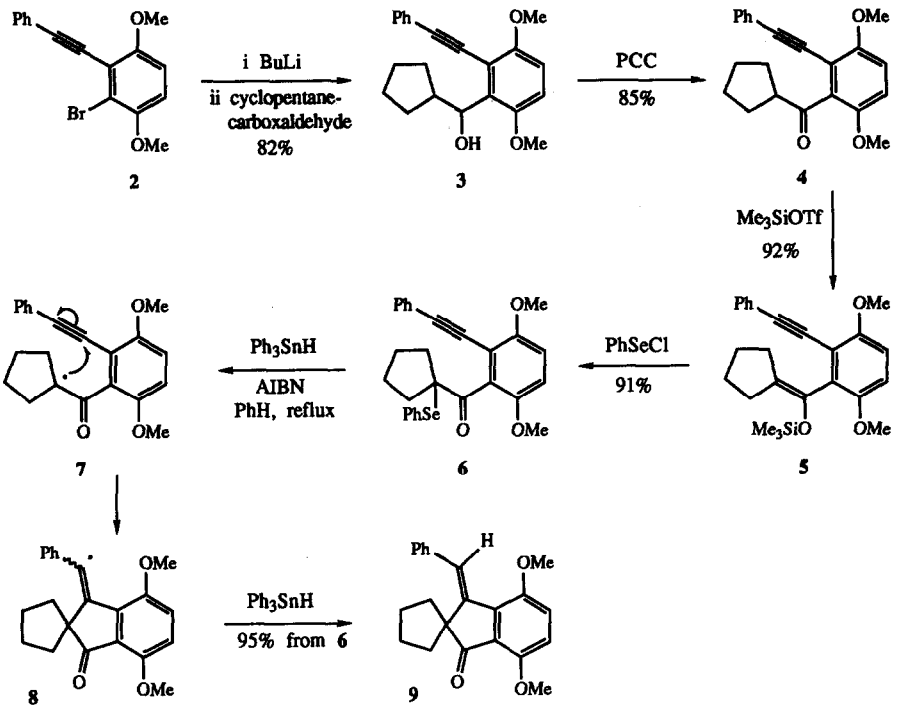
general process of radical spirocyclization.[2] This methodology is illustrated in Scheme 1 for a simple model study.

The reactions shown in the Scheme all worked without incident, but the silyl enol ether **5** is unusual in that it can be chromatographed on silica gel without hydrolysis. The radical cyclization **6**→**7**→**8**→**9** was done thermally in refluxing benzene, and proceeded in high yield to afford the product as a single stereoisomer with *Z* double bond geometry. However, the corresponding experiment with the more advanced model **10**[3] (see Scheme 2) was much less efficient and revealed a problem that is sometimes met in radical cyclizations.

The early parts of the sequence (**10**→**11**→**12**) proceeded well, but the required final product (**13**) was isolated in only 48% yield (as a mixture of geometrical isomers). A very significant amount (41% yield) of a

byproduct was formed by intramolecular hydrogen abstraction (**12**→**14**) followed by 6-*endo*-trigonal closure (**14**→**15**). It is clear that the adjacent *peri* substituent forces the critical *O*-methyl group on ring E (see **12**)

Scheme 1



close to the vinyl radical. In principle, **14** could give **13**, by reaction with stannane. However, this appears not to be the case because, when the reaction was done using triphenyltin deuteride, a deuteriated analogue of **13** was obtained in which the deuterium was located only [^{1}H NMR (400 MHz)] on the vinyl carbon (PhCD= instead of PhCH=).

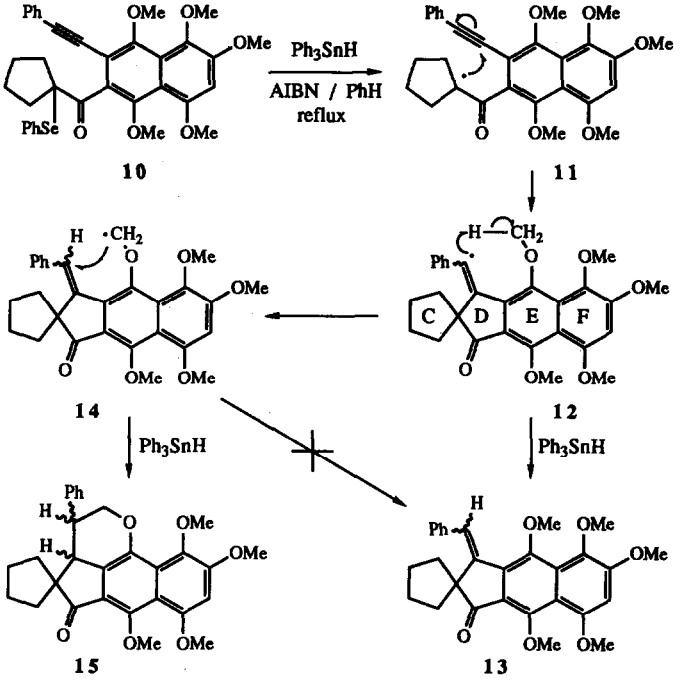
We sought to improve the selectivity between the pathways leading to **13** and **15** by trying the radical cyclization at room temperature with triphenyltin hydride in the presence of triethylborane and air.[4] Unfortunately, the method did not work with selenide **10**,[5] and we were left therefore, with the task of avoiding or suppressing the undesired intramolecular hydrogen transfer.

Our first approach aimed at the preparation of highly oxygenated naphthalenes in which the *peri* oxygens are linked as shown in **16** (R = Me or aryl, X = C or Si). Such oxygen protection would make the intramolecular hydrogen abstraction (*cf.* **12**→**14**, Scheme 2) sterically impossible, but we never verified this method because the few attempts to generate compounds of type **16** were all very unpromising.

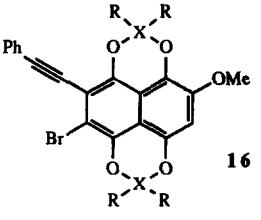
Since the hydrogen transfer did not occur — at least to any appreciable extent — with radicals of type **8** (see Scheme 1) we sought ways of building up the F-ring (*cf.* structure 1) *after* the radical cyclization. To this end, compound **9** was converted into quinone **19** (Scheme 3). Cleavage of the exocyclic double bond in **9** was best done by ozonolysis (94% yield) rather than by vicinal hydroxylation (osmium tetroxide, *ca.* 77%) and glycol cleavage (periodic acid, *ca.* 63%). Reduction of the carbonyl groups of **17** gave a mixture of diols [mainly (≥95%) *trans*] which were then acetylated (**17**→**18**). Finally, oxidation [ammonium cerium(IV)

nitrate] afforded the desired quinone **19** [which was almost exclusively (98%) the *trans* isomer]. Although quinone **19** did react with dienes **20**,[6] **21**,[7] and **22**[8] the initial adducts were sensitive and readily formed complex mixtures. We were, in fact, never able to isolate any useful products representing the CDEF ring

Scheme 2

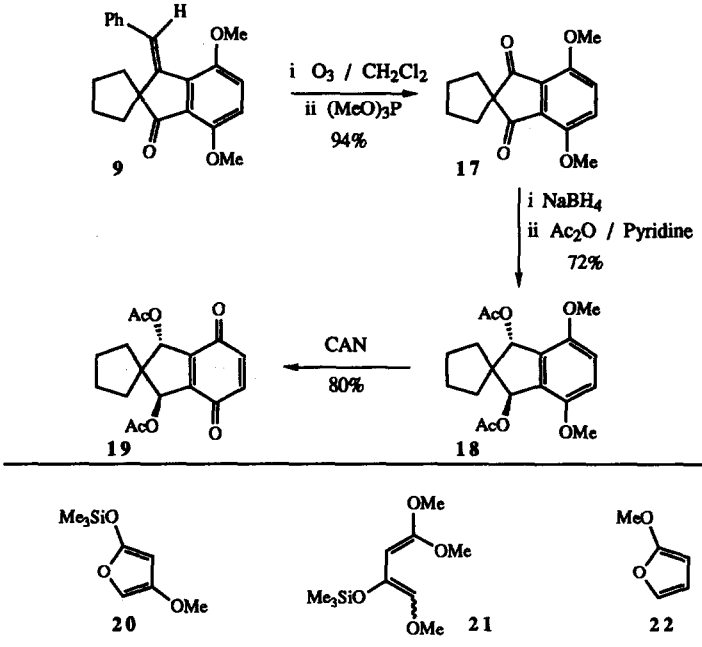


system of fredericamycin A, and so this approach was set aside. We have, however, been able to solve the abstraction problem — or, at least to suppress it very largely — by making use of isotope effects.[9] This was achieved by replacing the critical *O*-methyl by an *O*-trideuteriomethyl group. As chance would have it, the route we had followed in preparing selenide **10** (see Scheme 2) readily accommodated the required change and we had only to use, at the appropriate stage, a deuteriated methylating reagent (CD_3OTs) instead of dimethyl sulfate.



