NH_4Cl, dried over $MgSO_4$, and concentrated. The residue was chromatographed (silica gel, 7 g; 1:5 CH_2Cl_2–ether) to give 80 mg of crystalline **7f** (79%): mp 110–111 °C (recrystallized from AcOEt–hexane); $[\alpha]^{19}_D$ –56.4° (*c* 2.38, MeOH); ^1H NMR (90 MHz) 1.36 (3 H, d, *J* = 6.7 Hz), 3.31 (1 H, d, *J* = 7.2 Hz), 3.81 (3 H, s), 4.60 (1 H, dd, *J* = 3.2, 7.2 Hz), 4.86 (2 H, br), 5.00 (1 H, dq, *J* = 3.2, 6.7 Hz); IR (KBr) 3450, 3300, 3270, 2230, 1720, 1602, 1432, 1495, 1480, 1335, 1320, 1260, 1138, 1075, 1033, 998, 935, 755. Anal. Calcd for $C_8H_{11}NO_5$: C, 47.76; H, 5.51; N, 6.96. Found: C, 47.56; H, 5.81; N, 6.82.

(4*R*,5*S*)-Methyl 5-[(Carbamoyl)oxy]-4-[(triethylsilyl)oxy]-2-hexynoate (7g). Alcohol **7f** (282 mg, 1.40 mmol) was stirred with imidazole (220 mg, 3.23 mmol) and Et_3SiCl (0.26 mL, 1.55 mmol) in dry DMF (2 mL) at room temperature for 1.5 h and chromatographed directly on silica gel column (15 g; 20:1 → 2:1 hexane–ether) to afford colorless oil **7g** (440 mg, 100%): $[\alpha]^{20}_D$ –47.9° (*c* 1.61, $CHCl_3$); ^1H NMR (90 MHz) 0.48–1.15 (15 H, m), 1.32 (3 H, d, *J* = 6.5 Hz), 3.78 (3 H, s), 4.60 (1 H, d, *J* = 4.0 Hz), 4.87 (1 H, dq, *J* = 4.0, 6.5 Hz), 4.88 (2 H, br); IR (film) 3480, 3370, 3270, 3195, 2950, 2920, 2880, 2340, 1715, 1600, 1456, 1435, 1412, 1385, 1320, 1250, 1155, 1080, 1040, 1005, 972, 955, 890, 810, 750, 730.

(4*R*,5*S*)-Methyl (*E*)-5-[(Carbamoyl)oxy]-4-[(triethylsilyl)oxy]-2-hexenoate (4b). A solution of **7g** (51.5 mg, 0.163 mmol) in MeOH (5 mL) was stirred with 5 mg of 5% Pd on $CaCO_3$ poisoned with lead under H_2 atmosphere (1 atm) at room temperature for 10 min; the reaction was carefully followed by TLC analysis, which indicated the reaction completed within 10 min. The mixture was filtered through Celite, and the concentrated filtrate was chromatographed (silica gel 1 g, 2:1 hexane–ether) to afford **4b** as a colorless oil (50 mg, 97%): $[\alpha]^{18}_D$ +13.7° (*c* 2.89, $CHCl_3$); ^1H NMR (200 MHz) 0.5–0.7 (6 H, m), 0.8–1.1 (9 H, m), 1.23 (3 H, d, *J* = 6.6 Hz), 3.75 (3 H, s) 4.62 (2 H, br), 4.84 (1 H, dq, *J* = 4.4, 6.6 Hz), 5.43 (1 H, ddd, *J* = 1.2, 4.4, 8.5 Hz), 5.87 (1 H, dd, *J* = 1.2, 11.8 Hz), 6.14 (1 H, dd, *J* = 8.5, 11.8 Hz); IR (film) 3470, 3370, 3295, 3195, 2955, 2925, 2880, 1722, 1654, 1601, 1460, 1440, 1410, 1376, 1332, 1235, 1204, 1182, 1146, 1082, 1035, 1005, 820, 750, 730. Anal. Calcd for $C_{14}H_{27}NO_5Si$: C, 52.97; H, 8.57; N, 4.41. Found: C, 53.08; H, 8.51; N, 4.75.

(4*R*,5*R*,6*S*)-5-[(Triethylsilyl)oxy]-4-[(methoxycarbonyl)methyl]-6-methylperhydro-1,3-oxazin-2-one (6). To a stirred suspension of *t*-BuOK (160 mg, 1.43 mmol) in dry THF (35 mL) was added quickly a solution of **4b** (423 mg, 1.33 mmol) in dry THF (15 mL) at 0 °C under Ar atmosphere. After 20 min at 0 °C, 1 mL of saturated aqueous NH_4Cl and 40 mL of AcOEt were added, and the mixture was stirred vigorously at room temperature for 5 min and filtered through Celite. The filtrate was concentrated under reduced pressure to give crude product **6**; its 400-MHz ^1H NMR spectrum did not show any signal derived from the 4*S* epimer. The crude residue was chromatographed on silica gel column (5 g) with 5:1 ether–hexane as eluent to afford pure colorless oil **6** (397 mg, 94%): $[\alpha]^{18}_D$ +35.8° (*c* 1.30, $CHCl_3$); ^1H NMR (400 MHz) 0.67 (6 H, q, *J* = 8.2 Hz), 0.98 (9 H, t, *J* = 8.2 Hz), 1.39 (3 H, d, *J* = 6.6 Hz), 2.37 (1 H, dd, *J* = 10.6, 16.5 Hz), 2.83 (1 H, dd, *J* = 2.5, 16.5 Hz), 3.38 (1 H, t, *J* = 8.5 Hz), 3.58 (1 H, dddd, *J* = 0.4, 2.5, 8.5, 10.6 Hz), 3.74 (3 H, s), 4.16 (1 H, dq, *J* = 8.5, 6.6 Hz), 5.91 (1 H, br); IR (film) 3350, 3260, 3140, 2960, 2925, 2890, 1735, 1720, 1455, 1440, 1412, 1400, 1360, 1330, 1296, 1240, 1200, 1174, 1126, 1078, 1006, 858, 746, 732.

(3*R*,4*R*,5*S*)-3-Benzamido-5-hydroxy-5-hexanolide (15). Carbamate **6** (21 mg, 0.066 mmol) was heated at 60 °C with 0.5 mL of 1 N aqueous NaOH in EtOH (1 mL) for 12 h. The mixture was cooled to 0 °C and small pieces of dry ice were added until the precipitation ceased, followed by the addition of $NaHCO_3$ (30 mg, 0.36 mmol) and a solution of PhCOCl (41 mg, 0.29 mmol) in acetone (0.5 mL). After 12 h at room temperature, concentrated HCl was added until pH of the mixture became ca. 2. Diluted with saturated aqueous NH_4Cl, the mixture was extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated. The residue was chromatographed (silica gel, 2 g; 1:1 hexane–AcOEt) and recrystallized from AcOEt–hexane to give **15** (12 mg, 73%) as colorless needles: mp 152–154 °C; $[\alpha]^{20}_D$ +42° (*c* 0.41, EtOH); ^1H NMR (200 MHz) 1.38 (3 H, d, *J* = 6.6 Hz), 2.63 (1 H, dd, *J* = 4.6, 18.5 Hz), 2.96 (1 H, br d, *J* = 4.2 Hz, OH), 3.17 (1 H, dd, *J* = 9.1, 18.5 Hz), 4.08 (1 H, ddq, *J* = 4.2, 4.9, 6.6 Hz), 4.34 (1 H, dd, *J* = 3.6, 4.9 Hz), 4.88 (1 H, dddd, *J* = 3.6, 4.6, 7.1, 9.1 Hz), 6.93 (1 H, br d, *J* = 7.1 Hz, NH), 7.52 (3 H, m), 7.84 (2 H, m); IR (KBr) 3325, 3050, 3010, 2955, 2920, 2860, 1740, 1720, 1638, 1598, 1575, 1542, 1492, 1455, 1408, 1382, 1370, 1338, 1320, 1284, 1258, 1216, 1187, 1135, 1100, 1086, 1035, 1026, 1004, 964, 922, 850, 692. Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.55; H, 6.28; N, 5.62.

***N*-Benzoylristosamine (2b).** To a stirred solution of **15** (61 mg, 0.24 mmol) in dry THF (10 mL) was added dropwise 1.23 mL of 1 M DIBAL in hexane at –98 °C under Ar atmosphere. After 50 min at the same temperature the reaction was quenched with 1 mL of 5:1 mixture of MeOH–H_2O, and then the cold bath was removed. The mixture was stirred at room temperature for 30 min and filtered through Celite. The filtrate was concentrated and chromatographed on silica gel (5 g) column with 5:1 AcOEt–hexane as eluent to give crystalline **2b** (40 mg, 65%), recrystallized from AcOEt–hexane: mp 132–134 °C; $[\alpha]^{28}_D$ –10° (after 10 min), –24° (after 3 h, constant) (*c* 0.20, EtOH); ^1H NMR (400 MHz, Me_2SO-d_6; 2:1 anomeric mixture of furanose after 1 h) [major anomer] 1.07 (3 H, d, *J* = 6.5 Hz, H6), 1.77 (1 H, ddd, *J* = 2.3, 4.7, 13.4 Hz, H2), 2.31 (1 H, ddd, *J* = 5.3, 9.1, 13.4 Hz, H2), 3.64 (1 H, ddq, *J* = 4.4, 4.9, 6.5 Hz, H5), 3.89 (1 H, dd, *J* = 4.9, 5.3 Hz, H4), 4.40 (1 H, dddd, *J* = 4.7, 5.3, 7.8, 9.1 Hz, H3), 4.69 (1 H, d, *J* = 4.4 Hz, C5-OH), 5.40 (1 H, dt, *J* = 2.3, 5.3, Hz, H1), 6.35 (1 H, d, *J* = 5.3 Hz, Cl-OH), 7.49 (3 H, m), 7.84 (2 H, m), 8.40 (1 H, d, *J* = 7.8 Hz, NH), [minor isomer] 1.09 (3 H, d, *J* = 6.2 Hz, H6), 2.04 (2 H, dd, *J* = 3.7, 7.8 Hz, H2), ~3.68 (1 H, m, H5), 3.68 (1 H, m, H4), 4.57 (1 H, d, *J* = 3.0 Hz, C5-OH), 4.65 (1 H, dq, *J* = 5.3, 7.8 Hz, H3), 5.40 (1 H, m, H1), 6.36 (1 H, d, *J* = 5.3 Hz, C1-OH), 7.49 (3 H, m), 7.84 (2 H, m), 8.56 (1 H, d, *J* = 7.8 Hz, NH); IR (KBr) 3360, 3295, 3075, 2970, 2920, 1635, 1580, 1540, 1492, 1448, 1405, 1320, 1154, 1076, 1062, 1044, 1032, 1020, 995, 935, 918, 876, 860, 820, 802, 700.

