The synthesis and some chemical reactions of a 5a-methyl 2*H*-naphtho[1,8-*bc*]furan[1]

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This paper is dedicated to Professors David B. MacLean and Ian Spenser

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A synthesis of the tricycle **19** has been completed in 14% overall yield from guaiacol. Several chemical transformations of this compound including its reduction to an octahydro naphtho[1,8-*bc*]furan and conversion to the hitherto unknown azuleno-[8,1-*bc*]furan ring system are described.

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Utilisant le guaïacol comme produit de départ on a réalisé une synthèse du tricycle **19** avec un rendement global de 14%. On décrit plusieurs transformations chimiques de ces composés, y compris sa réduction en un octahydro naptho[1,8-*bc*]furane et sa conversion dans le système cyclique de l'azuléno[8,1-*bc*]furane inconnu jusqu'à maintenant.

[Traduit par la rédaction]

The 2*H*-naphtho[1,8-*bc*]furan structural unit occurs at various oxidation levels in some terpenes and fungal metabolites. Its 5a-methyl (angular methyl) derivative **1** is a particularly important target for synthetic chemists because the development of an efficient general method for the preparation of **1** and closely related tricycles will be a significant step towards the synthesis of many natural products such as the pentacyclic marine quinones **2** and **3** (1), the fungal metabolites of *Gliocladium virens* **4** and **5** (2), and *Penicillium wortmanni* **6** (3). Some synthetic activity in this area has already been recorded by Kanematsu et al. (4) who applied their "furan transfer" protocol to prepare **7** in 6.3% yield from α-furyl methanol. In addition, both Xestoquinone **2** and Halenaquinone **3** have been synthesized in low yields (5) but in these instances the naphtho-[1,8-*bc*]furan unit was generated after the aromatic rings A and B had been attached. Very recently an oxidized variant, the furanocyclohexadienone lactone **8**, has been prepared (6) as part of a synthetic program directed at Wortmannin. We now report some of our synthetic work in this area.

The benzofuran ester **9** prepared from 2-methoxy-5-methylphenol as previously described (7) was saponified and the resulting acid **10** was converted to the diazoketone **11** through the acid chloride. All of several attempts to cyclize this material to the desired tricycle **12** via cationic intermediates with trifluoroacetic acid or boron trifluoride (8), or via carbenoids with rhodium(II) acetate (9) or silver oxide, failed to provide any isolable and identifiable product.[3] It was therefore apparent that the angular methyl group had to be introduced by different methods. The benzofuran **13**, prepared as described earlier (7) in 33% overall yield from 2-methoxyphenol, was subjected to one-carbon chain homologation in 63% yield by the Arndt–Eistert sequence to produce the acid **17** through the usual intermediates **14–16**. Intramolecular Friedel–Crafts cyclization to **18** was easily accomplished by either polyphosphoric acid (PPA) at 90°C (81%) or trifluoroacetic acid – trifluoroacetic anhydride (TFA–TFAA) in dry methylene chloride at 25°C (87%). Birch reduction[4] with potassium/liquid ammonia/*tert*-butanol followed by methylation (4.5 equiv. lithium bromide, followed by methyl iodide in THF–water) gave a 76% yield of the desired 5a-methylated-2*H*-naphthofuran **19**. The addition of the lithium bromide to exchange the potassium enolate for the lithium is necessary to preserve the selectivity of the methylation step. Without it, methylation on both sides of the C-5 carbonyl group was observed. The loss of the methoxyl group *para* to the C-5 carbonyl was not unexpected (10). The 200-MHz ^{1}H NMR spectrum of the product shows only one signal for the 5a methyl group at 1.36 ppm and no evidence could be found for the existence of more than one diastereomer in the product. The *cis* configuration at C-2a,5a was assigned to this product by the examination of models and was confirmed by an X-ray structure of a crystalline derivative (vide infra). This synthetic route provides the angularly methylated 2*H*-naphthofuran in 14% overall yield from 2-methoxyphenol. Although this was a reasonably efficient process there appeared to be room for improvement in the fact that the methoxyl group of the starting material was lost in the Birch reduction step and a great increase in efficiency would be possible if *o*-iodophenol, a commercial material, was used instead of guaiacol. The tedious *o*-iodination procedure necessary with the latter could then be avoided. Thus the benzofuran ester **20** was prepared from *o*-iodophenol as before (7) in two steps in 61% yield and homologated by the same Arndt–Eistert protocol to the ester **21** in 52% yield (32% overall from *o*-iodophenol). Unfortunately every attempt made, and a great many were tried, to cyclize the ester **21**, the acid **22**, or diazoketone **23** failed. All acidic reagents in Friedel–Crafts reactions, carbenoids, as well as the use of a Cu(I) triflate-promoted cyclization of a selenate ester **24** (11) failed. Mild conditions returned the starting material and forcing ones caused its destruction. The requirement for a *para*-methoxy group in a similar intramolecular Friedel–Crafts cyclization has been noted previously (12). In the hope that the benzofuran might cyclize better than the dihydrobenzofuran **22**, the methyl ester of the latter was dehydrogenated quantitatively with dichlorodicyanobenzoquinone (DDQ) in dioxan and saponified to provide the acid **25**. Friedel–Crafts cyclization with PPA or through the acid chloride with aluminum chloride was again not successful. The cyclopentanone **26** was the only isolable product (20% yield).