The synthesis of selenide **10** involves the silylated naphthalene **23** (see Scheme 4). In the normal course of events (leading eventually to compound **10** of Scheme 2)[3] the silyl group is removed[10] and the

Scheme 3

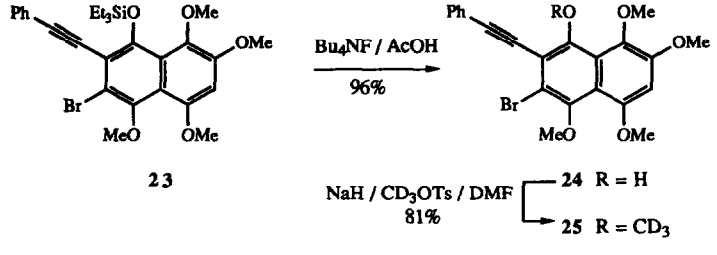


resulting naphthol (**24**, Scheme 4) is methylated with dimethyl sulfate. In the present context, the naphthol was treated instead with methyl-d_3 *p*-toluenesulfonate[11] and sodium hydride (**24**→**25**), and the next steps followed exactly our previous route[3] (of the nondeuteriated series): Halogen-metal exchange, followed by condensation with cyclopentanecarboxaldehyde, gave alcohol **26**, and this was oxidized (DDQ) to the corresponding ketone **27**. Finally, the phenylseleno group was introduced via the silyl enol ether (**27**→**28**→**29**).

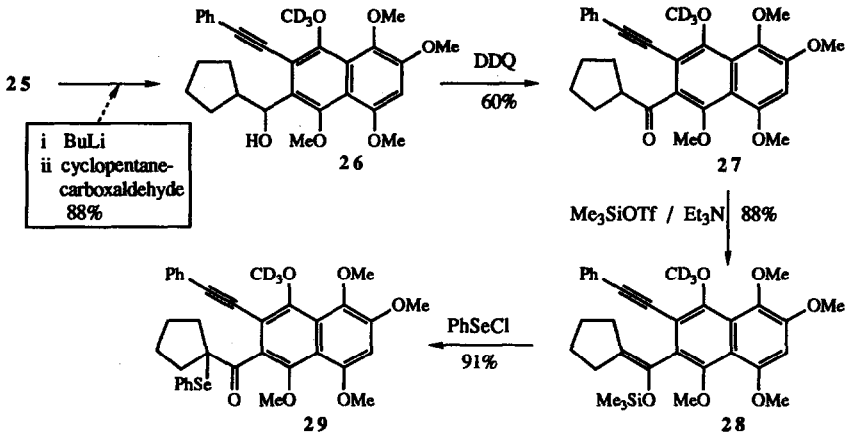
When the deuteriated selenide **29** was treated under our standard conditions (refluxing benzene) with triphenyltin hydride and AIBN (Scheme 5), the spirocyclic compounds **31** were formed in ≥70% yield and little material (**32**) resulting from the undesired abstraction pathway was formed. The ratio **31**:**32** was now 9.7:1,[12] which represents a substantial improvement over the ratio for the nondeuteriated series [**13**:**15** = 1.15:1 to 1.40:1].

As far as we are aware, isotopic modification of a protecting group (here *O*-methyl) has not been used before in synthetic radical chemistry, and the standard reference work[13] does not mention such a technique. Deuteriated protecting groups have, however, been used to simplify NMR spectra.[14]

Scheme 4 (first part)



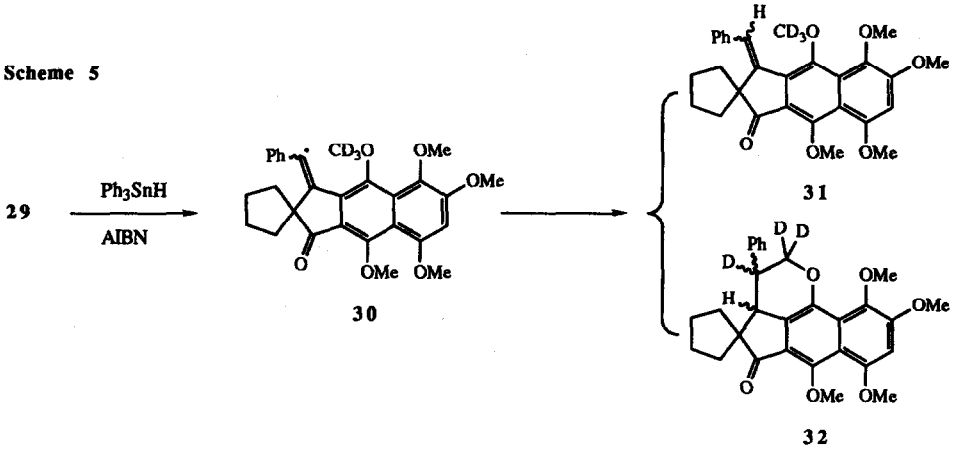
Scheme 4 (continued)



Our results implied that the abstraction problem had been solved, and so we felt it worthwhile to use compounds **13** and **31** to practice forming the quinone system of fredericamycin A.

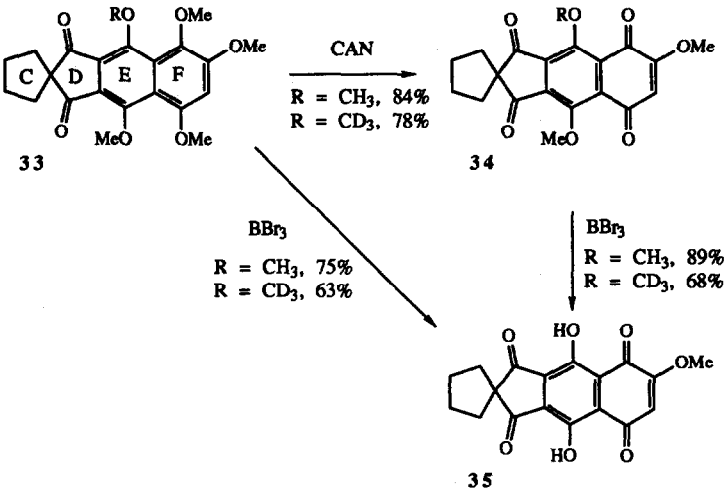
Compound **13** had previously been converted[3] into the spirodiketone **33** (R = CH_3) (Scheme 6) by

Scheme 5



vicinal hydroxylation and glycol cleavage, and we now sought to degrade it further to the quinone **35**. Reaction with ammonium cerium(IV) nitrate served to convert ring F of **33** (R = CH_3) into a quinone (**33**→**34**)[15] and then exposure to boron tribromide gave the desired quinone **35** as a red, crystalline substance. The selective demethylation could also be done directly by treating the fully methylated compound **33** (R = CH_3) with boron tribromide. This reagent, and other Lewis acids, have, of course, been used for selective demethylations,[16] but there appear to be few close analogies[15a] for selective demethylation of polyalkoxynaphthalenes. The tautomer shown for **35** is an arbitrary assignment, but is probably the major tautomer.[17]

Scheme 6



Finally, the deuteriated compound **31** was converted into **33** (R = CD_3) by vicinal hydroxylation and glycol cleavage, and we then repeated the experiments of Scheme 6, using the deuteriated material. These experiments worked without incident.

Experimental

Standard experimental techniques were used.[18] Solutions were evaporated at room temperature. The symbols s', d', t', q' in ^{13}C NMR spectra refer to zero, one, two, and three attached hydrogens, respectively.

α-Cyclopentyl[3,6,dimethoxy-2-(phenylethynyl)phenyl]methanol (3).

n-Butyllithium (1.5 M in hexanes, 0.53 mL, 0.79 mmol) was injected dropwise into a stirred and cooled (-78°C) solution of bromide **2** (264 mg, 0.78 mmol) in ether (6 mL). The mixture was stirred for an additional 30 min, and cyclopentanecarboxaldehyde[19] (77.1 mg, 0.78 mmol) in ether (3 mL plus 1 mL as a rinse) was then added over *ca.* 3 min. The cooling bath was left in place for 2 h, by which time the temperature had risen to 0°C. Saturated aqueous ammonium chloride (10 mL) was added, and the mixture was extracted with ether (2 x 25 mL). The combined organic extracts were washed with brine and dried ($MgSO_4$). Evaporation of the solvent and flash chromatography of the residue over the silica gel (2 x 15 cm), using 7:13 ethyl acetate-hexane, gave alcohol **3** as a homogeneous [^1H NMR (300 MHz)], white solid (228.4 mg, 82%): mp 123.0-123.5°C; FTIR (neat) 3560, 2953, 1590, 1477 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.21--1.76 (m, 7 H), 1.88--1.98 (m, 1 H), 2.48--2.62 (m, 1 H), 3.69 (d, *J* = 9.2 Hz, 1 H), 3.85 (s, 3 H), 3.87 (s, 3 H), 5.04 (t, *J* = 9.2 Hz, 1 H), 6.75 (d, *J* = 8.8 Hz, 1 H), 6.86 (d, *J* = 8.8 Hz, 1 H), 7.32--7.39 (m, 3 H), 7.50--7.56 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 25.40 (t'), 25.51 (t'), 29.13 (t'), 30.48 (t'), 46.49 (d'), 55.91 (q'), 56.47 (q'), 76.56 (d'), 84.11 (s'), 98.7 3 (s'), 109.52 (d'), 111.97 (d'), 112.64 (s'), 123.47 (s'), 128.37 (d'), 131.52 (d'), 135.21 (s'), 151.40 (s'), 154.73 (s'); exact mass *m/z* calcd for $C_{22}H_{24}O_3$ 336.1725, found 336.1721. Anal. Calcd for $C_{22}H_{24}O_3$: C, 78.54; H, 7.19. Found: C, 78.51; H, 7.26.