Model Studies in the Quassimarin Series: Total Synthesis of De-A-quassimarin

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trans-Decalone **5** has been converted into (±)-de-A-quassimarin (**6**) via a sequence of transformations involving (a) introduction of a latent acetic acid unit into the C(14) position of **13**, (b) construction of the C(8),C(13) epoxymethano ether bridge, (c) elaboration of the trans-diaxial arrangement of hydroxyl groups at C(11) and C(12), and (d) adjustment of the oxidation state at C(7) for eventual δ-lactone formation.

Synthetic studies on quassinoids,[1] bitter principles of simaroubaceous plants, continue to occupy the attention of numerous synthetic organic chemists worldwide.[2] Much of the activity in this area has been due in part to the fact

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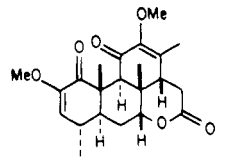
that these natural products possess a wide spectrum of biological properties including in vivo antileukemic, antiviral, antimalarial, antifeedant, and amoebicidal activity.[3] Rapid advances in structural studies on simaroubaceous bitter constituents have given rise to nearly 100 known quassinoids. Early synthetic efforts in the quassinoid area have culminated in total syntheses of quassin (1)[4] and castelanolide (2).[5] The main focus of synthetic activity today is centered around quassimarin (3) and bruceantin (4).



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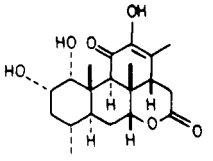

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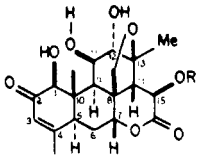
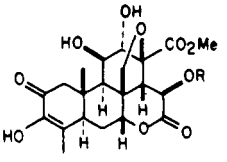
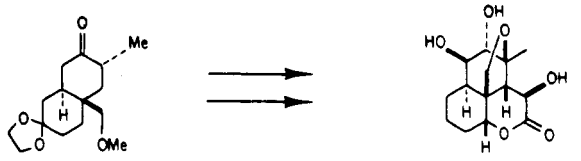


3 R = COC(OAc)(Me)Et



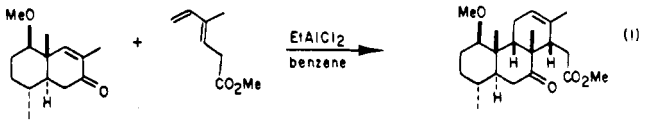
4 R = COCH=C(Me)C_3H_7

Our preliminary investigation into the synthesis of quassimarin concentrated on construction of a BCDE tetracyclic system possessing the C(8),C(13) epoxymethano bridge[6] (steroid numbering) common to many naturally occurring quassinoids. We wish to describe below the details of our early model studies which have resulted in a total synthesis of de-A-quassimarin (6). The synthetic strategy leading to 6 should permit access to quassimarin and bruceantin.



5 6

From the very beginning of our synthetic efforts on quassimarin we realized that elaboration of the C(8),C(13) epoxymethano bridge and the ring D δ-lactone constituted formidable challenges. In addition, our previous work in the quassin area,[4] wherein a Diels–Alder strategy was employed to construct the carbocyclic framework (cf. eq 1),



(1)

suggested starting with a preformed trans-fused BC ring system (cf. decalone 5) so as to avoid potential problems that may arise during the course of inverting the stereocenter at C(9). Compound 5 possesses sufficient functionality for elaboration of the remaining four stereocenters on ring C including the epoxymethano bridge and the ring D δ-lactone.

Decalone 5 is readily available via a three-step sequence from the known octalin 7.[7] Allylic oxidation of 7 employing Collins reagent gives rise to octalone 8 (R = H).

7 8

Treatment of enone 8 successively with lithium diisopropylamide in tetrahydrofuran–hexamethylphosphoramide at −78 °C and methyl iodide affords octalone 8 (R = CH_3) in 65% yield. Reduction (lithium, liquid ammonia) of enone in 8 (R = CH_3) provides in 96% yield decalone 5.

The synthetic strategy for introduction of the C(8),C(13) epoxymethano ether bridge into substrate 5 was, to some extent, guided by a serendipitous observation made some years ago in connection with an attempt to prepare octalone 10 from bromo ketone 9 under standard dehydrobromination conditions.[6] Exposure of bromo ketone 9 to lithium bromide and lithium carbonate in dimethylformamide at 140 °C for 20 min provided less than 1% of the desired octalone 10. Surprisingly, a 90% yield of tricyclic ketone 11 was obtained. After the fact, one need not employ lithium bromide and lithium carbonate. The reaction proceeds in 93% yield when conducted in dimethylformamide at 140 °C for just a few minutes.

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(3) Polnsky, J. In "Chemistry and Biological Activity of the Quassinoids" *The Chemistry and Chemical Taxonomy of the Rutales*; Waterman, P. G., Grundon, M. F., Eds.; Academic: New York, 1983; p 247.

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(6) For a preliminary account of this work, see: Kanai, K.; Zelle, R. E.; Sham, H.-L.; Grieco, P. A.; Callant, P. *J. Org. Chem.* **1984**, *49*, 3867.

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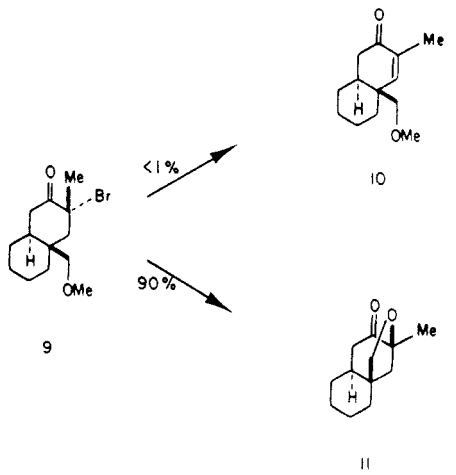
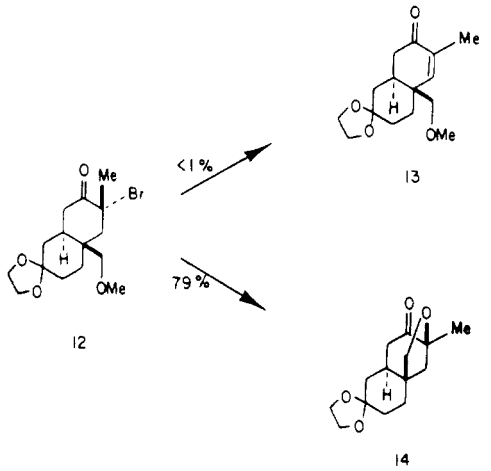
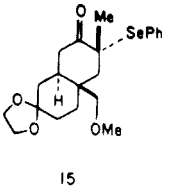


Application of this novel epoxymethano bridging reaction to the case at hand necessitates prior introduction of a suitable two-carbon appendage into the C(14) position of compound **5** presumably through some type of 1,4-addition to octalone **13** or its equivalent. However attempts to prepare **13** from bromo ketone **12** met with no success.



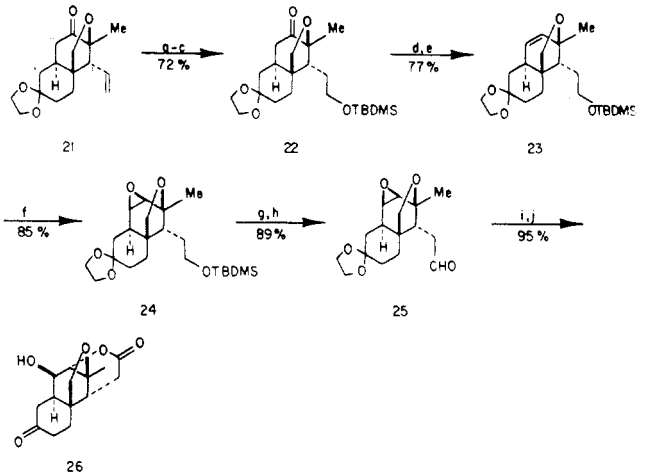
Not unexpectedly bromo ketone **12**, when subjected to dehydrobromination employing the conditions described above, behaved similarly to **9**, giving rise to a 79% yield of **14** as a crystalline compound, mp 97.5–98.5 °C, with less than 1% of **13** being detected.

Enone **13** was successfully prepared by employing selenium-based methodology. Transformation of decalone **5** into its thermodynamic silyl enol ether utilizing the procedure of Miller and McKean[8] followed by selenenylation with benzeneselenenyl chloride in benzene provided decalone **15**. Oxidation of **15** with hdyrogen peroxide in methylene chloride containing pyridine provided crystalline octalone **13**, mp 63.5–64.5 °C.



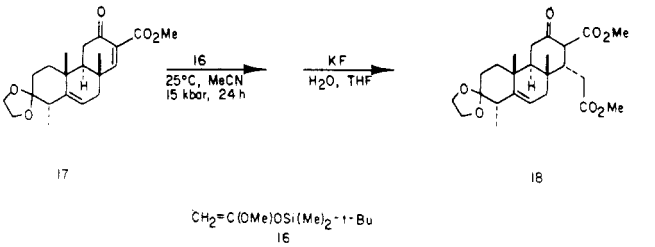
Attempts to add a variety of acetic acid equivalents to enone **13** were uniformly unsuccessful. It is of interest to note that in a recent report by Heathcock,[9] addition of

Scheme I. Synthesis of Tetracyclic Ketone 26[a]

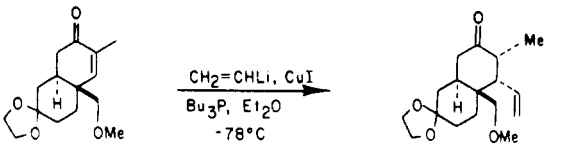


[a] (a) B_2H_6, THF; H_2O_2, NaOH, (b) TBDMSCl, DMAP, Et_3N, CH_2Cl_2; (c) CrO_3·2Py, CH_2Cl_2; (d) $TsNHNH_2$, HCl, THF; (e) excess LDA, THF; (f) MCPBA, CH_2Cl_2; (g) n-Bu_4NF, THF; (h) CrO_3·2Py, CH_2Cl_2; (i) Ag_2O, NaOH, EtOH; (j) TsOH, acetone.

ketene acetal **16** to the "very reactive" Michael acceptor **17** required 15 kbar at 24 h to drive the reaction to completion. After extensive experimentation with octalone



13, we settled on an organocopper reagent[10] derived from equimolar amounts of copper(I) iodide and vinyllithium and 2.6 equiv of tri-*n*-butylphosphine. Conjugate addition proceeded smoothly in ether at −78 °C, giving rise to **19**, mp 98–100 °C, in 95% yield.

