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A Novel Oxidative Intramolecular [4+2]Cycloaddition of Silylene-Protected Dihydroxystyrene Derivatives Leading to *peri*-Hydroxy Polycyclic Aromatic Compounds: A Synthesis of the ABCD Ring System of Fredericamycin A

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Heating of the silylene protected dihydroxystyrene generated from the *o*-hydroxyacetophenone (3a) at 130—150 °C for 15—48 h in a sealed tube gave intramolecular [4+2]cycloaddition products (5 and 6). The addition of chloranil to the reaction mixture brought about an oxidative intramolecular [4+2]cycloaddition to give the linearly condensed *peri*-hydroxy aromatic compound (7a) in excellent yield. The generality of this cycloaddition and application to a short and efficient synthesis of the ABCD ring system of fredericamycin A are described.

Keywords intramolecular [4+2]cycloaddition; *peri*-hydroxy polycyclic aromatic compound; oxdative cycloaddition; silylene derivative; fredericamycin A

Development of an efficient synthesis of naturally occurring *peri*-hydroxy aromatic compounds,[1] such as anthracyclines,[2] nogalamycin,[3] olivomycin,[4] bostrycin,[5] granaticin,[6] fredericamycin A,[7] and other antitumor polycyclic antibiotics, has been the subject of intensive study. The regioselective ring annulation is the critical step in the synthesis of these compounds. Among many approaches to them,[1] an intramolecular [4+2]cycloaddition reaction of alkoxystyrene derivatives having a suitable dienophile in the side chain, was expected to be a useful and straightforward method. The trials, however, were unsuccessful. One reason for this failure was the elimination of the alkoxy (or hydroxy) group from the cyclized product under the thermal conditions, leading to stable aromatization products.[8] Several years ago, we found a novel oxidative cycloaddition reaction of silylene-protected dihydroxystyrene derivatives with dienophiles, which gave the *peri*-hydroxy polycyclic aromatic compounds without loss of the α-hydroxyl group (Chart 1).[9] This approach should provide a short and efficient synthetic method for *peri*-hydroxy polycyclic compounds if the cycloaddition reaction can be extended to the intramolecular system. The conditions, however, were not suitable and gave a miserable yield of the intramolecular cycloaddition products. In connection with that work, we have recently communicated an efficient oxidative intramolecular [4+2]cycloaddition of *o*-hydroxyphenyl ketone having a suitable dienophile in the side chain leading to the *peri*-hydroxy aromatic compound in extremely high yield.[10] We now give a full account of this work and additional studies on the intramolecular [4+2]cycloaddition of other *o*-hydroxyphenyl ketones leading to the ABCD ring system of fredericamycin A.

Synthesis of 2,3-Dihydro-1*H*-benz[*f*]isoindol-1-ones (7a—c) and 2,3-Dihydro-1*H*-benz[*f*]indene Derivatives (21a, b and 22) The starting *o*-hydroxyphenyl ketones (**3a—c**) were prepared from *o*-hydroxyacetophenone in 4 steps. Hydroxymethylation of the acetyl group of *o*-hydroxyacetophenone with formaldehyde vapor under basic condition followed by dehydration with concentrated H_2SO_4 in benzene gave the known vinyl ketone (**1**).[11] Michael addition of aniline to **1** gave the terminal amino compound (**2**), which was condensed with α,β-unsaturated carboxylic acids by using a dehydrating agent, dicyclohexylcarbodiimide (DCC) or (trimethylsilyl)ethoxyacetylene,[12] to give the amides (**3a—c**) in considerable yields (Chart 2).

Initially, the dimethylsilylene derivative (**4a**) isolated by the reaction of **3a** with dichlorodimethylsilane (Me_2SiCl_2)/triethylamine (Et_3N) was heated under the same conditions as in the case of the intermolecular cycloaddition to give the cycloaddition products, **5** and **6**, in 15% and 11% yields, respectively. The yield of the products was dramatically improved when the reaction was performed without isolation of **4a** to give a 92% combined yield of **5** and **6** in a 35 : 57 ratio. Variation of the substituents on the silicon atom among dimethyl, diethyl, and diphenyl groups resulted in a slight increase in the ratio of **5** *vs.* **6** from 35 : 57 to 48 : 52. Although the yield of cycloadducts (**5** and **6**) was improved, the desired fully aromatized *peri*-hydroxy adduct (**7a**) could not be obtained at all.[13] After many unsuccessful trials,[14–16] an excellent result was obtained by addition of chloranil (0.136 mmol) in the reaction of **3a** (0.054 mmol), dichlorosilane (0.108 mmol), and Et_3N (0.217 mmol), which produced **7a** selectively in high yield (97%) (Chart 3).

Other *o*-hydroxyphenyl ketones (**3b, c**) gave the corresponding *peri*-hydroxy polycyclic compounds (**7b, c**) in excellent yeilds (Table I). It should be noted that the initially formed moisture-sensitive *Z*-olefin intermediates (**4**)[17] could be regenerated under the reaction conditions and underwent intramolecular Diels–Alder reaction to give the adducts, which were readily oxidized with chloranil to the stable *peri*-hydroxy polycyclic aromatic compounds (**7a—c**) irreversibly in high yields.

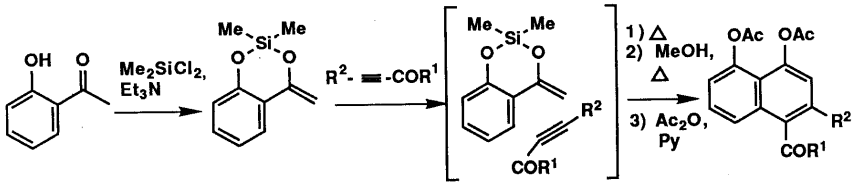
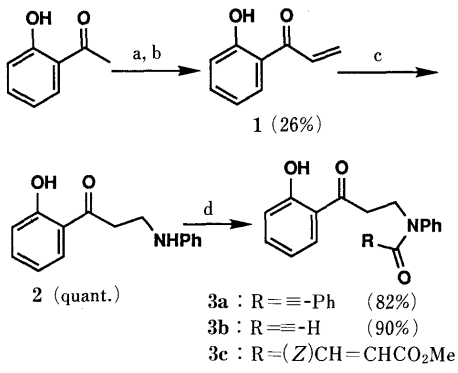


Chart 1

Next, we examined the generality of the cycloaddition in other *o*-hydroxyphenyl ketone systems. The starting *o*-hydroxyphenyl ketones (**16a—c** and **17**) were prepared from *o*-anisaldehyde (**8a**) or 2,5-dimethoxybenzaldehyde (**8b**) in several steps through intermediates (**12a—c** and **13a, b**) as outlined in Chart 4. The iodide (**10**) was prepared from γ-butyrolactone *via* the intermediates **18**, **19**, and **20** in 4 steps. Details of the preparation of **16a—c** and **17** are given in the experimental section.

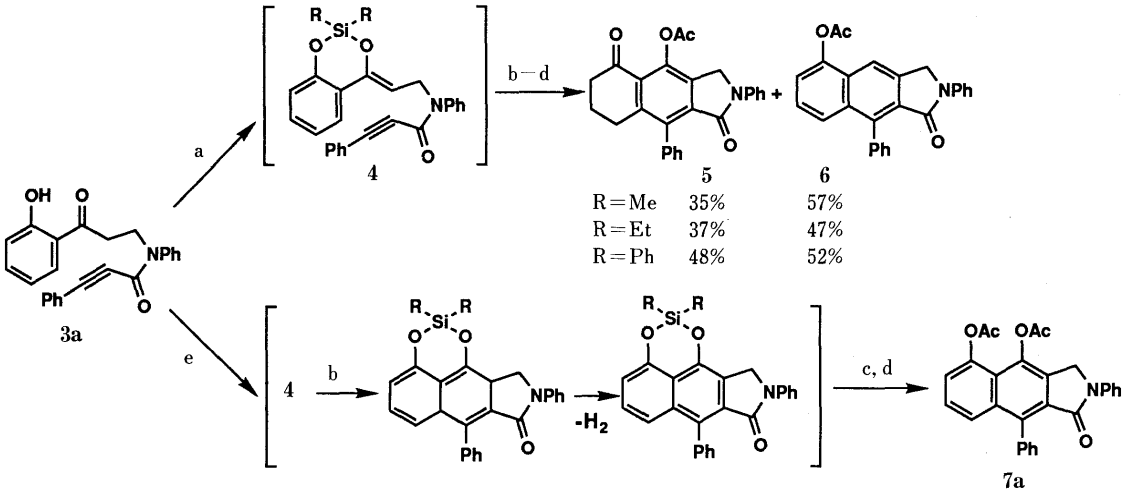


reagents : (a) LDA, $(HCHO)_n$, THF; (b) conc. H_2SO_4, C_6H_6; (c) aniline, EtOH; (d) α,β-unsaturated carboxylic acid (RCO_2H), CH_2Cl_2/DCC or TMS-≡-OEt, HgO

Chart 2

Thermal treatment of the dimethylsilylene derivatives of dihydroxystyrene derivatives (**16a—c** and **17**) as in the case of the synthesis of **7a—c** from **3a—c** gave the corresponding *peri*-hydroxy compounds (**21a, b**, **22**) in fair yields (Table II). The terminal silyl groups [trimethylsilyl (TMS) and *tert*-butyldimethylsilyl (TBDMS)] were eliminated under the reaction conditions and the bulky TBDMS group merely decreased the yield (entry 2). Even though the electron-withdrawing carbonyl function of the dienophile part was present on the opposite side of the acetylene bond, cyclization occurred smoothly (entry 4).

