Synthesis of Khellin and Its Analogues via Chromium Carbene Complexes

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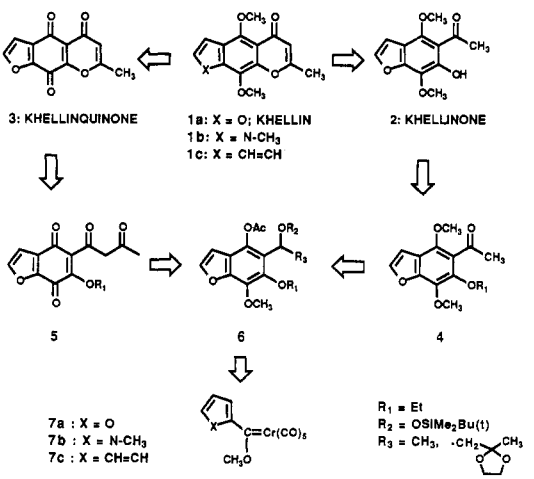
The synthesis of khellin, a lipid-altering and antiatherosclerotic furochromone, has been accomplished by two different routes in six and seven steps, respectively. The key steps in two alternative approaches are the cycloaddition reactions of a furan–methoxy chromium carbene complex **7a** with two types of alkoxyalkynes **10a** and **10b** to provide the direct construction of the benzofuran acetates **6a** and **6b**, which bear the functional groups necessary for formation of the γ-pyrone ring. The reactions of **7a** with alkoxyalkynes in the presence of acetic anhydride and triethylamine in THF provided the acetate derivatives of the desired benzofurans in fair to good yields. The alkoxyalkyne **10a** introduces the acetyl group precursor and **10b** bears the masked β-diketone unit. The benzofuran acetate **6a** leads to khellinone in four steps by direct conversion of the acetate to a methyl ether, the conversion of the silyloxy to the ketone, and the selective cleavage of the ethyl ether. The other benzofuran acetate **6b**, leads to khellinquinone in five steps by the direct conversion of the acetate to the methyl ether, the conversion of the silyloxy ether to a ketone, oxidation of the *p*-dimethoxybenzene ring, and sequential aqueous acid-catalyzed pyrone ring formation. Khellinone and khellinquinone are converted to khellin independently by the known procedures. These two synthetic routes are applied to the syntheses of khellin analogues, such as the pyrrole and phenyl analogues of khellin **1b** and **1c**, using the reactions of the corresponding pyrrolyl or phenyl chromium carbene complexes **7b**, **7c** with **10a** and **10b**.

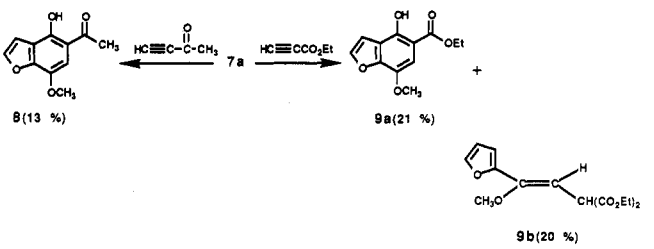
Khellin (**1a**)[1] is one member of a group of the furochromones isolated from Ammi-Visnaga, a perennial herbaceous plant which grows wild in many Mediterranean countries.[2] Along with analogues, such as ammiol and visnagan, khellin was found to possess desirable lipid-altering activity,[3] for example, decreasing the atherogenic VLDL + LDL cholesterol fraction, and elevating the antiatherogenic HDL cholesterol fraction in animal models as well as in humans.[4] These activities prompted us to consider new approaches to furochromone synthesis. Previous strategies for the synthesis of natural furochromone have a common feature of construction the furan ring onto a carefully constructed substituted benzene ring. The problem encountered in the previous syntheses was the need to differentiate the four oxygen substituents on the benzene ring, which required many additional steps. In this paper, we describe two new approaches to furochromones. They provide a formal total synthesis of **1a** and a general methodology for the synthesis of furochromone analogues required for structure–activity evaluation in the atherosclerosis area.

Our strategy (Scheme I) involves the cycloaddition reaction of a furan chromium carbene complex (**7a**)[5] with an alkoxyalkyne for direct construction of highly substituted benzofuran derivatives **6**, which bear the functional groups necessary for formation of the γ-pyrone ring. Since khellinone (**2**) and khellinquinone (**3**) have previously been converted to **1a**,[1c,i,2] our strategy also relies on (i) selective cleavage of the protecting group (R = Et) from the intermediate **4** and (ii) acid–catalyzed pyrone ring formation from the β-diketone **5**. The key step for our two synthetic approaches is the cycloaddition reaction of **7a** with an appropriate alkoxyalkyne to form the intermediate **6**. One strength of this synthetic strategy is the flexibility and the practicality for analogue formation. The furan ring in **1a** can be replaced by a pyrrole or a phenyl ring for formation of A-ring modified khellin analogues (**1b** and **1c**) by reactions of a pyrrole or a phenyl carbene complex **7b** and

Scheme I



Scheme II



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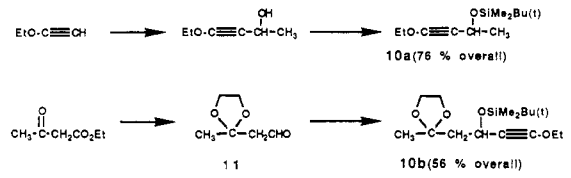
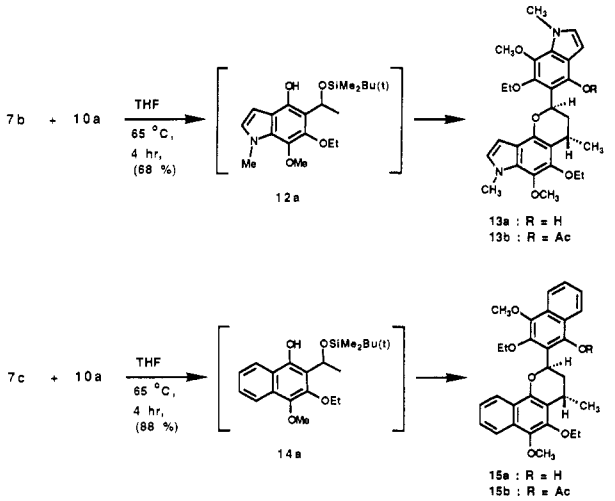
Scheme III



Scheme IV



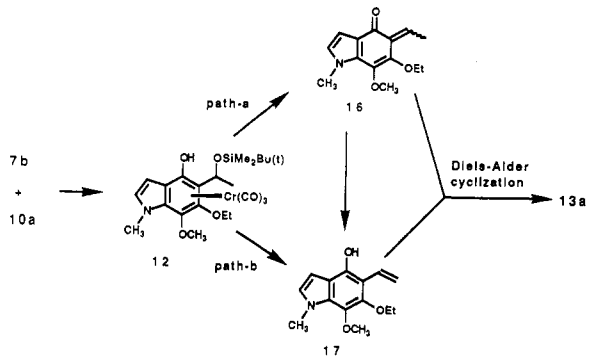
7c with the same alkoxyalkynes.

Results and Discussion

The carbene complexes **7a–c** were prepared according to the procedure of Fisher,[6] from the reaction of aryllithium and chromium hexacarbonyl, followed by methylation with trimethyloxonium tetrafluoroborate. Our preliminary work has shown that preparation of the benzofuran ketone directly by the reaction of **7a** with alkynes, such as acetylacetylene and ethyl propiolate, resulted in poor yields of cycloadducts **8** (13%)[7] and **9a** (21%),[8] respectively (Scheme II). For this reason, longer but higher yielding routes were developed, in which the complexes were reacted with precursors to **4** and **5** where the ketone was protected as a silylated alcohol **10a** and the β-diketone was protected as a silyl alcohol and a ketal **10b**. Regioselectivity of the reaction of **7** with **10** could be controlled by introducing a bulky protecting group, such as *tert*-butyldimethylsilyl group, for the alcohol at the α-position of the alkyne.[9] The alkyne **10a** was prepared as shown in Scheme III from ethoxyacetylene by lithiation and quenching with acetaldehyde to give an alcohol, which was protected with a silyl group. On the other hand, ethyl acetoacetate was converted to the aldehyde **11** in three steps, by protection of the ketone, reduction of the ester, and oxidation of the alcohol. Then, lithioethoxyacetylide was reacted with **11**, producing an alcohol, which was protected with a silyl group to give **10b**.

The reaction of **10a** with **7b** in THF at 65 °C under argon was complete in 4 h (Scheme IV), providing a single product **13a** as an oil in 68% yield.[10] Physical properties of **13a** suggest that the structure of the product is the

Scheme V



dimer of the expected indole **12a**. Acetylation of the product led to a crystalline monoacetate **13b**, which was subjected to X-ray crystallographic analysis to reveal the structure as **13b**,[11] where the two indole skeletons are linked together through a pyrone ring. Furthermore, the two ethoxy groups are adjacent to the two methoxy groups. A parallel process was observed with the reaction of **7c** with **10a**. Under identical reaction conditions, the dimeric structure **15a** of the expected naphthol **14a** was isolated as an oil in 88% yield. This is the first example of an electron-rich alkoxyalkyne participating in the carbene cycloaddition process. However, **7a** was unreactive with **10a** under the identical conditions, resulting in recovery of **7a**.

A plausible pathway for formation of the dimer is shown for **7b** in Scheme V. The well-established cycloaddition pathway[12] produces the indolohydroquinone **12a**, perhaps partly or largely present with chromium tricarbonyl coordinated to the arene ring. Elimination of the side-chain oxygen unit is assisted by the phenyl group, to give the transient *o*-quinonemethide **16** (path a). Isomerization by a proton shift would provide the styryl derivative **17**. Alternatively, direct elimination of a trialkylsilanol could provide **17** (path b). Then, Diels–Alder cycloaddition between **16** and **17** would lead to the observed dimer product **13a**. The elimination process to give **16** is unexpectedly facile but has close parallels in a proposed general mechanism of action of quinone antibiotics (bioreductive alkylation).[13] The structure of the intermediate **12a** requires that the carbene carbon attach to the ethoxy-bearing carbon of the alkyne with high regioselectivity. This is consistant with earlier observations with unsymmetrical alkynes and can be rationalized in terms of a dominating steric effect.[9]

Dimer formation was suppressed by using the method of in situ protection.[14] With this method, **7a** was activated and reacted with **10a** and **10b**, producing the desired benzofuran derivatives. The results from cyclization are shown in Table I. The reaction of **7a** with **10a** (1.5 molar equiv) was carried out in the presence of 2.0 molar equiv each of acetic anhydride and triethyl amine in THF at 65

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(11) **13b**: $C_{30}H_{36}N_4O_7 \cdot (CH_2Cl_2)$, M_r = 536.1·84.93, triclinic, *P*1, a = 10.313 (2) Å, b = 12.146 (2) Å, c = 13.302 (3) Å, α = 83.26 (2)°, β = 109.88 (2)°, γ = 97.42 (1)°, V = 1549.0 (13) Å^3, Z = 2, D_m = 1.21, D_c = 1.39 g/cm^3, Cu Kα, λ = 1.5418, μ(Cu Kα) = 2.2 cm^{-1}, T = 123 K, R = 0.094 for 5123 unique reflections. Fractional coordinates and an isotropic temperature factors have been deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK.
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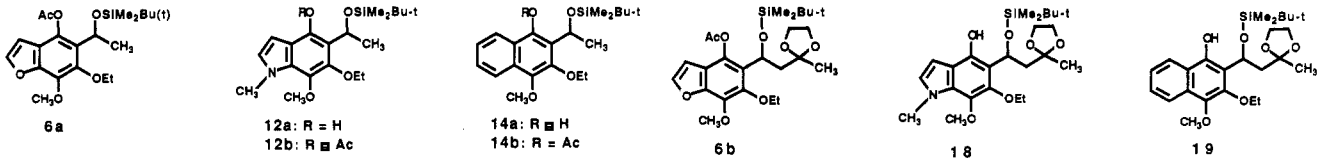
Table I



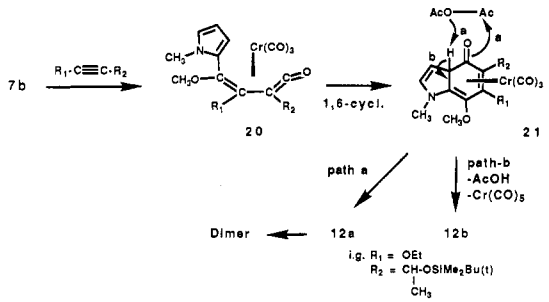
entry	complex	alkyne[a]	Ac_2O, molar equiv	Et_3N, molar equiv	time, h	products,[b] %
1	**7a**	**10a**	2.0	2.0	10	**6a** (43)
2	**7a**	**10a**	2.0	0.0	72	**6a** (36)
3	**7a**	**10b**	2.0	2.0	72	**6b** (28)
4	**7b**	**10a**	1.1	0.0	5	**12a** (26) + **12b** (41)
5	**7b**	**10a**	1.1	1.1	10	**12a** (0) + **12b** (46)
6	**7b**	**10a**	0.0	1.0	4	**13a** (13)
7	**7b**	**10b**	1.1	1.1	8	**18** (38)
8	**7c**	**10a**	1.1	0.0	4	**14a** (52) + **14b** (12)
9	**7c**	**10a**	1.1	1.1	3	**14a** (0) + **14b** (54)
10	**7c**	**10a**	0.0	1.0	4	**15a** (29)
11	**7c**	**10b**	1.1	1.1	5	**19** (45)
12	**7b**	**10a**	AcOH[c]	0.0	6	**12a** (19)
13	**7c**	**10a**	AcOH[c]	0.0	6	**14a** (50)

[a] 1.5 molar equiv of the alkyne was used. [b] Isolated yield after flash column chromatography. [c] 1.0 molar equiv of AcOH was used.