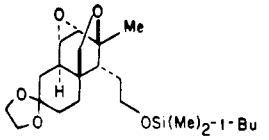


Application of the epoxymethano bridging reaction to bromo ketone **20**, derived from ketone **19** by silyl enol ether formation [$(Me_3Si)_2NH$, Me_3SiI, C_5H_{12}] and bromination [NBS, THF], proceeded efficiently in dimethylformamide at 150 °C (20 min), affording in ca. 75% overall yield from **19** crystalline tricyclic material **21**, mp 117–118 °C.

With the elements of ring E fully in place our efforts were focused on elaboration of the trans-diaxial arrange-

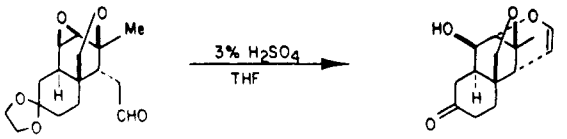
(8) Miller, R. D.; McKean, D. R. *Synthesis* **1979**, 730.
(9) Heathcock, C. H.; Mahaim, C.; Schlecht, M. F.; Utawanit, T. *J. Org. Chem.* **1984**, *49*, 3264.
(10) Suzuki, M.; Suzuki, T.; Kawagishi, T.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1247.

ment of hydroxyl groups at C(11) and C(12) (Scheme I). Prior to manipulation of the carbonyl at C(12), the terminal vinyl group in **21** was subjected to hydroboration. The resultant primary alcohol was protected as a tert-butyldimethylsilyl ether. Note that during the hydroboration the carbonyl at C(12) is reduced, thus necessitating an oxidation after silylation. The tosylhydrazone of ketone **22** upon treatment with lithium diisopropylamide in tetrahydrofuran provided olefin **23**, which offers several avenues for incorporation of the trans-diaxial hydroxyl groups. In view of the fact that the C(14) α-oriented siloxyethyl group blocks the exo (α) face of the C(11),C(12) double bond, it was anticipated that epoxidation of **23** would give rise to predominantly, if not exclusively, β-epoxide **24**. Epoxidation with *m*-chloroperbenzoic acid in methylene chloride gave rise to the desired epoxide **24** in 85% isolated yield. In addition approximately 10% of the "unwanted" α-epoxide **27** was isolated. In principle acid-catalyzed opening of epoxide **27** might well give rise to the desired arrangement of hydroxyl groups (vide infra).



27

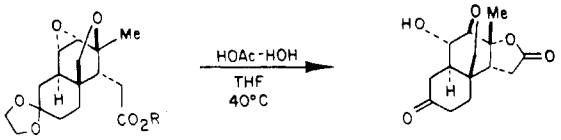
In advance of manipulating the epoxide functionality in compound **24**, it was more advantageous to correct the oxidation state at C(16). Toward this end, compound **24** was exposed to fluoride ion in tetrahydrofuran followed by oxidation (Collins) of the resultant primary alcohol giving rise to crystalline aldehyde **25**, mp 103–104 °C. Treatment of **25** with dilute sulfuric acid in tetrahydrofuran results in enol ether formation with establishment of the desired stereochemistry at C(12) and loss of the ketal at C(5). The formation of **28** proceeded in 82% yield;



28

however, we were never able to add the elements of water or methanol to the enol ether. To circumvent this problem, aldehyde **25** was oxidized to the corresponding acid, which upon exposure to *p*-toluenesulfonic acid in acetone gave rise to **26** in 95% overall yield.

In principle the acid or ester **29** derived from the "unwanted" α-epoxide **27** could give way to tetracyclic lactone **26** upon acid treatment. However treatment of **29** (R = CH_3) with acetic acid–water–tetrahydrofuran, 3:1:1, at 40 °C provided in >90% yield the rearranged γ-lactone **30**. After the fact this result is not surprising since the C(13) oxygen atom is very nicely set up to migrate upon protonation and ring opening of the epoxide unit.



29 30

With all the stereocenters in ring C established, (cf. compound **26**) the task at hand centered on elaboration of the ring D δ-lactone which required incorporation of an oxygen substituent into the C(7) position of compound **26**. Protection of the C(11) hdyroxyl in compound **26** as is its methoxymethyl ether using standard conditions provided **32** in 75–80% yield. The preparation of **32** was accom-

31 32

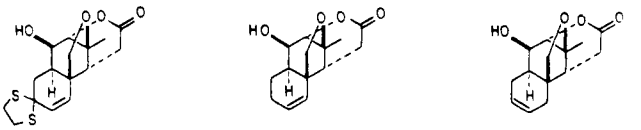
panied by formation of ca. 15–20% of a mixture of enol ethers of which methoxymethyl enol ether **31** predominated. The formation of **31** was of no real consequence since exposure of the crude residue containing **31** and **32** to 1 N hydrochloric acid at ambient temperature for 40 min gave rise to a 95% of **32**, mp 152–153 °C.

The Saegusa method[11] for converting a ketone into an α,β-unsaturated ketone appeared to be the procedure of choice for incorporating a double bond into the C(6),C(7) position of **32**. Silyl enol ether formation using a modification of the Miller[8] procedure followed by treatment with palladium acetate in acetonitrile afforded in 95% yield a mixture of enones **33**, mp 174.5–176.0 °C, and **34** in a ratio of 2.5:1. Of critical importance to success was

33 34

the ratio of silyl enol ethers produced in the initial step. The solvent of choice for this transformation was carbon tetrachloride–chloroform–pentane, 1:1:2.[14]

Transformation of tetracyclic ketone **33** into **6** requires (1) removal of the C(5) carbonyl, (2) introduction of the δ-lactone unit via a halolactonization–dehalogenation sequence, and (3) hydroxylation of the δ-lactone. Toward this end, a solution of **33** in methylene chloride was treated with ethanedithiol and boron trifluoride etherate, which generated a near quantitative yield of crystalline dithioketal **35**, mp 282–284 °C. During the course of the ke-

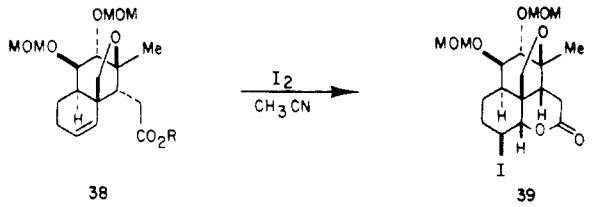


35 36 37

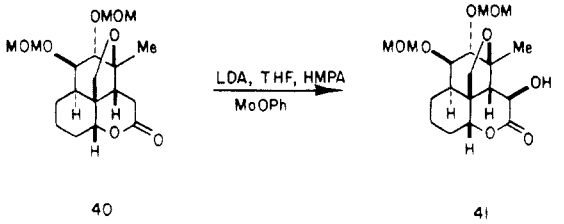
talization reaction the C(11) methoxymethyl ether is cleaved. Desulfurization of **35** in absolute ethanol with W-2 Raney nickel provided in 74% yield olefin **36**, mp 185–186 °C, along with 12% of the isomerized olefin **37**, which could readily be separated on silica gel. Transformation of **37** into **38** (R = H) was best carried out via a three-step sequence involving hydrolysis of the lactone, conversion of the resultant dihydroxy carboxylic acid into ester **38** (R = MOM), and hydrolysis of the ester. The overall yield for this process was 90%. Failure to employ excess chloromethyl methyl ether gives very low yields of **38** (R = H) due to the fact that alkylation of the two hindered hydroxyl groups is slow relative to the carboxyl unit. Subjection of **38** (R = H) to iololactonization proceeded smoothly in 82% yield, giving rise to iodo lactone **39**. Deiodination (Bu_3SnH, AIBN, benzene, reflux) pro-

(11) Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011.

vided **40**, mp 113–114 °C, in 97% yield.



Hydroxylation[12] of the lithium enolate derived from lactone **40** provided a 52% (91% based on recovered starting lactone) yield of crystalline lactone **41**. Cleavage



of the protecting groups in **41** employing dimethyl sulfide and boron trifluoride[13] etherate in methylene chloride afforded de-A-quassimarin (**6**), mp 230–233 °C, in 82% isolated yield.

The strategy employed above to synthesize de-A-quassimarin, which features a novel method for the construction of the C(8),C(13) epoxymethano ether bridge, should be amenable to quassimarin and related quassinoids. In particular, intermediate tetracyclic ketone **32** should permit via a ring A annulation sequence access to quassimarin. Efforts along these lines are in progress.

Experimental Section

Melting points were determined on a Fisher-Johns hot-stage melting point apparatus and are uncorrected. Infrared spectra (IR) were determined on a Perkin-Elmer 298 grating infrared spectrometer, and nuclear magnetic resonance (NMR) spectra were recorded at 90 (Varian EM-390), 300 (Varian XL-300), or 360 MHz (Nicolet NT-360) as indicated. Chemical shifts are reported in parts per million (δ) relative to Me_4Si (δ = 0.00) as an internal standard. High-resolution mass spectra were recorded on a Kratos MS-80 spectrometer.

All sovlents are reagent grade unless otherwise stated. "Dry" solvents were dried immediately before use. Tetrahydrofuran was distilled from sodium benzophenone ketyl. Dimethyl sulfoxide (Me_2SO), hexamethylphosphoramide (HMPA), pyridine, and diisopropylamine were distilled from calcium hydride. Methylene chloride was dried by passing through a column of alumina (Woelm, basic activity I) and was stored over molecular sieves (type 3A). Chromium trioxide was dried over phosphorus pentoxide. Thin-layer chromatography (TLC) was carried out on Analtech (Uniplate) glass plates precoated with silica gel GF (250 μm). Column chromatographic separations were performed on silica gel (Merck silica gel 60, 70–230 mesh ASTM).