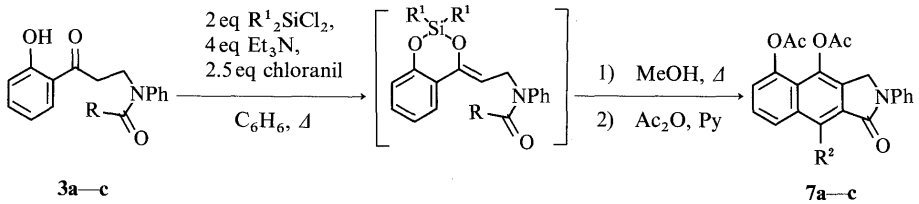
Application for Synthesis of the ABCD Ring System of Fredericamycin A (23) Fredericamycin A (**23**), isolated from *Streptomyces griseus*,[7] exhibits a potent *in vitro* cytotoxic activity[18] and has a unique structure involving a single chiral center at the spiro junction of the CD ring system. Although extensive efforts to achieve a total synthesis of **23**,[19] including one completed total synthesis of racemic **23**,[20] have been made, there is no report on



reagents : (a) R_2SiCl_2, Et_3N, C_6H_6; (b) heat in a sealed tube; (c) MeOH, reflux; (d) Ac_2O, pyridine; (e) R_2SiCl_2, Et_3N, chloranil, C_6H_6

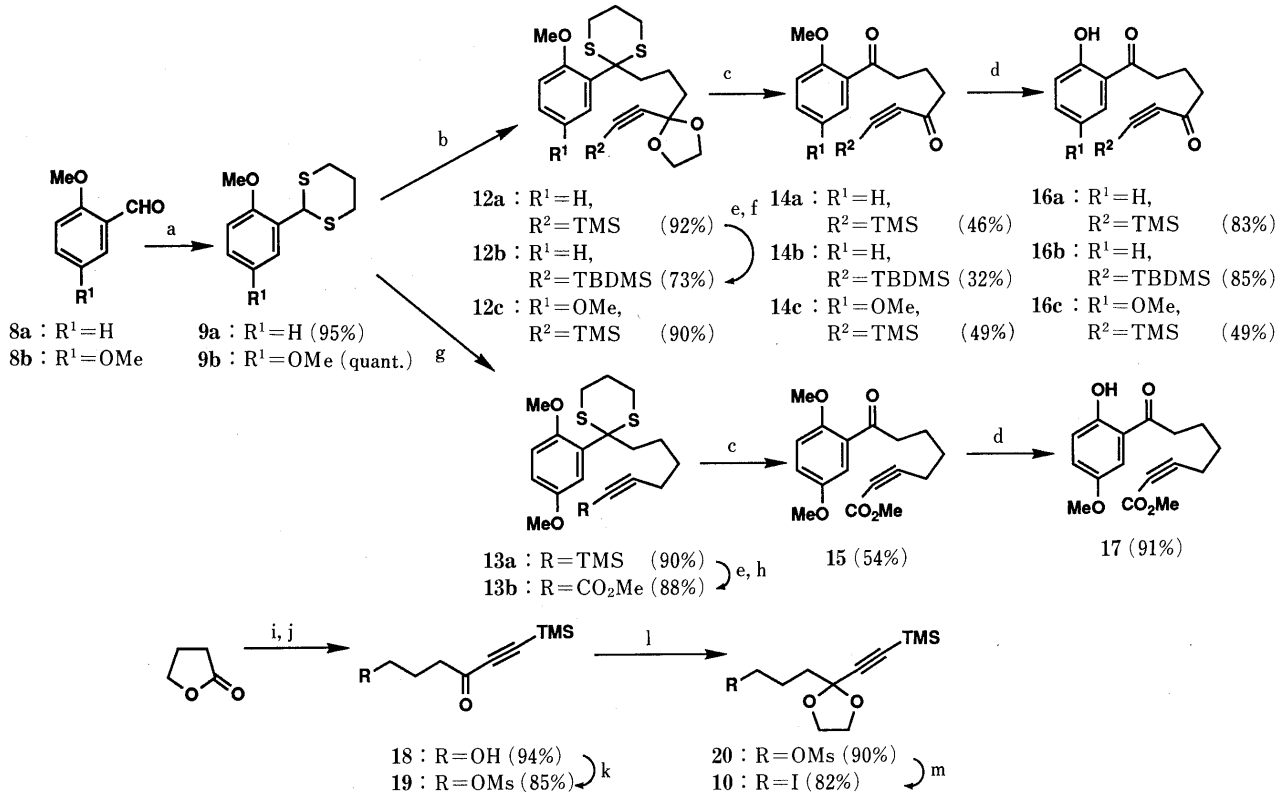
Chart 3

TABLE I. Oxidative Intramolecular [4+2]Cycloaddition of **3a—c**



3a—c **7a—c**

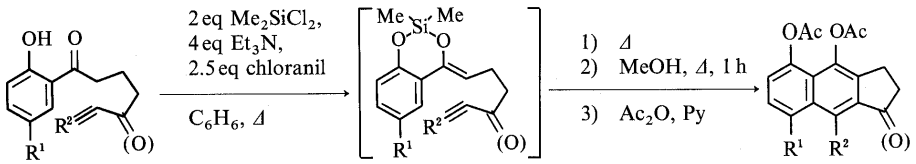
Entry	R	R^1	Reaction time (h)		R^2	Product Yields (%)
1	—≡—Ph	Me	48	**7a**	Ph	97
2	—≡—Ph	Ph	48	**7a**	Ph	92
3	—≡—H	Me	7	**7b**	H	84
4	—≡—H	Ph	48	**7b**	H	75
5	(Z) -CH=$CHCO_2Me$	Me	18	**7c**	CO_2Me	64
6	(Z) -CH=$CHCO_2Me$	Ph	48	**7c**	CO_2Me	65



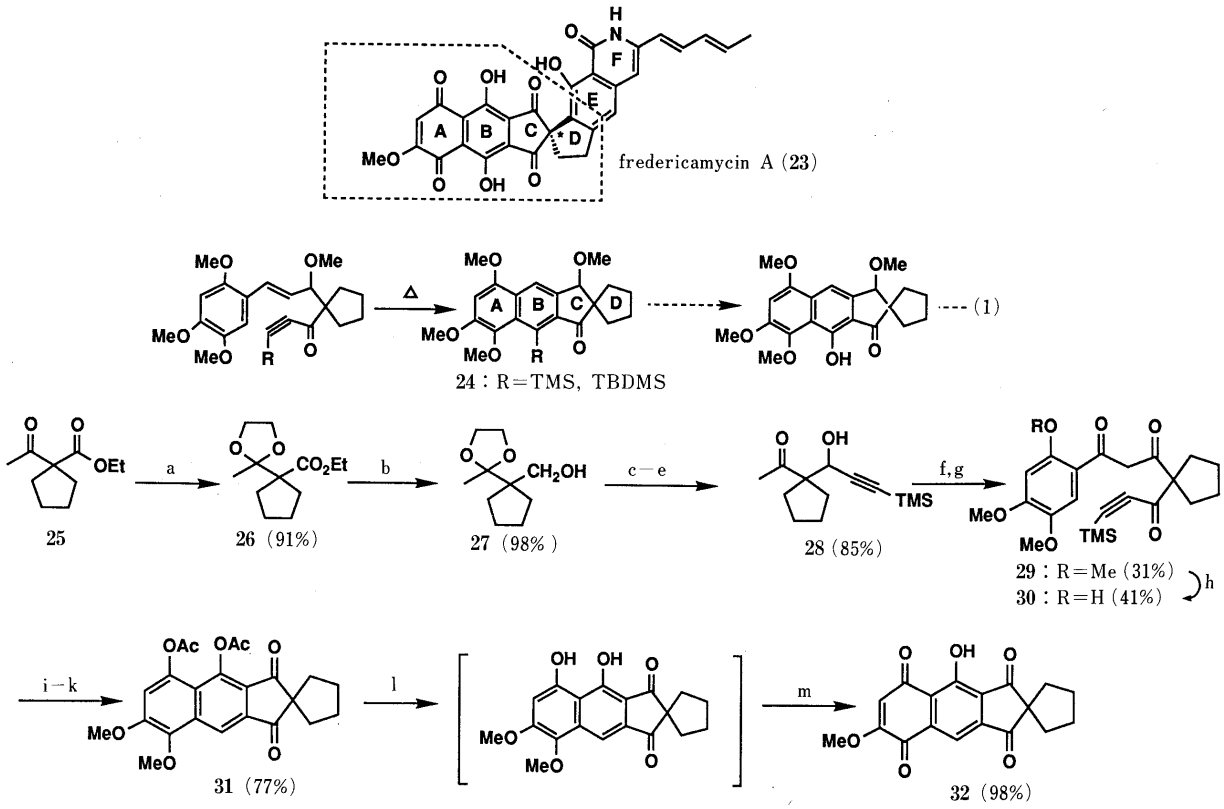
reagents : (a) propanedithiol, BF_3 Et_2O, CH_2Cl_2; (b) LDA, **10**, THF; (c) PIDA, *p*-TsOH, MeOH; (d) $AlCl_3$, CH_2Cl_2; (e) TBAF, THF; (f) *n*-BuLi, TBDMSCl, THF; (g) LDA, 6-iodo-1-(trimethylsilyl)-1-hexyne (**11**), THF; (h) *n*-BuLi, $ClCO_2Me$, THF; (i) TMS-≡-Li, THF; (j) AcOH, CH_2Cl_2; (k) MsCl, pyridine, CH_2Cl_2; (l) $(CH_2OH)_2$, *p*-TsOH, C_6H_6; (m) NaI, acetone

Chart 4

TABLE II. Oxidative Intramolecular [4+2]Cycloaddition of **16a—c** and **17**



Entry	Starting compound	Reaction time (h)	Product	Yield (%)
1	**16a**: R^2=TMS	15	**21a**	66
2	**16b**: R^2=TBDMS	48		22
3	**16c**	15	**21b**	61
4	**17**	22	**22**	62



reagents : (a) $(CH_2OH)_2$, *p*-TsOH, C_6H_6; (b) $LiAlH_4$, Et_2O; (c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; (d) TMS-≡-Li, THF; (e) *p*-TsOH, acetone; (f) 2 eq LDA, HMPA, 2,4,5-trimethoxybenzoyl chloride, THF; (g) DMSO, DCC, pyridinium trifluoroacetate, C_6H_6; (h) 4 eq $AlCl_3$, CH_2Cl_2; (i) Me_2SiCl_2, Et_3N, chloranil, C_6H_6, heat in a sealed tube; (j) MeOH, reflux; (k) Ac_2O, pyridine; (l) 80% aqueous CF_3CO_2H; (m) PIFA, 33% aqueous CH_3CN

Chart 5

the synthesis of optically active **23**. Very recently, Toyota and Terashima reported an elegant synthesis of 2,2-tetramethylene-benz[*f*]indanes (**24**) by an intramolecular Diels–Alder reaction of dienynes as exemplified in Eq. 1.[21] It is expected to be a useful method for the synthesis of optically active **23**, because it has potential for construction of the asymmetric spiro junction of the CD ring system. The conversion of the silyl group on the B-ring of **24** thus obtained into an OH group was, unfortunately, quite difficult and failed in our hands. Therefore, we examined the synthesis of the ABCD ring system of **23** using the present oxidative intramolecular [4+2]cycloaddition reaction of silylene-protected dihydroxystyrene derivatives.