[Cyclopentyl][3,6-dimethoxy-2-(phenylethynyl)phenyl]methanone (4).

Alcohol **3** (1.28 g, 3.79 mmol) in dichloromethane (25 mL) was added at room temperature to a stirred mixture of pyridinium chlorochromate (3.30 g, 15.2 mmol) and 3Å molecular sieves (8.0 g) in dichloromethane (62.0 mL). Stirring was continued for 6 h, ether (100 mL) was then added, and the suspension was filtered through a pad (5 x 6 cm) of Celite, which was washed well with 1:1 ether-dichloromethane. The combined filtrates were evaporated, and flash chromatography of the residue over the silica gel (6 x 15 cm), using 3:7 ethyl acetate-hexane, gave ketone **4** (1.08 g, 85%) as a homogeneous [^1H NMR (300 MHz)] solid: mp 88.5-89.3°C; FTIR (neat) 1700, 1575 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.51--1.90 (m, 6 H), 1.99--2.12 (m, 2 H), 3.44--3.55 (m, 1 H), 3.79 (s, 3 H), 3.90 (s, 3 H), 6.85 (d, *J* = 9.0 Hz, 1 H), 6.89 (d, *J* = 9.0 Hz, 1 H), 7.31--7.38 (m, 3 H), 7.48--7.53 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 26.30 (t'), 29.04 (t'), 52.95 (d'), 56.71 (q'), 56.95 (q'), 83.57 (s'), 97.84 (s'), 110.62 (s'), 112.10 (d'), 112.82 (d'), 123.44 (s'), 128.56 (d'), 128.74 (d'), 131.95 (d'), 136.31 (s'), 149.71 (s'),

154.66 (s'), 207.96 (s'); exact mass *m/z* calcd for $C_{22}H_{22}O_3$ 334.1569, found 334.1571. Anal. Calcd for $C_{22}H_{22}O_3$: C, 79.02; H, 6.63. Found: C, 78.86; H, 6.60.

[Cyclopentylidene[3,6-dimethoxy-2-(phenylethynyl)phenyl]methoxy]trimethylsilane (5).

Trimethylsilyl triflate (1.79 g, 5.34 mmol) was injected into a stirred and cooled (ice bath) mixture of ketone **4** (1.79 g, 5.34 mmol) and triethylamine (11.45 mL) in dry dichloromethane (182 mL). The mixture was stirred for 1 h. Saturated aqueous sodium bicarbonate (50 mL) was added and the mixture was extracted with dichloromethane (2 x 150 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica (5 x 15 cm), using 1:4 ethyl acetate-hexane, gave silyl enol ether **5** (2.00 g, 92%) as a homogeneous [^{1}H NMR (300 MHz)], white solid: mp 87.0-88.0°C; FTIR (CH_2Cl_2 cast) 1320, 1177, 1167, 1126 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.01 (s, 9 H), 1.49--1.80 (m, 4 H), 1.84--1.98 (m, 1 H), 2.28--2.52 (m, 2 H), 2.52--2.67 (m, 1 H), 3.81 (s, 3 H), 3.89 (s, 3 H), 6.81 (d, *J* = 9.6 Hz, 1 H), 6.85 (d, *J* = 9.6 Hz, 1 H), 7.28--7.38 (m, 3 H), 7.45--7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 0.00 (q'), 25.88 (t'), 26.61 (t'), 28.57 (t'), 29.04 (t'), 55.65 (q'), 55.84 (q'), 85.01 (s'), 95.73 (s'), 109.89 (d'), 111.49 (d'), 113.29 (s'), 123.40 (s'), 126.28 (s'), 127.33 (d'), 127.62 (d'), 130.94 (d'), 131.60 (s'), 135.08 (s'), 151.31 (s'), 153.62 (s'); exact mass *m/z* calcd for $C_{25}H_{30}O_3Si$ 406.1964, found 406.1979. Anal. Calcd for $C_{25}H_{30}O_3Si$: C, 73.85; H, 7.44. Found: C, 74.09, H, 7.57.

[1-(Phenylseleno)cyclopentyl][3,6-dimethoxy-2-(phenylethynyl)phenyl]methanone (6).

Benzeneselenenyl chloride (1.00 g, 5.2 mmol) in THF (4 mL plus 1 mL as a rinse) was added to a stirred and cooled (-78°C) solution of silyl enol ether **5** (1.42 g, 3.50 mmol) in THF (60 mL). Stirring was continued for 2 h, and the mixture was then diluted with ethyl acetate (500 mL) and washed with saturated aqueous sodium bicarbonate, water, and brine. The organic layer was dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (5 x 15 cm), using 1:3 ethyl acetate-hexane, gave selenide **6** (1.56 g, 91%) as a homogeneous [^{1}H NMR (300 MHz)], yellow oil: FTIR (CH_2Cl_2 cast) 1682, 1476, 1436 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.68--1.78 (m, 2 H), 1.80--1.98 (m, 4 H), 2.20--2.38 (m, 2 H), 3.71 (s, 3 H), 3.88 (s, 3 H), 6.85 (s, 2 H), 7.25--7.45 (m, 8 H), 7.63--7.68 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 24.57 (t'), 36.62 (t'), 55.93 (q'), 56.67 (q'), 65.39 (s'), 83.93 (s'), 97.79 (s'), 111.01 (s'), 111.73 (d'), 112.42 (d'), 123.09 (s'), 128.19 (d'), 128.40 (d'), 128.54 (d'), 128.69 (d'), 129.45 (d'), 131.67 (d'), 134.54 (s'), 137.54 (d'), 149.36 (s'), 154.54 (s'), 204.92 (s'); exact mass *m/z* calcd for $C_{28}H_{26}SeO_3$ 490.1047, found 490.1049.

4,7-Dimethoxy-3-(phenylmethylene)spiro[2*H*-indene-2,1'-cyclopentan]-1(3*H*)-one (9).

Azobisisobutyronitrile (10.0 mg, 0.061 mmol) was tipped into a solution of selenide **6** (336 mg, 0.69 mmol) in dry benzene (10.0 mL) under argon. The mixture was lowered into an oil-bath set at 80°C and, as soon as the solution began to reflux, triphenyltin hydride (0.26 mL, 1.02 mmol) in dry benzene (3 mL plus 0.5 mL as a rinse) was added over *ca.* 2 min. Refluxing was continued for 20 min and the solvent was then evaporated. Flash chromatography of the residue over silica gel (3 x 15 cm), using increasing amounts of ethyl acetate in hexane (from 25% to 40%), gave spiroketone **9** (217 mg, 95%) as a homogeneous [^{1}H NMR (300 MHz)] solid: mp 172.5-174.0°C; FTIR (CH_2Cl_2 cast) 1708, 1494 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.24--1.42 (m, 2 H), 1.65--2.05 (m, 6 H), 3.92 (s, 3 H), 3.93 (s, 3 H), 6.81 (d, *J* = 12 Hz, 1 H), 7.11 (d, *J* = 12 Hz, 1 H), 7.23--7.40 (m, 5 H), 8.06 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 26.97 (t'), 37.12 (t'), 55.83 (q'), 56.04 (q'), 58.91 (s'), 110.76 (d'), 117.86 (d'), 122.98 (s'), 126.76 (d'), 128.02 (d'), 128.92 (d'), 129.00 (d'), 137.96 (s'), 138.89 (s'), 143.55 (s'), 150.80 (s'), 151.92 (s'), 208.13 (s'); exact mass *m/z* calcd for $C_{22}H_{22}O_3$ 334.1569, found 334.1568. Anal. Calcd for $C_{22}H_{22}O_3$: C, 79.02; H, 6.63. Found: C, 78.66; H, 6.66. Irradiation of one of the methoxy signals in the ^{1}H NMR spectrum caused a nuclear Overhauser enhancement of 9% in the vinyl hydrogen signal.

4,7-Dimethoxyspiro[2*H*-indene-2,1'-cyclopentane]-1,3-dione (17).