(±)-4′,4′a,5′,6′-Tetrahydro-4′a-(methoxymethyl)spiro[1,3-dioxolane-2,2′(1′*H*)-naphthalen)-7′(3′*H*)-one (8, R = H). To a solution of dry chromium trioxide (201.5 g, 2.02 mol) in 3.0 L of dry methylene chloride containing 326 mL of dry pyridine under argon was added 500 g of Celite followed by the dropwise addition of olefin **7** (40.0 g, 0.17 mmol) in 144 mL of dry methylene chloride. The mixture was stirred at 25 °C for 36 h. The reaction was quenched by the addition of 600 g of solid sodium bisulfate. The reaction was filtered through a pad of silica gel–magnesium sulfate. The solvent was removed in vacuo, affording 40.1 g of a crude enone **8** (R = H), which upon crystallization from diisopropyl ether provided 20.7 g of enone **8** (R = H). The mother liquor was concentrated under reduced pressure. The residue was chromatographed on 500 g of silica gel. Elution with hexane–ether (2:1) gave 8.3 g of starting material (21%) and 3.7 g of additional enone **8** (R = H) as a crystalline material. There was thus obtained 24.4 g (58%) of pure enone **8** (R = H): R_f 0.30 (hexane–ether, 1:1); IR ($CHCl_3$) 2995, 2960, 2935, 2890, 2831, 1654, 1617, 1595, 1473, 1445, 1416, 1380, 1350, 1333, 1317, 1274, 1244, 1195, 1172, 1107, 1030, 1020, 976, 950, 882, 830, 700, 657 cm^{-1}; NMR (90 MHz, CCl_4) δ 1.16–2.70 (m, 10 H), 3.33 (s, 3 H)8 3.43 (s, 2 H), 3.88 (s, 4 H), 5.66 (s, 1 H). An analytical sample was obtained by recrystallization from ether–hexane, mp 86–87 °C. Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.79; H, 7.91.

***trans*-(±)-4′,4′a,5′,6′-Tetrahydro-4′a-(methoxymethyl)-6′-methylspiro[1,3-dioxolane-2,2′(1′*H*)-naphthalen]-7′(3′*H*)-one (8, R = CH_3).** To a stirred solution of lithium diisopropylamide (88 mmol), prepared from 15.4 mL of diisopropylamine and 56.4 mL of *n*-butyllithium (1.6 M in hexane) in 100 mL of anhydrous tetrahydrofuran at −78 °C under argon was added a solution of 18.5 g (73.4 mmol) of enone **8** (R = H) in 150 mL of dry tetrahydrofuran over a 30-min period. After the addition was complete, the reaction mixture was stirred for 30 min and was treated with 22.4 mL (0.29 mol) of methyl iodide. Stirring was continued at −78 °C for 0.5 h and at 0 °C for 1 h. The reaction mixture was quenched with saturated ammonium chloride solution. The product was isolated by extraction with ether. The combined ethereal extracts were washed with brine and dried over anhydrous magnesium sulfate. The solvent was removed in vacuo. The residue was chromatographed on 700 g of silica gel. Elution with hexane–ether (1:1) gave 12.7 g (65%) of enone **8** (R = CH_3) R_f 0.38 (hexane–ether, 1:3); IR ($CHCl_3$) 3040, 3010, 2985, 2949, 2881, 1665, 1623, 1474, 1454, 1420, 1376, 1359, 1334, 1314, 1218, 1185, 1090, 1064, 1035, 1017, 998, 965, 949, 883, 840, 830 cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 1.08 (d, 3 H, J = 7 Hz), 1.20–1.75 (m, 9 H), 3.36 (s, 3 H), 3.46 (s, 2 H), 3.96 (s, 4 H), 5.83 (s, 1 H)] and 0.88 g (4.7%) of starting material.

(4′aα,6′β,8′aβ)-(±)-Hexahydro-4′a-(methoxymethyl)-6′-methylspiro[1,3-dioxolane-2,2′(1′*H*)-naphthalen]-7′(3′*H*)-one (5). To a solution of lithium (841 mg, 0.12 mol) in 300 mL of anhydrous ammonia at −78 °C under argon was added a solution of 5.35 g (20.2 mmol) of enone **8** (R = CH_3) in 45 mL of dry tetrahedronfuran containing 2 mL of dry *tert*-butyl alcohol. After the addition was complete, the reaction mixture was stirred for 20 min. The reaction was quenched with 1,3-butadiene followed by the addition of ammonium chloride. After evaporation of the liquid ammonia, the product was isolated by extraction with ether. The combined ether extracts were washed with brine and dried over anhydrous magnesium sulfate. The solvent was removed in vacuo. The residue was chromatographed on 150 g of silica gel. Elution with hexane–ether (2:1) gave 5.19 g (96%) of ketone **5** as a crystalline compound: R_f 0.42 (hexane–ether, 1:2); IR ($CHCl_3$) 3009, 2935, 2891, 2815, 1710, 1480, 1460, 1448, 1378, 1370, 1095, 1058, 983, 945 cm^{-1}; NMR (90 MHz, CCl_4) δ 0.98 (d, 3 H, J = 6 Hz), 1.06–2.60 (m, 12 H), 3.36 (s, 3 H), 3.58 (d, 2 H, J = 3 Hz), 3.86 (s, 4 H). An analytical sample was obtained by recrystallization from hexane, mp 71–72 °C. Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 67.03; H, 8.98.

***trans*-(±)-4′,4′a,8′,8′a-Tetrahydro-4′a-(methoxymethyl)-6′-methylspiro[1,3-dioxolane-2,2′(1′*H*)-naphthalen]-7′-(3′*H*)-one (13).** To a solution of ketone **5** (985 mg, 3.67 mmol) in 55 mL of dry pentane at −23 °C under argon was added 0.93 mL (4.40 mmol) of hexamethyldisilazane. After the mixture was stirred for 10 min, 0.57 mL (4.04 mmol) of trimethylsilyl iodide was added. The reaction mixture was warmed to room temperature. After being stirred for 2 h, the reaction was quenched with an ice-cooled saturated sodium bicarbonate solution and was extracted with hexane. The combined organic extracts were

(12) Vedejs, E.; Engler, D. A.; Telschow, J. E. *J. Org. Chem.* **1978**, *43*, 188.

(13) Kieczykowski, G. R.; Schlessinger, R. H. *J. Am. Chem. Soc.* **1978**, *100*, 1938. Kuji, K.; Kawabata, T.; Fujita, E. *Chem. Pharm. Bull.* **1980**, *28*, 3662.

(14) Efforts to improve the ratio of silyl enol ethers concentrated on modifying the Miller procedure[8] since attempts to employ lithium diisopropylamide in tetrahydrofuran followed by trapping with trimethylsilyl chloride led to disappointingly low yields of product. Numerous solvent combinations were examined with Me_3Si–HMDS in an attempt to increase the formation of the desired silyl enol ether. Use of methylene chloride–pentane (1:5) (−20 → 0 °C, 2 h) provided the desired enol ether in a ratio of 1.8:1 in 94% yield. Chloroform–pentane (1:1) (−20 → 0 °C, 3.5 h) afforded in 95% yield the desired enol ether in a ratio of 1.8:1. Use of methylene chloride (−20 → 0 °C, 1.5 h) improved the ratio to 2:1; however, the yield was only 44%.

washed with brine and dried over sodium sulfate. The solvent was removed in vacuo. The oily residue was chromatographed on 28 g of silica gel. Elution with hexane–ether (3:1) gave 1.22 g (98%) of the corresponding thermodynamic trimethylsilyl enol ether as a colorless oil [R_f 0.68 (hexane–ether, 1:1); IR (CCl_4) 2943, 2881, 2870, 2828, 2800, 1460, 1445, 1288, 1264, 1254, 1181, 1093, 985, 845 cm^{-1}; NMR (60 MHz, CCl_4) δ 0.13 (s, 9 H), 1.03–2.10 (m, 11 H), 1.5 (s, 3 H), 3.06–3.40 (m, 2 H), 3.27 (s, 3 H), 3.83 (s, 4 H)], which was used directly in the next reaction.

To a solution of the above trimethylsilyl enol ether (1.22 g, 3.6 mmol) in 15 mL of dry benzene at 0 °C under argon was added a solution of 688 mg (3.6 mmol) of benzeneselenenyl chloride in 30 mL of dry benzene. The reaction mixture was warmed to room temperature over 20 min. The solvent was removed in vacuo. The residue was dissolved in 25 mL of methylene chloride containing 0.8 mL of pyridine and was cooled to 0 °C. Hydrogen peroxide (3.6 mL of a 30% aqueous solution) was added dropwise. After being stirred for 30 min, the reaction mixture was quenched with ice-cooled saturated sodium bicarbonate solution. The product was extracted with ether. The organic extracts were washed with brine and dried over anhydrous magnesium sulfate. The solvent was removed in vacuo. The residue was chromatographed on 30 g of silica gel. Elution with hexane–ether (1:1) gave 915 mg (95%) of enone **13**: R_f 0.38 (hexane–ether, 1:2); IR ($CHCl_3$) 2920, 2872, 1665, 1445, 1356, 1182, 1070, 972, 940, 892, 814 cm^{-1}; NMR (90 MHz, CCl_4) δ 0.90–2.47 (m, 9 H), 1.72 (s, 3 H), 3.28 (s, 3 H), 3.52 (d, 2 H, J = 4.5 Hz), 3.86 (s, 4 H), 6.46 (s, 1 H). An analytical sample was obtained by recrystallization from hexane mp 63.5–64.5°C. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.32. Found: C, 67.97; H, 8.34.

(4′aα,5′β,6′β,8′aβ)-(±)-Hexahydro-4′a-(methoxymethyl)-6′-methyl-5′-vinylspiro[1,3-dioxolane-2,2′(1′*H*)-naphthalen]-7′(3′*H*)-one (19). To a suspension of cuprous iodide (6.99 g, 36.7 mmol) in 110 mL of dry ether under argon was added 23.8 mL (95.5 mmol) of tri-*n*-butylphosphine. After being stirred for 10 min, the suspension became a clear solution. To this solution at −78 °C was added 32.8 mL (36.7 mmol) of vinyllithium (1.1 M in ether). After 20 min, a solution of enone **13** (1.95 g, 7.34 mmol) in 6 mL of dry ether was added to the vinyl copper reagent. The reaction mixture was stirred at −78 °C for 1 h, at −23 °C for 30 min, and at 0 °C for 10 min. The reaction was quenched with an ice-cooled saturated ammonium chloride solution. The product was extracted with ether. The ethereal extracts were washed with brine and dried over anhydrous magnesium sulfate. The solvent was removed in vacuo. The residue was chromatographed on 70 g of silica gel. Elution with hexane–ether (2:3) gave 2.06 g (95%) of bicyclic ketone **19**: mp 98–100 °C; R_f 0.32 (hexane–ether, 1:2); IR ($CHCl_3$) 2929, 2885, 2808, 1708, 1456, 1443, 1414, 1360, 1261, 1205, 1174, 1086, 1060, 975, 942 cm^{-1}; NMR (220 MHz, $CDCl_3$) δ 0.90 (d, 2 H, J = 9 Hz), 1.27–1.91 (m, 7 H), 2.1–1.4 (m, 3 H), 2.73–2.95 (m, 2 H), 3.41 (s, 3 H), 3.70 (d, 1 H, J = 10 Hz), 3.82 (d, 1 H, J = 10 Hz), 3.90 (s, 4 H), 5.0–5.5 (m, 3 H). Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.39; H, 8.99.