The requisite *o*-hydroxyphenyl ketone (**30**) was prepared from the known *β*-ketoester (**25**)[22] in 8 steps. Acetalization of **25** followed by reduction of the acetal (**26**) gave the alcohol (**27**) in 89% yield. Oxidation of **27** followed by treatment with lithium trimethylsilylacetylide gave the ethynyl alcohol, which was deprotected to give the *β*-ketoalcohol (**28**) in 85% overall yield from **27**. The dianion of **28** was aroylated with 2,4,5-trimethoxybenzoyl chloride to give the *β*-diketoalcohol, which was oxidized to give the triketone (**29**) in 31% overall yield from **28**. Selective demethylation of **29** with aluminum trichloride ($AlCl_3$) at room temperature gave the requisite *o*-hydroxyphenyl ketone (**30**) in 41% yield. Thermal treatment of **30** under the conditions described above caused oxidative intramolecular cycloaddition to give the desired *peri*-hydroxy aromatic compound, which was acetylated to give the acetate (**31**) in 77% overall yield from **30**. Deacetylation of **31** followed by oxidation with phenyliodosyl bis(trifluoroacetate)[PIFA, $PhI(OCOCF_3)_2$][23] gave the quinone (**32**), which is a key partial structure of **23** (Chart 5).

Application of this methodology to a total synthesis of optically active fredericamycin A is under investigation.

Experimental

All boiling and melting points are uncorrected. Infrared (IR) absorption spectra were recorded on a JASCO HPIR-102 spectrophotometer, ^{1}H-nuclear magnetic resonance (^{1}H-NMR) spectra were determined on a Hitachi R-22 (90 MHz) or JEOL JNM-GX500 (500 MHz) spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were obtained by the electron impact (EI) method on an ESCO EMD-05A (for EI-MS) or a JEOL JMS-D300 (for EI- and exact MS) mass spectrometer. E. Merck silica gel 60 (70—230 mesh ASTM) for column chromatography and E. Merck precoated thin layer chromatography (TLC) plates, Silica gel F_{254} for preparative TLC (prep. TLC) were used. Organic layers were dried with anhydrous $MgSO_4$. Tetrahydrofuran (THF) was distilled from the sodium benzophenone dianion under nitrogen.

2-Hydroxyphenyl Vinyl Ketone (1) *o*-Hydroxyacetophenone (7.23 ml, 60.0 mmol) was added dropwise at −78 °C under nitrogen to an anhydrous THF solution of lithium diisopropylamide (LDA), prepared from *n*-BuLi (1.6 N in hexane, 89.0 ml, 144 mmol), diisopropylamine (20.1 ml, 144 mmol) and anhydrous THF (100 ml), and the mixture was stirred for 1 h under the same conditions. Then HCHO vapor obtained by heating paraformaldehyde (7.00 g) at 180 °C was introduced into the reaction vassel with vigorous stirring under nitrogen at 0 °C. The reaction mixture was poured into saturated aqueous NH_4Cl, and acidified (pH=3) with concentrated HCl. After extraction with Et_2O and AcOEt, the organic layer was washed with saturated aqueous $NaHCO_3$ and brine successively, dried, and then evaporated under reduced pressure. Purification of the residue by column chromatography on silica gel (benzene : AcOEt=

5:1—1:1, and Et_2O) followed by recrystallization from hexane–CH_2Cl_2 gave 3.50 g (35%) of pure 2′-hydroxyethyl 2-hydroxyphenyl ketone.

Concentrated H_2SO_4 (50.0 mg) was added to a benzene solution (21 ml) of 2′-hydroxyethyl 2-hydroxyphenyl ketone (1.00 g, 6.02 mmol). The reaction mixture was refluxed for 80 min with a Dean–Stark apparatus. The resultant mixture was poured into saturated aqueous $NaHCO_3$, and extracted with ether. The organic layer was washed with brine, dried, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (benzene) to give 670 mg (75%) of pure **1** as a yellow oil: bp 65—67 °C (1.2—1.3 mmHg) (lit.[11] bp 67—68 °C (1—2 mmHg)). IR ($CHCl_3$) ν: 3040, 1640, 1620 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 5.92 (dd, 1H, J=10, 2 Hz, vinyl-H), 6.51 (dd, 1H, J=16, 2 Hz, vinyl-H), 6.77—7.59 (m, 4H, vinyl-H and ArH×3), 7.78 (dd, 1H, J=8, 2 Hz, 3-H), 12.50 (s, 1H, OH).

3-Anilino-1-(2-hydroxyphenyl)-1-propanone (2) An EtOH (160 ml) solution of **1** (1.99 g, 13.4 mmol) was added dropwise over 30 min to an EtOH (100 ml) solution of aniline (1.25 g, 13.4 mmol) at room temperature. The solvent was removed by evaporation under reduced pressure to give a crude solid. Recrystallization from hexane–AcOEt gave 3.40 g (quant.) of pure **2** as colorless crystals: mp 65—67 °C. IR ($CHCl_3$) ν: 3010, 1640, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.23 (t, 2H, J=6 Hz, $COCH_2$), 3.58 (t, 2H, J=6 Hz, NCH_2), 6.51—7.71 (m, 10H, ArH×9 and NH), 12.26 (s, 1H, OH). MS m/z: 241 (M^+). *Anal.* Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.59; H, 6.19; N, 5.78.

***N*-[3-(2-Hydroxyphenyl)-3-oxo-propyl]-*N*-phenyl-phenylpropiolamide (3a)** DCC (206 mg, 1.00 mmol) was added to a CH_2Cl_2 (2 ml) solution of **2** (241 mg, 1.00 mmol) and phenylpropiolic acid (146 mg, 1.00 mmol) at room temperature. The reaction mixture was stirred under the same conditions for 25 h. After filtration to remove the precipitate, the filtrate was evaporated under reduced pressure to give a crude residue. The residue was purified by column chromatography on silica gel (hexane: AcOEt=5:1) to give 302 mg (82%) of pure **3a** as colorless crystals: mp 111—112 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) ν: 3000, 2210, 1640, 1630, 1595 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.40 (t, 2H, J=8 Hz, $COCH_2$), 4.24 (t, 2H, J=8 Hz, NCH_2), 6.71—7.82 (m, 14H, ArH×14), 12.02 (s, 1H, OH). MS m/z: 369 (M^+). *Anal.* Calcd for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79. Found: C, 78.19; H, 4.94; N, 3.80.

***N*-[3-(2-Hydroxyphenyl)-3-oxo-propyl]-*N*-phenyl-Propiolamide (3b)** This was prepared from **2** (241 mg, 1.00 mmol) and propiolic acid (75.0 μl, 1.20 mmol) by the same procedure as described for the preparation of **3a**. Purification by column chromatography on silica gel (hexane: AcOEt=2:1) gave pure **3b** (262 mg, 90%) as colorless crystals: mp 134—135 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) ν: 3300, 3010, 2100, 1640, 1595 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.80 (s, 1H, C≡CH), 3.36 (t, 2H, J=8 Hz, $COCH_2$), 4.20 (t, 2H, J=8 Hz, NCH_2), 6.76—7.78 (m, 9H, ArH×9), 12.04 (s, 1H, OH). MS m/z: 293 (M^+). *Anal.* Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.47; H, 5.02; N. 4.69.

***N*-[3-(2-Hydroxyphenyl)-3-oxo-propyl]maleinanilic Acid, Methyl Ester (3c)** A CH_2Cl_2 (0.3 ml) solution of maleic acid monomethyl ester (49.0 mg, 0.373 mmol) was added dropwise to a mixture of (trimethylsilyl)ethoxyacetylene (90.0 μl, 0.525 mmol), a catalytic amount of HgO (0.24 mg, 1.1 μmol) and dry CH_2Cl_2 (1.2 ml), and the mixture was stirred at room temperature for 1 h. Then a CH_2Cl_2 solution of **2** (75.0 mg, 0.311 mmol) was added dropwise and the whole was stirred at room temperature for 6 h. After addition of (trimethylsilyl)ethoxyacetylene (90.0 μl, 0.525 mmol) and maleic acid monomethyl ester (49.0 mg, 0.373 mmol), the reaction mixture was stirred at room temperature for 15 h. Removal of the solvent under reduced pressure gave the crude product. Purification by column chromatography on silica gel (hexane: AcOEt=3:1) gave pure **3c** (63.2 mg, 58%) as colorless crystals: mp 105—107 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) ν: 1725, 1640, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.42 (t, 2H, J=8 Hz, $COCH_2$), 3.73 (s, 3H, OCH_3), 4.18 (t, 2H, J=8 Hz, NCH_2), 5.73 (d, 1H, J=12 Hz, vinyl-H), 6.22 (d, 1H, J=12 Hz, vinyl-H), 6.72—7.89 (m, 9H, ArH×9). 12.09 (s, 1H, OH). MS m/z: 353 (M^+). *Anal.* Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.86; H, 5.25, N, 3.87.