An ozone-oxygen stream was bubbled through a stirred and cooled (-78°C) solution of spiroketone **9** (200 mg, 0.60 mmol) in dichloromethane (9 mL) until the starting material had just disappeared [3 min, TLC control (silica gel, 1:1 ethyl acetate-hexane)]. Trimethyl phosphite (0.20 mL, 1.8 mmol) was injected, the cold bath was removed, and stirring was continued overnight. Evaporation of the solvent and flash chromatography of the residue over silica gel (2 x 15 cm), using 1:1 ethyl acetate-hexane, gave spirodiketone **17** as a homogeneous [^{1}H NMR (200 MHz)], light yellow solid (154 mg, 94%): mp 124-127°C; FTIR (CH_2Cl_2 cast) 1795, 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.93 (s, 8 H), 3.97 (s, 6 H), 7.22 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 27.34 (t'), 35.44 (t'), 56.47 (q'), 60.48 (s'), 119.71 (d'), 129.11 (s'), 150.97 (s'), 203.09 (s'); exact mass *m/z* calcd for $C_{15}H_{16}O_4$ 269.1049, found 260.1049.

***trans*-1,3-Dihydro-4,7-dimethoxyspiro[2*H*-indene-2,1'-cyclopentane]-1,3-diol diacetate (18).**

Sodium borohydride (156 mg, 4.14 mmol) was added to a stirred and cooled (0°C) solution of spirodiketone **17** (179 mg, 0.69 mmol) in methanol (15.0 mL) and stirring was continued for 6 h. Saturated aqueous ammonium chloride (20 mL) was added and the mixture was extracted with ether (2 x 50 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. The residue was dissolved in dry dichloromethane (15.0 mL) and the solution was stirred at 0°C for 5 min. Acetic anhydride (0.16 mL), pyridine (0.16 mL), and DMAP (10.0 mg) were then added, and stirring at 0°C was continued for 3 h. Evaporation of the solvent and flash chromatography the residue over silica gel (2 x 15 cm), using 3:7 ethyl acetate-hexane, gave the diacetate **18** (172 mg, 72%) as a clear oil composed mainly (95% by ^1H NMR) of the *trans* isomer: FTIR ($CHCl_3$ cast) 1736, 1501, 1263, 1229 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ.1.38--1.89 (m, 8 H), 2.08 (s, 6 H), 3.74 (s, 6 H), 6.36 (s, 2 H), 6.72 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 21.07 (q'), 24.73 (t'), 31.30 (t'), 55.94 (q'), 58.69 (s'), 78.21 (d'), 112.11 (d'), 130.49 (s'), 150.55 (s'), 170.65 (s'); exact mass *m/z* calcd for $C_{19}H_{24}O_6$ 348.1572, found 348.1581.

***trans*-1,3-Bisacetoxy-1,3-dihydro[2*H*-indene-2,1'-cyclopentane]-4,7-dione (19).**

A solution of ammonium cerium(IV) nitrate (425 mg, 0.78 mmol) in water (2 mL) was added at room temperature to a stirred solution of diacetate **18** (136 mg, 0.39 mmol) in acetonitrile (10 mL). After 5 min the mixture was poured into water (30 mL) and extracted with ether (2 x 30 mL). The organic extract was washed with brine and dried ($MgSO_4$). Evaporation of the solvent and flash chromatography of the residue over silica gel (2 x 15 cm), using 1:3 ethyl acetate-hexane, gave quinone **19** (98.2 mg, 80%) as a yellow solid consisting mainly (98% by ^1H NMR) of the *trans* isomer: FTIR ($CHCl_3$ cast) 1745, 1667 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.43--1.88 (m, 8 H), 2.07 (s, 6 H), 6.18 (s, 2 H), 6.71 (s, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 20.82 (q'), 24.30 (t'), 31.13 (t'), 57.16 (s'), 77.49 (d'), 137.07 (d'), 145.96 (s'), 169.92 (s'), 184.38 (s'); exact mass *m/z* calcd for $C_{13}H_{12}O_3$ 216.0787 (M - $C_4H_6O_3$), found 216.0788. Anal. Calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 63.77; H, 5.68.

Radical cyclization of 10 using triphenyltin deuteride. 4,5,6,8,9-Pentamethoxy-3-(phenylmethylene-1-d)spiro[2*H*-benz[f]indene-2,1'-cyclopentan]-1(3*H*)-one (13, PhCD= instead of PhCH=).

Azobisisobutyronitrile (2.5 mg, 0.015 mmol) was tipped into a solution of selenide **10** (97 mg, 0.154 mmol) in dry benzene (2.0 mL) and the mixture was maintained under a static pressure of argon. The reaction flask was lowered into an oil-bath and, as soon as the solution began to reflux, triphenyltin deuteride (82 mg, 0.235 mmol) in dry benzene (1.0 mL plus 0.5 mL as a rinse) was added over 2-3 min. Refluxing was continued overnight, and the mixture was then cooled and evaporated. Flash chromatography of the residue over silica gel (1.5 x 10 cm), using 1:4 ethyl acetate-hexane, gave the desired product (**13** with PhCD= instead of PhCH=) (23 mg, 31.5%) and abstraction products (31 mg, 42.5%), the former as a yellow foam and the latter as a yellow solid. The desired product had: FTIR (CH_2Cl_2 cast) 2934, 1707, 1596, 1571 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.32--2.22 (br m, 8 H), 3.21 (s, 1 H, OMe of minor isomer), 3.58 (s, 1 H, OMe of minor isomer), 3.80--4.06 (seven overlapping singlets, five of which are due to the major isomer, 13 H), 6.70 (s, 1 H), 7.10--7.40 (m, 5 H); [the deuteriated compound lacks signals at δ 6.70 (s, minor isomer) and δ 8.32 (s, major isomer) which occur in the spectrum of the nondeuteriated material]; exact mass *m/z* calcd for $C_{29}H_{29}DO_6$ 475.2106, found 475.2113. The compounds decomposed before we could obtain a ^{13}C NMR spectrum. The abstraction products were separated by flash chromatography into two fractions. One fraction was very largely (*ca.* 89%) a single isomer and had ^1H NMR ($CDCl_3$, 200 MHz) δ 0.74--2.20 (br m, 8 H), 3.22 (dd, *J* = 11.0, 3.5 Hz, 1 H), 3.81 (s, 3 H), 3.90--4.07 (series of singlets, 9 H), 4.30 (t, *J* = 11.0 Hz, 1 H), 4.54 (dd, *J* = 11.0, 3.5 Hz, 1 H), 6.69 (s, 1 H), 7.19--7.44 (m, 5 H). The other fraction, which was a mixture (3:2) of the above isomer (major component) and a second, had: FTIR (CH_2Cl_2 cast) 1708, 1612, 1597, 1588 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.79--2.24 (br m, 8 H), 3.21 (dd, *J* =11.0, 3.5 Hz, 0.6 H), 3.41 (m, 0.4 H), 3.70--4.04 (series of singlets, 12 H), 4.29 (t, *J* = 11.0 Hz, 0.6 H), 4.53 (m, 1 H), 4.76 (dd, *J* = 11.0, 3.0, Hz 0.4 H), 6.69 and 6.71 (two singlets, 1 H), 6.92--7.17 (m, signals of minor isomer, 2 H), 7.21--7.42 (m, signals of major isomer, 3 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 25.15 (t'), 25.30 (t'), 25.77 (t'), 26.03 (t'), 32.99 (t'), 33.12 (t'), 33.87 (t'), 38.34 (t'), 39.30 (d'), 40.04 (d'), 47.54 (t'), 57.20 (q'), 57.33 (q'), 62.04 (q'), 62.45 (q'), 62.50 (s'), 63.07 (s'), 63.20 (q'), 63.44 (q'), 72.37 (t'), 74.08 (t'), 98.25 (d'), 98.33 (d'), 117.86 (s'), 118.06 (s'), 121.24 (s'), 121.49 (s'), 125.76 (s'), 126.97 (d'), 127.46 (d'), 127.67 9 (s'), 127.74 (s'), 128.19 (d'), 128.42 (d'), 128.95 (d'), 137.80 (s'), 139.30 (s'), 140.97 (s'), 143.13 (s'), 143.69 (s'), 150.17 (s'), 150.52 (s'), 152.45 (s'), 156.59 (s'), 156.73 (s'), 206.58 (s'), 207.22 (s'); exact mass *m/z* calcd for $C_{29}H_{29}DO_6$ 475.2106, found 475.2107.

HPLC Separation of nondeuteriated abstraction products.