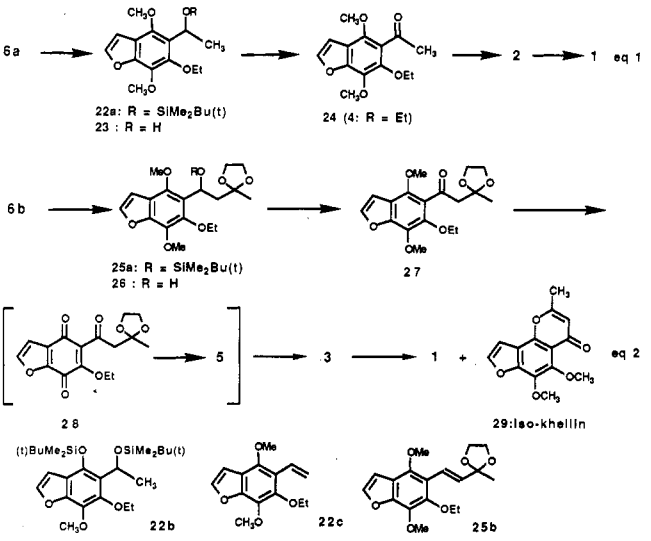
°C under argon. After 10 h under these conditions, the benzofuran acetate **6a** was isolated as a single product in 43% yield (entry 1). Without NEt_3 (entry 2), the reaction took 72 h for completion to give **6a** in 36% yield. The reaction of **7a** with **10b** in the presence of Ac_2O and NEt_3 required at least 72 h for completion, producing the benzofuran acetate **6b** in 28% yield (entry 3). The regiochemistry of the products was determined based on the result from X-ray analysis of **13b**. The parallel process was applied to **7b** and **7c**. Heating a THF solution of **7b**, **10a** and Ac_2O at 65 °C for 6 h produced the free indole **12a** and the indole acetate **12b** in 26% and 41% yield, respectively (entry 4). The same reaction which was carried out with NEt_3 (entry 5) produced only **12b** in 46% yield. On the other hand, the reaction of **7b** and **10b** in the presence of Ac_2O and NEt_3 was complete in 10 h, giving the indole **18** as a single product in 38% yield (entry 7). Similar results were obtained from the reactions of **7c** with **10a** and **10b**. The complex **7c** was heated at 65 °C in THF with **10a** and Ac_2O for 4 h to produce the free naphthol **14a** and the naphthol acetate **14b** in 52% and 12% yield, respectively (entry 8). The same reaction with NEt_3 produced only **14b** in 54% yield (entry 9). The reaction of **7c** with **10b** in the presence of Ac_2O and NEt_3 formed only the free naphthol **19** in 45% yield (entry 11). No dimer formation was detected in these reactions. Increased amounts of Ac_2O and NEt_3 for these reactions did not change the yields and the ratio of the phenol and the acetate. It is presumed that, in the reaction of **10b** with **7b** or **7c**, acetylation was inhibited by the steric hindrance of the bulky substituent and the relatively short reaction time. The reaction of **7b** with **10a** and NEt_3 (entry 6) produced only the dimer **13a** in 13% yield, while the reaction of **7c** with **10a** and NEt_3 (entry 10) also resulted in formation of the dimer **15a** (29%). The presence of acetic acid also suppressed dimer formation (entry 12, 13), producing the phenol. The indoles **12a**, **12b**, and **18** and the naphthols **14a**, **14b**, and **19** served as the key intermediates for the synthesis of **1b** and **1c** (Scheme VIII and IX).

A plausible pathway for the in-situ protection is outlined for **7b** in Scheme VI. The 1,6-cycloaddition from the vinyl ketene intermediate **20** generates the cyclohexadienone chromium **21**, which aromatizes to **12a** by a proton shift (path a). In the presence of acetic anhydride, this could be rapidly acetylated during aromatization, proceeding by path b. Thus, path a could be blocked. Triethylamine

Scheme VI



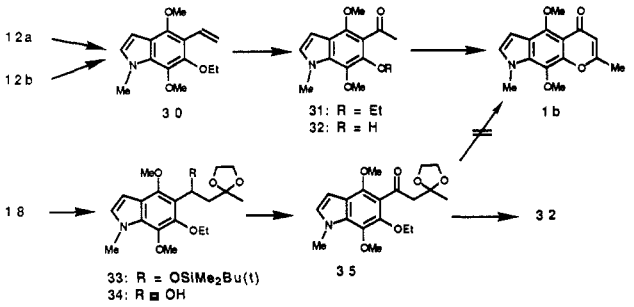
Scheme VII



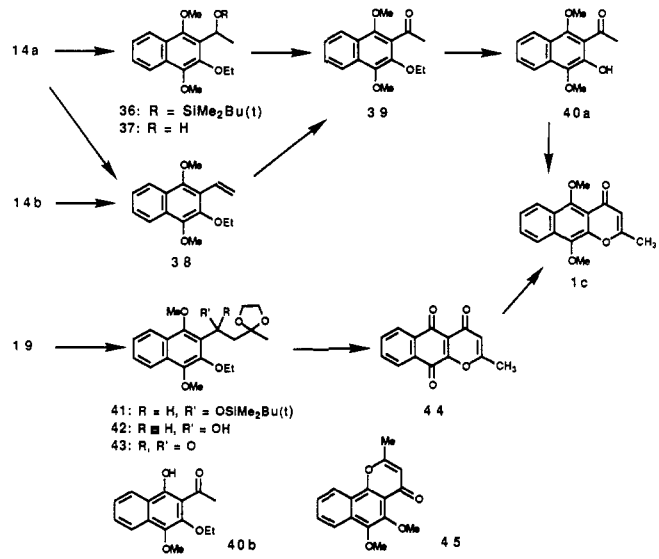
works as an acid scavenger for the generated acetic acid; otherwise, the acid generated during the process could cleave the acetate to form the free phenol. Since **7a** was inert to cycloaddition with **10a**, **10b**, it is apparent that the role of Ac_2O and NEt_3 in this reaction is more than solely as in situ acetylation reagents. Presumably, they act either as a Lewis acid or by reducing the electron density of the carbene carbon by acetylation of a metal ligand.

For the intermediate **6a**, the route to **1a** requires the conversion of the acetate to the methyl ether, the selective cleavage of the ethyl ether, and acid-catalyzed pyrone ring formation. The first of these objectives was carried out

Scheme VIII



Scheme IX



without isolation of the intermediate free phenol, which was labile and readily lost trialkylsilanol providing an olefin (Scheme VII, eq 1). Thus, treatment of **6a** with 2.2 molar equiv of sodium hydride and 10 molar equiv of methyl iodide in THF and HMPA directly produced the methyl ether **22a** in 54% yield along with the disilyl ether **22b** and the olefin **22c** in 6% and 19% yields, respectively. The same reaction, which was carried out without HMPA, provided **22a** in 79% yield and recoved **6a** (12%). The reaction presumably proceeds by initial formation of ketene from the acetate by base and then methylation of the sodium phenoxide with methyl iodide. The alcohol **23** was freed from its silyl ether with tetra-*n*-butylammonium fluoride in DMF at 25 °C[15] and was oxidized by pyridinium dichromate in dry CH_2Cl_2[16] to produce the ketone **24**. Selective cleavage of the ethyl ether was effected with 10 molar equiv of BF_3·Et_2O in dry CH_2Cl_2,[17] providing **2** in 97% yield. No demethylated product was detected. According to the procedure of Spath,[1c,2] **2** was converted to **1** (83%) through a Claisen type condensation and subsequent acid-catalyzed pyrone ring formation.

Khellin was also generated by an alternate route from **6b** (Scheme VII, eq 2). As described above, direct conversion of the acetate to the methyl ether with sodium hydride and methyl iodide in THF provided **25a** and the olefin **25b** in 68% and 23% yield, respectively. Cleavage of the silyl protecting group from **25a** with tetra-*n*-butylammonium fluoride in DMF at 55 °C produced an alcohol **26** in 89% yield. Oxidation of the alcohol **26** with pyridinium dichromate in dry CH_2Cl_2 gave a 35% yield of the ketone **27** along with the recovery of **26** (30%). Attempts to cleave the ethyl ether of **27** under the conditions described above were unsuccessful, resulting in the recovery of **27**. Oxidation of the *p*-dimethoxybenzene ring of **27** with ceric ammonium nitrate (3 molar equiv) in a mixture of acetonitrile and water (3:1 mixture) at 0 °C[18] led to the quinone **28**, which decomposed under purification conditions, and was directly treated with aqueous acid. Treatment with 1 N HCl in MeOH at 25 °C cleaved the ketal to generate the β-diketone **5**, which, under aqueous acid conditions, spontaneously cyclized to form the pyrone ring, providing **3** in 70% yield. Reduction of the quinone **3** with $NaHSO_3$ in the presence of catalytic amounts of concentrated HCl at 100 °C, followed by methylation,[2] generated **1a** (50%) and iso-khellin (**29**, 10%).[19] These two synthetic pathways to **1a** were applied to formation of the khellin analogues **1b** and **1c**.

A pyrrole analogue of khellin **1b** was generated from the indoles **12a**, **12b**, and **20a** as shown in Scheme VIII. Methylation of **12a** with NaH and MeI in THF (with or without HMPA) at 0 °C resulted in elimination of trialkylsilanol, giving the olfein **30** as a single product in 77% yield. Attempts to convert the acetate **12b** directly to the methyl ether under the conditions described earlier also caused elimination of the side-chain oxygen unit, forming **30** in 65% yield. The Wacker procedure (treatment with oxygen gas in the presence of palladium chloride and cuprous chloride in DMF–H_2O for 15 h)[20] converted the olefin to the ketone **31** in 77% yield. Selective cleavage of the ethyl ether with excess BF_3·Et_2O provided the phenol **32** in 86% yield. As described for conversion of **2** to **1a**, a Claisen type condensation of **32** with EtOAc, followed by acid-catalyzed pyrone ring formation, gave **1b** in 80% yield. The other indole intermediate **18** was methylated to give **33**, which was deprotected to free the alcohol **34**. Oxidation of the alcohol with $Pd(PPh_3)_4$ in the presence of NaH, phenyl bromide, and 18-crown-6 in DMF at 75 °C[21] provided the ketone **35** (48%) and the recovery of **34** (51%). The attempt to form the corresponding quinone by oxidation of the *p*-dimethoxybenzene ring of **35** was troublesome, resulting in decomposition of the material. Treatment of **35** with excess BF_3·Et_2O, for selective cleavage of the ethyl ether, generated **32** in 48% yield. The reaction presumably proceeded with cleavage of the ketal to form the β-diketone, which underwent the retro Aldol reaction generating **31**, followed by cleavage of the ethyl ether.

Benzochromone **1c**[22] was generated from the naphthols **14a**, **14b**, and **19** in processes parallel to that described for **1a** (Scheme IX). Treatment of **14a** with NaH (2 molar equiv) and MeI (4 molar equiv) in THF and HMPA at 0 °C produced the methyl ether **36** in 90% yield. The same reaction without HMPA resulted in elimination of trialkylsilanol, giving the olefin **38** as a single product in 99% yield. The olefin **38** was also generated from **14b** by treatment with NaH and MeI in THF (83%). Cleavage

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of the silyl protecting group of **36** with *n*-Bu_4NF in DMF at 55 °C, followed by oxidation of the alcohol **37** with PDC in CH_2Cl_2, provided the ketone **39** in 35% overall yield (with recovery of **37**, 30%). Treatment of **39** with excess BF_3·Et_2O in CH_2Cl_2 afforded the deethylated **40a** (83%) as well as the demethylated product **40b** (10%). A Claisen type condensation of **40a**, followed by acid-catalyzed pyrone ring formation, provided the desired **1c** in 84% yield. From the intermediate **19**, **1c** was also generated using the khellinquinone route. Methylation of **19** to **41**, removal of the silyl group to give **42**, and oxidation of the alcohol provided the ketone **43** in 35% overall yield. Treatment of **43** with excess BF_3·Et_2O in dry CH_2Cl_2, in an attempt to cleave the ethyl ether selectively, resulted in formation of **40a** and **40b** in 31% and 6% yield, respectively, along with the recovery of **43** (29%). Oxidation of **43** with ceric ammonium nitrate (3 molar equiv) in acetonitrile and water at 0 °C, followed by acid treatment, produced the quinone **44** (89%), which was reduced and methylated. Benzochromone **1c** and the isomer **45**[19b] were obtained in 71% and 28% yields, respectively.