General Procedure for Intramolecular [4+2]Cycloaddition Reaction of Silylene-Protected Dihydroxystyrene Derivatives Obtained from *o*-Hydroxyphenylketones (3a—c, 16a—c, 17, and 30) Method A: A mixture of *o*-hydroxyphenyl ketone (0.100 mmol), Me_2SiCl_2 (0.200 mmol), Et_3N (0.400 mmol) in benzene (10 ml) was refluxed under nitrogen for 6 h and then stirred at room temperature for 12 h. The reaction mixture was diluted with dry benzene. The precipitate was filtered off, and the filtrate was concentrated under reduced pressure. The residue was diluted with dry benzene and heated in a sealed tube at 130—150 °C for 48 h. The reaction mixture was evaporated under reduced pressure, then diluted with MeOH and refluxed for 1 h. After concentration, the crude desilylated product was acetylated by a usual method with acetic anhydride in pyridine to give the acetate, which was purified by preparative TLC to give the pure acetylated cycloadducts.

Method B: A mixture of *o*-hydroxyphenyl ketone (0.100 mmol), dichlorodialkylsilane (0.200 mmol), Et_3N (0.400 mmol) and benzene (10 ml) was heated in a sealed tube at 130—150 °C for 48 h. The reaction mixture was worked up as described under method A to give the acetylated cycloadducts.

Method C: A suspension of *o*-hydroxyphenyl ketone (0.100 mmol), dichlorodialkylsilane (0.200 mmol), Et_3N (0.400 mmol), chloranil (0.250 mmol) and benzene (10 ml) was heated in a sealed tube at 130—150 °C for 15—48 h. The reaction mixture was worked up as described under method A to give the acetylated cycloadducts.

4-Acetoxy-2,9-diphenyl-2,3,5,6,7,8-hexahydro-1*H*-benz[*f*]isoindole-1,5-dione (5) and 5-Acetoxy-2,9-diphenyl-2,3-dihydro-1*H*-benz[*f*]isoindol-1-one (6) These were prepared from **3a** by method A or B. Purification by preparative TLC gave pure **5** and **6**. **5**: pale yellow crystals; mp 227—229 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) ν: 1770, 1705, 1690 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.97—2.07 (m, 2H, 7-CH_2), 2.49 (s, 3H, $COCH_3$), 2.66 (t, 2H, J=7 Hz, 6-CH_2), 2.73 (t, 2H, J=7 Hz, 8-CH_2), 4.78 (s, 2H, 3-CH_2), 7.08—7.79 (m, 10H, ArH×10). MS m/z: 411 (M^+). *Anal.* Calcd for $C_{26}H_{21}NO_4$: C, 75.90; H, 5.14; N, 3.40. Found: C, 75.66; H, 5.02; N, 3.29. **6**: colorless crystals; mp 235—238 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) ν: 1760, 1695 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.54 (s, 3H, $COCH_3$), 5.03 (s, 2H, 3-CH_2), 7.15 (t, 1H, J=8.0 Hz, ArH), 7.33—7.48 (m, 6H, ArH×6), 7.49—7.58 (m, 3H, ArH×3), 7.66 (d, 1H, J=8.5 Hz, ArH), 7.86 (dd, 2H, J=8.0, 1.0 Hz, ArH×2), 8.02 (s, 1H, 4-CH). MS m/z: 393 (M^+). *Anal.* Calcd for $C_{26}H_{19}NO_3$: C, 79.37; H, 4.87; N, 3.56. Found: C, 79.28; H, 4.69; N, 3.58.

4,5-Diacetoxy-2,9-diphenyl-2,3-dihydro-1*H*-benz[*f*]isoindol-1-one (7a) This was prepared from **3a** (20.0 mg, 54.2 μmol) by method C. Purification by preparative TLC gave pure **7a** (23.6 mg, 97%) as colorless crystals: mp 280—285 °C (dec.) (hexane–CH_2Cl_2). IR ($CHCl_3$) ν: 1775, 1765, 1700 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.47 (s, 3H, $COCH_3$), 2.53 (s, 3H, $COCH_3$), 4.83 (s, 2H, 3-CH_2), 7.15 (t, 1H, J=7.3 Hz, ArH), 7.26 (dd, 1H, J=7.0, 1.2 Hz, ArH), 7.34—7.46 (m, 6H, ArH×6), 7.51—7.57 (m, 4H, ArH×4), 7.71 (dd, 1H, J=8.5, 1.2 Hz, ArH), 7.79 (br d, 1H, J=8.0 Hz, 8-CH). MS m/z: 451 (M^+). *Anal.* Calcd for $C_{28}H_{21}NO_5$: C, 74.49; H, 4.69; N, 3.10. Found: C, 74.28; H, 4.49; N, 3.06.

4,5-Diacetoxy-2-phenyl-2,3-dihydro-1*H*-benz[*f*]isoindol-1-one (7b) This was prepared from **3b** (40.0 mg, 0.136 mmol) by method C. Purification by preparative TLC gave pure **7b** (43.0 mg, 84%) as colorless crystals: mp 241—243 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) ν: 1775, 1700 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.44 (s, 3H, $COCH_3$), 2.49 (s, 3H, $COCH_3$), 4.84 (s, 2H, 3-CH_2), 7.22 (tt, 1H, J=7.3, 1.2 Hz, 4′-CH), 7.27 (dd, 1H, J=8.5, 1.2 Hz, 6-CH), 7.45 (td, 2H, J=7.3, 1.2 Hz, 3′ and 5′-CH), 7.56 (t, 1H, J=8.5 Hz, 7-CH), 7.86 (dd, 2H, J=7.3, 1.2 Hz, 2′ and 6′-CH), 7.98 (dd, 1H, J=8.5, 1.2 Hz, 8-CH), 8.41 (s, 1H, 9-CH). MS m/z: 375 (M^+). *Anal.* Calcd for $C_{22}H_{17}NO_5$: C, 70.39; H, 4.56; N, 3.73. Found: C, 70.58; H, 4.58; N, 3.81.

4,5-Diacetoxy-9-methoxycarbonyl-2-phenyl-2,3-dihydro-1*H*-benz[*f*]-isoindol-1-one (7c) This was prepared from **3c** (20.0 mg, 56.7 μmol) by method C. Purification by preparative TLC gave pure **7c** (16.0 mg, 65%) as colorless crystals: mp 230—232 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) ν: 1770, 1740, 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.44 (s, 3H, $COCH_3$), 2.49 (s, 3H, $COCH_3$), 4.15 (s, 3H, OCH_3), 4.84 (s, 2H, 3-CH_2), 7.22 (tt, 1H, J=7.3, 1.2 Hz, 4′-CH), 7.31 (dd, 1H, J=8.5, 1.2 Hz, 6-CH), 7.43 (td, 2H, J=7.3, 1.2 Hz, 3′ and 5′-CH), 7.62 (t, 1H, J=8.5 Hz, 7-CH), 7.82 (dd, 1H, J=7.3, 1.2 Hz, 2′ and 6′-CH), 7.91 (dd, 1H, J=8.5, 1.2 Hz, 8-CH). MS m/z: 433 (M^+). *Anal.* Calcd for $C_{24}H_{19}NO_7$: C, 66.50; H, 4.41; N, 3.23. Found: C, 66.63; H, 4.36; N, 3.50.

6-Hydroxy-3-oxo-1-trimethylsilyl-1-hexyne (18) A solution of *n*-BuLi (1.6 N in hexane, 6.30 ml, 10.2 mmol) was added dropwise to an anhydrous THF (7 ml) solution of trimethylsilylacetylene (1.44 ml, 10.2 mmol) at −40 °C under nitrogen. The mixture was stirred under the same conditions for 30 min, then added dropwise to an anhydrous THF (13 ml) solution of γ-butyrolactone (0.854 ml, 11.2 mmol) at −40 °C under nitrogen. The reaction mixture was stirred under the same conditions for 1 h and kept at −40 °C. The mixture was introduced into a CH_2Cl_2 (200 ml) solution of acetic acid (0.600 ml, 10.5 mmol) at room temperature, and the whole was washed with brine. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was dried, and concentrated under reduced pressure. Purification of the residue by column chromatography on silica

gel (hexane : AcOEt = 2 : 1) gave **18** (1.69 g, 94%) as a colorless oil: bp 145—165 °C (0.11 mmHg) (dec.). IR ($CHCl_3$) *v*: 2960, 2150, 1670 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.24 (s, 9H, $Si(CH_3)_3$), 1.91 (quint, 2H, J = 6 Hz, CH_2), 2.69 (t, 2H, J = 6 Hz, $COCH_2$), 3.67 (t, 2H, J = 6 Hz, OCH_2). MS *m/z*: 184 (M^+). *Anal.* Calcd for $C_9H_{16}O_2Si$: C, 58.65; H, 8.75. Found: C, 58.91; H, 8.85.