(3′α,5′aα,9′aα,10′*S)-(±)-Tetrahydro-3′-methyl-10′-vinylspiro[1,3-dioxolane-2,7′(3′*H*)-[1*H*-3,9a]methano[2]benzoxepin]-4′(5′*H*)-one (21).** To a solution of ketone **19** (5.0 g, 0.017 mol) in 340 mL of dry pentane at −23 °C under argon was added 7.17 mL (0.034 mol) of hexamethyldisilazane. After the mixture was stirred for 10 min, 4.16 mL (0.031 mol) of trimethylsilyl iodide was added dropwise at −23 °C. The reaction mixture was warmed to room temperature and stirred for 4 h. The reaction was quenched with an ice-cooled saturated sodium bicarbonate solution and was extracted with hexane. The organic extracts were washed with brine and dried over anhydrous sodium sulfate. The solvent was removed in vacuo, leaving 6.2 g (100%) of the corresponding thermodynamic trimethylsilyl enol ether as a colorless liquid [R_f 0.68 (hexane–ether, 1:2); NMR (90 MHz, CCl_4) δ 0.16 (s, 9 H)8 0.83–2.00 (m, 9 H), 1.5 (s, 3 H), 2.65 (d, 1 H, J = 9 Hz), 3.30 (s, 3 H), 3.10–3.53 (dd, 2 H), 3.84 (s, 4 H), 4.80–5.73 (m, 3 H, CH=CH_2)] a portion of which was used directly in the next reaction.

To a solution of the above silyl enol ether (2.18 g, 5.94 mmol) in 62 mL of dry tetrahydrofuran at −23 °C under argon was added 1.1 g (5.94 mmol) of *N*-bromosuccinimide. After the reaction mixture was stirred at −23 °C for 15 min, the temperature was warmed to 0 °C over 15 min. The reaction was quenched with an ice-cooled saturated sodium bicarbonate solution. The product was isolated by extraction with ether. The organic extracts were washed with brine and dried over magnesium sulfate. The solvent was removed in vacuo, leaving 2.20 g of crude α-bromo ketone **20**, which was dissolved in 40 mL of dry dimethylformamide. The reaction mixture was heated at 150 °C for 20 min. After the mixture was cooled to 25 °C, the reaction was quenched with a saturated sodium bicarbonate solution and was extracted with ether. The combined ethereal extracts were washed with brine and dried over magnesium sulfate. The solvent was removed in vacuo. The residue was chromatographed on 55 g of silica gel. Elution with hexane–ether (1:1) gave 1.23 g (75% overall yield) of tricyclic ketone **21** as a crystalline solid: R_f 0.45 (hexane–ether, 1:2); IR ($CHCl_3$) 2980, 2929, 2880, 1745, 1449, 1381, 1370, 1289, 1179, 1144, 1068, 1016, 835 cm^{-1}; NMR (90 MHz, CCl_4) δ 1.12 (s, 3 H), 1.28–2.41 (m, 10 H), 3.63 (d, 1 H, J = 8 Hz), 3.83 (s, 4 H), 4.30 (d, 1 H, J = 8 Hz), 5.00–5.70 (m, 3 H). An analytical sample was prepared by recrystallization from hexane, mp 117–118 °C. Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.99. Found: C, 69.09; H, 7.95.

(3′α,5′aα,9′aα,10′*S)-(±)-Tetrahydro-10′-[2-(*tert*-butyldimethylsiloxy)ethyl]-3′-methylspiro[1,3-dioxolane-2,7′-(3′*H*)-[1*H*-3,9a]methano[2]benzoxepin]-4′(5′*H*)-one (22).** To a solution of ketone **21** (4.30 g, 15.5 mmol) in 100 mL of dry tetrahydrofuran at 0 °C under argon was added dropwise over 40 min 69 mL (69 mmol) of a 1.0 M solution of borane in tetrahydrofuran. After addition was complete, stirring was continued at 0 °C for 6 h and at room temperature for 20 h. The reaction was quenched at 0 °C by the addition of 26 mL of water, followed by 26 mL of a 3 N aqueous sodium hydroxide solution and 26 mL of 30% hydrogen peroxide. After an additional 20 h at ambient temperature, the organic layer was decanted, and the remaining aqueous layer was washed with ethyl acetate. The combined organic layers were washed with 10% aqueous sodium thiosulfate and brine. The organic layer was dried over anhydrous magnesium sulfate. Evaporation of the solvent in vacuo gave 5.18 g of the crude diol, which was used immediately in the next reaction.

To a solution of the above crude diol in 85 mL of methylene chloride was added triethylamine (2.58 mL, 18.5 mmol), 4-(dimethylamino)pyridine (75 mg, 0.61 mmol), and dimethyl-*tert*-butylsilyl chloride (2.56 g, 17.0 mmol) at room temperature. After 48 h, the reaction mixture was taken up in ethyl acetate and washed with water, saturated aqueous ammonium chloride, and brine. The organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent in vacuo gave a crude monosilylated alcohol, which was used immediately in the next reaction.

To a flask equipped with a mechanical stirrer containing dry methylene chloride (550 mL) and dry pyridine (25.0 mL, 309 mmol) cooled to 0 °C was added portionwise 15.5 g (155 mmol) of chromium trioxide. After 1 h, 80 g of Celite was added, the reaction mixture was warmed to room temperature, and stirring was continued for 1 h. A solution of the above crude alcohol in 50 mL of methylene chloride was added to the vigorously stirred reaction vessel cooled to 0 °C. The reaction mixture was stirred at 0 °C for 30 min and was treated with 46 g of sodium bisulfate and 600 mL of ether. After being stirred for an additional 10 min at room temperature, the reaction mixture was filtered through a pad of silica gel–magnesium sulfate–Celite. Evaporation of the solvent in vacuo gave 7.70 g of the crude product, which was purified on 200 g of silica gel. Elution with hexane–ethyl acetate (4:1) gave 4.57 g (72% overall yield from ketone **21**) of pure **22**: R_f 0.57 (hexane–ether, 1:2); IR ($CHCl_3$) 2940, 2920, 2865, 2842, 1715, 1440, 1370, 1355, 1249, 1169, 1115, 1091, 1059, 1005, 940, 900, 825 cm^{-1}; NMR (90 MHz, CCl_4) δ 0.03 (s, 6 H), 0.86 (s, 9 H), 1.18 (s, 3 H), 1.23–2.20 (m, 12 H), 3.60 (m, 3 H), 3.83 (s, 4 H), 4.25 (d, 1 H, J = 8 Hz). Anal. Calcd for $C_{22}H_{38}O_5Si$; C, 64.35; H, 9.33. Found: C, 64.24; H, 9.39.

(3′α,5′aα,9′aα,10′*S)-(±)-*tert*-Butyldimethyl[2-(5′a,6′,8′,9′-tetrahydro-3′-methylspiro[1,3-dioxolane-2,7′-(3′*H*)-[1*H*-3,9a]methano[2]benzoxepin]-10′-yl)ethoxy]silane (23).** To a solution of ketone **22** (2.36 g, 5.72 mmol) in 45 mL of dry tetrahydrofuran was added 2.16 g (11.6 mmol) of *p*-toluenesulfonylhydrazine and 0.21 mL of concentrated hydrochloric acid. The reaction was stirred at room temperature for

1.5 h. Removal of the solvent in vacuo provided the corresponding hydrazone, which was used directly in the next reaction.

To a stirred solution of lithium diisopropylamide (63 mmol) [prepared from 40.3 mL of *n*-butyllithium (1.56 M in hexane) and 9.6 mL of dry diisopropylamine in 100 mL of dry tetrahydrofuran at −78°C under argon] was added a solution of the above hydrazone in 30 mL of dry tetrahydrofuran. The reaction mixture was stirred at −78 °C for 30 min and at 25 °C for 2 h. The mixture was quenched with saturated ammonium chloride solution. The product was isolated by extraction with ether. The ethereal extracts were washed with brine and dried over magnesium sulfate. The solvent was removed in vacuo. The residue was chromatographed on 80 g of silica gel. Elution with hexane–ether (1:1) gave 1.74 g (77% overall yield) of olefin **23**: R_f 0.64 (hexane–ether, 1:2); IR ($CHCl_3$) 2980, 2940, 2920, 2864, 2840, 1670, 1455, 1439, 1370, 1244, 1154, 1078, 999, 938, 825 cm^{-1}; NMR (90 MHz, CCl_4) δ 0.03 (s, 6 H), 0.89 (s, 9 H), 1.18 (s, 3 H), 1.10–2.04 (m, 9 H), 2.43 (m, 1 H), 3.28–3.93 (m, 4 H), 3.90 (s, 3 H), 5.32 (s, 2 H). Anal. Calcd for $C_{22}H_{38}O_4Si$; C, 66.96; H, 9.71. Found: C, 67.21; H, 9.86.