In summary, we have described two very facile syntheses of khellin in overall yields of 13% and 5% resulting from only six and seven steps, respectively. Two synthetic pathways were successfully applied for formation of khellin analogues. These results exploited the utility of the cycloaddition reaction of aryl chromium carbene complexes with alkynes in natural product synthesis.

Experimental Section

General Procedure. All melting points are uncorrected. ^1H NMR spectra were recorded at 80 or 300 MHz. Chemical shifts are reported as values in parts per million relative to tetramethylsilane (δ 0.00) as an internal standard. All chromatographic isolations were accomplished by medium-pressure liquid chromatography using a flash column packed with silica gel-60 (230–400 mesh ASTM). Analytical thin-layer chromatography (TLC) was conducted on 20 × 20 cm precoated glass plates (silica gel 60 F-254, 0.25 mm layer thickness). Preparative TLC was conducted on 20 × 20 cm precoated glass plates with 2 or 1.5 mm layer thickness (silica gel GR).

Materials. Dry solvents were freshly distilled from an appropriate drying agent and stored under an argon atmosphere. Tetrahydrofuran (THF) was predried over molecular sieves (4 Å) and distilled over sodium metal benzophenone ketyl immediately prior to use at atmospheric pressure under argon. All other solvents and reactants were ACS reagent grade unless described otherwise. "Ether" refers to anhydrous diethyl ether. *n*-Butyllithium was purchased as a 1.6 M solution in *n*-hexane. Phenyllithium was purchased as a 2.0 M solution in benzene/ether (3:1). Trimethyloxonium tetrafluoroborate (BF_3·Et_2O) was purchased and was used without further purification, or synthesized by literature procedure. Pentacarbonyl(2-furylmethoxycarbene)chromium(0) (**7a**) and pentacarbonyl(phenylmethoxycarbene)chromium(0) (**7c**) were synthesized by literature procedures.[6]

Preparation of Pentacarbonyl[(*N*-methyl-2-pyrrolyl)methoxycarbene]chromium(0) (7b). In a 500-mL three-necked round-bottomed flask, evacuated and filled with argon three times, were placed *N*-methylpyrrole (9 mL, 0.1 mol) and THF (100 mL) via syringe, the flask was cooled at −78 °C (dry ice–acetone bath), *n*-butyllithium (62 mL, 0.1 mol, 1.6 M in *n*-hexane solution) was introduced slowly via syringe over a period of 20 min, and the resulting solution was stirred at −20 °C for 15 h under argon. In a 1000-mL three-necked round-bottomed flask, evacuated and filled with argon three times, were placed chromium hexacarbonyl (22 g, 0.1 mol) and anhydrous ether (150 mL), and, to this cooled (wet ice bath) suspension, the yellow solution of lithiopyrrole was introduced using a liquid transferring cannula. During this procedure most of the $Cr(CO)_6$ was dissolved, and the solution turned deep red. The solvent was removed by rotary evaporation (bath temperature was kept under 45 °C), the black residue was dissolved in 200 mL of H_2O, and Me_3O·BF_4 (15 g, 0.101 mol) was added portionwise to the aqueous solution. The aqueous layer was extracted with ether (3 × 300 mL), dried (Na_2SO_4), filtered, and concentrated to give a dark red oil. Purification by flash column chromatography (elution by ether/*n*-hexane, 1/1) gave **7b** as orange yellow needles (19.6 g, 62%): MS 315 (M^+), 287 (M^+ − CO), 259 (M^+ − 2CO), 231 (M^+ − 3CO), 203 (M^+ − 4CO), 175 (M^+ − 5CO), 160, 145, 132, 52 (Cr); IR (Nujol) 2053, 1984, 1400, 1343, 1323; ^1H NMR ($CDCl_3$) δ 7.73 (1 H, d, d, J = 1.5, 2.4 Hz, C_5-H in pyrrole), 6.79 (1 H, d, d, J = 1.5, Hz, C_3-H in pyrrole), 6.28 (1 H, d, d, J = 1.0, 2.4, Hz, C_4-H in pyrrole), 4.71 (3 H, s, OCH_3), 3.73 (3 H, s, N-CH_3). Anal. Calcd for $C_{12}H_9NO_6Cr$: C, 45.75; H, 2.88; N, 4.44. Found: C, 45.82; H, 3.02; N, 4.38.

Preparation of 3-[(*tert*-Butyldimethylsilyl)oxy]-1-ethoxy-1-butyne (10a). (a) 1-Ethoxy-3-hydroxy-1-butyne. To a cooled (−78 °C, dry ice–actone bath) solution of the lithio ethoxyacetylide (0.16 mol), prepared from ethoxyacetylene (15 mL, 0.16 mol) and *n*-BuLi (108 mL, 0.16 mol); 1.6 mmol/mL *n*-hexane solution) in THF (400 mL), was slowly added acetaldehyde (15 mL, 0.27 mol) via syringe. The mixture was warmed to 0 °C, stirred at this temperature for 1 h, poured into a mixture of ice–H_2O. The organic layer was separated, and the aqueous layer was extracted with ether. The extracts were combined, washed (brine), dried (Na_2SO_4), filtered, and concentrated. Purification by short path distillation at bp 48–50 °C (0.2 mmHg) gave the acetylene as a colorless oil (17 g, 95%): ^1H NMR ($CDCl_3$) δ 4.55 (1 H, q, J = 6.5 Hz, $CH_3CH(OH)CC$), 4.09 (2 H, q, J = 7.1 Hz, $CCOCH_2CH_3$), 1.86 (1 H, br s, OH), 1.41 (3 H, d, J = 6.5 Hz, $CH_3CH(OH)CC$), 1.36 (3 H, t, J = 7.1 Hz, $CCOCH_2CH_3$).

(b) Compound 10a. The alcohol (11.8 g, 0.104 mol) was protected by treatment with *tert*-butyldimethylsilyl chloride (18.7 g, 0.12 mol) in the presence of imidazole (17.6 g, 0.26 mol) in DMF (90 mL) at 25 °C for 24 h. Purification by distillation at bp 48–52 °C (0.1 mmHg) gave **10a** as a colorless oil (18.7 g, 79%): MS 228 (M^+), 114; IR (neat) 2983, 2958, 2931, 2858, 2266, 1474, 1464, 1256, 1251, 1091, 1045 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.56 (1 H, q, J = 6.5 Hz, $CH_3CH(OP)CC$), 4.06 (2 H, q, J = 7.0 Hz, $CCOCH_2CH_3$), 1.37 (3 H, d, J = 6.4 Hz, $CH_3CH(OP)C$), 1.35 (3 H, t, J = 7.0 Hz, $COCH_2CH_3$), 0.90 (9 H, s, *t-Bu*Si), 0.11 (6 H, br s, CH_3SiCH_3). Anal. Calcd for $C_{12}H_{24}O_2Si$: C, 63.10; H, 10.59. Found: C, 62.77; H, 10.54.

Preparation of 3-[(*tert*-Butyldimethylsilyl)oxy]-1-ethoxy-5,5-(ethylenedioxy)-1-butyne (10b). (a) Ethyl 3,3-(Ethylenedioxy)butyrate. To a cooled (wet ice bath) solution of ethyl acetoacetate (50 g, 0.384 mol) and dry ethylene glycol (95.5 g, 1.54 mol) in dry CH_2Cl_2 (700 mL) was added BF_3·Et_2O (50 mL) under argon over a period of 30 min, and the resulting solution was stirred at 25 °C for 48 h. The reaction mixture was diluted with CH_2Cl_2 (500 mL), washed with H_2O (3 × 300 mL), dried (Na_2SO_4), filtered, and concentrated. The product was purified by distillation at bp 55–58 °C (0.05 mmHg) to give the ketal (65 g, 96%): ^1H NMR ($CDCl_3$) δ 4.15 (2 H, q, J = 7.1 Hz, $CO_2CH_2CH_3$), 3.98 (4 H, s, OCH_2CH_2O), 2.66 (2 H, s, RCH_2CO_2Et), 1.43 (3 H, s, terminal CH_3), 1.26 (3 H, t, J = 7.1 Hz, $CO_2CH_2CH_3$).

(b) 3,3-(Ethylenedioxy)butanol. The ketal-ester (37.8 g, 0.217 mol) was reduced by treatment with LAH (8.35 g) in THF (600 mL) under argon at 0 °C. Purification by distillation at bp 34–38 °C (0.2 mmHg) gave the alcohol as a colorless oil (28 g, 97%): ^1H NMR ($CDCl_3$) δ 3.99 (4 H, s, OCH_2CH_2O), 3.91–3.66 (2 H, m, RCH_2CH_2OH), 2.77 (1 H, t, J = 5.6 Hz, OH), 1.94 (2 H, t, J = 5.7 Hz, RCH_2CH_2OH), 1.36 (3 H, s, terminal CH_3).

(c) 3,3-(Ethylenedioxy)butanal (11). Oxidation of the alcohol (6.2 g, 47 mmol) with PDC (15.2 g, 70 mmol) in dry CH_2Cl_2 gave the aldehyde as a colorless oil (bp 80–85 °C (13 mmHg), 4.31 g, 70%): ^1H NMR ($CDCl_3$) δ 8.32 (1 H, t, J = 2.8 Hz, $RCHO$), 4.00 (4 H, s, OCH_2CH_2O), 2.75–2.65 (2 H, m, RCH_2CHO), 1.43 (3 H, s, terminal CH_3).

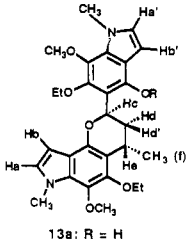
(d) 1-Ethoxy-5,5-(ethylenedioxy)-3-hydroxy-1-hexyne. To a cooled (−78 °C, dry ice–actone bath) solution of the lithio ethoxyacetylide (50 mmol), prepared from ethoxyacetylene and *n*-BuLi (mL, 50 mmol); 1.6 mmol/mL hexane solution) in THF (100 mL), was slowly added 3,3-(ethylenedioxy)butanal (5.3 g, 50 mmol) via syringe. The mixture was warmed to 0 °C, stirred at this temperature for 1 h, and poured into a mixture of ice–H_2O. The organic layer was separated, and the aqueous layer was extracted with ether. The extracts were combined, washed (brine), dried (Na_2SO_4), filtered, and concentrated. Purification by short

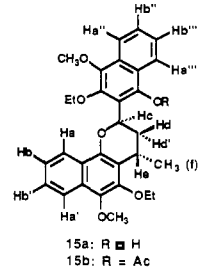
path distillation at bp 150 °C (0.01 mmHg) gave the acetylene as a yellow oil (6.65 g, 66%): ^{1}H NMR ($CDCl_3$) δ 4.75–4.55 (1 H, m, $CH_2CH(OH)C$), 4.09 (2 H, q, J = 7.1 Hz, $COCH_2CH_3$), 3.99 (4 H, s, OCH_2CH_2O), 3.75 (1 H, s, OH), 2.20–1.80 (2 H, m, $CH_2CH(OH)C$), 1.38 (3 H, t, $COCH_2CH_3$), 1.36 (3 H, s, terminal CH_3).

(e) Compound 10b. The alcohol (14.3 g, 71.42 mmol) was protected by treatment with *tert*-butyldimethylsilyl chloride (12.93 g, 85.78 mmol) in the presence of imidazole (12.61 g, 185.2 mmol) in DMF (80 mL) at 25 °C for 24 h. Purification by flash column chromatography (silica gel, 250 g; *n*-hexane) gave **10b** as a yellow oil (bp 150 °C (0.01 mmHg), 17.82 g, 79%): MS 314 (M^+), 257, 87; IR (neat) 2958, 2931, 2858, 2266, 1472, 1380, 1255, 1146, 1108, 1056, 1009 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.60 (1 H, t, J = 6.2 Hz, $CH_2CH(OSiR_3)$), 4.06 (2 H, q, J = 7.1 Hz, $CCOCH_2CH_3$), 3.92 (4 H, s, OCH_2CH_2O), 2.03 (2 H, d, J = 6.2 Hz, $CH_2CH(OSiR_3)$), 1.41 (3 H, s, terminal CH_3), 1.35 (3 H, t, $COCH_2CH_3$), 0.90 (9 H, s, *t*-*Bu*Si), 0.14, 0.12 (2 × 3 H, 2 s, CH_3SiCH_3). Anal. Calcd for $C_{16}H_{30}O_4Si$: C, 61.11; H, 9.62. Found: C, 61.35; H, 9.56.