For comparison with the abstraction products obtained from the experiment with selenide **10** and triphenyltin deuteride, some of the material from our normal (triphenyltin hydride) experiments[3] was separated by HPLC [Whatman Magnum Partisil Column [2.5 x 2.2 (i.d.) cm; 1:1 ethyl acetate-hexane]. Two fractions were obtained. One was a single isomer and had: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.77--1.05 (m, 1 H), 1.15--1.79 (m, 6 H), 2.00--2.19 (m, 1 H), 3.22 (dt, *J* = 11.0, 3.5 Hz, 1 H), 3.72 (d, *J* = 11.0 Hz, 1 H), 3.82 (s, 3 H), 3.97 (s, 3 H), 3.99 (s, 6 H), 4.30 (t, *J* = 11.0 Hz, 1 H), 4.53 (dd, *J* = 11.0, 3.5 Hz, 1 H), 6.69 (s, 1 H), 7.22--7.43 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 25.79 (t'), 26.05 (t'), 33.15 (t'), 33.93 (t'), 40.15 (d'), 47.59 (d'), 57.27 (q'), 57.40 (q'), 62.08 (q'), 63.21 (s'), 63.49 (q'), 72.42 (t'), 98.45 (d'), 117.92 (s'), 121.25(s'), 125.82 (s'), 127.49 (d'), 127.74 (s'), 128.21 (d'), 128.98 (d'), 137.89 (s'), 139.34 (s'), 143.13 (s'), 150.21 (s'), 152.49 (s'), 156.63 (s'), 206.57 (s'). The other fraction contained some (*ca.* 25%) of the first material and had: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.74--2.27 (br m, 8 H), 3.39--3.47 (m, 1 H), 3.72 (s, 3 H), 3.92 (d, *J*= *ca.* 2.5 Hz, 1 H), 3.99 (s, 9 H), 4.52 (dd, *J* = 11.0, 1.5 Hz, 1 H), 4.75 (dd, *J* = 11.0, 3.0 Hz, 1 H), 6.71 (s, 1 H), 6.94--7.18 (m, 5 H). We were unable to obtain the ^{13}C NMR spectrum for this fraction.

3-Bromo-4,5,7,8-tetramethoxy-2-(phenylethynyl)-1-naphthalenol (24).

(a) [[3-Bromo-4,5,7,8-tetramethoxy-2-(phenylethynyl)-1-naphthalenyl]oxy]triethylsilane.

A solution of sodium dithionite (2.03 g, 12 mmol) and tetrabutylammonium bromide (100 mg, 0.31 mmol) in water (50 mL) was added to a solution of 2-bromo-5,6,8-trimethoxy-3-(phenylethynyl)-4-[(triethylsilyl)oxy]-1-naphthalenol[3] (2.43 g, 4.5 mmol) in dichloromethane (150 mL), and the mixture was stirred vigorously at room temperature for 30 min under argon. Dimethyl sulfate (4.0 mL, 24 mmol), followed by 2N aqueous sodium hydroxide (21 mL, 42 mmol) were then added, each in one portion, and stirring was continued overnight. The organic phase was separated and the aqueous layer was extracted with dichloromethane (3 x 25 mL). The combined organic extracts were washed with 10% aqueous ammonium hydroxide solution (1 x 50 mL) and with water (1 x 50 mL), dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (3.5 x 18 cm), using increasing amounts of ethyl acetate in hexane (from 10% to 20%), gave **23** (2.05 g, 82%) as a homogeneous [^{1}H NMR (300 MHz)] yellow solid: FTIR ($CHCl_3$ cast) 1600, 1357 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.78--0.96 (m, 15 H), 3.70 (s, 3 H), 3.83 (s, 3 H), 3.98 (s, 3 H), 4.01 (s, 3 H), 6.66 (s, 1 H), 7.33--7.43 (m, 3 H), 7.61--7.67 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 5.25 (t'), 6.92 (q'), 57.27 (q'), 61.52 (q'), 61.93 (q'), 87.76 (s'), 97.91 (s'), 99.63 (d'), 115.26 (s'), 115.47 (s'), 117.48 (s'), 123.82 (s'), 124.70 (s'), 128.36 (d'), 131.53 (d'), 138.43 (s'), 148.16 (s'), 150.00 (s'), 150.13 (s'), 152.44 (s'); exact mass, *m/z* calcd for $C_{28}H_{33}{}^{79}BrO_5Si$ 556.1280, found 556.1272. A small portion was recrystallized from dichloromethane-petroleum ether: mp 99-101 °C. Anal. Calcd for $C_{28}H_{33}BrO_5Si$: C, 60.32; H, 5.97. Found: C, 60.30; H, 5.85.

(b) 3-Bromo-4,5,7,8-tetramethoxy-2-(phenylethynyl)-1-naphthalenol (24).

Tetrabutylammonium fluoride (1.0 M in THF, 6.9 mL, 6.8 mmol) was added rapidly to a stirred solution of silyl ether **23** (1.92 g, 3.4 mmol) in a mixture of dry THF (30 mL) and glacial acetic acid (2.0 mL). Stirring at room temperature was continued for 30 min. The solution was then diluted with dichloromethane (150 mL) and washed with water (1 x 100 mL), saturated aqueous sodium bicarbonate (1 x 100 mL), and water (1 x 100 mL). The organic layer was dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 20 cm), using increasing amounts of ethyl acetate in hexane (from 20% to 35%), gave naphthol **24** (1.47 g, 96%) as a homogeneous [^{1}H NMR (200 MHz)] yellow solid: mp 154-155°C; FTIR ($CHCl_3$ cast) 3230, 1809, 1383, 1343, 1035 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz), δ 3.82 (s, 3 H), 3.98 (s, 3 H), 4.00 (s, 3 H), 4.02 (s, 3 H), 6.73 (s, 1 H), 7.30--7.40 (m, 3 H), 7.61--7.70 (m, 2 H), 10.77 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 56.75 (q'), 57.09 (q'), 61.49 (q'), 62.47 (q'), 85.24 (s'), 98.25 (s'), 98.63 (d'), 105.77 (s'), 115.86 (s'), 116.57 (s'), 118.58 (s'), 123.51 (s'), 128.22 (d'), 131.65 (d'), 136.31 (s'), 146.03 (s'), 148.15 (s'), 152.40 (s'), 153.31 (s'); exact mass *m/z* calcd for $C_{22}H_{19}{}^{79}BrO_5$ 442.0416, found 442.0410. Anal. Calcd for $C_{22}H_{19}BrO_5$: C, 59.61; H, 4.33. Found: C, 59.64; H, 4.48.

2-Bromo-1,5,6,8-tetramethoxy-4-(methoxy-d$_3$)-3-(phenylethynyl)naphthalene (25).

Methyl-d$_3$ *p*-toluenesulfonate[11] (1.22 g, 6.44 mmol) was tipped into a solution of naphthol **24** (1.425 g, 3.21 mmol) in dry DMF (20 mL), and sodium hydride (60%w/w dispersion in oil, 0.24 g, 6.0 mmol) was then added. The mixture was stirred at room temperature for 2.5 h. Saturated aqueous ammonium chloride (40 mL) was added and the mixture was extracted with dichloromethane (3 x 125 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated at room temperature, first under water-pump vacuum and then under oil pump vacuum (to remove DMF). Flash chromatography of the residue over silica gel (2.5 x 18 cm), using increasing amounts of ethyl acetate in hexane (from 30% to 40%), gave the deuteriated ether **25** (1.32 g,

89%) as a pale yellow solid which was recrystallised from dichloromethane-hexane to afford the pure material (1.21 g, 81%): mp 146-147 °C; FTIR ($CHCl_3$ cast) 1599, 1356, 1203, 1046 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.85 (s, 3 H), 3.86 (s, 3 H), 4.00 (s, 3 H), 4.02 (s, 3 H), 6.79 (s, 1 H), 7.34--7.44 (m, 3 H), 7.61--7.70 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 56.74 (q'), 57.36 (q'), 61.51 (q'), 62.10 (q'), 85.39 (s'), 98.24 (s'), 99.07 (d'), 114.57 (s'), 117.38 (s'), 118.59 (s'), 123.35 (s'), 125.34 (s'), 128.36 (d'), 128.59 (d'), 131.71 (d'), 137.07 (s'), 150.30 (s'), 150.77 (s'), 152.91 (s'), 154.38 (s'); exact mass *m/z* calcd for $C_{23}H_{18}D_3{}^{79}BrO_5$ 459.0761, found 459.0762. A satisfactory analysis was obtained[3] for the corresponding nondeuteriated compound.