(1′aα,2′α,4′aα,8′aα,8′bα,9′*R*)-(±)-*tert*-Butyl[2-(hexahydro-2′-methylspiro[1,3-dioxolane-2,7′(2′*H*)-[4*H*-2,4a]methanooxireno[*d*][2]benzoxepin]-9′-yl)ethoxy]dimethylsilane (24).** To a solution of olefin **23** (1.74 g, 4.41 mmol) in 182 mL of dry methylene chloride was added 5.98 g (34 mmol) of *m*-chloroperbenzoic acid. After being stirred at room temperature for 24 h, the reaction was quenched with 1 N sodium hydroxide solution. The product was extracted with methylene chloride and ether. The combined organic extracts were washed with brine and dried over magnesium sulfate. The solvent was removed in vacuo. The residue was chromatographed on 80 g of silica gel. Elution with hexane–ether (1:1) gave 181 mg (10%) of α-epoxide **27** [R_f 0.50 (hexane–ether, 1:2); NMR (220 MHz, $CDCl_3$) δ 0.06 (s, 6 H), 0.90 (s, 9 H), 1.45 (s, 3 H), 1.27–1.91 (m, 9 H), 2.33 (dd, 1 H, J = 5 Hz and J = 12.5 Hz), 2.68 (d, 1 H, J = 4 Hz), 2.90 (d, 1 H, J = 4 Hz), 3.53 (m, 3 H), 3.97 (s, 4 H), 4.09 (d, 1 H, J = 10 Hz)] and 1.54 g (85%) of desired β-epoxide **24** as an oil: R_f 0.30 (hexane–ether, 1:2); IR (CCl_4) 2944, 2920, 2860, 1443, 1372, 1250, 1189, 1138, 1080, 1020, 940, 900, 873, 832 cm^{-1}; NMR (90 MHz, CCl_4) δ 0.04 (s, 6 H), 0.90 (s, 9 H), 1.37 (s, 3 H), 1.23–2.03 (m, 10 H), 2.70 (d, 1 H, J = 3.5 Hz), 2.83 (dd, 1 H, J = 3.0 Hz and J = 3.5 Hz), 3.17 (d, 1 H, J = 8 Hz), 3.60 (m, 2 H), 3.88 (s, 4 H), 3.93 (d, 1 H, J = 8 Hz). Anal. Calcd for $C_{22}H_{38}O_5Si$; C, 64.35; H, 9.33. Found: C, 64.07; H, 9.43.

(1′aα,2′α,4′aα,8′aα,8′bα,9′*R*)-(±)-(Hexahydro-2′-methylspiro[1,3-dioxolane-2,7′(2′*H*)-[4*H*-2,4a]methanooxireno[*d*]-benzoxepin]-9′-yl)acetaldehyde (25).** To a solution of epoxide **14** (1.75 g, 4.25 mmol) in 60 mL of dry tetrahydrofuran was added 4.02 g (12.8 mmol) of tetra-*n*-butylammonium fluoride (1 M in THF). After the mixture was stirred at room temperature under argon for 30 min, the solvent was removed in vacuo. The residue was chromatographed on 45 g of silica gel. Elution with ethyl acetate gave 1.27 g (100%) of the corresponding epoxy alcohol [R_f 0.24 (hexane–ether, 1:3); IR ($CHCl_3$) 3610, 3450, 2925, 2867, 1445, 1376, 1355, 1292, 1240, 1135, 1078, 1015, 942, 900, 870 cm^{-1}; NMR (90 MHz, CCl_4) δ 1.17–1.80 (m, 10 H), 1.40 (s, 3 H), 2.23 (s, 1 H, OH), 2.75 (d, 1 H, J = 3.5 Hz), 2.87 (dd, 1 H, J = 3.5 Hz and J = 2.5 Hz), 3.18 (d, 1 H, J = 8 Hz), 3.57 (m, 2 H), 3.90 (s, 4 H), 3.97 (d, 1 H, J = 8 Hz)], which was used directly in the next reaction.

To a solution of dry chromium trioxide (8 g, 0.08 mol) in 200 mL of dry methylene chloride containing 12.9 mL (0.16 mol) of pyridine under argon was added 20 g of Celite 545 followed by the dropwise addition of the above epoxy alcohol (1.27 g, 4.25 mmol) in 30 mL of dry methylene chloride. The reaction mixture was stirred at room temperature for 15 min and was quenched by the addition of 20 g of solid sodium bisulfate. The reaction was filtered over a pad of silica gel–magnesium sulfate. After the solvent was removed in vacuo, the residue was chromatographed on 40 g of silica gel. Elution with ether gave 1.13 g (89%) of epoxy aldehyde **25**: R_f 0.58 (ethyl acetate); IR (CCl_4) 2945, 2924, 2865, 2810, 2710, 1730, 1450, 1380, 1300, 1248, 1210, 1190, 1170, 1140, 1082, 1025, 945, 905, 878 cm^{-1}; NMR (90 MHz, CCl_4) δ 1.30 (s, 3 H), 1.25–1.80 (m, 7 H), 1.97 (t, 1 H, J = 6 Hz), 2.33 (d, 2 H, J = 6 Hz), 2.70 (d, 1 H, J = 4 Hz), 2.85 (dd, 1 H, J = 4 Hz and J = 2 Hz), 3.25 (d, 1 H, J = 8 Hz), 3.88 (s, 4 H), 3.98 (d, 1 H, J = 8 Hz), 9.74 (s, 1 H). An analytical sample was obtained by recrystallization from hexane–ether, mp 103–104 °C. Anal. Calcd for $C_{16}H_{22}O_5$: C, 65.29; H, 7.53. Found: C, 65.08; H, 7.70.

(1α,2α,6α,6aα,10aβ,13*S*)-(±)-Octahydro-1-hydroxy-13-methyl-6a,2,6-(methanoxymetheno)-2*H*-3-benzoxocine-4,9-(1*H*)-dione (26).** To a solution of aldehyde **25** (1.13 g, 3.8 mmol) in 50 mL of 95% ethanol and 25 mL of water was added 2.61 g (1.12 mmol) of silver(I) oxide, followed by the addition of 11.4 mL of a 1 M sodium hydroxide solution. After the mixture was stirred at room temperature for 10 min, the solid was filtered. The solvent was removed in vacuo. The residue was acidified by the addition of 0.5 N hydrochloric acid and was extracted with ethyl acetate. The organic extracts were washed with brine and dried over anhydrous magnesium sulfate. The solvent was removed in vacuo, affording 1.1 g of the crude epoxy acid, which was used directly in the next reaction.

To a solution of the above epoxy acid (1.1 g, 3.7 mmol) in 93 mL of acetone was added 264 mg (1.54 mmol) of *p*-toluenesulfonic acid. After the reaction was stirred for 7.5 h at room temperature, the reaction was quenched with a saturated sodium bicarbonate solution. The product was extracted with ethyl acetate. The organic extracts were washed with water and dried over magnesium sulfate. After the solvent was removed in vacuo, the residue was chromatographed on 35 g of silica gel. Elution with ethyl acetate gave 959 mg (95%) of pure lactone **26** as a crystalline solid: mp 187–188 °C; R_f 0.32 (ethyl acetate); IR ($CDCl_3$) 3525, 2967, 2921, 2868, 2240, 1740, 1720, 1450, 1410, 1357, 1365, 1279, 1235, 1210, 1190, 1180, 1135, 1080, 1052, 1037, 1002, 965 cm^{-1}; NMR (90 MHz, $CDCl_3$) δ 1.45 (s, 3 H), 1.13–2.40 (m, 7 H), 2.57–2.70 (m, 2 H), 2.90 (d, 2 H, J = 10 Hz), 3.56–3.83 (m, 2 H), 4.2 (dd, 1 H), 4.37 (d, 1 H, J = 9.0 Hz). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.16; H, 6.93.

(1α,2α,6α,6aα,10aβ,13*S*)-(±)-Octahydro-13-methyl-1-[methoxymethoxy]-6a,2,6-(methanoxymetheno)-2*H*-3-benzoxocine-4,9(1*H*)-dione (32).** To a solution of alcohol **26** (328 mg, 1.23 mmol) in 3 mL of methylene chloride at room temperature were added *N*,*N*-diisopropylethylamine (4.3 mL, 24.7 mmol) and chloromethyl methyl ether (0.95 mL, 12.5 mmol). After 60 h, the reaction mixture was diluted with ethyl acetate and was washed with water, 5% hydrochloric acid, and brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure, providing 445 mg of a crude product. The product which contains ca. 20% of methoxymethyl enol ether was used directly in the next reaction.

A solution of the above residue in 20 mL of tetrahydrofuran cooled to 0 °C was treated with 1.2 mL of 1 N hydrochloric acid. After 15 min at 0 °C, the reaction temperature was warmed to room temperature, where stirring was continued for an additional 30 min. The reaction mixture was taken up in ethyl acetate and was washed with a saturated aqueous sodium bicarbonate solution and brine. The organic layer was dried over anhydrous magnesium sulfate. Evaporation of the solvent in vacuo gave 380 mg of the crude product, which was purified on 8 g of silica gel. Elution with methylene chloride–acetone (9:1) gave 364 mg (95%) of crystalline **32**: R_f 0.37 (methylene chloride–acetone, 6:1); IR ($CHCl_3$) 2950, 1725, 1365, 1035 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 4.67 (AB q, 2 H, J = 7.2 Hz, $\Delta\nu_{AB}$ = 34.4 Hz), 4.52 (d, 1 H, J = 7.8 Hz), 4.32 (t, 1 H, J = 1.5 Hz), 3.76 (dd, 1 H, J = 5.4, 1.5 Hz), 3.68 (dd, 1 H, J = 7.8, 1.5 Hz), 3.40 (s, 3 H), 2.88 (dd, 1 H, J = 15.0, 12.9 Hz), 2.79 (one part of ABX, 1 H, J_{AB} = 19.8 Hz, J_{AX} = 5.4 Hz, $\Delta\nu_{AB}$ = 62.0 Hz), 2.58 (one part of AB, 1 H, J = 19.8 Hz, $\Delta\nu_{AB}$ = 62.0 Hz), 2.5–2.1 (m, 4 H), 2.00 (d, 1 H, J = 5.4 Hz), 1.85 (one part of ABXY, 1 H, J_{AB} = 13.5 Hz, J_{AX} = 13.5 Hz, J_{AY} = 4.2 Hz, $\Delta\nu_{AB}$ = 34.3 Hz), 1.74 (one part of ABXY, 1 H, J_{AB} = 13.5 Hz, J_{AX} = 6.3 Hz, J_{AY} = 2.7 Hz, $\Delta\nu_{AB}$ = 34.3 Hz), 1.53 (s, 3 H). Recrystallization from isopropyl alcohol provided analytically pure **32**, mp 152–153 °C. Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.14. Found: C, 61.74; H, 7.06.

(1α,2α,6α,6aα,10aβ,13*S*)-(±)-4,5,6,6a,10,10a-Hexahydro-13-methyl-1-[methoxymethoxy]-6a,2,6-(methanoxymetheno)-2*H*-3-benzoxocine-4,9(1*H*)-dione (33).** To a solution of ketone **32** (334 mg, 1.08 mmol) in 12 mL of carbon tetrachloride–chloroform–pentane (1:1:2) cooled to −20 °C was added hexamethyldisilazane (455 μL, 2.16 mmol) and iodotrimethylsilane (230 μL, 1.62 mmol). After 6 h at −20 °C, the reaction temperature was warmed to 0 °C, where stirring was continued for an additional 2 h. The reaction mixture was quenched with saturated aqueous

sodium bicarbonate, and the product was isolated by extraction with ether. The organic layer was washed with 10% aqueous sodium thiosulfate, saturated aqueous sodium bicarbonate, and brine. The organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent gave 451 mg of crude trimethylsilyl enol ether, which was used immediately in the next reaction.