Reaction of 7b with 10a. Preparation of the Dimer (13a) and the Acetate (13b). A solution of **7b** (3.0 g, 9.5 mmol) and **10a** (3.5 g, 15.2 mmol) in 350 mL of THF was heated at 65 °C (bath temperature) for 5 h under argon. The mixture was cooled, and the solvent was removed by rotary evaporation. The black residue was chromatographed using a flash column (silica gel, 300 g). Elution by 30% ether in *n*-hexane provided **13a** as a brown oil (1.53 g, 68%): MS (FAB) 494 (M^+), 248, 247, 218; IR (neat) 3406, 1634, 1493, 1462, 1321, 1060 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.02 (1 H, s, ArO*H*), 6.85–6.75 (2 H, m, J_{ab} = 3.1 Hz, 2 Ha, Ha'), 6.53–6.45 (2 H, dd, J_{ab} = 3.1 Hz, Hb, Hb'), 5.75 (1 H, dd, J_{cd} = 11.3 Hz, $J_{cd'}$ = 1.9 Hz, Hc), 4.25–4.00 (4 H, m, 2 $ArOCH_2CH_3$), 3.96, 3.93, 3.91, 3.77 (4 × 3 H, 4 s, 2 of $ArOCH_3$, 2 of N-CH_3), 3.40–3.00 (1 H, m, He), 2.4–2.1 (1 H, m, $J_{bb'}$ = 13.0 Hz, J_{cd} = 12.0 Hz, J_{de} = 6.0 Hz, Hd), 2.05–1.75 (1 H, m, $J_{cd'}$ = 2.0 Hz, $J_{de} \approx 0$ Hz, Hd'), 1.50 (3 H, d, J = 6.8 Hz, CH_3-f), 1.40 (6 H, t, J = 7.0 Hz, 2 of $ArOCH_2CH_3$).

Compound **13a** was acetylated by treatment with Ac_2O in dry pyridine at 25 °C. Purification by flash column chromatography (silica gel, elution by 30% ether in *n*-hexane) gave **13b** as colorless crystals: mp 119–120 °C; high resolution MS mol wt 536.2523, Calcd 536.2522; IR (Nujol) 1766, 1624, 1490, 1464 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.86 (1 H, d, J_{ab} = 3.1 Hz, Ha), 6.71 (1 H, $J_{a'b'}$ = 3.1 Hz, Ha'), 6.41 (1 H, d, Hb), 6.22 (1 H, d, Hb'), 5.70 (1 H, dd, J_{cd} = 12.0 Hz, $J_{cd'}$ = 2.0 Hz, Hc), 4.25–4.00 (4 H, m, 2 of $ArOCH_2CH_3$), 3.97, 3.95, 3.93, 3.77 (4 × 3 H, 4 s, 2 of $ArOCH_3$, 2 of N-CH_3), 3.30–3.20 (1 H, m, He), 2.74–2.6 (1 H, m, $J_{dd'}$ = 13.3 Hz, J_{de} = 5.4 Hz, Hd), 2.01 (3 H, s, $ArOCOCH_3$), 1.83–1.75 (1 H, dd, $J_{d'e}$ = 1.0 Hz, Hd'), 1.47 (3 H, d, J = 7.0 Hz, CH_3-f), 1.42 (3 H, t, J = 6.9 Hz, $ArOCH_2CH_3$), 1.35 (3 H, t, J = 7.0 Hz, $ArOCH_2CH_3$). Anal. Calcd for $C_{30}H_{36}N_2O_7$: C, 67.14; H, 6.76; N, 5.22. Found: C, 66.90; H, 6.69; N, 5.11.





Reaction of Pentacarbonyl[phenylmethoxycarbene]-chromium(0) (7c) with 10a. Preparation of the Dimer (15a) and the Acetate (15b). A solution of **7c** (3.0 g, 9.5 mmol) and **10a** (3.5 g, 15.2 mmol) in THF (350 mL) was heated at 65 °C (bath temperature) for 4 h under argon. The mixture was cooled, and the solvent was removed by rotary evaporation. The black residue was chromatographed using a flash column (silica gel, 300 g). Elution by 5% ether in *n*-hexane provided **15a** as a yellow oil (2.1 g, 88%): MS 488 (M^+), 345, 244, 229, 216, 201; IR (neat) 3411, 1631, 1596, 1454 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.35 (1 H, s, ArO*H*), 8.30–7.95 (4 H, m, Ha, Ha', Ha'', Ha'''), 7.60–7.31 (4 H, m, Hb, Hb', Hb'', Hb'''), 5.93 (1 H, dd, J_{cd} = 11.8 Hz, $J_{cd'}$ = 2.0 Hz, Hc), 4.50–4.10 (4 H, m, 2 of $ArOCH_2CH_3$), 3.95 (2 × 3 H, 2 s, 2 of $ArOCH_3$), 3.50–3.10 (1 H, m, He), 2.75–1.90 (2 H, m, Hd, Hd'), 1.56 (3 H, d, J = 6.6 Hz, CH_3-f), 1.47 (3 H, t, J = 7.0 Hz, $ArOCH_2CH_3$), 1.44 (3 H, t, J = 7.1 Hz, $ArOCH_2CH_3$).

Compound **15a** was acetylated by treatment with Ac_2O in dry pyridine at 25 °C. Purification by flash column chromatography (silica gel, elution by 5% ether in *n*-hexane) gave **15b** as a yellow oil: high-resolution MS mol wt 530.2300, calcd 530.2304; IR (neat) 1770, 1626, 1596, 1455, 1373, 1196, 1059 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.25–7.90 (4 H, m, Ha, Ha', Ha'', Ha'''), 7.76–7.20 (4 H, m, Hb, Hb', Hb'', Hb'''), 5.82 (1 H, d, J_{cd} = 11.8 Hz, $J_{cd'}$ = 2.0 Hz, Hc), 4.45–4.10 (4 H, 2 overlapped q, $ArOCH_2CH_3$), 4.02, 3.94 (2 × 3 H, 2 s, 2 of $ArOCH_3$), 3.00–2.60 (1 H, m, He), 2.50–2.00 (2 H, m, Hd, Hd'), 2.03 (3 H, s, $ArOCOCH_3$), 1.51 (3 H, d, J = 6.1 Hz, CH_3-f), 1.47 (3 H, t, J = 6.9 Hz, $ArOCH_2CH_3$), 1.34 (3 H, t, J = 7.0 Hz, $ArOCH_2CH_3$). Anal. Calcd for $C_{32}H_{34}O_7$: C, 72.43; H, 6.46. Found: C, 72.52; H, 6.53.

Reaction of 7a with 10a in the Presence of Ac_2O and NEt_3 in THF. Preparation of 4-Acetoxy-5-[1-[(*tert*-butyldimethylsilyl)oxy]ethyl]-6-ethoxy-7-methoxybenzofuran (6a). A solution of **7a** (1.5 g, 5.0 mmol), **10a** (3.0 g, 15 mmol), Ac_2O (1.0 mL, 10 mmol), and NEt_3 (1.4 mL, 10 mmol) in THF (150 mL) was heated at 65 °C under argon for 10 h. The mixture was cooled, and the solvent was removed by rotary evaporation to give a black oil. Purification by flash column chromatography (silica gel, 250 g; 20% ether in *n*-hexane) gave **6a** as a brown oil (893 mg, 43%): high-resolution MS mol wt 408.1977, calcd 408.1968; IR (neat) 1770, 1627, 1480, 1204 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.51 (1 H, d, J = 2.3 Hz, C_2-H), 6.53 (1 H, d, J = 2.3 Hz, C_3-H), 5.36 (1 H, q, J = 6.6 Hz, $ArCH(OP)CH_3$), 4.15–3.95 (2 H, q, J = 7.1 Hz, $ArOCH_2CH_3$), 4.11 (3 H, s, $ArOCH_3$), 2.33 (3 H, s, $ArOCOCH_3$), 1.56 (3 H, d, J = 6.6 Hz, $ArCHCH_3$), 1.41 (3 H, t, J = 7.1 Hz, $ArOCH_2CH_3$), 0.87 (9 H, s, *t*-*Bu*Si), 0.04, 0.03 (2 × 3 H, 2 s, CH_3SiCH_3). Anal. Calcd for $C_{21}H_{32}O_6Si$: C, 61.73; H, 7.90. Found: C, 61.51; H, 8.04.

Reaction of 7a with 10b in the Presence of Ac_2O and NEt_3 in THF. Preparation of 4-Acetoxy-5-[1-[(*tert*-butyldimethylsilyl)oxy]-3,3-(ethylenedioxy)butyl]-6-ethoxy-7-methoxybenzofuran (6b). A solution of **7a** (3.0 g, 9.9 mmol), **10b** (3.0 g, 10 mmol), Ac_2O (1.9 mL, 20 mmol), and NEt_3 (2.8 mL, 20 mmol) in THF (280 mL) was heated at 65 °C under argon for 72 h. The mixture was cooled, and the solvent was removed by rotary evaporation to give a black oil. Purification by flash column chromatography (silica gel, 300 g; 20% ether in *n*-hexane) afforded **6b** as a brown oil (1.4 g, 28%): MS 494 (M^+), 393, 351, 293, 115, 87; IR (neat) 1769, 1478, 1264, 1053 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.51 (1 H, d, J = 3.2 Hz, C_2-H), 6.52 (1 H, d, J = 3.2 Hz, C_3-H), 5.65–5.40 (1 H, m, $ArCH(OP)CH_3$), 4.25–3.95 (2 H, q, J = 7.0 Hz, $ArOCH_2CH_3$), 4.09 (4 H, s, OCH_2CH_2O), 3.88 (3 H, s, $ArOCH_3$), 2.32 (3 H, s, $ArOCOCH_3$), 1.55–1.20 (8 H, m, $ArCH(OP)CH_2$, $ArOCH_2CH_3$, terminal-CH_3), 0.92 (9 H, s, *t*-*Bu*Si), 0.14 (6 H, s, CH_3SiCH_3). Anal. Calcd for $C_{25}H_{38}O_8Si$: C, 60.70; H, 7.74. Found: C, 60.45; H, 7.71.

Reaction of 7b with 10a. Preparation of 5-[1-[(*tert*-Butyldimethylsilyl)oxy]ethyl]-6-ethoxy-4-hydroxy-7-methoxyindole (12a) and the Acetate (12b). (a) In the Presence of Ac_2O in THF. A solution of **7b** (1.0 g, 3.2 mmol), **10a** (1.5 g, 4.8 mmol), and Ac_2O (0.3 mL, 3.2 mmol) in THF (150 mL) was heated at 65 °C under argon for 5 h. The mixture was cooled, and the solvent was removed by rotary evaporation to give a black oil. Purification by flash column chromatography (silica gel, 250 g; 30% ether in *n*-hexane) gave **12a** as a brown oil (309 mg, 26%) and **12b** as a brown oil (553 mg, 41%). **12a**: MS 379 (M^+), 363, 247, 218; IR (neat) 3334, 1637, 1494, 1324, 1288, 1056 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.86 (1 H, s, ArO*H*), 6.78 (1 H, d, J = 3.1 Hz, C_2-H), 6.49 (1 H, d, J = 3.1 Hz, C_3-H), 5.45 (1 H, q, J = 6.3 Hz, $ArCH(OP)CH_3$), 4.09 (2 H, q, J = 7.0 Hz, $ArOCH_2CH_3$), 3.93 (3 H, s, $ArOCH_3$), 3.85 (3 H, s, NCH_3), 1.51 (3 H, d, J = 6.3 Hz, $ArCH(OP)CH_3$), 1.41 (3 H, t, J = 7.0 Hz, $ArOCH_2CH_3$), 0.92 (9 H, s, *t*-*Bu*Si), 0.16, –0.07 (2 × 3 H, 2 s, CH_3SiCH_3). Anal. Calcd for $C_{20}H_{33}NO_4Si$: C, 63.28; H, 8.76; N, 3.69. Found: C, 63.25; H, 8.81; N, 3.52. **12b**: high-resolution MS mol wt 421.2280, calcd 421.2284; IR (neat) 1767, 1627, 1205, 1058 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.84 (1 H, d, J = 3.1 Hz, C_2-H), 6.17 (1 H, d, J = 3.1 Hz, C_3-H), 5.36 (1 H, q, J = 6.5 Hz, $ArCH(OP)CH_3$), 4.10 (2 H, q, J = 7.1 Hz, $ArOCH_2CH_3$), 3.93 (3 H, s, $ArOCH_3$), 2.33 (3 H, s, $ArOCOCH_3$), 3.85 (3 H, s, NCH_3), 1.57 (3 H, d, J = 6.5 Hz, $ArCHCH_3$), 1.42

(3 H, t, J = 7.1 Hz, $ArOCH_2CH_3$), 0.87 (9 H, s, *t*-BuSi), 0.04, −0.06 (2 × 3 H, 2 s, CH_3SiCH_3). Anal. Calcd for $C_{22}H_{35}NO_5Si$: C, 62.67; H, 8.37; N, 3.32. Found: C, 62.56; H, 8.47; N, 3.17.

(b) In the Presence of Ac_2O and NEt_3 in THF. A solution of **7b** (10 g, 31.7 mmol), **10a** (15 g, 48 mmol), Ac_2O (3.0 mL, 32 mmol), and NEt_3 (4.5 mL, 32 mmol) in THF (800 mL) was heated at 65 °C under argon for 10 h. The mixture was cooled, and the solvent was removed by rotary evaporation to give a black oil. Purification by flash column chromatography (silica gel, 450 g; 20% ether in *n*-hexane) afforded 6.1 g (46%) of **12b**.