α-Cyclopentyl-1,5,6,8-tetramethoxy-4-(methoxy-d_3)-3-(phenylethynyl)-2-naphthalenemethanol (26).

n-Butyllithium (1.6 M in hexanes, 1.84 mL, 2.94 mmol) was added dropwise over *ca.* 1 min to a stirred and cooled (-78°C) solution of bromide **25** (679 mg, 1.47 mmol) in dry THF (16 mL). Halogen-metal exchange was monitored by TLC (silica, 1:1 ethyl acetate-hexane) and, after 5 min, a solution of freshly distilled cyclopentanecarboxaldehyde[19] (363 mg, 3.70 mmol) in THF (2 mL plus 1 mL as a rinse) was injected rapidly. The brownish orange color of the solution faded within 30 sec. Stirring was continued for 20 min at -78°C and saturated aqueous ammonium chloride (20 mL) was added. The mixture was allowed to attain room temperature and was extracted with dichloromethane (3 x 60 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 20 cm), using increasing amounts of ethyl acetate in hexane (from 20% to 50%), gave alcohol **26** (621 mg, 88%) as a homogeneous [^1H NMR (200 MHz)], yellow foam: FTIR ($CHCl_3$ cast) 3550, 2951, 1601, 1381, 1047 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.26--1.84 (m, 7 H), 1.92--2.14 (m, 1 H), 2.68--2.93 (m, 1 H), 3.59 (d, J = 11 Hz, 1 H), 3.84 (s, 3 H), 3.87 (s, 3 H), 3.98 (s, 3 H), 4.02 (s, 3 H), 5.09 (t, J = 11 Hz, 1 H), 6.78 (s, 1 H), 7.35--7.45 (m, 3 H), 7.52--7.66 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 25.61 (t'), 29.28 (t'), 31.04 (t'), 46.98 (d'), 56.83 (q'), 57.12 (q'), 62.09 (q'), 63.30 (q'), 75.24 (d'), 85.16 (s'), 98.67 (d'), 99.43 (s'), 114.66 (s'), 116.82 (s'), 123.19 (s'), 125.47 (s'), 128.53 (d'), 128.64 (d'), 131.35 (d'), 131.56 (s'), 137.02 (s'), 150.38 (s'), 150.44 (s'), 153.12 (s'), 154.57 (s'); exact mass *m/z* calcd for $C_{29}H_{29}D_3O_6$ 479.2387, found 479.2390.

α-Cyclopentyl-1,5,6,8-tetramethoxy-4-(methoxy-d_3)-3-(phenylethynyl)-2-naphthalenylmethanone (27).

2,3-Dichloro-5,6-dicycano-1,4-benzoquinone (836 mg, 3.7 mmol) was added to a stirred solution of alcohol **26** (883 mg, 1.8 mmol) in dry dioxane (20 mL). The black suspension was stirred overnight at 100 °C, cooled to room temperature, diluted with 1:1 ethyl acetate-hexane (50 mL), and filtered through a pad of aluminium oxide (neutral, grade III, 10 x 5 cm). The pad was washed with 1:1 ethyl acetate-hexane (2 L) and ethyl acetate (500 mL). Evaporation of the filtrate and flash chromatography of the residue over silica gel (2.5 x 20 cm), using 1:5 ethyl acetate-hexane, gave impure material which was purified by flash chromatography over silica gel (2.5 x 20 cm), using first 1:1 dichloromethane-petroleum ether and then 1:4:5 ethyl acetate-dichloromethane-petroleum ether, to afford pure [^1H NMR (300 MHz)] ketone **27** (525 mg, 60%) as a yellow solid: FTIR ($CHCl_3$ cast) 2070, 1600, 1364, 1046 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.46--1.62 (m, 2 H), 1.62--1.76 (m, 2 H), 1.76--1.91 (m, 2 H), 1.98--2.12 (m, 2 H), 3.48--3.60 (m, 1 H), 3.73 (s, 3 H), 3.83 (s, 3 H), 3.97 (s, 3 H), 3.98 (s, 3 H), 6.74 (s, 1 H), 7.28--7.37 (m, 3 H), 7.46--7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 26.00 (t'), 29.15 (t'), 53.09 (d'), 56.71 (q'), 62.04 (q'), 64.11 (q'), 83.85 (s'), 97.65 (s'), 97.84 (d'), 112.58 (s'), 116.54 (s'), 123.14 (s'), 126.25 (s'), 128.30 (d'), 128.48 (d'), 131.52 (d'), 133.40 (s'), 136.89 (s'), 148.87 (s'), 151.11 (s'), 153.58 (s'), 153.98 (s'), 208.15 (s'); exact mass *m/z* calcd for $C_{29}H_{27}D_3O_6$ 477.2231, found 477.2229. A sample was recrystallized from dichloromethane-petroleum ether: mp 109-111°C. A satisfactory analysis was obtained[3] for the corresponding nondeuteriated compound.

[Cyclopentylidene[1,5,6,8-tetramethoxy-4-(methoxy-d_3)-3-(phenylethynyl)-2-naphthalenyl]methoxy]trimethylsilane (28).

Trimethylsilyl triflate (0.50 mL, 2.66 mmol) was added to a stirred and cooled (ice bath) mixture of ketone **27** (516 mg, 1.15 mmol) and triethylamine (1.0 mL, 7.17 mmol) in dichloromethane (30 mL). The solution was stirred at 0°C for 2 h, and then saturated aqueous sodium bicarbonate (30 mL) was added. The organic layer was separated and the aqueous phase was extracted with dichloromethane (2 x 50 mL). The combined organic layers were dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.5 x 20 cm), using increasing amounts of ethyl acetate in hexane (from 15% to 20%), gave the silyl enol ether **28** (525 mg, 88%) as a pale yellow, homogeneous [^1H NMR (200 MHz)] solid: FTIR ($CHCl_3$ cast) 2070, 1800, 1363, 1341, 1050, 876, 848 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.00 (s, 9 H), 1.48--1.73 (m, 4 H), 1.80--1.92 (m, 1 H), 2.26--2.65 (m, 3 H), 3.75 (s, 3 H), 3.85 (s, 3 H), 3.93 (s, 3 H), 3.97

(s, 3 H), 6.72 (s, 1 H), 7.25--7.37 (m, 3 H), 7.45--7.51 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 0.89 (q'), 26.61 (t'), 27.26 (t'), 29.25 (t'), 30.13 (t'), 56.79 (q'), 57.44 (q'), 62.06 (q'), 62.37 (q'), 86.18 (s'), 96.16 (s'), 98.64 (d'), 116.95 (s'), 117.63 (s'), 124.03 (s'), 125.91 (s'), 126.30 (s'), 128.12 (d'), 128.35 (d'), 129.48 (s'), 131.57 (d'), 136.31 (s'), 136.95 (s'), 150.49 (s'), 151.53 (s'), 153.57 (s'), 153.84 (s'); exact mass *m/z* calcd for $C_{32}H_{35}D_3O_6Si$ 549.2625, found 549.2622. A sample was recrystallized from dichloromethane-petroleum ether: mp 175-177°C. A satisfactory analysis was obtained[3] for the corresponding nondeuteriated compound.

[1-(Phenylseleno)cyclopentyl][1,5,6,8-tetramethoxy-4-(methoxy-d_3)-3-(phenylethynyl)-2-naphthalenyl]methanone (29).

Benzeneselenenyl chloride (211 mg, 1.10 mmol) was tipped into a stirred and cooled (-78°C) solution of silyl enol ether **28** (484 mg, 0.88 mmol) in dry THF (16 mL). After 1 h, the cooling-bath was removed and stirring was continued for 2 h. The red solution was diluted with dichloromethane (1 x 100 mL) and washed with saturated aqueous sodium bicarbonate (1 x 50 mL), and water (1 x 50 mL). The organic layer was dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using 1:3 ethyl acetate-petroleum ether, gave the phenylseleno ketone **29** (506 mg, *ca.* 91%) as a orange foam containing trace impurities (TLC, silica, 1:1 ethyl acetate-hexane) but suitable for the next stage: FTIR ($CHCl_3$ cast) 2070, 1800, 1363, 1046 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.64--1.79 (m, 2 H), 1.80--2.05 (m, 4 H), 2.23--2.38 (m, 2 H), 3.74 (s, 3 H), 3.87 (s, 3 H), 3.98 (s, 3 H), 4.02 (s, 3 H), 6.79 (s, 1 H), 7.22--7.37 (m, 6 H), 7.44--7.57 (m, 2 H), 7.72--7.78 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 24.33 (t'), 36.82 (t'), 56.79 (q'), 57.12 (q'), 62.13 (q'), 63.43 (q'), 65.57 (s'), 84.65 (s'), 97.92 (s'), 98.40 (d'), 113.21 (s'), 116.63 (s'), 123.24 (s'), 126.24 (s'), 128.27 (d'), 128.46 (d'), 128.52 (d'), 128.66 (d'), 129.52 (s'), 131.65 (d'), 131.85 (s'), 137.01 (s'), 137.65 (s'), 148.71 (s'), 151.15 (s'), 153.70 (s'), 154.25 (s'), 206.16 (s'); exact mass *m/z* calcd for $C_{35}H_{31}D_3O_6Se$ 633.1708, found 633.1694. A satisfactory analysis was obtained[3] for the corresponding nondeuteriated compound.

5,6,8,9-Tetramethoxy-4-(methoxy-d_3)-3-(phenylmethylene)spiro[2*H*-benz[f]indene-2,1'-cyclopentan]-1(3*H*)-one (31) and 3,3a-Dihydro-6,7,9,10-tetramethoxy-3-phenylspiro[4*H*-benz[5,6]indeno[7,1-bc]pyran-4,1'-cyclopentan]-5(2*H*)-one-2,2,3-d_3 (32).