A solution of the above crude silyl enol ether in 5 mL of acetonitrile was treated with a solution of palladium(II) acetate (484 mg, 2.16 mmol) in 27 mL of acetonitrile at room temperature. After 12 h, the reaction mixture was quenched with saturated aqueous sodium bicarbonate, and the product was isolated by extraction with methylene chloride. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. After evaporation of the solvent in vacuo, there was obtained 437 mg. Purification of 70 g of silica gel using ether–methylene chloride–methanol (20:2:1) afforded 225 mg (73% overall yield from ketone **32**) of desired enone **33**: R_f 0.46 (ether–methanol, 11:1); IR ($CHCl_3$) 2930, 1740, 1690, 1380, 1035 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 6.29 (AB q, 2 H, J = 10.1 Hz, $\Delta\nu_{AB}$ = 114.0 Hz), 4.69 (AB q, 2 H, J = 7.2 Hz, $\Delta\nu_{AB}$ = 35.6 Hz), 4.37 (s, 1 H), 4.36 (d, 1 H, J = 7.9 Hz), 3.86 (d, 1 H, J = 2.9 Hz), 3.66 (dd, 1 H, J = 7.9, 1.5 Hz), 3.42 (s, 3 H), 2.83 (dd, 1 H, J = 15.8, 12.2 Hz), 2.81 (one part of ABX, 1 H, J_{AB} = 19.8 Hz, J_{AX} = 7.6 Hz, $\Delta\nu_{AB}$ = 66.6 Hz), 2.63 (one part of AB, 1 H, J = 19.8 Hz, $\Delta\nu_{AB}$ = 66.6 Hz), 2.5–2.35 (m, 2 H), 2.30 (d, 1 H, J = 7.6 Hz), 1.54 (s, 3 H). Recrystallization from isopropyl alcohol afforded analytically pure enone **33**, mp 174.5–176 °C. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.34; H, 6.54. Found: C, 62.49; H, 6.60.

Continued elution with ether–methylene chloride–methanol (10:1:1) provided 91 mg (27%) of isomeric enone **34**: R_f 0.35; IR ($CHCl_3$) 3015, 2945, 1740, 1685, 1360, 1020 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 6.22 (s, 1 H), 4.69 (AB q, 2 H, J = 7.2 Hz, $\Delta\nu_{AB}$ = 14.9 Hz), 4.41 (s, 1 H), 4.32 (br s, 1 H), 4.27 (d, 1 H, J = 7.9 Hz), 3.82 (d, 1 H, J = 7.9 Hz), 3.38 (s, 3 H), 2.84 (one part of ABX, 1 H, J_{AB} = 19.4 Hz, J_{AX} = 9.0 Hz, $\Delta\nu_{AB}$ = 77.5 Hz), 2.63 (one part of AB, 1 H, J_{AB} = 19.4 Hz, $\Delta\nu_{AB}$ = 77.5 Hz), 2.6–2.4 (m, 2 H), 2.25 (dd, 1 H, J = 9.0 Hz, 1.3 Hz), 2.04 (t, 2 H, J = 7.0 Hz), 1.56 (s, 3 H). Anal. Calcd for $C_{16}H_{20}O_6$: m/e 308.1260. Found: m/e 308.1259.

(1α,2α,6α,6aα,10aβ,13S*)-(±)-Octahydro-1-hydroxy-13-methylspiro[1,3-dithiolane-2,9-[9*H*-6a,2,6](methanoxymetheno)[4*H*-3]benzoxocin]-4-one (35). A solution of enone **33** (441 mg, 1.43 mmol) in 45 mL of methylene chloride cooled to 0 °C was treated with 0.41 mL (4.89 mmol) of 1,2-ethanedithiol followed by 0.19 mL (1.54 mmol) of boron trifluoride etherate. The reaction mixture was warmed to room temperature and was stirred for 5 h. The solvent was removed under reduced pressure, and the remaining solid was washed with ether, affording crystalline dithioacetal, which was homogeneous on TLC (ether–methanol, 30:1; R_f 0.49). The crystalline material was taken up in methylene chloride and was washed with brine. The organic layer was dried over anhydrous magnesium sulfate. Evaporation of the solvent in vacuo gave 477 mg (98%) of pure crystalline **35**: mp 282–284 °C; IR (Nujol) 3375, 1730, 1030 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 6.06 (dd, 1 H, J = 9.7, 0.7 Hz), 5.17 (d, 1 H, J = 9.7 Hz), 4.23 (t, 1 H, J = 1.8 Hz), 4.05 (d, 1 H, J = 8.6 Hz), 3.95 (ddd, 1 H, J = 10.4, 2.9, 1.8 Hz), 3.59 (dd, 1 H, J = 8.6, 1.5 Hz), 3.5–3.3 (m, 4 H), 2.83 (d, 1 H, J = 10.4 Hz, OH), 2.72 (one part of ABX, 1 H, J_{AB} = 19.8 Hz, J_{AX} = 7.9 Hz, $\Delta\nu_{AB}$ = 38.4 Hz), 2.62 (one part of AB, 1 H, J = 19.8 Hz, $\Delta\nu_{AB}$ = 38.4 Hz), 2.42 (one part of ABX, 1 H, J_{AB} = 13.0 Hz, J_{AX} = 11.9 Hz, $\Delta\nu_{AB}$ = 34.4 Hz), 2.32 (one part of AB, 1 H, J = 13 Hz, $\Delta\nu_{AB}$ = 34.4 Hz), 2.13 (d, 1 H, J = 8.3 Hz), 2.01 (br d, 1 H, J = 13.0 Hz), 1.52 (s, 3 H). Anal. Calcd for $C_{16}H_{20}O_4S_2$: m/e 340.0803. Found: m/e 340.0804.

(1α,2α,6α,6aα,10aβ,13S*)-(±)-4,5,6,6a,10,10a-Hexahydro-13-methyl-1-hydroxy-4*H*-6a,2,6-(methanoxymetheno)-2*H*-3-benzoxocin-4-one (36). A solution of dithioacetal **35** (79 mg, 0.23 mmol) in 15 mL of absolute ethanol containing ca. 1.7 g of Raney nickel (W-2) was refluxed for 2 h. After cooling to room temperature, the reaction mixture was filtered through a pad of silica gel–Celite, and the remaining solid was washed with 30 mL of methanol. The combined filtrates were evaporated in vacuo, leaving 69 mg of material. Chromatography on 20 g of silica gel (hexane–acetone–1-butanol, 11:2:1) gave 5 mg (6%) of recovered dithioacetal **35** and 59 mg of a crude isomeric mixture of olefins. Further purification of this mixture on 10 g of silica gel using methylene chloride/acetone (19:1) gave in order of elution 7 mg (12%) of the undesired olefin **37** [R_f 0.44 (methylene chloride–acetone, 9:1); IR ($CHCl_3$) 3510, 3025, 2885, 1735, 1385, 1060 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 5.72 (m, 1 H), 5.62 (m, 1 H), 4.30 (t, 1 H, J = 2.0 Hz), 4.10 (d, 1 H, J = 8.3 Hz), 3.83 (ddd, 1 H, J = 11.2, 5.0, 1.8 Hz), 3.47 (dd, 1 H, J = 8.3, 1.8 Hz), 3.01 (d, 1 H, J = 11.2 Hz, OH) 2.74 (one part of ABX, 1 H, J_{AB} = 19.8 Hz, J_{AX} = 7.7 Hz, $\Delta\nu_{AB}$ = 30.9 Hz), 2.7 (m, 1 H), 2.65 (one part of AB, 1 H, J = 19.8 Hz, $\Delta\nu_{AB}$ = 30.9 Hz), 2.24 (dq, 1 H, J = 18.0, 2.2 Hz), 2.09 (br d, 1 H, J = 7.6 Hz), 1.93 (d, 1 H, J = 7.6 Hz), 1.86 (m, 1 H), 1.72 (dd, 1 H, J = 18.0, 4.7 Hz), 1.53 (s, 3 H). Anal. Calcd for $C_{14}H_{18}O_4$: m/e 250.1205. Found: m/e 250.1199.] and 43 mg (74%) of the desired olefin **36** as a crystalline compound: R_f 0.37; IR ($CHCl_3$) 3535, 2940, 1730, 1360, 1040 cm^{-1}; NMR (360 MHz) $CDCl_3$ δ 5.97 (dt, 1 H, J = 9.7, 3.6 Hz), 5.18 (d, 1 H, J = 9.7 Hz), 4.24 (t, 1 H, J = 2.0 Hz), 4.01 (one part of AB, 1 H, J = 9.0 Hz, $\Delta\nu_{AB}$ = 151.1 Hz), 3.88 (ddd, 1 H, J = 10.4, 4.3, 1.8 Hz), 3.59 (one part of ABX, 1 H, J_{AB} = 9.0 Hz, J_{AX} = 1.1 Hz, $\Delta\nu_{AB}$ = 151.1 Hz), 2.87 (d, 1 H, J = 10.4 Hz, OH), 2.70 (one part of ABX, 1 H, J_{AB} = 19.8 Hz, J_{AX} = 7.6 Hz, $\Delta\nu_{AB}$ = 29.0 Hz), 2.64 (one part of AB, 1 H, J = 19.8 Hz, $\Delta\nu_{AB}$ = 29.0 Hz), 2.25–2.15 (m, 2 H), 2.09 (d, 1 H, J = 7.6 Hz), 1.9–1.7 (m, 2 H), 1.66 (br d, 1 H, J = 11.5 Hz), 1.52 (s, 3 H). Recrystallization from isopropyl alcohol gave analytically pure olefin **35**, mp 185–186 °C. Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.45; H, 7.26.

Carboxylic Acid 38 (R = H). A solution of lactone **36** (29 mg, 0.12 mmol) in 1.2 mL of methanol cooled to 0 °C was treated dropwise with 0.6 mL of a 1 N aqueous sodium hydroxide solution. After 2 h at 0 °C, the reaction temperature was warmed to room temperature, where stirring was continued for an additional 20 h. The reaction mixture was acidified with 5% hydrochloric acid, and the product was isolated by extraction with ethyl acetate. The combined organic layers were washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent in vacuo gave 31 mg of the crude diol acid, which was used directly in the next reaction.