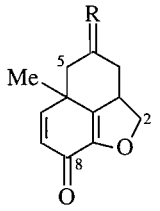
The chemical properties of **19** were investigated next. Attempts were made to deoxygenate the carbonyl group at C-5. Initially the thioketal – Raney Ni desulfurization and the tosylhydrazone–hydride reduction (13) were contemplated. How-

[1]Dedicated to Professors David MacLean and Ian Spenser for their outstanding contributions to Organic Chemistry.

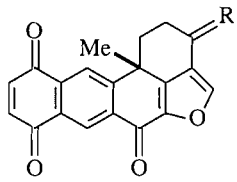
[2]Author to whom correspondence may be addressed.

[3]G. Weeratunga and R. Rodrigo, unpublished results.

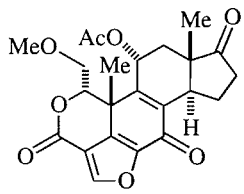
[4]For a recent review of the Birch reduction see ref. 10*b*.



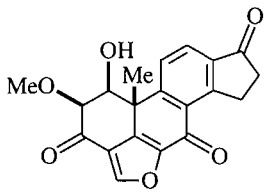
1 (R = H, H)
7 (2,2*a* dehydro R = H, H)
12 (R = O)



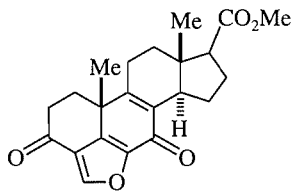
2 (R = H, H) Xestoquinone
3 (R = O) Halenaquinone



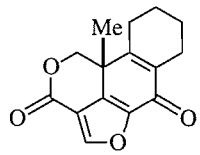
6 Wortmannin



4 Viridin



5 Virone



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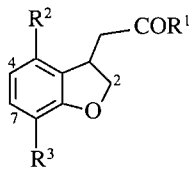
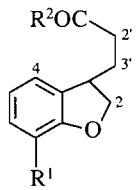
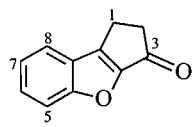


9 (R^1 = OEt, R^2 = Me, R^3 = OMe)
10 (R^1 = OH, R^2 = Me, R^3 = OMe)
11 (R^1 = CHN_2, R^2 = Me, R^3 = OMe)
13 (R^1 = OEt, R^2 = H, R^3 = OMe)
14 (R^1 = OH, R^2 = H, R^3 = OMe)
15 (R^1 = CHN_2, R^2 = H, R^3 = OMe)
20 (R^1 = OEt, R^2 = R^3 = H)
23 (R^1 = CHN_2, R^2 = R^3 = H)