Reaction of 7b with 10b in the Presence of Ac_2O and NEt_3 in THF. Preparation of 5-[1-[(*tert*-Butyldimethylsilyl)oxy]-3,3-(ethylenedioxy)butyl]-6-ethoxy-4-hydroxy-7-methoxyindole (18). A solution of **7b** (1.5 g, 4.8 mmol), **10b** (2.0 g, 6.4 mmol), Ac_2O (0.5 mL, 5.0 mmol), and NEt_3 (0.7 mL, 5.0 mmol) in THF (150 mL) was heated at 65 °C under argon for 8 h. The mixture was cooled, and the solvent was removed by rotary evaporation to give a black oil. Purification by flash column chromatography (silica gel, 250 g; 25% ether in *n*-hexane) isolated **18a** as a yellow oil (844 mg, 38%) and **18b** as a yellow oil (210 mg, 10%). **18a**: MS 465 (M^+), 364, 306, 272, 247, 87; IR (neat) 3352, 1650, 1638, 1492, 1473, 1379, 1307, 1252 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.34 (1 H, s, ArO*H*), 6.77 (1 H, d, J = 3.1 Hz, C_2-H), 6.48 (1 H, d, J = 3.1 Hz, C_3-H), 5.55 (1 H, dd, J = 3.3 Hz, 11.1 Hz, $ArCH(OP)CH_2$), 4.12 (2 H, q, J = 7.1 Hz, $ArOCH_2CH_3$), 3.93 (7 H, br s, OCH_2CH_2O, $ArOCH_3$), 3.84 (3 H, s, NCH_3), 2.50–1.75 (2 H, m, $ArCH(OP)CH_2$), 1.46 (3 H, s, terminal CH_3), 1.44 (3 H, t, J = 7.1 Hz, $ArOCH_2CH_3$), 0.89 (9 H, s, *t*-BuSi), 0.19, −0.03 (2 × 3 H, 2 s, CH_3SiCH_3). Anal. Calcd for $C_{24}H_{39}NO_6Si$: C, 61.90; H, 8.44; N, 3.01. Found: C, 61.71; H, 8.24; N, 2.94. **18b**: MS 449 (M^+), 392, 348, 262, 161, 87; IR (neat) 1650, 1602, 1510, 1402, 1250, 1219, 1113, 1047 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.77 (1 H, d, J = 2.3 Hz, C_2-H), 6.48 (1 H, d, J = 2.3 Hz, C_3-H), 5.35–5.20 (1 H, m, $ArCH(OP)CH_2$), 4.20–3.80 (2 H, m, $ArOCH_2CH_3$), 3.95 (4 s, OCH_2CH_2O), 3.84 (3 H, s, NCH_3), 2.50–1.80 (2 H, m, $ArCH(OP)CH_2$), 1.46 (3 H, s, terminal CH_3), 1.44 (3 H, t, J = 7.0 Hz, $ArOCH_2CH_3$), 0.85 (9 H, s, *t*-BuSi), 0.10, −0.02 (2 × 3 H, 2 s, CH_3SiCH_3). Anal. Calcd for $C_{23}H_{35}NO_6Si$: C, 61.42; H, 7.85; N, 3.12. Found: C, 61.10; H, 8.58; N, 3.30.

Reaction of 7c with 10a. Preparation of 2-[1-[(*tert*-Butyldimethylsilyl)oxy]ethyl]-3-ethoxy-1-hydroxy-4-methoxynaphthalene (14a) and the Acetate (14b). (a) In the Presence of Ac_2O in THF. A solution of **7c** (2.5 g, 8.0 mmol), **10a** (2.5 g, 12.0 mmol), and Ac_2O (0.8 mL, 8.0 mmol) in THF (240 mL) was heated at 65 °C under argon for 4 h. The mixture was cooled, and the solvent was removed by rotary evaporation to give a black oil. Purification by flash column chromatography (silica gel, 250 g; 10% ether in *n*-hexane) gave **14a** as a yellow oil (1.56 g, 52%) and **14b** as a yellow oil (410 mg, 12%). **14a**: MS 376 (M^+), 244, 229, 201; IR (neat) 3299, 1631, 1598 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.31 (1 H, s, ArO*H*), 8.25–7.85 (2 H, m, C_5-H, C_8-H), 7.50–7.30 (2 H, m, C_6-H, C_7-H), 5.56 (1 H, q, J = 6.2 Hz, $ArCH(OP)CH_3$), 4.23 (2 H, q, J = 7.1 Hz, $ArOCH_2CH_3$), 3.99 (3 H, s, $ArOCH_3$), 1.54 (3 H, d, J = 6.2 Hz, $ArCH(OP)CH_3$), 1.42 (3 H, t, J = 7.1 Hz, $ArOCH_2CH_3$), 0.93 (9 H, s, *t*-BuSi), 0.19, −0.09 (2 × 3 H, 2 s, CH_3SiCH_3). Anal. Calcd for $C_{21}H_{32}O_4Si$: C, 66.98; H, 8.57. Found: C, 66.71; H, 8.70. **14b**: high-resolution MS mol wt 418.2166, calcd 418.2175; IR (neat) 1772, 1597, 1374, 1203, 1047 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.16–7.90 (1 H, m, C_8-H), 7.70–7.30 (3 H, m, C_5-H, C_6-H, C_7-H), 5.46 (1 H, q, J = 6.6 Hz, $ArCH(OP)CH_3$), 4.21 (2 H, q, J = 7.1 Hz, $ArOCH_2CH_3$), 3.90 (3 H, s, $ArOCH_3$), 2.41 (3 H, s, $ArOCOCH_3$), 1.60 (3 H, d, J = 6.6 Hz, $ArCH(OP)CH_3$), 1.44 (3 H, t, J = 7.1 Hz, $ArOCH_2CH_3$), 0.89 (9 H, s, *t*-BuSi), 0.04, −0.02 (2 × 3 H, 2 s, CH_3SiCH_3). Anal. Calcd for $C_{23}H_{34}O_5Si$: C, 65.99; H, 8.19. Found: C, 66.00; H, 8.21.

(b) In the Presence of Ac_2O and NEt_3 in THF. A solution of **7c** (2.0 g, 6.4 mmol), **10a** (2.0 g, 9.6 mmol), Ac_2O (0.7 mL, mmol), and NEt_3 (0.9 mL, mmol) in THF (180 mL) was heated at 65 °C under argon for 3 h. The mixture was cooled, and the solvent was removed by rotary evaporation to give a black oil. Purification by flash column chromatography (silica gel, 300 g; 10% ether in *n*-hexane) afforded 1.44 g (54%) of **14b**.

Reaction of 7c with 10b in the Presence of Ac_2O and NEt_3 in THF. Preparation of 2-[1-[(*tert*-Butyldimethylsilyl)oxy]-3,3-(ethylenedioxy)butyl]-3-ethoxy-1-hydroxy-4-methoxynaphthalene (19). A solution of **7c** (1.5 g, 4.8 mmol), **10b** (1.84 g, 5.9 mmol), Ac_2O (0.5 mL, 5.0 mmol), and NEt_3 (0.7 mL, 5.0 mmol) in THF (150 mL) was heated at 65 °C under argon for 6 h. The mixture was cooled, and the solvent was removed by rotary evaporation to give a black oil. Purification by flash column chromatography (silica gel, 250 g; 10% ether in *n*-hexane) isolated **19** as a yellow oil (1.00 mg, 45%): high-resolution MS mol wt 462.2429, calcd 462.2437; IR (neat) 3319, 1631, 1597, 1582, 1463, 1378, 1258 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.81 (1 H, s, ArO*H*), 8.25–7.90 (2 H, m, C_5-H, C_8-H), 7.55–7.30 (2 H, m, C_6-H, C_7-H), 5.65 (1 H, m, $ArCH(OP)CH_2$), 4.24 (2 H, q, J = 7.2 Hz, $ArOCH_2CH_3$), 3.93 (4 H, br s, OCH_2CH_2O), 3.87 (3 H, s, $ArOCH_3$), 2.60–2.30 (2 H, m, $ArCH(OP)CH_2$), 1.48 (3 H, s, terminal CH_3), 1.46 (3 H, t, J = 7.2 Hz, $ArOCH_2CH_3$), 0.90 (9 H, s, *t*-BuSi), 0.22, −0.06 (2 × 3 H, 2 s, CH_3SiCH_3). Anal. Calcd for $C_{25}H_{38}O_6Si$: C, 64.90; H, 8.28. Found: C, 64.88; H, 8.25.

Direct Conversion of the Acetate to the Methyl Ether. Preparation of 5-[1-[(*tert*-Butyldimethylsilyl)oxy]ethyl]-4,7-dimethoxy-6-ethoxybenzofuran (22a). (a) Without HMPA. To a cooled (wet ice bath) suspension of NaH (690 mg, 14.4 mmol, 50% oil dispersion, washed with dry hexane) in THF (50 mL) was dropwise added a THF (50 mL) solution of **6a** (1.95 g, 4.8 mmol) via syringe under argon, and the mixture was stirred at this temperature for 1 h. MeI (3 mL, 48 mmol) was added to the solution, the cooling bath was removed, and the mixture was stirred at 25 °C for 24 h under argon. The mixture was poured into a mixture of ice (200 mL) and H_2O, the organic layer was separated, and the aqueous layer was extracted with ether (3 × 100 mL). The organic layers were combined, washed (brine, 2 × 150 mL), dried (Na_2SO_4), filtered, and concentrated to give a yellow oil. Thick-layer chromatography (silica gel, 2000 μm; 10% ether in *n*-hexane) provided **22a** as a yellow oil (985 mg, 54%), the silyl ether **22b** as white needles (mp 78.5–80 °C, 132 mg, 6%), and the olefin **22c** as a yellow oil (201 mg, 19%). **22a**: MS 380 (M^+), 323, 308, 294, 276, 264; IR (neat), 1480, 1378, 1345, 1247, 1132, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.51 (1 H, d, J = 2.2 Hz, C_2-H), 6.81 (1 H, d, J = 2.2 Hz, C_3-H), 5.46 (1 H, q, J = 6.6 Hz, $ArCH(OP)CH_3$), 4.16 (2 H, q, J = 7.0 Hz, $ArOCH_2CH_3$), 4.07, 3.94 (2 × 3 H, 2 s, 2 of $ArOCH_3$), 1.62 (3 H, d, J = 6.6 Hz, $ArCH(OP)CH_3$), 1.42 (3 H, t, J = 7.0 Hz, $ArOCH_2CH_3$), 0.87 (9 H, s, Si*Bu-t*), 0.09, −0.04 (2 × 3 H, 2 s, CH_3SiCH_3). Anal. Calcd for $C_{20}H_{32}O_5Si$: C, 63.12; H, 8.48. Found: C, 63.44; H, 8.63. **22b**: high-resolution MS mol wt 480.2757, calcd 480.2727; IR (Nujol) 1473, 1347, 1135, 1053 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.44 (1 H, d, J = 2.1 Hz, C_2-H), 6.72 (1 H, d, J = 2.1 Hz, C_3-H), 5.40 (1 H, q, J = 6.6 Hz, $ArCH(OP)CH_3$), 4.20 (2 H, q, J = 7.0 Hz, $ArOCH_2CH_3$), 4.06 (3 H, s, $ArOCH_3$), 1.66 (3 H, d, J = 6.6 Hz, $ArCH(OP)CH_3$), 1.43 (3 H, t, J = 7.0 Hz, $ArOCH_2CH_3$), 1.09 (9 H, s, Si*Bu-t*), 0.84 (9 H, s, Si*Bu-t*), 0.17, 0.129, 0.08, −0.09 (4 × 3 H, 4 s, 2 of CH_3SiCH_3). Anal. Calcd for $C_{25}H_{44}O_5Si_2$: C, 62.45; H, 9.22. Found: C, 62.37; H, 9.23. **22c**: high-resolution MS mol wt 248.1033, calcd 248.1048; IR (neat) 1607, 1474, 1383, 1338, 1247, 1132, 1067 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52 (1 H, d, J = 2.2 Hz, C_2-H), 6.84 (1 H, d, J = 2.2 Hz, C_3-H), 7.09–6.72 (1 H, m, $ArCH{=}CH_2$), 6.19–5.37 (2 H, m, $ArCH{=}CH_2$), 4.05 (2 H, q, J = 7.1 Hz, $ArOCH_2CH_3$), 4.07, 3.91 (2 × 3 H, 2 s, 2 of $ArOCH_3$), 1.39 (3 H, t, J = 7.1 Hz, $ArOCH_2CH_3$).

(b) With HMPA. To a cooled (wet ice bath) suspension of NaH (990 mg, 19.4 mmol, 50% oil dispersion, washed with dry hexane) in HMPA (5 mL) and THF (100 mL) was dropwise added a THF (50 mL) solution of **6a** (3.6 g, 8.8 mmol) via syringe under argon, and the mixture was stirred at this temperature for 1 h. MeI (3.5 mL, 53 mmol) was added to the solution, the cooling bath was removed, and the mixture was stirred at 25 °C for 24 h under argon. The mixture was poured onto a mixture of ice and H_2O (200 mL), the organic layer was separated, and the aqueous layer was extracted with ether (3 × 100 mL). The organic layers were combined, washed (brine, 2 × 150 mL), dried (Na_2SO_4), filtered, and concentrated to give a yellow oil. Flash column chromatography (silica gel, 400 g; 10% ether in *n*-hexane) provided **22a** (2.64 g, 79%) and **6a** (420 mg, 12%).