4-Oxo-6-trimethylsilyl-5-hexynyl Methanesulfonate (19) A mixture of **18** (1.46 g, 7.90 mmol), pyridine (0.960 ml, 11.9 mmol), methanesulfonyl chloride (0.735 ml, 9.50 mmol), and CH_2Cl_2 (80 ml) was stirred at room temperature for 14 h. Further methanesulfonyl chloride (0.37 ml, 4.8 μmol) and pyridine (0.48 ml, 5.9 μmol) were added to the mixture, and the whole was stirred at room temperature for 22 h. Then MeOH (1 ml) was added, and the mixture was washed with brine. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was dried, and evaporated under reduced pressure. Purification of the residure by column chromatography on silica gel (hexane : AcOEt = 2 : 1) gave **19** (1.76 g, 85%) as a colorless oil: bp 106 °C (0.19 mmHg) (dec.). IR ($CHCl_3$) *v*: 2150, 1675, 1360, 1175 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.24 (s, 9H, $Si(CH_3)_3$), 2.11 (quint, 2H, J = 6 Hz, CH_2), 2.77 (t, 2H, J = 6 Hz, $COCH_2$), 3.02 (s, 3H, SO_2CH_3), 4.28 (t, 2H, J = 6 Hz, OCH_2). Exact MS Calcd for $C_9H_{15}O_4SSi$ ($M^+ - CH_3$): 247.0458. Found: 247.0438, and Calcd for $C_9H_{15}O_2Si$ ($M^+ - SO_2CH_3$): 183.0838. Found: 183.0818.

4,4-Ethylenedioxy-6-trimethylsilyl-5-hexynyl Methanesulfonate (20) A benzene (30 ml) solution of **19** (500 mg, 1.91 mmol), ethylene glycol (1.06 ml, 19.1 mmol), and a catalytic amount of *p*-TsOH (150 mg, 0.871 mmol) was refluxed for 3 h under azeotropic conditions. The resulting mixture was diluted with AcOEt, washed with saturated aqueous $NaHCO_3$, dried, and concentrated under reduced pressure. Purification by column chromatography on silica gel (hexane : AcOEt = 2 : 1) gave **20** (525 mg, 90%) as a colorless oil: bp 105—115 °C (0.25 mmHg) (dec.). IR ($CHCl_3$) *v*: 2970, 1355, 1170 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.18 (s, 9H, $Si(CH_3)_3$), 1.96—2.11 (m, 4H, $CH_2 \times 2$), 3.00 (s, 3H, SO_2CH_3), 3.91—4.16 (m, 4H, OCH_2CH_2O), 4.20—4.38 (m, 2H, OCH_2). Exact MS Calcd for $C_{12}H_{22}O_5SSi$ (M^+): 306.0956. Found: 306.0931.

3,3-Ethylenedioxy-6-iodo-1-trimethylsilyl-1-hexyne (10) A Mixture of **20** (1.19 g, 3.89 mmol), sodium iodide (1.46 g, 9.72 mmol), and acetone (30 ml) was stirred at room temperature for 4 d. The reaction mixture was diluted with CH_2Cl_2, then washed with aqueous $Na_2S_2O_3$, and brine successively. The organic layer was dried an evaporated under reduced pressure. Purification of the residure by column chromatography on silica gel (hexane : AcOEt = 10 : 1) gave **10** (1.13 g, 82%) as a colorless oil: bp 95—105 °C (0.26 mmHg). IR ($CHCl_3$) *v*: 2970, 2910, 845 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.16 (s, 9H, $Si(CH_3)_3$), 1.94—2.10 (m, 4H, $CH_2 \times 2$), 3.25 (t, 2H, J = 7 Hz, ICH_2), 3.92—4.07 (m, 4H, OCH_2CH_2O). Exact MS Calcd for $C_{11}H_{19}O_2SiI$ (M^+): 338.0199. Found: 338.0204.

2-(2-Methoxyphenyl)-1,3-dithiane (9a) $BF_3 \cdot Et_2O$ (2.44 ml, 20.0 mmol) was added dropwise to a dry CH_2Cl_2 (20 ml) solution of *o*-anisaldehyde (**8a**, 2.41 ml, 20.0 mmol) and propanedithiol (2.00 ml, 19.9 mmol) at 0 °C under nitrogen. The reaction mixture was stirred at room temperature for 20 h, and then poured into aqueous KOH. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried, and evaporated under reduced pressure. Purification of the residure by column chromatography on silica gel (benzene) gave **9a** (4.28 g, 95%) as colorless crystals: mp 127—128.5 °C (benzene). IR ($CHCl_3$) *v*: 2910, 2840, 1590, 1490, 1250 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.79—2.26 (m, 2H, CH_2), 2.71—3.26 (m, 4H, $SCH_2 \times 2$), 3.83 (s, 3H, OCH_3), 5.65 (s, 1H, SCH), 6.75—7.59 (m, 4H, $ArH \times 4$). MS *m/z*: 226 (M^+). *Anal.* Calcd for $C_{11}H_{14}OS_2$: C, 58.37; H, 6.23; S, 28.33. Found: C, 58.39; H, 6.30; S, 28.33.

3,3-Ethylenedioxy-7-(2-methoxyphenyl)-7,7-propylenedithio-1-trimethylsilyl-1-heptyne (12a) *n*-BuLi (1.6 N in hexane, 0.150 ml, 0.243 mmol) was added dropwise to an anhydrous THF (1 ml) solution of **9a** (50.0 mg, 0.221 mmol) at −78 °C under nitrogen, and the mixture was stirred under the same conditions for 30 min. An anhydrous THF (2 ml) solution of **10** (75.0 mg, 0.221 mmol) was added dropwise to the anion solution at the same temperature. The reaction mixture was stirred at −78 °C for 1 h, and then allowed to warm to room temperature for 1 h. Aqueous NH_4Cl was added to the solution, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried, and concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel (hexane : AcOEt = 5 : 1) gave pure **12a** (93.7 mg, 97%) as a colorless oil: IR ($CHCl_3$) *v*: 2960, 2900, 2840, 1595 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.11 (s, 9H, $Si(CH_3)_3$), 1.39—1.41 (m, 2H, CH_2), 1.76—1.80 (m, 2H, CH_2), 1.95—1.97 (m, 2H, CH_2), 2.50—2.53 (m, 2H, SCH_2CH_2), 2.77—2.79 (m, 4H, $SCH_2 \times 2$), 3.85 (s, 3H, OCH_3), 3.87—4.01 (m, 4H, $OCH_2 \times 2$), 6.90—6.95 (m, 2H, $ArH \times 2$), 7.23—7.24 (m, 1H, ArH), 7.87 (dd, 1H, J = 7.3, 1.2 Hz, ArH). Exact MS Calcd for $C_{22}H_{32}O_3S_2Si$ (M^+): 436.1559. Found: 436.1541.

1,5-Dioxo-1-(2-methoxyphenyl)-7-trimethylsilyl-6-heptyne (14a) Phenyliodosyl diacetate [PIDA, $PhI(OCOCH_3)_2$] (1.12 g, 3.47 mmol) was added to a MeOH (10 ml) solution of **12a** (1.01 g, 2.32 mmol), and the mixture was stirred at room temperature for 15 min, then the reaction was quenched with saturated aqueous $NaHCO_3$, and the whole was extracted with CH_2Cl_2. The extract was dried, and concentrated under reduced pressure. A catalytic amount of *p*-TsOH was added to an acetone (10 ml) solution of the residue, and the solution was stirred for 10 min at room temperature. The reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane : AcOEt = 5 : 1) to give **14a** (320 mg, 46%) as a colorless oil: IR ($CHCl_3$) *v*: 3000, 2960, 2145, 1670, 1595 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.23 (s, 9H, $Si(CH_3)_3$), 2.05 (quint, 2H, J = 7.3 Hz, CH_2), 2.67 (t, 2H, J = 7.3 Hz, $COCH_2$), 3.03 (t, 2H, J = 7.1 Hz, $COCH_2$), 3.90 (s, 3H, OCH_3), 6.95 (d, 1H, J = 7.9 Hz, ArH), 7.00 (t, 1H, J = 7.9 Hz, ArH), 7.45 (td, 1H, J = 7.9, 1.8 Hz, ArH), 7.68 (dd, 1H, J = 7.9, 1.8 Hz, ArH). Exact MS Calcd for $C_{17}H_{22}O_3Si$ (M^+): 302.1336. Found: 302.1336.

1,5-Dioxo-1-(2-hydroxyphenyl)-7-trimethylsilyl-6-heptyne (16a) Powdered anhydrous $AlCl_3$ (155 mg, 1.16 mmol) was added to a dry CH_2Cl_2 (10 ml) solution of **14a** (87.8 mg, 0.291 mmol). The mixture was stirred at room temperature for 90 min. The reaction was quenched with aqueous $(CO_2H)_2$, and the whole was extracted with $CHCl_3$. The combined organic layer was washed with brine, dried, and concentrated under reduced pressure. Purification of the residue by preparative TLC (hexane : AcOEt = 5 : 1) gave **16a** (69.8 mg, 83%) as a pale yellow oil. IR ($CHCl_3$) *v*: 2960, 2150, 1670, 1635, 1610 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.24 (s, 9H, $Si(CH_3)_3$), 2.11 (quint, 2H, J = 7.3 Hz, CH_2), 2.73 (t, 2H, J = 7.3 Hz, $COCH_2$), 3.06 (t, 2H, J = 7.3 Hz, $COCH_2$), 6.90 (t, 1H, J = 8.0 Hz, ArH), 6.98 (d, 1H, J = 8.0 Hz, ArH), 7.47 (td, 1H, J = 8.0, 1.2 Hz, ArH), 7.75 (dd, 1H, J = 8.0, 1.2 Hz, ArH), 12.25 (s, 1H, OH). Exact MS Calcd for $C_{16}H_{20}O_3Si$ (M^+): 288.1181. Found: 288.1181.