To a solution of the above diol-acid in 1 mL of methylene chloride was added *N,N*-diisopropylethylamine (1.2 mL, 6.89 mmol) and chloromethyl methyl ether (0.26 mL, 3.43 mmol). The reaction mixture was refluxed for 5.5 h. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate and was washed with 5% hydrochloric acid and brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. There was obtained 47 mg of crude **38** (R = MOM), which was used immediately in the next reaction.

A solution of the above ester in 1.2 mL of methanol cooled to 0 °C was treated dropwise with 0.6 mL of 1 N aqueous sodium hydroxide. After 1 h at 0 °C, the reaction temperature was warmed to room temperature, where stirring was continued for an additional 20 h. The reaction mixture was acidified with 5% hydrochloric acid, and the product was extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous sodium sulfate. Evaporation of the solvent in vacuo gave 43 mg of crude acid, which was purified on 5 g of silica gel. Elution with methylene chloride/acetone (4:1) gave 37 mg (90% overall yield from lactone **36**) of **38** (R = H) as an oil: R_f 0.39 (methylene chloride–acetone, 2:1); IR ($CHCl_3$) 2935, 1710, 1380, 1025 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 12.0–9.5 (br s, 1 H), 5.85 (dt, 1 H, J = 9.9, 3.6 Hz), 5.25 (d, 1 H, J = 9.9 Hz), 4.66 (AB q, 2 H, J = 6.9 Hz, $\Delta\nu_{AB}$ = 36.2 Hz), 4.63 (AB q, 2 H, J = 6.9 Hz, $\Delta\nu_{AB}$ = 32.9 Hz), 4.10 (d, 1 H, J = 7.8 Hz), 3.71 (d, 1 H, J = 5.1 Hz), 3.53 (s, 1 H), 3.42 (d, 1 H, J = 7.8 Hz), 3.40 (s, 3 H), 3.39 (s, 3 H), 2.81 (one part of ABX, 1 H, J_{AB} = 16.2 Hz, J_{AX} = 7.5 Hz, $\Delta\nu_{AB}$ = 110.0 Hz), 2.44 (one part of ABX, 1 H, J_{AB} = 16.2 Hz, J_{AX} = 6.5 Hz, $\Delta\nu_{AB}$ = 110.0 Hz), 2.26 (t, 1 H, J = 6.9 Hz), 2.15–1.60 (m, 5 H), 1.37 (s, 3 H). Anal. Calcd for $C_{18}H_{28}O_7$: m/e 356.1835. Found: m/e 356.1843.

Iodo Lactone 39. A solution of acid **38** (R = H) (18 mg, 0.051 mmol) in 0.5 mL of acetonitrile cooled to −20 °C was treated with a solution of iodine (128 mg, 0.50 mmol) in 1 mL of acetonitrile. After being stirred for 1 h at −20 °C, the reaction mixture was diluted with ether and was washed with saturated aqueous sodium bicarbonate, 10% aqueous sodium thiosulfate, saturated aqueous sodium bicarbonate, and brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under

reduced pressure. There was obtained 24 mg of crude material, which was purified on 5 g of silica gel. Elution with methylene chloride–acetone (16:1) gave 20 mg (82%) of crystalline **39**: R_f 0.49 (methylene chloride–acetone, 7:1); IR ($CHCl_3$) 2955, 1730, 1025 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 4.75 (d, 1 H, J = 6.8 Hz), 4.7–4.5 (m, 6 H), 3.74 (d, 1 H, J = 5.0 Hz), 3.63 (dd, 1 H, J = 8.3, 1.4 Hz), 3.61 (s, 1 H), 3.43 (s, 3 H), 3.38 (s, 3 H), 3.27 (one part of ABX, 1 H, J_{AB} = 19.1 Hz, J_{AX} = 13.7 Hz, $\Delta\nu_{AB}$ = 239.4 Hz), 2.60 (one part of ABX, 1 H, J_{AB} = 19.1 Hz, J_{AX} = 6.5 Hz, $\Delta\nu_{AB}$ = 239.4 Hz), 2.2–2.0 (m, 5 H), 1.52 (br d, 1 H, J = 9.4 Hz), 1.37 (s, 3 H). Recrystallization from isopropyl alcohol afforded analytically pure iodo lactone, mp 150–151 °C. Anal. Calcd for $C_{18}H_{27}IO_7$: C, 44.83; H, 5.64. Found: C, 45.12; H, 5.76.

Tetracyclic Lactone 40. A solution of iodo lactone **39** (70 mg, 0.15 mmol) and tributyltin hydride (240 μL, 0.76 mmol) in 8 mL of benzene containing 12 mg (0.073 mmol) of 2,2′-azobisisobutyronitrile was heated under reflux for 40 min. After cooling to room temperature, the reaction mixture was passed through a short column of silica gel by eluting with hexane followed by methylene chloride and ethyl acetate. The combined ethyl acetate fractions were washed with 5% hydrochloric acid, saturated aqueous sodium bicarbonate, and brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. There was obtained 83 mg of crude product, which was purified on 10 g of silica gel. Elution with methylene chloride–acetone (11:1) gave 50 mg (97%) of crystalline **40**: R_f 0.40 (methylene chloride–acetone, 6:1); IR ($CHCl_3$) 2950, 1720, 1030 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 4.65 (AB q, 2 H, J = 7.0 Hz, $\Delta\nu_{AB}$ = 43.4 Hz), 4.61 (AB q, 2 H, J = 6.7 Hz, $\Delta\nu_{AB}$ = 44.1 Hz) 4.36 (t, 1 H, J = 2.6 Hz), 4.33 (d, 1 H, J = 7.6 Hz), 3.73 (d, 1 H, J = 5.4 Hz), 3.59 (s, 1 H) 3.40 (s, 3 H), 3.38 (s, 3 H), 3.36 (dd, 1 H, J = 7.6, 1.4 Hz), 3.29 (one part of ABX, 1 H, J_{AB} = 18.9 Hz, J_{AX} = 13.3 Hz, $\Delta\nu_{AB}$ = 234.1 Hz), 2.63 (one part of ABX, 1 H, J_{AB} = 18.9 Hz, J_{AX} = 6.5 Hz, $\Delta\nu_{AB}$ = 234.1 Hz), 2.15–2.0 (m, 2 H), 1.96 (dd, 1 H, J = 13.3 Hz, 6.5 Hz), 1.8–1.55 (m, 5 H), 1.37 (s, 3 H). Recrystallization from isopropyl alcohol gave analytically pure lactone **40**, mp 113–114 °C. Anal. Calcd for $C_{18}H_{28}O_7$: C, 60.66; H, 7.92. Found: C, 60.71; H, 8.06.

α-Hydroxy Lactone 41. To 0.55 M tetrahydrofuran solution of lithium diisopropylamide (1.8 mL, 0.99 mmol) cooled to −78 °C was added dropwise a solution of lactone **40** (35 mg, 0.098 mmol) in 6 mL of tetrahydrofuran followed by hexamethylphosphoramide (0.4 mL, 2.30 mmol) in 2 mL of tetrahydrofuran. After being stirred for 1 h, the reaction temperature was warmed to −20 °C, where stirring was continued for an additional 2 h. The reaction mixture was cooled to −78 °C and was treated with oxodiperoxymolybdenum (pyridine) (hexamethylphosphoric triamide) (640 mg, 1.47 mmol) at once. After being stirred at −78 °C for 2 h, the reaction mixture was gradually warmed to room temperature, and stirring was continued for an additional 12 h. The reaction mixture was diluted with ethyl acetate and washed with 5% hydrochloric acid and brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. There was obtained 350 mg of crude material, which was purified on 15 g of silica gel. Elution with methylene chloride–acetone (7:1) gave 15 mg (43%) of recovered lactone **40**. Continued elution with methylene chloride–acetone (5:1) gave 19 mg (52%) of crystalline **41**: R_f 0.33 (methylene chloride–acetone, 4:1); IR ($CHCl_3$) 3570, 2945, 1725, 1030 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 4.98 (d, 1 H, J = 11.9 Hz), 4.68 (ABq, 2 H, J = 6.8 Hz, $\Delta\nu_{AB}$ = 40.8 Hz), 4.65 (AB q, 2 H, J = 6.8 Hz, $\Delta\nu_{AB}$ = 39.4 Hz), 4.44 (t, 1 H, J = 2.7 Hz), 4.28 (d, 1 H, J = 7.2 Hz), 3.78 (d, 1 H, J = 5.8 Hz), 3.67 (s, 1 H), 3.41 (s, 3 H), 3.40 (s, 3 H), 3.39 (dd, 1 H, J = 7.2, 1.1 Hz), 2.9 (br s, 1 H, OH), 2.2–2.0 (m, 2 H), 2.01 (d, 1 H, J = 11.9 Hz), 1.8–1.5 (m, 5 H), 1.51 (s, 3 H). Recrystallization from isopropyl alcohol gave analytically pure α-hydroxy lactone **41**, mp 135–136 °C. Anal. Calcd for $C_{18}H_{28}O_8$: C, 58.05; H, 7.58. Found: C, 57.73; H, 7.65.

De-A-quassimarin (6). To a solution of **41** (17 mg, 0.046 mmol) in 0.5 mL of methylene chloride cooled to 0 °C was added methyl sulfide (0.5 mL) followed by boron trifluoride etherate (56 μL, 0.46 mmol). After 1 h at 0 °C, the reaction temperature was warmed to room temperature, where stirring was continued for an additional 1 h. The reaction mixture was diluted with ethyl acetate and washed with brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. There was obtained 19 mg of crude product, which was purified on 5 g of silica gel. Elution with ethyl acetate/methanol (19:1) gave 10 mg (82%) of **6**: R_f 0.37 (ethyl acetate–methanol, 16:1); IR ($CHCl_3$) 3600–3100, 2935, 1715, 1375, 1130 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 5.20 (d, 1 H, J = 11.9 Hz), 4.40 (t, 1 H, J = 2.7 Hz), 4.23 (d, 1 H, J = 7.9 Hz), 3.84 (br s, 1 H), 3.79 (d, 1 H, J = 4.7 Hz), 3.44 (dd, 1 H, J = 7.9, 1.4 Hz), 3.16 (br s, 1 H, OH), 2.47 (d, 1 H, J = 9.4 Hz, OH), 2.25 (br s, 1 H, OH), 2.15–2.05 (m, 2 H), 2.06 (d, 1 H, J = 11.9 Hz), 1.8–1.5 (m, 5 H), 1.56 (s, 3 H). Recrystallization from ether–isopropyl alcohol gave crystalline **6**, mp 230–233 °C. Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.07; H, 7.13.

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