16 (R^1 = R^2 = OMe)
17 (R^1 = OMe, R^2 = OH)
21 (R^1 = H, R^2 = OMe)
22 (R^1 = H, R^2 = OH)
24 (R^1 = H, R^2 = SeMe)
25 (R^1 = H, 2,3-dehydro, R^2 = OH)



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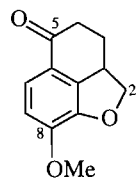

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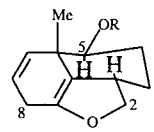
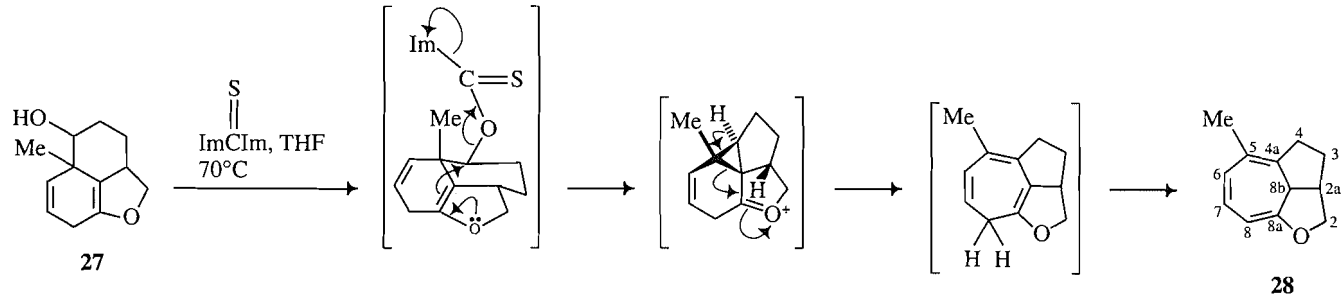
19



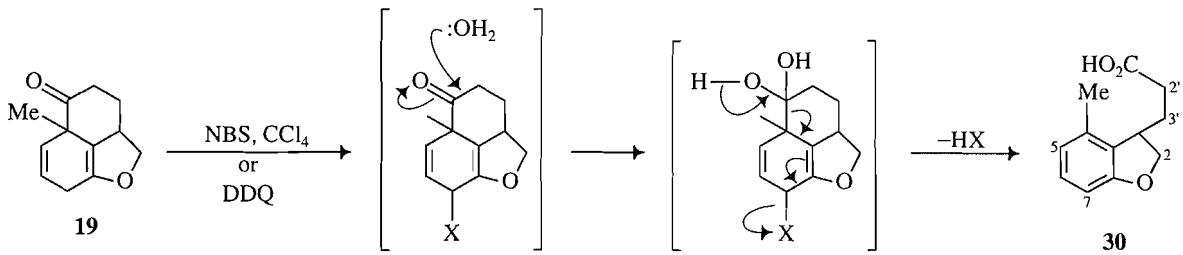
27 (R = H)
31 (R = Me)