1-*tert*-Butyldimethylsilyl-3,3-ethylenedioxy-7-(2-methoxyphenyl)-7,7-propylenedithio-1-heptyne (12b) A mixture of **12a** (707 mg, 1.62 mmol) and tetrabutylammonium fluoride (1 M in anhydrous THF, 4.86 ml, 4.86 mmol) was stirred at room temperature overnight. The mixture was diluted with CH_2Cl_2, washed with H_2O and brine, dried, and evaporated under reduced pressure. Purification of the residue by column chromatography on silica gel (hexane : AcOEt = 2 : 1) gave 3,3-ethylenedioxy-7-(2-methoxyphenyl)-7,7-propylenedithio-1-heptyne (500 mg, 85%). *n*-BuLi (1.6 N in hexane, 0.613 ml, 0.992 mmol) was added dropwise to an anhydrous THF (3 ml) solution of the desilylated compound (300 mg, 0.827 mmol) at −78 °C under nitrogen, and the mixture was stirred under the same conditions for 1 h. A THF (3 ml) solution of *tert*-butyldimethylchlorosilane (249 mg, 1.65 mmol) was added to the anion solution at −78 °C. The mixture was stirred under the same condition for 30 min, and then allowed to warm to room temperature for 3 h. The reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried, and concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel (hexane : AcOEt = 10 : 1) gave **12b** (343 mg, 86%) as a colorless oil: IR ($CHCl_3$) *v*: 2960, 2860, 1590 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H, $Si(CH_3)_2$), 0.88 (s, 9H, $SiC(CH_3)_3$), 1.39—1.44 (m, 2H, CH_2), 1.77—1.80 (m, 2H, CH_2), 1.94—1.96 (m, 2H, CH_2), 2.50—2.53 (m, 2H, SCH_2CH_2), 2.76—2.79 (m, 4H, $SCH_2 \times 2$), 3.84 (s, 3H, OCH_3), 3.88—4.01 (m, 4H, $OCH_2 \times 2$), 6.91 (d, 1H, J = 8.0 Hz, ArH), 6.93 (t, 1H, J = 8.0 Hz, ArH), 7.24 (td, 1H, J = 8.0, 1.2 Hz, ArH), 7.86 (dd, 1H, J = 8.0, 1.2 Hz, ArH). Exact MS Calcd for $C_{25}H_{38}O_3S_2Si$ (M^+): 478.2031. Found: 478.2036.

7-*tert*-Butyldimethylsilyl-1,5-dioxo-1-(2-methoxyphenyl)-6-heptyne (14b) This was prepared from **12b** by the same procedure as described for the synthesis of **14a**. The reaction of **12b** (295 mg, 0.617 mmol) and PIDA (298 mg, 0.926 mmol) gave **14b** (68.3 mg, 32%) as a pale yellow oil: IR ($CHCl_3$) *v*: 2930, 2850, 2145, 1665, 1595 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.17 (s, 6H, $Si(CH_3)_2$), 0.96 (s, 9H, $SiC(CH_3)_3$), 2.06 (quint, 2H, J = 7.3 Hz, CH_2), 2.67 (t, 2H, J = 7.3 Hz, $COCH_2$), 3.03 (t, 2H, J = 7.3 Hz, $COCH_2$), 3.89 (s, 3H, OCH_3), 6.95 (d, 1H, J = 8.0 Hz, ArH), 6.99 (t, 1H, J = 8.0 Hz, ArH), 7.45 (td, 1H, J = 8.0, 1.8 Hz, ArH), 7.68 (dd, 1H, J = 8.0, 1.8 Hz, ArH). Exact MS Calcd for $C_{20}H_{28}O_3Si$ (M^+): 344.1805. Found: 344.1787.

7-*tert*-Butyldimethylsilyl-1,5-dioxo-1-(2-hydroxyphenyl)-6-heptyne (16b)

Reaction of **14b** (56.8 mg, 0.165 mmol) with anhydrous $AlCl_3$ (88.0 mg, 0.660 mmol) by the same procedure as described for the synthesis of **16a** gave **16b**. Purification by column chromatography on silica gel (hexane : AcOEt = 8 : 1) gave pure **16b** (46.2 mg, 85%) as a pale yellow oil: IR ($CHCl_3$) ν: 2950, 2930, 2850, 2150, 1670, 1640, 1610 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.18 (s, 6H, $Si(CH_3)_2$), 0.96 (s, 9H, $SiC(CH_3)_3$), 2.11 (quint, 2H, J=7.3 Hz, CH_2), 2.73 (t, 2H, J=7.3 Hz, $COCH_2$), 3.07 (t, 2H, J=7.3 Hz, $COCH_2$), 6.89 (td, 1H, J=8.5, 1.2 Hz, ArH), 6.99 (dd, 1H, J=8.5, 1.2 Hz, ArH), 7.47 (td, 1H, J=8.5, 1.2 Hz, ArH), 7.76 (dd, 1H, J=8.5, 1.2 Hz, ArH), 12.25 (s, 1H, OH). Exact MS Calcd for $C_{19}H_{26}O_3Si$ (M^+): 330.1649. Found: 330.1643.

2-(2,5-Dimethoxyphenyl)-1,3-dithiane (9b) This was prepared from 2,5-dimethoxybenzaldehyde (**8b**) by the same procedure as described for the synthesis of **9a**. Reaction of **8b** (0.913 g, 5.50 mmol) and propanedithiol (0.500 ml, 4.98 mmol) with $BF_3 \cdot Et_2O$ (0.46 ml, 5 mmol) gave **9b** (1.45 g, quant.) as colorless crystals: mp 126—129 °C (hexane–AcOEt). IR ($CHCl_3$) ν: 3010, 2950, 2910, 2850, 1500 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.84—2.37 (m, 2H, CH_2), 2.77—3.33 (m, 4H, $SCH_2 \times 2$), 3.79 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 5.66 (s, 1H, SCH), 6.76—7.25 (m, 3H, ArH × 3). MS m/z: 256 (M^+). *Anal.* Calcd for $C_{12}H_{16}O_2S_2$: C, 56.22; H, 6.29; S, 25.01. Found: C, 55.92; H, 6.32; S, 25.15.

7-(2,5-Dimethoxyphenyl)-3,3-ethylenedioxy-7,7-propylenedithio-1-trimethylsilyl-1-heptyne (12c) Reaction of **9b** (250 mg, 0.977 mmol) and **10** (330 mg, 0.977 mmol) by the same procedure as described for the synthesis of **12a** gave **12c**. Purification by column chromatography on silica gel (hexane : AcOEt = 10 : 1) gave pure **12c** (412 mg, 90%) as a colorless oil: IR ($CHCl_3$) ν: 2970, 2910, 2840, 1610, 1580 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.10 (s, 9H, $Si(CH_3)_3$), 1.29—2.89 (m, 12H, $CH_2 \times 3$ and $CH_2 \times 3$). 3.82 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.81—4.13 (m, 4H, OCH_2CH_2O), 6.68—6.93 (m, 2H, 3′ and 4′-CH), 7.53 (d, 1H, J=2 Hz, 6′-CH). Exact MS Calcd for $C_{23}H_{34}O_4S_2Si$ (M^+): 466.1665. Found: 466.1660.

1-(2,5-Dimethoxyphenyl)-1,5-dioxo-7-trimethylsilyl-6-heptyne (14c) Reaction of **12c** (2.20 g, 4.72 mmol) with PIDA (2.28 g, 7.09 mmol) by the same procedure as described for the synthesis of **14a** gave **14c**. Purification by column chromatography on silica gel (hexane : AcOEt = 5 : 1) gave pure **14c** (862 mg, 49%) as a colorless oil: IR ($CHCl_3$) ν: 3010, 2970, 2840, 2160, 1670 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.16 (s, 9H, $Si(CH_3)_3$), 1.98 (quint, 2H, J=7.1 Hz, CH_2), 2.61 (t, 2H, J=7.1 Hz, $COCH_2$), 2.97 (t, 2H, J=7.1 Hz, $COCH_2$), 3.72 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 6.76—7.19 (m, 3H, ArH × 3). Exact MS Calcd for $C_{18}H_{24}O_4Si$ (M^+): 332.1444. Found: 332.1445.

1,5-Dioxo-1-(2-hydroxy-5-methoxyphenyl)-7-trimethylsilyl-6-heptyne (16c) Reaction of **14c** (140 mg, 0.422 mmol) and anhydrous $AlCl_3$ (224 mg, 1.68 mmol), by the same proceudre as described for the synthesis of **16a**, gave **16c**. Purification by column chromatography on silica gel (hexane : AcOEt = 5 : 1) gave pure **16c** (66.0 mg, 49%) as pale yellow crystals: mp 50.5—52 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) ν: 2960, 2150, 1670, 1645 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.25 (s, 9H, $Si(CH_3)_3$), 2.09 (quint, 2H, J=7.0 Hz, CH_2), 2.74 (t, 2H, J=7.0 Hz, $COCH_2$), 3.03 (t, 2H, J=7.0 Hz, $COCH_2$), 3.81 (s, 3H, OCH_3), 6.86—7.26 (m, 3H, ArH × 3), 11.90 (s, 1H, OH). Exact MS Calcd for $C_{17}H_{22}O_4Si$ (M^+): 318.1285. Found: 318.1268.

2-(2,5-Dimethoxyphenyl)-2-(6-trimethylsilyl-5-hexynyl)-1,3-dithiane (13a) This was prepared from **9b** (2.00 g, 7.81 mmol) and 6-iodo-1-trimethylsilyl-1-hexyne[24] (**11**, 2.54 g, 8.59 mmol) by the same procedure as described for the synthesis of **12a**. Purification by column chromatography on silica gel (hexane : AcOEt = 10 : 1) gave pure **13a** (2.87 g, 90%) as a pale yellow oil: IR ($CHCl_3$) ν: 3000, 2950, 2900, 2820, 2160 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.08 (s, 9H, $Si(CH_3)_3$), 1.19—2.83 (m, 14H, $CH_2 \times 3$ and $CH_2 \times 4$), 3.78 (s, 6H, $OCH_3 \times 2$), 6.72—7.45 (m, 3H, ArH × 3). Exact MS Calcd for $C_{21}H_{32}O_2S_2Si$ (M^+): 408.1613. Found: 408.1613.