Preparation of 4,7-Dimethoxy-6-ethoxy-5-(1-hydroxyethyl)benzofuran (23). A solution of **22a** (600 mg, 1.58 mmol) and n-$Bu_4NF{\cdot}3H_2O$ (1.5 g, 4.8 mmol) in dry DMF (20 mL) was stirred at 25 °C under argon for 20 h by the standard procedure.[13] The mixture was diluted with ether (250 mL), and the ether layer was washed (brine, 3 × 150 mL), dried (Na_2SO_4), filtered, and

concentrated to give a yellow oil. Thick-layer chromatography (silica gel, 200 μm; 50% ether in *n*-hexane) provided **23** as yellow oil (355 mg, 85%): high-resolution MS mol wt 266.1151, calcd 266.1154; IR (neat) 3467, 1613, 1480, 1385, 1343, 1245, 1132, 1059 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52 (1 H, d, J = 2.1 Hz, C_2-H), 6.83 (1 H, d, J = 2.1 Hz, C_3-H), 5.40–5.10 (1 H, m, ArC*H*(OP)CH_3), 4.21 (2 H, q, J = 7.0 Hz, ArOC*H*$_2$$CH_3$), 4.05 (6 H, s, 2 of ArOC*H*$_3$), 3.73 (1 H, d, J = 8.2 Hz, OH), 1.56 (3 H, d, J = 6.9 Hz, ArCH-(OP)C*H*$_3$), 1.44 (3 H, t, J = 7.0 Hz, ArOCH$_2$C*H*$_3$). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.14; H, 6.81. Found: C, 63.19; H, 6.80.

Preparation of 5-Acetyl-4,7-dimethoxy-6-ethoxybenzofuran (24 = 4). The alcohol (**23**, 1.35 g, 5.1 mmol) was oxidized with PDC (4.0 g, 10.2 mmol) in dry CH_2Cl_2 (200 mL) at 25 °C by the standard procedure.[14] After a usual workup procedure, the product was purified by thick-layer chromatography (silica gel, 2000 μm; 35% ether in *n*-hexane) to give the recoved **23** (168 mg, 12%) and **4** as a yellow oil (711 mg, 53%): high-resolution MS mol wt 264.1006, calcd 264.0998; IR (neat) 1707, 1611, 1479, 1384, 1352, 1137, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.55 (1 H, d, J = 2.3 Hz, C_2-H), 6.86 (1 H, d, J = 2.3 Hz, C_3-H), 4.23 (2 H, q, J = 7.0 Hz, ArOC*H*$_2$$CH_3$), 4.07, 3.98 (2 × 3 H, 2 s, 2 of ArOC*H*$_3$), 2.53 (3 H, s, ArC(O)C*H*$_3$), 1.33 (3 H, t, J = 7.0 Hz, ArOCH$_2$C*H*$_3$). Anal. Calcd for $C_{14}H_{16}O_5$: C, 63.62; H, 6.10. Found: C, 63.72; H, 6.19.

Selective Cleavage of the Ethyl Ether. Preparation of Khellinone (2). To a cooled (wet ice bath) solution of **4** (103 mg, 0.39 mmol) in dry CH_2Cl_2 (70 mL) was dropwise added BF_3·Et_2O (0.5 mL, 0.41 mmol) via syringe under argon. The bath was removed, and the yellow solution was stirred at 25 °C for 15 h and diluted with CH_2Cl_2 (50 mL). The organic layer was washed with H_2O (3 × 100 mL), dried (Na_2SO_4), filtered, and concentrated. Purification by thick-layer chromatography (silica gel, 2000 μm; developed by ether/*n*-hexane, 1/3) gave **2** as yellow crystals (89 mg, 97%, mp 97–99 °C; lit. mp 97.5–100 °C[1c,f]). Physical behavior of the product was the same as that of the authentic sample obtained from alkaline degradation of khellin.

Preparation of Khellin (1) from 2. According to the procedure of Spath,[2] a mixture of **2** (80 mg, 0.339 mmol) and NaH (163 mg, 3.39 mmol, 50% oil dispersion) in EtOAc (15 mL) was heated at reflux under argon for 6 h. The solution was cooled, poured into a mixture of ice and H_2O, and acidified (pH ~1.0) with concentrated HCl. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), and the extracts were combined, washed (H_2O), dried ($MgSO_4$), filtered, and concentrated. The yellow residue was dissolved in MeOH (30 mL) and 1 N HCl (15 mL) and stirred at 25 °C for 24 h. The solvent was removed by rotary evaporation, and the residue was dissolved in H_2O (50 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), and the extracts were combined, washed (H_2O), dried (Na_2SO_4), filtered, and concentrated. Purification by thick-layer chromatography (silica gel, 200 μm; ether) gave **1** (73 mg, 83%, mp 148–150 °C; undepressed on admixture with a natural specimen, mp 151–152 °C). Physical behavior of the product was the same as that of the authentic sample.

Direct Conversion of the Acetate to the Methyl Ether. Preparation of 5-[1-[(*tert*-Butyldimethylsilyl)oxy]-3,3-(ethylenedioxy)butyl]-4,7-dimethoxy-6-ethoxybenzofuran (25a). To a cooled (wet ice bath) suspension of NaH (155 mg, 3.2 mmol, 50% oil dispersion, washed with dry hexane) in THF (30 mL) was dropwise added a THF (20 mL) solution of **6b** (500 mg, 1.04 mmol) via syringe under argon, and the mixture was stirred at this temperature for 1 h. MeI (1 mL, 16 mmol) was added to the solution, the cooling bath was removed, and the mixture was stirred at 25 °C for 24 h under argon. The mixture was poured onto a mixture (200 mL) of ice and H_2O, the organic layer was separated, and the aqueous layer was extracted with ether (3 × 100 mL). The organic layers were combined, washed (brine, 2 × 150 mL), dried (Na_2SO_4), filtered, and concentrated to give a yellow oil. The thick-layer chromatography (silica gel, 2000 μm; 10% ether in *n*-hexane) provided **25a** (a yellow oil, 330 mg, 68%) and the olefin **25b** (a yellow oil, 80 mg, 23%). **25a**: high-resolution MS mol wt 466.2395, calcd 466.2387; IR (neat) 1614, 1478, 1377, 1343, 1246, 1132, 1063 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50 (1 H, d, J = 2.2 Hz, C_2-H), 6.81 (1 H, d, J = 2.2 Hz, C_3-H), 5.60–5.30 (1 H, m, ArC*H*(OP)CH_2), 4.04 (4 H, s, OC*H*$_2$$CH_2$O), 4.15 (2 H, q, J = 7.0 Hz, ArOC*H*$_2$$CH_3$), 3.97, 3.86 (2 × 3 H, 2 s, 2 of ArOC*H*$_3$), 2.70–1.80 (2 H, m, ArCH(OP)C*H*$_2$), 1.44 (3 H, t, J = 7.0 Hz, ArOCH$_2$C*H*$_3$), 1.32 (3 H, s, terminal CH_3), 0.83 (9 H, s, *t*-*Bu*Si), 0.14 (6 H, s, C*H*$_3$SiC*H*$_3$). Anal. Calcd for $C_{24}H_{38}O_7Si$: C, 61.77; H, 8.21. Found: C, 62.12; H, 8.28. **25b**: high-resolution MS mol wt 334.12256, calcd 334.1416; IR (neat) 1476, 1385, 1267, 1043 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52 (1 H, d, J = 2.2 Hz, C_2-H), 6.82 (1 H, d, J = 2.2 Hz, C_3-H), 6.71 (2 H, m, ArC*H*=CH_2), 6.20–5.35 (2 H, m, ArCH=C*H*$_2$), 4.15 (2 H, q, J = 7.1 Hz, ArOC*H*$_2$$CH_3$), 4.07, 3.90 (2 × 3 H, 2 s, 2 of ArOC*H*$_3$), 3.99 (4 H, s, OC*H*$_2$C*H*$_2$O), 1.39 (3 H, s, terminal CH_3), 1.40 (3 H, t, q, J = 7.1 Hz, ArOCH$_2$C*H*$_3$).

Preparation of 4,7-Dimethoxy-6-ethoxy-5-[1-hydroxy-3,3-(ethylenedioxy)butyl]benzofuran (26). Cleavage of the *tert*-butyldimethylsilyl group from **25a** (1.39 g, 3.2 mmol) was accomplished with *n*-Bu_4NF·$3H_2O$ (3.0 g, 9.6 mmol) in DMF (50 mL) using the procedure for **22a**. Thick-layer chromatography (silica gel, 2000 μm; 50% ether in hexane) gave the recovered **25a** (41 mg, 3%) and **26** as a yellow oil (985 mg, 87%): high-resolution MS mol wt 352.1505, calcd 352.1522; IR (neat) 3519, 1480, 1384, 1343, 1131, 1062 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.51 (1 H, d, J = 2.2 Hz, C_2-H), 6.82 (1 H, d, J = 2.2 Hz, C_3-H), 5.57–5.30 (1 H, m, ArC*H*(OH)CH_2), 4.20 (2 H, q, J = 7.0 Hz, ArOC*H*$_2$$CH_3$), 4.01 (7 H, br s, ArOC*H*$_3$, OC*H*$_2$C*H*$_2$O), 4.05 (3 H, s, ArOC*H*$_3$), 3.63 (1 H, s, OH), 2.70–1.80 (2 H, m, ArCH(OH)C*H*$_2$), 1.48 (3 H, s, terminal CH_3), 1.44 (3 H, t, J = 7.0 Hz, ArOCH$_2$C*H*$_3$). Anal. Calcd for $C_{18}H_{24}O_7$: C, 61.35; H, 6.86. Found: C, 61.14; H, 6.90.

Preparation of 4,7-Dimethoxy-6-ethoxy-5-[1-oxo-3,3-(ethylenedioxy)butyl]benzofuran (27). Oxidation of the alcohol (**26**, 686 mg, 1.95 mmol) was accomplished with PDC (2.2 g, 5.85 mmol) in dry CH_2Cl_2 (150 mL) as described for **4**. Purification by thick-layer chromatography (silica gel, 2000 μm; 35% ether in *n*-hexane) gave the recovery of **26** (206 mg, 30%) and **27** as a yellow oil (238 mg, 35%): high-resolution MS mol wt 350.1372, calcd 350.1365; IR (neat) 1714, 1478, 1384, 1347, 1136, 1064 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.55 (1 H, d, J = 2.2 Hz, C_2-H), 6.85 (1 H, d, J = 2.2 Hz, C_3-H), 4.12 (2 H, q, J = 7.0 Hz, ArOC*H*$_2$$CH_3$), 4.07, 3.97 (2 × 3 H, 2 s, 2 of ArOC*H*$_3$), 3.93 (4 H, br s, OC*H*$_2$C*H*$_2$O), 3.21 (2 H, s, ArCOC*H*$_2$), 1.54 (3 H, s, terminal CH_3), 1.33 (3 H, t, J = 7.0 Hz, ArOCH$_2$C*H*$_3$). Anal. Calcd for $C_{18}H_{22}O_7$: C, 61.70; H, 6.33. Found; C, 61.49; H, 6.28.

Preparation of Khellinquinone (3). A solution of ceric ammonium nitrate (1.36 g, 2.48 mmol) in H_2O (10 mL) was dropwise added to a cooled (wet ice bath) solution of **27** (290 mg, 0.828 mmol) in CH_3CN (20 mL) over a period of 10 min, and the resulting orange solution was stirred at this temperature for 2 h under argon. The mixture was diluted with H_2O (50 mL) and the aqueous layer was extracted with $CHCl_3$ (3 × 100 mL). The extracts were combined, washed (H_2O), dried (Na_2SO_4), filtered, and concentrated. The brown oil was dissolved in 1 N HCl (10 mL) and THF (20 mL) and stirred at 25 °C for 24 h. The mixture was diluted with H_2O (20 mL) and extracted with $CHCl_3$ (3 × 100 mL). The extracts were combined, washed (H_2O), dried (Na_2SO_4), filtered, and concentrated. The remaining brown solid was recrystallized from EtOH–ether–*n*-hexane to give **3** as a yellow powder (139 mg, 73% based on **27**, mp 204–208 °C; lit. mp 196–202 °C[1b,i]). Physical behavior of the product was the same as that of the authentic sample obtained from oxidation of Khellin.

Preparation of Khellin (1) and Isokhellin (29) from 3. Conversion of **3** (70 mg, 0.3 mmol) to **1** was accomplished, using the literature procedure,[2] by reduction ($NaHSO_3$, catalytic HCl, 100 °C) and dimethylation (MeI, K_2CO_3, acetone, reflux, 5 h), giving **1** (39 mg, 50%) and isokhellin as white needles (**29**, 7.0 mg, 10%, mp 170–175 °C; lit. mp 179–180 °C[1c]). Physical behavior of the product was the same as that of the authentic sample obtained from acid treatment of Khellin, followed by dimethylation.