Azobisisobutyronitrile (2 mg) was added to a solution of selenide **29** (170 mg, 0.27 mmol) in dry benzene (4.0 mL), and the mixture was lowered into an oil-bath set at 80°C. As soon as refluxing began a solution of triphenyltin hydride (151 mg, 0.52 mmol) in dry benzene (0.5 mL plus 2 x 0.3 mL as a rinse) was injected rapidly. Refluxing was continued overnight, and the mixture was cooled to room temperature and evaporated. Flash chromatography of the residue over silica gel (2.5 x 15 cm), using mixtures of ethyl acetate-dichloromethane-petroleum ether (from 1:1:9 to 1:1:3), gave olefinic ketone **31** (96.5 mg, *ca.* 75%) as a yellow foam and abstraction product **32** (5.5 mg, *ca.* 4%) as a pale yellow foam. Compound **31**, which was not absolutely pure, but was suitable for the next step, was a mixture of two isomers [^{1}H NMR (200 MHz)] and had: FTIR ($CHCl_3$ cast) 1709, 1366, 1047 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.38--1.50 (m, 1 H), 1.75--2.07 (m, 6 H), 2.12--2.25 (m, 1 H), 3.59 (s, 1.14 H), 3.86 (s, 1.86 H), 3.97 (s, 1.86 H), 4.00 (s, 1.14 H), 4.01 (s, 3 H), 4.05 (s, 1.86 H), 4.07 (s, 1.14 H), 6.69 (s, 0.38 H), 6.74 (s, 0.38 H), 6.75 (s, 0.62 H), 7.13--7.42 (m, 5 H), 8.30 (s, 0.62 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 26.97 (t'), 27.06 (t'), 56.62 (q'), 57.40 (q'), 60.24 (s'), 62.15 (q'), 62.48 (q'), 62.79 (q'), 63.39 (q'), 65.40 (s'), 97.53 (d'), 97.78 (d'), 118.00 (s'), 121.24 (s'), 124.61 (s'), 126.59 (d'), 126.80 (d'), 127.09 (d'), 128.04 (d'), 128.23 (d'), 128.63 (d'), 128.97 (d'), 130.60 (d'), 133.70 (s'), 134.75 (s'), 137.08 (s'), 137.70 (s'), 138.26 (s'), 139.12 (s'), 141.81 (s'), 142.58 (s'), 147.82 (s'), 148.13 (s'), 152.77 (s'), 152.83 (s'), 153.79 (s'), 156.66 (s'), 156.70 (s'), 204.09 (s'), 206.90 (s'); exact mass *m/z* calcd for $C_{29}H_{27}D_3O_6$ 477.2231, found 477.2209.

Abstraction product **32** consisted of a mixture of two isomers [^{1}H NMR (200 MHz)] and had: FTIR ($CHCl_3$ cast) 2933, 1708, 1599, 1365, 1051, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.75--1.10 (m, 2 H), 1.17--1.41 (m, 3 H), 1.49--1.79 (m, 3 H), 1.82--2.22 (m, 1 H), 3.70--4.01 (eight singlets, 12 H), 6.59 (s, 0.65 H), 6.70 (s, 0.35 H), 6.97--7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 25.15 (t'), 25.29 (t'), 25.77 (t'), 26.04 (t'), 32.99 (t'), 33.13 (t'), 33.91 (t'), 38.39 (t'), 46.08 (d'), 47.43 (d'), 57.24 (q'), 57.37 (q'), 62.05 (q'), 62.47 (q'), 62.61 (s'), 63.16 (s'), 63.22 (q'), 63.46 (q'), 98.34 (d'), 98.43 (d'), 117.91 (s'), 118.10 (s'), 121.23 (s'), 121.48 (s'), 125.78 (s'), 126.98 (d'), 127.45 (d'), 127.72 (s'), 128.17 (d'), 128.43 (d'), 128.95 (d'), 130.09 (d'), 137.86 (s'), 139.27 (s'), 140.95 (s'), 143.10 (s'), 143.66 (s'), 150.18 (s'), 150.53 (s'), 152.45 (s'), 156.60 (s'), 156.73 (s'), 206.55 (s'), 207.19 (s'); exact mass *m/z* calcd for $C_{29}H_{27}D_3O_6$ 477.2231, found 477.2231.

4,6,9-Trimethoxyspiro[2*H*-benz[f]indene-2,1'-cyclopentane]-1,3,5,8-tetrone (34, R = CH_3).

A solution of ammonium cerium(IV) nitrate (40 mg, 0.073 mmol) in water (0.5 mL) was added quickly to a stirred solution of spirodiketone **33** (R = CH_3) (11.4 mg, 0.029 mmol) in acetonitrile (1.0 mL). Stirring at room temperature was continued for 10 min (TLC control, silica, 1:2 ethyl acetate-hexane). The mixture was diluted with ethyl acetate (20 mL) and washed with water (2 x 25 mL). The organic extract was dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1 x 10 cm), using 1:2 ethyl acetate-hexane, gave quinone **34** (R = CH_3) (8.9 mg, 84%) as homogeneous [TLC (silica, 1:2 ethyl acetate-hexane), ^1H NMR (200 MHz)], yellow crystals: mp 179-181°C; FTIR (CH_2Cl_2 cast) 2943, 1711, 1684, 1652, 1623 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.95 (br s, 8 H), 3.87 (s, 3 H), 4.05 (s, 3 H), 4.07 (s, 3 H), 6.11 (s, 1 H); ^{13}C NMR ($CDCl_3$, 106.1 MHz) δ 27.51 (t'), 35.88 (t'), 56.72 (q'), 61.37 (s'), 63.41 (q'), 63.46 (q'), 110.80 (d'), 131.58 (s'), 132.48 (s'), 138.51 (s'), 139.75 (s'), 153.52 (s'), 154.19 (s'), 160.02 (s'), 178.35 (s'), 182.67 (s'), 200.83 (s'); exact mass *m/z* calcd for $C_{20}H_{18}O_7$ 370.1053, found 370.1045.

4,9-Dihydroxy-6-methoxyspiro[2*H*-benz[f]indene-2,1'-cyclopentane]-1,3,5,8-tetrone (35).
(a) By demethylation of 34 (R = CH_3).

Boron tribromide (1.75 M in dichloromethane, 130 μL, 0.23 mmol) was added dropwise to a stirred and cooled (-78°C) solution of quinone **34** (R = CH_3) (8.4 mg, 0.023 mmol) in dry dichloromethane (1.5 mL). The solution became deep red during the addition. Stirring at -78°C was continued for 20 min after the addition. Water (20 mL) and dichloromethane (20 mL) were then added and the mixture was allowed to separate into two phases. The organic layer was was washed with 10%v/v hydrochloric acid (1 x 20 mL) and with water (1 x 20 mL), dried (Na_2SO_4), and evaporated. Flash chromatography of the residue over silica gel (1 x 10 cm) with 100:50:0.5 dichloromethane-ethyl acetate-acetic acid gave the crude product. This was dissolved at room temperature in dichloromethane and the solution was diluted with ethyl acetate and allowed to stand for 24 h. Crystals of pure [TLC, silica, 100:50:1 dichloromethane-ethyl acetate-acetic acid; ^1H NMR (200 MHz)] hydroxy quinone **35** (6.9 mg, 89%) were obtained: mp 247-249°C; FTIR (CH_2Cl_2 cast) 1708, 1599 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.86--2.08 (m, 8 H), 3.98 (s, 3 H), 6.27 (s, 1 H), 12.50 (s, 1 H), 13.15 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 27.37 (t'), 35.71 (t'), 57.31 (q'), 60.92 (s'), 111.05 (d'), 117.67 (s'), 117.80 (s'), 135.50 (s'), 137.29 (s'), 152.78 (s'), 153.60 (s'), 161.17 (s'), 183.38 (s'), 188.64 (s'), 201.05 (s'), 201.12 (s'); exact mass *m/z* calcd for $C_{18}H_{14}O_7$ 342.0739, found 342.0741.

Irradiation of the vinyl hydrogen signal in the ^1H NMR spectrum caused a nuclear Overhauser enhancement of 14% in the methoxy signal.

(b) By demethylation of 33 (R = CH_3).

Boron tribromide (1.75 M in dichloromethane, 160 μL, 0.28 mmol) was added dropwise to a stirred and cooled (-78°C) solution of spirodiketone **33** (R = CH_3) (7.4 mg, 0.019 mmol) in dry dichloromethane (1.0 mL). The solution became deep red during the addition. Stirring at -78°C was continued for 20 min after the addition. Water (20 mL) and dichloromethane (20 mL) were then added and the mixture was allowed to separate into two phases. The organic layer was was washed with 10%v/v hydrochloric acid (1 x 20 mL) and with water (1 x 20 mL), dried (Na_2SO_4), and evaporated. The residue was dissolved in chloroform (2 mL) that had been shaken with concentrated hydrochloric acid, and the mixture was stirred for 2 h and then evaporated. Flash chromatography of the residue over silica gel (1 x 10 cm) with 100:50:0.5 dichloromethane-ethyl acetate-acetic acid gave the crude product. This was dissolved at room temperature in dichloromethane and the solution was diluted with ethyl acetate and allowed to stand 24 h. Crystals of pure [TLC, silica, 100:50:1 dichloromethane-ethyl acetate-acetic acid; ^1H NMR (200 MHz)] hydroxy quinone **35** (4.8 mg, 75%) were obtained, identical with material made as described above.