Methyl 8-(2,5-Dimethoxyphenyl)-8,8-propylenedithio-2-octynoate (13b) A mixture of **13a** (1.18 g, 2.89 mmol) and tetrabutylammonium fluoride (1 M in anhydrous THF, 14.5 ml, 14.5 mmol) was stirred at room temperature for 3 d. The mixture was diluted with CH_2Cl_2, washed with H_2O and brine, dried, and evaporated under reduced pressure. Purification of the residue by column chromatography on silica gel (AcOEt) gave 2-(2,5-dimethoxyphenyl)-2-(5-hexynyl)-1,3-dithiane (950 mg, 98%) as a colorless oil. IR ($CHCl_3$) ν: 3310, 3000, 2950, 2830, 2120 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.73—2.84 (m, 15H, $CH_2 \times 3$, $CH_2 \times 4$, and C≡CH), 3.79 (s, 6H, $OCH_3 \times 2$), 6.76—7.51 (m, 3H, ArH × 3). MS m/z: 336 (M^+). *Anal.* Calcd for $C_{18}H_{24}O_2S_2$: C, 64.25; H, 7.19; S, 19.05. Found: C, 64.10; H, 7.35; S, 18.89. *n*-BuLi (1.6 N in hexane, 1.90 ml, 2.46 mmol) was added dropwise to a THF (10 ml) solution of 2-(2,5-dimethoxyphenyl)-2-(5-hexynyl)-1,3-dithiane (750 mg, 2.23 mmol) at −78 °C under nitrogen, and the mixture was stirred under the same conditions for 30 min. Methyl chloroformate (0.517 ml, 6.70 mmol) was added to the anion solution at −78 °C. The mixture was stirred under the same conditions for 10 min, and then allowed to warm to room temperature for 20 min. The reaction mixture was quenched with saturated aqueous NH_4Cl and the mixture was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried, and concentrated under reduced pressure. Purification by column chromatography on silica gel (hexane : AcOEt = 10 : 1) gave **13b** (790 mg, 90%) as a colorless oil. IR ($CHCl_3$) ν: 3000, 2950, 2830, 2230, 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.79—2.83 (m, 14H, $CH_2 \times 3$ and $CH_2 \times 4$), 3.70 (s, 3H, OCH_3), 3.88 (s, 6H, $OCH_3 \times 2$), 6.74—7.45 (m, 3H, ArH × 3). MS m/z: 394 (M^+). *Anal.* Calcd for $C_{20}H_{26}O_4S_2$: C, 60.89; H, 6.64; S, 16.25. Found: C, 60.74; H, 6.71; S, 16.04.

Methyl 8-(2,5-Dimethoxyphenyl)-8-oxo-2-octynoate (15) This was prepared from **13b** (20.0 mg, 50.8 μmol) by the same procedure as described for the synthesis of **14a**. Purification of the residue by column chromatography on silica gel (hexane : AcOEt = 4 : 1) gave **15** (8.40 mg, 54%) as colorless crystals: mp 62—62.5 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) ν: 3010, 2960, 2840, 2240, 1710, 1670 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.62—1.85 (m, 4H, $CH_2 \times 2$), 2.36 (t, 2H, J=7 Hz, C≡CCH_2), 2.98 (t, 2H, J=7 Hz, $COCH_2$), 3.73 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 6.81—7.25 (m, 3H, ArH × 3). MS m/z: 304 (M^+). *Anal.* Calcd for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 66.95; H, 6.63.

Methyl 8-(2-Hydroxy-5-methoxyphenyl)-8-oxo-2-octynoate (17) This was prepared from **15** (235 mg, 0.774 mmol) by the same procedure as described for the synthesis of **16a**. Purification of the residue by preparative TLC (hexane : AcOEt = 10 : 1) gave **17** (203 mg, 91%) as pale yellow crystals: mp 47.5—48 °C (hexane). IR ($CHCl_3$) ν: 3020, 2960, 2240, 1705, 1645, 1620 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.70 (quint, 2H, J=7.3 Hz, CH_2), 1.89 (quint, 2H, J=7.3 Hz, CH_2), 2.42 (t, 2H, J=7.3 Hz, C≡CCH_2), 3.02 (t, 2H, J=7.3 Hz, $COCH_2$), 3.75 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 6.93 (d, 1H, J=9 Hz, 3-CH), 7.11 (dd, 1H, J=9, 3 Hz, 4-CH), 7.18 (d, 1H, J=3 Hz, 6-CH), 11.9 (s, 1H, OH). MS m/z: 290 (M^+). *Anal.* Calcd for $C_{16}H_{18}O_5$: C, 66.20; H, 6.25. Found: C, 66.21; H, 6.29.

4,5-Diacetoxy-2,3-dihydro-1*H*-benz[*f*]indene-1-one (21a) This was prepared from **16a** (26.2 mg, 91.0 μmol) by method C. Purification by preparative TLC (hexane : AcOEt = 1 : 1) gave **21a** (17.9 mg, 66%) as colorless crystals: mp 177.5—179.5 °C (hexane–benzene). IR ($CHCl_3$) ν: 3020, 1760, 1715 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.43 (s, 3H, $COCH_3$), 2.46 (s, 3H, $COCH_3$), 2.79 (t, 2H, J=6.4 Hz, 2-CH_2 or 3-CH_2), 3.11 (t, 2H, J=6.4 Hz, 2-CH_2 or 3-CH_2), 7.25—7.28 (m, 1H, 6-CH or 8-CH), 7.51 (t, 1H, J=8.5 Hz, 7-CH), 7.95 (d, 1H, J=8.5 Hz, 6-CH or 8-CH), 8.27 (s, 1H, 9-CH). Exact MS Calcd for $C_{17}H_{14}O_5$ (M^+): 298.0842. Found: 298.0844.

4,5-Diacetoxy-7-methoxy-2,3-dihydro-1*H*-benz[*f*]indene-1-one (21b) This was prepared from **16c** (20.3 mg, 63.0 μmol) by method C. Purification by preparative TLC (hexane : AcOEt = 1 : 1) gave **21b** (12.8 mg, 61%) as colorless crystals: mp 158—160.5 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) ν: 3030, 1770, 1760, 1715 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.40 (s, 3H, $COCH_3$), 2.45 (s, 3H, $COCH_3$), 2.78 (t, 2H, J=6.8 Hz, 2-CH_2 or 3-CH_2), 3.09 (t, 2H, J=6.8 Hz, 2-CH_2 or 3-CH_2), 4.01 (s, 3H, OCH_3), 6.78 (d, 1H, J=8.5 Hz, 6-CH or 7-CH), 7.15 (d, 1H, J=8.5 Hz, 6-CH or 7-CH), 8.75 (s, 1H, 9-CH). Exact MS Calcd for $C_{18}H_{16}O_6$ (M^+): 328.0944. Found: 328.0929.

8,9-Diacetoxy-5-methoxy-4-methoxycarbonyl-2,3-dihydro-1*H*-benz[*f*]-indene (22) This was prepared from **17** (25.4 mg, 87.6 μmol) by method C. Purification by preparative TLC (hexane : AcOEt = 3 : 1) gave **22** (20.2 mg, 62%) as colorless crystals: mp 167—169 °C (hexane–benzene). IR ($CHCl_3$) ν: 3010, 2840, 1775, 1765, 1730 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.14 (quint, 2H, J=7.3 Hz, 2-CH_2), 2.36 (s, 3H, $COCH_3$), 2.37 (s, 3H, $COCH_3$), 2.88 (t, 2H, J=7.3 Hz, 1-CH_2 or 3-CH_2), 2.99—3.08 (m, 2H, 1-CH_2 or 3-CH_2), 3.92 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 6.78 (d, 1H, J=8.2 Hz, 6-CH or 7-CH), 6.99 (d, 1H, J=8.2 Hz, 6-CH or 7-CH). Exact MS Calcd for $C_{20}H_{20}O_7$ (M^+): 372.1209. Found: 372.1215.

Ethyl 1-Acetylcyclopentane-1-carboxylate (25) A mixture of ethyl acetoacetate (21.3 g, 0.164 mol), 1,4-dibromobutane (29.5 g, 0.137 mol), K_2CO_3 (113 g, 0.819 mol), and acetone (530 ml) was stirred at room temperature for 24 h. After removal of the solvent, the reaction mixture was diluted with AcOEt, washed with H_2O, dried, and concentrated under reduced pressure. The residue was purified by distillation under reduced pressure to give **25** (9.25 g, 37%) as a colorless oil: bp 116—120 °C (30 mmHg) (lit.[22] 120—128 °C (30 mmHg)). IR ($CHCl_3$) ν: 2970, 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.26 (t, 3H, J=7 Hz, CH_2CH_3), 1.53—1.76 (m, 4H, $CH_2 \times 2$), 1.99—2.22 (m, 4H, $CH_2 \times 2$), 2.13 (s, 3H, $COCH_3$), 4.20 (q, 2H, J=7 Hz, CH_2CH_3).

Ethyl 1-(1,1-Ethylenedioxyethyl)cyclopentane-1-carboxylate (26) Compound **25** (6.20 g, 33.7 mmol) was reacted with ethylene glycol (18.8 ml, 0.337 mol) under the same conditions as described for the synthesis of **20** to give **26** (7.00 g, 91%) as a colorless oil: bp 101 °C (0.31 mmHg). IR ($CHCl_3$) *v*: 3000, 2970, 2890, 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.24 (t, 3H, J=7 Hz, $CH_2\underline{CH_3}$), 1.33 (s, 3H, CH_3), 1.45—2.29 (m, 8H, $CH_2 \times 4$), 3.94 (s, 4H, $OCH_2 \times 2$), 4.15 (q, 2H, J=7 Hz, $\underline{CH_2}CH_3$). MS *m/z*: 213 ($M^+ - CH_3$). *Anal.* Calcd for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83. Found: C, 62.95; H, 9.03.