Preparation of 4,7-Dimethoxy-5-ethenyl-6-ethoxy-1-methylindole (30). (a) From 12a. Methylation of the free phenol of **12a** (500 mg, 1.3 mmol) was accomplished with NaH (120 mg, 2.6 mmol, 50% oil dispersion) and MeI (1.0 mL, 16 mmol) in THF (50 mL) using the procedure described for formation of **22a**. Purification by thick-layer chromatography (silica gel, 2000 μm; 40% ether in *n*-hexane) gave **30** as yellow oil (247 mg, 77%): high-resolution MS mol wt 261.1359, calcd 261.1365; IR (neat) 1608, 1484, 1388, 1307, 1289, 1233, 1108, 1042 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.83 (1 H, d, J = 3.2 Hz, C_2-H), 6.47 (1 H, d, J = 3.2 Hz, C_3-H), 6.90 (1 H, d, J = 11.3 Hz, ArC*H*=CH_2), 6.18–5.35 (2

H, m, ArCH=CH_2), 4.03 (2 H, q, J = 7.0 Hz, ArOCH_2CH$_3$), 3.95 (6 H, s, 2 of ArOCH_3), 3.89 (3 H, s, NCH_3), 1.40 (3 H, t, J = 7.0 Hz, ArOCH$_2$CH_3). Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.77; H, 7.35; N, 5.25.

(b) From 12b. Direct conversion of the acetate **12b** (9.27 g, 22 mmol) to the methyl ether was accomplished with NaH (2.6 g, 44 mmol, 50% oil dispersion) and MeI (10 mL, 160 mmol) in THF (300 mL) using the procedure described for formation of **22a**. Purification by flash column chromatography (silica gel, 300 g, elution by 10% ether in *n*-hexane) gave **30** (3.7 g, 65%).

Preparation of 5-Acetyl-4,7-dimethoxy-6-ethoxy-1-methylindole (31). $PdCl_2$ (620 mg, 3.4 mmol) and CuCl (1.69 g, 17 mmol) was dissolved in a mixture of DMF (100 mL) and H_2O (24 mL), and oxygen gas was introduced into the solution for 20 min. A solution of **30** (3.7 g, 14.2 mmol) in DMF (76 mL) was added, and the resulting mixture was treated by bubbling oxygen gas for 48 h at 25 °C. The catalyst was removed through filteration, and the filterate was diluted with ether (300 mL). The organic layer was washed (brine, 3 × 200 mL), dried (Na_2SO_4), filtered, and concentrated to give a brown oil. Flash column chromatography (silica gel, 300 g; 10% ether in *n*-hexane) gave the recovered **30** (270 mg, 7%). Further elution by 40% ether in *n*-hexane provided **31** as colorless crystals (mp 55.0–56.0 °C, 3.03 g, 77%): high-resolution MS mol wt 277.1306, calcd 277.1314; IR (Nujol) 1698, 1607, 1488, 1389, 1308, 1065 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.88 (1 H, d, J = 3.1 Hz, C_2-H), 6.50 (1 H, d, J = 3.1 Hz, C_3-H), 4.08 (2 H, q, J = 7.1 Hz, ArOCH_2CH$_3$), 3.97 (6 H, s, 2 of ArOCH_3), 3.94 (3 H, s, NCH_3), 2.55 (3 H, s, ArCOCH_3), 1.34 (3 H, t, J = 7.1 Hz, ArOCH$_2$CH_3). Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.96; H, 6.96; N, 5.05. Found: C, 64.73; H, 6.93; N, 4.91.

Preparation of 5-Acetyl-4,7-dimethoxy-6-hydroxy-1-methylindole (32). Selective cleavage of the ethyl ether **31** (470 mg, 1.7 mmol) was accomplished with BF_3·Et_2O (1.5 mL, 12.2 mmol) in dry CH_2Cl_2 (150 mL) using the procedure for formation of **2**. Purification by thick-layer chromatography (silica gel, 2000 μm; 50% ether in *n*-hexane) gave **32** as yellow needles (mp 103–105 °C, 362 mg, 86%): high-resolution MS mol wt 249.1009, calcd 249.1001; IR (Nujol) 1638, 1604, 1434, 1323 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 12.81 (1 H, d, ArOH), 6.80 (1 H, d, J = 3.3 Hz, C_2-H), 6.53 (1 H, d, J = 3.3 Hz, C_3-H), 4.08 (3.96 (2 × 3 H, 2 s, 2 of ArOCH_3), 3.93 (3 H, s, NCH_3), 2.73 (3 H, s, ArCOCH_3). Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.53; H, 6.16; N, 5.40.

Preparation of a Pyrrole Analogue of Khellin (1b). A Claisen type condensation and subsequent acid-catalyzed pyrone ring formation from **32** (500 mg, 2.0 mmol) was accomplished using the procedure described for formation of **1** from **2** with NaH (4805 mg, 10.0 mmol, 50% oil dispersion) and EtOAc (30 mL), followed by acid treatment (1 N HCl, THF, 25 °C). Purification by thick-layer chromatography (silica gel, 2000 μm; ether) gave **1b** as yellow crystals (mp 151.5–152.5 °C, 436 mg, 80%): high-resolution MS mol wt 273.1006, calcd 273.1001; IR (Nujol) 1652, 1608, 1393, 1053 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.97 (1 H, d, J = 3.2 Hz, C_2-H), 6.69 (1 H, d, J = 3.2 Hz, C_3-H), 5.99 (1 H, s, C_6-H), 4.04 (6 H, s, two of ArOCH_3), 4.02 (3 H, s, NCH_3), 2.37 (3 H, s, C_7-CH_3). Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.66; H, 5.61; N, 5.04.

Preparation of 5-[1-[(*tert*-Butyldimethylsilyl)oxy]-3,3-(ethylenedioxy)butyl]-4,7-dimethoxy-6-ethoxy-1-methylindole (33). The free phenol **18** (1.93 g, 4.14 mmol) was methylated by heating at reflux with MeI (5.1 mL, 82 mmol) and K_2CO_3 (8 g, 57 mmol) in dry acetone (110 mL) for 6 h under argon. After a usual workup procedure, the product was purified by flash column chromatography (silica gel, 250 g; 30% ether in *n*-hexane) to give **33** as a yellow oil (1.64 g, 83%): high-resolution MS mol wt 479.2692, calcd 479.2703; IR (neat) 1613, 1491, 1473, 1380, 1307, 1111, 1060, 1033 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.82 (1 H, d, J = 3.1 Hz, C_2-H), 6.45 (1 H, d, J = 3.1 Hz, C_3-H), 5.60–5.35 (1 H, m, ArCH(OP)CH$_2$), 4.16 (2 H, q, J = 7.0 Hz, ArOCH_2CH$_3$), 3.95 (4 H, s, OCH_2CH_2O), 3.99, 3.91 (2 × 3 H, 2 s, 2 of ArOCH_3), 3.88 (3 H, s, NCH_3), 2.70–2.40 (2 H, m, ArCH(OP)CH_2), 1.38 (3 H, t, J = 7.0 Hz, ArOCH$_2$CH_3), 1.33 (3 H, s, terminal CH$_3$), 0.83 (9 H, s, *t*-*Bu*Si), 0.15 (6 H, s, CH_3SiCH_3). Anal. Calcd for $C_{25}H_{41}NO_6Si$: C, 62.59; H, 8.62; N, 2.92. Found: C, 62.64; H, 8.70; N, 2.95.

Preparation of 4,7-Dimethoxy-6-ethoxy-5-[1-hydroxy-3,3-(ethylenedioxy)butyl]-1-methylindole (34). Cleavage of *tert*-butyldimethylsilyl group from **33** (540 mg, 1.127 mmol) was accomplished with *n*-Bu_4NF·3H_2O (1.1 g, 1.24 mmol) in DMF (20 mL) by the procedure for formation of **23**. Purification by thick-layer chromatography (silica gel, 2000 μm; 50% ether in *n*-hexane) gave the recovered **33** (86 mg, 16%) and **34** as a yellow oil (342 mg, 83%): high-resolution MS mol wt 365.1840, calcd 365.1838; IR (neat) 3522, 1614, 1492, 1447, 1430, 1404, 1389, 1307, 1249, 1129, 1071, 1056 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.83 (1 H, d, J = 3.1 Hz, C_2-H), 6.44 (1 H, d, J = 3.1 Hz, C_3-H), 5.56–5.31 (1 H, m, ArCH(OH)), 4.10 (2 H, q, J = 7.1 Hz, ArOCH_2CH$_3$), 4.01 (7 H, br s, ArOCH_3, OCH_2CH_2O), 3.95 (3 H, s, ArOCH_3), 3.91 (3 H, s, NCH_3), 3.60 (1 H, br s, OH), 2.70–2.00 (2 H, m, ArCH(OH)CH_2), 1.49 (3 H, s, terminal CH$_3$), 1.44 (3 H, t, J = 7.1 Hz, ArOCH$_2$CH_3). Anal. Calcd for $C_{19}H_{27}NO_6$: C, 62.45; H, 7.45; N, 3.83. Found: C, 62.57; H, 7.78; N, 3.76.

Preparation of 4,7-Dimethoxy-6-ethoxy-1-methyl-5-[1-oxo-3,3-(ethylenedioxy)butyl]indole (35). A DMF (50 mL) solution of **34** (329 mg, 0.9034 mmol), NaH (65 mg, 13.5 mmol), $(Ph_3P)_4Pd$ (2.09 g, 1.81 mmol), PhBr (0.95 mL, 9.03 mmol), and 18-crown-6 (478 mg, 1.91 mmol) was heated at 75–80 °C (bath temperature) under argon for 72 h. The mixture was cooled and diluted with ether (300 mL). The grayish black precipitate was filtered through a Celite cake, and the filterate was washed (brine, 3 × 200 mL), dried (Na_2SO_4), filtered, and concentrated. Thick-layer chromatography (silica gel, 2000 μm; 50% ether in *n*-hexane) afforded **34** (169 mg, 51%) and **35** as a yellow oil (150 mg, 48%): MS mol wt 363.1709, calcd 363.1682; IR (neat 1707, 1691, 1608, 1488, 1447, 1429, 1389, 1375, 1353, 1307, 1240, 1188, 1134, 1108 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.87 (1 H, d, J = 3.2 Hz, C_2-H), 6.49 (1 H, d, J = 3.2 Hz, C_3-H), 4.08 (2 H, q, J = 7.1 Hz, ArOCH_2CH$_3$), 3.971 (4 H, br s, OCH_2CH_2O), 3.94 (9 H, br s, NCH_3, 2 of ArOCH_3), 2.26 (2 H, s, ArCH(O)CH_2), 1.54 (3 H, s, terminal CH$_3$), 1.34 (3 H, t, J = 7.1 Hz, ArOCH$_2$CH_3). Anal. Calcd for $C_{19}H_{25}NO_6$: C, 62.80; H, 6.93; N, 3.85. Found: C, 62.61; H, 7.21; N, 3.82.

Preparation of 2-[1-[(*tert*-Butyldimethylsilyl)oxy]-ethyl]-1,4-dimethoxy-3-ethoxynaphthalene (36). Compound **14a** (500 mg, 1.33 mmol) was methylated by treatment with NaH (120 mg, 2.7 mmol, 50% oil dispersion) and MeI (0.35 mL, 5.3 mmol) in HMPA (1 mL) and THF (50 mL) under argon at 0 °C. After the standard workup procedure used for formation of **22a**, purification by thick-layer chromatography (silica gel, 2000 μm; 10% ether in *n*-hexane) gave **36** as a yellow oil (468 mg, 90%): MS mol wt 390.2223, calcd 390.2226; IR (neat) 1590, 1382, 1271, 1077 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.15–7.85 (2 H, m, C_5-H), C_8-H), 7.50–7.30 (2 H, m, C_6-H, C_7-H), 5.57 (1 H, q, J = 6.7 Hz, ArCH-(OP)CH$_3$), 4.19 (2 H, q, J = 7.1 Hz, ArOCH_2CH$_3$), 3.96 (3 H, s, ArOCH_3), 1.715 (3 H, s, ArCH(OP)CH_3), 1.45 (3 H, t, J = 7.1 Hz, ArOCH$_2$CH_3), 0.87 (9 H, s, *t*-*Bu*Si), 0.13, –0.03 (2 × 3 H, 2 s, CH_3SiCH_3). Anal. Calcd for $C_{22}H_{34}O_4Si$: C, 67.67; H, 8.68. Found: C, 68.05; H, 8.74.