5,6,8,9-Tetramethoxy-4-(methoxy-d_3)spiro[2*H*-benz[f]indene-2,1'-cyclopentane]-1,3-dione (33, R = CD_3).
(a) 3-Hydroxy-3-(hydroxyphenylmethyl)-5,6,8,9-tetramethoxy-4-(methoxy-d_3)spiro[2*H*-benz[f]indene-2,1'-cyclopentane]-1(3*H*)-dione.

A freshly prepared solution of osmium tetroxide in bench pyridine (4.1 mL, 11.3 mg per mL, 0.107 mmol of osmium tetroxide) was added with stirring to the radical cyclization products **31** (49.2 mg, 0.103 mmol) and the solution was stirred at room temperature for 1 h. The mixture was then diluted with ethyl acetate (50 mL) and was washed with 10 % aqueous sodium bisulfite (2 x 25 mL), 2 N aqueous hydrochloric acid (1 x 25 mL), and water (1 x 25 mL), dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1 x 15 cm), using 2:3 ethyl acetate-hexane, gave the required diols as a yellow, glassy solid (42.9 mg, 81%) which was a mixture of two isomers: FTIR (CH_2Cl_2 cast) 3475, 2947, 1719, 1599, 1382, 1350 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.55--2.45 (m, 9 H), 3.35--4.10 (nine singlets

corresponding to 12 H), 4.36 (br s, 0.6 H), 4.75 (br s, 0.4 H), 4.96 (br d, J = 8.0 Hz, 0.4 H), 5.01 (br s, 0.6 H), 6.65--7.25 (m including a singlet at δ 6.75, 6 H); ^{13}C NMR ($CHCl_3$, 75.47 MHz) δ 25.42 (t'), 25.68 (t'), 26.86 (t'), 27.31 (t'), 27.62 (t'), 27.75 (t'), 35.88 (t'), 37.69 (t'), 56.61 (q'), 57.31 (q'), 57.38 (q'), 62.32 (q'), 62.46 (q'), 63.25 (q'), 63.47 (q'), 66.66 (s'), 67.49 (s'), 78.58 (d'), 80.11 (d'), 84.56 (s'), 85.11 (s'), 97.47 (d'), 97.54 (d'), 117.89 (s'), 118.23 (s'), 123.45 (s'), 124.33 (s'), 127.40 (d'), 127.45 (d'), 127.62 (d'), 127.75 (d'), 127.81 (d'), 127.89 (d'), 128.20 (s'), 128.99 (s'), 135.10 (s'), 136.16 (s'), 137.04 (s'), 138.69 (s'), 140.28 (s'), 152.30 (s'), 152.81 (s'), 156.77 (s'), 156.84 (s'), 200.39 (s'), 201.37 (s'); exact mass m/z calcd for $C_{29}H_{29}D_3O_8$ 511.2285, found 511.2296.

(b) 5,6,8,9-Tetramethoxy-4-(methoxy-d_3)spiro[2*H*-benz[f]indene-2,1'-cyclopentane]-1,3-dione (33, R = CD_3).

Periodic acid (55 mg, 0.24 mmol) was added in one batch to a stirred solution of the above diols (37.5 mg, 0.073 mmol) in methanol (3.0 mL). After 2 h at room temperature (TLC control, silica, 1:3 ethyl acetate-hexane) the mixture was diluted with ethyl acetate (50 mL), washed with water (1 x 30 mL), and dried ($MgSO_4$). [The reaction must be stopped as soon as it is complete otherwise the yield is lower.] Evaporation of the solvent and flash chromatography of the residue over silica gel (1 x 8 cm) with 1:3 ethyl acetate-hexane gave the spirodiketone **33** (R = CD_3) (20.7 mg, 69%) as a homogeneous [^1H NMR (200 MHz)] yellow oil: FTIR ($CHCl_3$ cast) 1729, 1701, 1596, 1356 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.96--2.06 (m, 8 H), 3.88 (s, 3 H), 4.03 (s, 6 H), 4.06 (s, 3 H), 6.90 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 28.15 (t'), 36.56 (t'), 57.13 (q'), 58.03 (q'), 62.79 (q'), 62.99 (s'), 63.60 (q'), 100.48 (d'), 121.70 (s'), 124.75 (s'), 127.82 (s'), 131.55 (s'), 139.91 (s'), 154.08 (s'), 154.14 (s'), 157.38 (s'), 202.45 (s'), 203.86 (s'); exact mass m/z calcd for $C_{22}H_{21}D_3O_7$ 403.1710, found 403.1705. A satisfactory analysis was obtained[3] for the corresponding nondeuteriated compound.

6,9-Dimethoxy-4-(methoxy-d_3)spiro[2*H*-benz[f]indene-2,1'-cyclopentane]-1,3,5,8-tetrone (34, R = CD_3).

A solution of ammonium cerium(IV) nitrate (85.9 mg, 0.157 mmol) in water (1.0 mL) was added quickly to a stirred solution of spirodiketone **33** (R = CD_3) (23.4 mg, 0.058 mmol) in acetonitrile (2.0 mL). Stirring at room temperature was continued for 10 min (TLC control, silica, 2:3 ethyl acetate-hexane). The mixture was diluted with ethyl acetate (50 mL) and washed with water (2 x 25 mL). The organic extract was dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1 x 8 cm) with 2:3 ethyl acetate-hexane gave quinone **34** (R = CD_3) (16.9 mg, 78%) as homogeneous [TLC (silica, 2:3 ethyl acetate-hexane)] yellow crystals: mp 164-175°C; FTIR ($CHCl_3$ cast) 2880, 2080, 1713, 1686, 1653, 1625 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.98 (br s, 8 H), 3.89 (s, 3 H), 4.06 (s, 3 H), 6.14 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 27.48 (t'), 35.84 (t'), 56.67 (q'), 61.37 (s'), 63.35 (q'), 110.76 (d'), 131.56 (s'), 132.46 (s'), 138.46 (s'), 139.72 (s'), 153.46 (s'), 154.15 (s'), 160.03 (s'), 178.31 (s'), 182.61 (s'), 200.76 (s'), 200.82 (s'); exact mass m/z calcd for $C_{20}H_{15}D_3O_7$ 373.1241, found 373.1236.

4,9-Dihydroxy-6-methoxyspiro[2*H*-benz[f]indene-2,1'-cyclopentane]-1,3,5,8-tetrone (35).
(a) By demethylation of 34 (R = CD_3).

Boron tribromide (1.75 M in dichloromethane, 180 μL, 0.32 mmol) was added dropwise to a stirred and cooled (-78°C) solution of quinone **34** (R = CD_3) (12.3 mg, 0.033 mmol) in dry dichloromethane (2.0 mL). The solution became deep red during the addition. Stirring at -78°C was continued for 2 h after the addition. Water (20 mL) and dichloromethane (20 mL) were then added and the mixture was allowed to separate into two phases. The organic layer was was washed with 10%v/v hydrochloric acid (1 x 20 mL), and with water (1 x 20 mL), dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1 x 8 cm) with 100:50:0.5 dichloromethane-ethyl acetate-acetic acid gave the crude product (8.9 mg). This was dissolved at room temperature in dichloromethane and the solution was diluted with ethyl acetate and allowed to stand for 24 h. Crystals of pure [TLC, silica, 100:50:1 dichloromethane-ethyl acetate-acetic acid] quinone **35** (7.6 mg, 68%) were obtained, identical to a sample made in the nondeuteriated series.

(b) By demethylation of 33 (R = CD_3).

Boron tribromide (1.75 M in dichloromethane, 150 μL, 0.26 mmol) was added dropwise to a stirred and cooled (-78°C) solution of spirodiketone **33** (R = CD_3) (5.5 mg, 0.014 mmol) in dry dichloromethane (1.0 mL). The solution became deep red during the addition. Stirring at -78°C was continued for 2 h after the addition. Water (20 mL) and dichloromethane (20 mL) were then added and the mixture was allowed to separate into two phases. The organic layer was was washed with 10%v/v hydrochloric acid (1 x 20 mL), and with water (1 x 20 mL), dried (Na_2SO_4) and evaporated. The residue was dissolved in chloroform (2 mL) that had been shaken with concentrated hydrochloric acid, and the solution was stirred for 24 h and evaporated.

Flash chromatography of the residue over silica gel (1 x 8 cm) with 100:50:0.5 dichloromethane-ethyl acetate-acetic acid gave quinone **35** (2.9 mg, 63 %), identical to material made by the two-step route.

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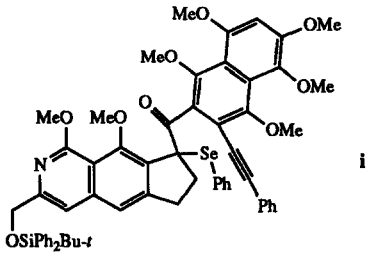

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