3,3-Ethylenedioxy-2,2-tetramethylene-1-butanol (27) An ether (1 ml) solution of **26** (38.6 mg, 0.169 mmol) was added dropwise to a suspension of $LiAlH_4$ (14.1 mg, 0.372 mmol) in ether (2 ml) at 0 °C, and the mixture was stirred for 15 min at the same temperature. The reaction was quenched with 5% HCl at 0 °C and the mixture was washed with H_2O. The aqueous layer was extracted with ether. The combined organic layer was washed with brine, dried, and concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel (hexane : AcOEt = 3 : 1) gave **27** (31.0 mg, 98%) as a colorless oil: bp 95 °C (0.25 mmHg). IR ($CHCl_3$) *v*: 3530, 2975, 2890 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.31 (s, 3H, CH_3), 1.44—2.04 (m, 8H, $CH_2 \times 4$), 2.87—3.11 (br s, 1H, OH), 3.49 (s, 2H, OCH_2), 3.98 (s, 4H, $OCH_2 \times 2$). MS *m/z*: 171 ($M^+ - CH_3$). *Anal.* Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.28; H, 9.93.

4-Hydroxy-3,3-tetramethylene-6-trimethylsilyl-5-hexyn-2-one (28) A dry CH_2Cl_2 (10 ml) solution of **27** (2.96 g, 15.9 mmol) was added dropwise to a mixture of $(COCl)_2$ (5.56 ml, 63.7 mmol), dimethyl sulfoxide (DMSO) (6.77 ml, 95.4 mmol), and dry CH_2Cl_2 (150 ml) at −78 °C, and the mixture was stirred at the same temperature for 30 min. Then Et_3N (15.5 ml, 0.111 mol) was added at −78 °C and the whole was stirred for 15 min. The reaction was quenched with H_2O, and the mixture was extracted with $CHCl_3$. The extract was washed with 3% HCl, saturated aqueous $NaHCO_3$, and brine, dried, and concentrated under reduced pressure to give the aldehyde (3.34 g). A THF (50 ml) solution of lithium trimethylsilylacetylide, which was prepared from trimethylsilyl acetylene (5.13 ml, 36.3 mmol) and *n*-BuLi (1.6 N in hexane, 22.4 ml, 36.3 mmol) was added dropwise to a THF (50 ml) solution of the above aldehyde at −45 °C and the mixture was stirred at the same temperature for 20 min and at room temperature for 20 min. The reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with CH_2Cl_2. The organic layer was washed with brine, dried, and concentrated under reduced pressure. A mixture of the residue, *p*-TsOH (200 mg, 1.16 mmol), and acetone (60 ml) was stirred at room temperature for 17 h. The reaction was quenched with saturated aqueous NH_4Cl, and the mixure was extracted with CH_2Cl_2. The extract was washed with brine, dried, and concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel (hexane : AcOEt = 4 : 1) gave **28** (3.21 g, 85% from **27**) as colorless crystals. mp 49—50 °C (hexane). IR ($CHCl_3$) *v*: 2960, 2175, 1685 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.15 (s, 9H, $Si(CH_3)_3$), 1.56—2.11 (m, 8H, $CH_2 \times 4$), 2.21 (s, 3H, $COCH_3$), 3.03 (d, 1H, J=7 Hz, OH), 4.54 (d, 1H, J=7 Hz, OCH). MS *m/z*: 238 (M^+). *Anal.* Calcd for $C_{13}H_{22}O_2Si$: C, 65.50; H, 9.30. Found: C, 65.44; H, 9.46.

4,4-Tetramethylene-1-(2,4,5-trimethoxyphenyl)-7-trimethylsilyl-6-heptyn-1,3,5-trione (29) A solution of **28** (1.01 g, 4.24 mmol) in anhydrous THF (8 ml) and hexamethylphosphoric triamide (HMPA, 1.61 ml, 9.24 mmol) were added dropwise at −78 °C to a solution of LDA in anhydrous THF (9 ml), obtained from dry diisopropylamine (1.29 ml, 9.24 mmol) and *n*-BuLi (1.6 N in hexane, 5.72 ml, 9.24 mmol). The mixture was stirred at the same temperature for 45 min. Then a solution of 2,4,5-trimethoxybenzoyl chloride (1.16 g, 5.04 mmol) in anhydrous THF (16 ml) was added dropwise at −78 °C and the whole was stirred at the same temperature for 35 min and at room temperature for 35 min. The reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with CH_2Cl_2. The organic layer was washed with brine, dried, and concentrated under reduced pressure to give a mixture of the *C*-acylated and the *O*-acylated products. A mixture of the crude acylated product (398 mg), DMSO (0.261 ml, 3.68 mmol), DCC (380 mg, 1.84 mmol), pyridinium trifluoroacetate (88.8 mg, 0.460 mmol), and dry benzene (7 ml) was stirred at room temperature for 5 h. The reaction was quenched with water, and the mixture was extracted with ether. The extract was washed with saturated aqueous $NaHCO_3$ and brine, dried, and concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel (hexane : AcOEt = 2 : 1) gave **29** (227 mg, 31% from **28**) as yellow crystals: mp 93—95 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) *v*: 2970, 2150, 1665, 1605, 1570 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.19 (s, 9H, $Si(CH_3)_3$), 1.64—1.71 (m, 4H, $CH_2 \times 2$), 2.18—2.22 (m, 2H, CH_2), 2.33—2.38 (m, 2H, CH_2), 3.888 (s, 3H, OCH_3), 3.893 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 6.50 (s, 1H, vinyl-H), 6.58 (s, 1H, ArH), 7.50 (s, 1H, ArH). MS *m/z*: 430 (M^+). *Anal.* Calcd for $C_{23}H_{30}O_6Si$: C, 64.16; H, 7.02. Found: C, 64.14; H, 7.06.

4,4-Tetramethylene-1-(4,5-dimethoxy-2-hydroxyphenyl)-7-trimethylsilyl-6-heptyn-1,3,5-trione (30) This was prepared from **29** (48.3 mg, 0.112 mmol) by the same procedure as described for the synthesis of **16a**. Purification by preparative TLC (hexane : AcOEt = 2 : 1) gave **30** (19.1 mg, 41%) as a yellow oil. IR ($CHCl_3$) *v*: 2950, 2150, 1660, 1610 cm^{-1}. ^{1}H-NMR (C_6D_6) δ: 0.03 (s, 2/3 × 9H, $Si(CH_3)_3 \times 2/3$), 0.05 (s, 1/3 × 9H, $Si(CH_3)_3 \times 1/3$), 2.08—2.57 (m, 8H, $CH_2 \times 4$), 3.13 (s, 3H, OCH_3), 3.36 (s, 2/3 × 3H, $OCH_3 \times 2/3$), 3.59 (s, 1/3 × 3H, $OCH_3 \times 1/3$), 3.84 (s, 1/3 × 2H, $COCH_2CO \times 1/3$), 6.24 (s, 2/3 × 1H, vinyl-H × 2/3), 6.32 (s, 1/3 × 1H, ArH × 1/3), 6.37 (s, 2/3 × 1H, ArH × 2/3), 6.99 (s, 2/3 × 1H, ArH × 2/3), 7.09 (s, 1/3 × 1H, ArH × 1/3), 12.6 (s, 2/3 × 1H, OH × 2/3), 13.1 (s, 1/3 × 1H, OH × 1/3). Exact MS Calcd for $C_{22}H_{28}O_6Si$ (M^+): 416.1652. Found: 416.1652.

4,5-Diacetoxy-7,8-dimethoxy-2,2-tetramethylene-benz[*f*]indane-1,3-dione (31) This was prepared from **30** (19.1 mg, 45.9 μmol) by method C. Purification by preparative TLC (hexane : AcOEt = 2 : 1) gave **31** (15.1 mg, 77%) as pale yellow crystals: mp 144—146 °C (hexane–CH_2Cl_2). IR ($CHCl_3$) *v*: 3020, 2980, 1770, 1735, 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.96—1.97 (m, 8H, $CH_2 \times 4$), 2.44 (s, 3H, $COCH_3$), 2.54 (s, 3H, $COCH_3$), 4.02 (s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 7.15 (s, 1H, ArH), 8.68 (s, 1H, ArH). MS *m/z*: 426 (M^+). *Anal.* Calcd for $C_{23}H_{22}O_8$: C, 64.78; H, 5.20. Found: C, 64.77; H, 5.05.

4-Hydroxy-7-methoxy-2,2-tetramethylene-benz[*f*]indane-1,3,5,8-tetrone (32) A mixture of **31** (24.6 mg, 57.7 μmol) and 80% aqueous trifluoroacetic acid (10 ml) was refluxed for 3 h. The reaction mixture was concentrated under reduced pressure. The residue was dissolved in 33% aqueous CH_3CN. To this solution, phenyliodosyl bistrifluoroacetate (PIFA) (245 mg, 0.570 mmol) was added at room temperature and the mixture was stirred at the same temperature overnight, then concentrated under reduced pressure. Purification by preparative TLC (CH_2Cl_2 : MeOH = 30 : 1) gave **32** (18.4 mg, 98%) as pale yellow crystals: mp 220—230 °C (dec.) (hexane–CH_2Cl_2). IR ($CHCl_3$) *v*: 2940, 1710, 1690, 1630, 1605 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.97 (m, 8H, $CH_2 \times 4$), 3.99 (s, 3H, OCH_3), 6.25 (s, 1H, vinyl-H), 8.17 (s, 1H, ArH), 13.28 (s, 1H, OH). Exact MS Calcd for $C_{18}H_{14}O_6$ (M^+): 326.0791. Found: 326.0801.

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