Preparation of 1,4-Dimethoxy-2-ethenyl-3-ethoxynaphthalene (38). (a) From 14a. Compound **14a** (5.82 g, 15.5 mmol) was treated with NaH (744 mg, 15.5 mmol, 50% oil dispersion) and MeI (7 mL, mmol) in THF (50 mL) under argon as described for formation of **22a**. Purification by flash column chromatography (silica gel, 250 g; 5% ether in *n*-hexane) gave **38** as a yellow oil (4.0 g, 99%): MS mol wt 258.1256, calcd 258.1257; IR (neat) 1623, 1589, 1457, 1380 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.20–7.90 (2 H, m, C_5-H, C_8-H), 7.55–7.250 (2 H, m, C_6-H, C_7-H), 7.10–6.75 (1 H, m, ArCH=CH$_2$), 6.37–6.15 (2 H, m, ArCH=CH_2), 4.14 (2 H, q, J = 7.1 Hz, ArOCH_2CH$_3$), 3.99, 3.85 (2 × 3 H, 2 s, ArOCH_3), 1.42 (3 H, t, J = 7.1 Hz, ArOCH$_2$CH_3). Anal. Calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.39; H, 7.14.

(b) From 14b. Treatment of **14b** (350 mg, 0.837 mmol) with NaH (200 mg, 4.1 mmol, 50% oil dispersion) and MeI (1 mL, mmol) in THF (50 mL) by the procedure as described for formation of **22a** afforded **38** (179 mg, 83%).

Preparation of 1,4-Dimethoxy-3-ethoxy-2-(1-hydroxyethyl)naphthalene (37). Cleavage of the silyl group from **36** (800 mg, 2.1 mmol) was accomplished with *n*-Bu_4NF (20 mL, 14 mmol, 0.7 M THF solution) under argon as described for **23**. Purification by flash column chromatography (silica gel, 250 g; 40% ether in *n*-hexane) gave **37** as a yellow oil (454 mg, 78%): MS mol wt 276.1360, calcd 276.1361; IR (neat) 3459, 1623, 1592, 1457, 1381, 1369 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.15–7.85 (2 H, m,

C_5-H), C_8-H), 7.55–7.35 (2 H, m, C_6-H, C_7-H), 5.50–5.15 (1 H, m, ArC*H*(OH)CH_3), 4.20 (3 H, m, OH, ArOC*H*$_2$$CH_3$), 3.95, 3.92 (2 × 3 H, 2 s, 2 of ArOC*H*$_3$), 1.64 (3 H, d, J = 6.8 Hz, ArCH(OH)C*H*$_3$), 1.49 (3 H, t, J = 7.1 Hz, ArOCH$_2$C*H*$_3$). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.41; H, 7.34.

Preparation of 2-Acetyl-1,4-dimethoxy-3-ethoxynaphthalene (39) from 38. The Wacker process to convert the olefin **38** (921 mg, 3.57 mmol) to the ketone was accomplished with oxygen gas in DMF–H_2O (9:1) mixture, 100 mL) in the presence of $PdCl_2$ (126 mg, 0.2 mmol) and CuCl (353 mg, 3.57 mmol). Thick-layer chromatography (silica gel, 2000 μm; 10% ether in *n*-hexane) gave the recovery of **38** (467 mg, 51%) and **39** as a yellow oil (410 mg, 42%): MS 247 (M^+), 259, 231; IR (neat) 1710, 1621, 1591, 1363, 1212, 1083 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.16–7.95 (2 H, m, C_5-H, C_8-H), 7.55–7.35 (2 H, m, C_6-H), C_7-H), 4.21 (2 H, q, J = 7.1 Hz, ArOC*H*$_2$CH$_3$), 3.98, 3.92 (2 × 3 H, 2 s, 2 of ArOC*H*$_3$), 2.60 (3 H, s, ArCOCH$_3$), 1.36 (3 H, t, J = 7.1 Hz, ArOCH$_2$C*H*$_3$). Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.03; H, 6.59.

Preparation of 2-Acetyl-1,4-dimethoxy-3-ethoxynaphthalene (39) from 37. Oxidation of the alcohol **37** (680 mg, 2.5 mmol) with PDC (1.7 g, 4.5 mmol) in dry CH_2Cl_2 (100 mL) at 25 °C by the standard procedure gave **39** (423 mg, 62%) and the recovery of **37** (176 mg, 26%).

Selective Cleavage of the Ethyl Ether. Preparation of 2-Acetyl-1,4-dimethoxy-3-hydroxynaphthalene (40a) and the Isomer (40b). Treatment of **39** (108 mg, 0.394 mmol) with BF_3·Et_2O (1.5 mL, 12.2 mmol) in dry CH_2Cl_2 (90 mL) was carried out as described for formation of **2**. Purification by thick-layer chromatography (silica gel, 2000 μm; 15% ether in *n*-hexane) gave **40a** as yellow needles (mp 76–77.5 °C, 80 mg, 83%) and **40b** as a yellow oil (10 mg, 10%). **40a**: MS mol wt 246.0890, calcd 246.0892; IR (neat) 1646, 1639, 1617, 1424, 1378 cm^{-1}; ^1H NMR ($CDCl_3$) δ 11.50 (1 H, s, ArO*H*), 8.20–7.95 (2 H, m, C_5-H, C_8-H), 7.60–7.20 (2 H, m, C_6-H, C_7-H), 3.99 (6 H, s, 2 of ArOC*H*$_3$), 2.87 (3 H, s, ArCOC*H*$_3$). Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.07; H, 5.86. **40b**: MS mol wt 260.1038, calcd 260.1048; IR (neat) 1622, 1572, 1477, 1375 cm^{-1}; ^1H NMR ($CDCl_3$) δ 13.68 (1 H, s, ArOH), 8.00–7.40 (2 H, m, C_5-H, C_8-H), 7.30–7.20 (2 H, m, C_6-H, C_7-H), 4.28 (2 H, q, J = 7.1 Hz, ArOC*H*$_2$CH$_3$), 3.92 (3 H, s, ArOC*H*$_3$), 2.80 (3 H, s, ArCOC*H*$_3$), 1.46 (3 H, t, J = 7.1 Hz, ArOCH$_2$C*H*$_3$).

Preparation of 5,8-Dimethoxy-6,7-benzochromone (1c) from 40a. A Claisen type condensation of **40a** (250 mg, 1.01 mmol) with NaH (487 mg, 10.1 mmol, 50% oil dispersion) and dry EtOAc (30 mL), followed by the pyrone ring formation, was accomplished using the process described for **1** from **2**. Purification by thick-layer chromatography (silica gel, 2000 μm; ether) gave **1c** as white crystals (230 mg, 84%, 143.5–144.5 °C; lit. mp 146 °C[22]): MS mol wt 270.0888, calcd 270.0892; IR (Nujol) 1666, 1639, 1620, 1593, 1559 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.45–8.10 (2 H, m, 2 ortho protons in Ph), 7.70–7.45 (2 H, m, 2 meta protons in Ph), 6.06 (1 H, d, J = 0.4 Hz, C_3-H), 4.08, 4.06 (2 × 3 H, 2 s, 2 of ArOC*H*$_3$), 2.42 (3 H, s, C_2-C*H*$_3$).

Preparation of 2-[1-[(*tert*-Butyldimethylsilyl)oxy]-3,3-(ethylenedioxy)butyl]-1,4-dimethoxy-3-ethoxynaphthalene (41). The phenol **19** (197 mg, 0.4 mmol) was methylated by heating at reflux in dry acetone (30 mL) with K_2CO_3 (800 mg, 5.8 mmol) and MeI (5 mL, 80 mmol). Purification by thick-layer chromatography (silica gel, 2000 μm; 25% ether in *n*-hexane) gave **41** as a yellow oil (179 mg, 94%): MS mol wt 476.2595, calcd 476.2595; IR (neat) 1622 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.20–7.90 (2 H, m, C_5-H, C_8-H), 7.55–7.30 (2 H, m, C_6-H, C_7-H), 5.70–5.40 (1 H, m, ArC*H*(OP)CH_2), 4.28 (2 H, q, J = 7.2 Hz, ArOC*H*$_2$$CH_3$), 4.03, 3.90 (2 × 3 H, 2 s, 2 of ArOC*H*$_3$), 3.94 (4 H, br s, OC*H*$_2$C*H*$_2$O), 2.80–2.20 (2 H, m, ArCH(OP)C*H*$_2$), 1.46 (3 H, t, J = 7.2 Hz, ArOCH$_2$C*H*$_3$), 1.40 (3 H, s, terminal CH_3), 0.83 (9 H, s, *t*-*Bu*Si), 0.20, –0.02 (2 × 3 H, 2 s, C*H*$_3$SiC*H*$_3$). Anal. Calcd for $C_{26}H_{40}O_6Si$: C, 65.51; H, 8.46. Found: C, 65.65; H, 8.45.

Preparation of 1,4-Dimethoxy-3-ethoxy-2-[1-hydroxy-3,3-(ethylenedioxy)butyl]naphthalene (42). Cleavage of the silyl protecting group of **41** (511 mg, 1.1 mmol) was accomplished with *n*-Bu_4NF·$3H_2O$ (1.04 g, 3.3 mmol) in DMF (20 mL) at 25 °C by the procedure for formation of **23**. Purification by thick-layer chromatography (silica gel, 2000 μm; 50% ether in *n*-hexane) gave **42** as a yellow oil (314 mg, 80%): MS mol wt 362.1728, calcd 362.1729; IR (neat) 3514, 1622, 1591, 1363, 1067 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.25–7.95 (2 H, m, C_5-H, C_8-H), 7.65–7.25 (2 H, m, C_6-H, H_7-H), 5.75–5.45 (1 H, m, ArC*H*(OP)CH_2), 4.40 (2 H, q, J = 7.1 Hz, ArOC*H*$_2$$CH_3$), 4.03 (4 H, br s, OC*H*$_2$C*H*$_2$O), 3.97, 3.93 (2 × 3 H, 2 s, 2 of ArOC*H*$_3$), 3.70 (1 H, d, J = 7.0 Hz, OH), 2.90–1.90 (2 H, m, ArCH(OP)C*H*$_2$), 1.50 (3 H, s, terminal CH_3), 1.48 (3 H, t, J = 7.2 Hz, ArOCH$_2$C*H*$_3$). Anal. Calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 65.90; H, 7.35.

Preparation of 1,4-Dimethoxy-3-ethoxy-2-[1-oxo-3,3-(ethylenedioxy)butyl]naphthalene (43). Oxidation of the alcohol **42** (150 mg, 0.414 mmol) with PDC (311 mg, 0.828 mmol) in dry CH_2Cl_2 (30 mL) was accomplished by the procedure for formation of **4**. Purification by thick-layer chromatography (silica gel, 2000 μm; 50% ether in *n*-hexane) gave the recovered **42** (65 mg, 43%) and **43** as a yellow oil (69 mg, 46%): MS mol wt 360.1584, calcd 360.1573; IR (neat) 1716, 1621, 1590, 1363, 1069 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.20–7.95 (2 H, m, C_5-H, C_8-H), 7.65–7.25 (2 H, m, C_6-H, C_7-H), 4.11 (2 H, q, J = 7.1 Hz, ArOC*H*$_2$CH$_3$), 3.97 (3 H, s, ArOC*H*$_3$), 3.94 (7 H, br s, ArOC*H*$_3$, OC*H*$_2$C*H*$_2$O), 3.29 (2 H, s, ArCOC*H*$_2$), 1.58 (3 H, s, terminal CH_3), 1.37 (3 H, t, J = 7.1 Hz, ArOCH$_2$C*H*$_3$). Anal. Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.72; H, 6.80.

Treatment of 43 with BF_3·Et_2O. Treatment of **43** (50 mg, 0.139 mmol) with BF_3·Et_2O (0.5 mL, mmol) in dry CH_2Cl_2 (30 mL) was pursued as described for formation of **2**. Purification by thick-layer chromatography (silica gel, 2000 μm; 15% ether in *n*-hexane) gave **39** (11 mg, 29%), **40a** (11 mg, 31%), and **40b** (2.0 mg, 6%).

Preparation of 5,8-Dimethoxy-6,7-benzochromone (1c) and 5,6-Dimethoxy-7,8-benzochromone (45) from 43. Conversion of **43** (192 mg, 0.533 mmol) to the benzochromones **1c** and **45** was accomplished by the two-step procedure for formation of **1a** from **27**. Oxidation by CAN (877 mg, 1.6 mmol) in H_2O (10 mL) at 0 °C, followed by acid treatment with 1 N HCl (7 mL) in THF (14 mL) gave **44** (115 mg, 89%), which was reduced ($NaHSO_3$, concentrated HCl) and dimethylated (MeI, K_2CO_3, acetone, reflux). Purification by thick-layer chromatography (silica gel, 2000 μm; ether) gave **1c** (92 mg, 71%) and **45** as white crystals (36 mg, 28%, mp 129.5–130 °C; ref. mp 130 °C[22]): MS mol wt 270.0899, calcd 270.0892; IR (Nujol) 1669, 1461, 1446, 1375, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.45–8.10 (2 H, m, 2 ortho protons in Ph), 7.75–7.45 (2 H, m, 2 meta protons in Ph), 6.23 (1 H, d, J = 0.4 Hz, C_3-H), 4.07, 3.98 (2 × 3 H, 2 s, 2 of ArOC*H*$_3$), 2.46 (3 H, s, C_2-C*H*$_3$).