ever, neither derivative could be obtained under the usual conditions but extensive decomposition of **19** took place instead. Reduction of the C-5 carbonyl group with sodium borohydride in ethanol could be accomplished in 93% yield to provide the alcohol **27** with the hydroxyl group in an apparently equatorial orientation ($J_{4,5}$ = 4.4 and 11.1 Hz). Attempts were now made to prepare the bromide or tosylate Treatment of the alcohol **27** with carbon tetrabromide and triphenylphosphine in methylene chloride or with 1,2-bis(triphenylphosphino) ethane tetrabromide (14) in the same solvent resulted in a complex mixture of products. Tosyl chloride in the presence of dimethylaminopyridine at 0°C also provoked decomposition. A recent report (15) suggests that even neopentyl alcohols can be deoxygenated efficiently by conversion to the 2,4,6-trichlorophenoxy thiocarbonyl ester followed by treatment with tributyl tin hydride. When this method was applied to **27**, extensive decomposition again resulted and the ^{1}H NMR spectrum of the product mixture showed aromatic absorption. An attempt was then made to prepare an imidazole thioester. Treatment of **19** with thiocarbonyldiimidazole in refluxing THF produced a 48% yield of a material identified as the azulenofuran **28**. The 250-MHz ^{1}H NMR spectrum showed the presence of three vinyl protons at 5.53 (1H) and 6.14 (2H) ppm. Irradiation of the former produced a clean AB pattern for H-6 and H-7 at 6.14 ppm. The proton at C-2a was found at 3.08 ppm as a multiplet that was coupled to a doublet at 2.91 ppm (H-8b) and to the protons at C-2 and C-3. The ^{13}C NMR spectrum was also in accord with this structure. No report could be found in the literature of the preparation or natural occurrence of this simple tricyclic system. It must arise in this instance by participation of the enol ether oxygen in displacing the imidazole ester at C-5 (Scheme 1). This proposal is supported by the fact that the 8a,8b-dihydro derivative of **27** (vide infra) when treated with thiocarbonyldiimidazole did provide the thioimidazole ester **29** in 65% yield.

In view of the presence of a carbonyl group in the natural products **2–6** at a position corresponding to C-8 of **19** it was decided to attempt oxidation at this allylic methylene group. Various chromium(VI) species (e.g., PDC, CrO_3 – dimethyl pyrazole (DMP)), DDQ, and allylic bromination with *N*-bromosuccinimide (NBS) caused decomposition, and the mixtures of products obtained showed aromatic signals in their ^{1}H NMR spectra. Thus in both the allylic bromination and DDQ oxidations the dihydrobenzofuran carboxylic acid **30** was obtained and characterized, in yields of 74 and 31%, respectively. Its formation is rationalized in Scheme 2 (X = Br or a positive charge). The first step (also the rate-determining step) in oxidations with quinones is generally believed to be hydride abstraction from the substrate; the cation (or ion pair) subsequently goes on to product(s). Since it appeared that the combination of positive centres at the C-5 and C-8 led to ring-opening



SCHEME 1. The ring expansion of **27**



(X = Br or a positive charge)

SCHEME 2. The aromatization of **19**

and aromatization, the C-5 methyl ether **31** was prepared from the alcohol **27** in 82% yield by successive treatment with *n*-BuLi in THF–HMPA at −78°C and using excess methyl iodide. Every attempt at oxidation of this compound with various Cr(VI) and Ce(IV) reagents, DDQ, and NBS led to decomposition and the production of mixtures displaying aromatic signals in the ^{1}H NMR spectra.

Isobenzofurans are among the most reactive dienes known (16) and have been shown (17) to react even with cyclohexene to provide adducts in good yield. The isobenzofuran **33** (18), generated in situ with glacial acetic acid from the hydroxyphthalan **32**, was reacted with **19** in refluxing carbon tetrachloride for 2h. A crystalline product obtained in 50% yield displayed ^{1}H NMR signals consistent with the presence of both the methoxylated benzene ring and the tricyclic dienophile **19**. However, the vinyl protons of the 6,7 double bond were still present in the NMR spectrum of this compound at 5.19 (dd, H-7, $J_{6,7}$ = 10, $J_{7,8}$ = 3.65 Hz) and 5.98 ppm (dd, H-6, $J_{6,7}$ = 10 and $J_{6,8}$ = 1.7 Hz), suggesting that the reaction had taken place at C-8 and that the product **34** was not a Diels–Alder adduct. When dissolved in ethanol and stirred for 20 min with one drop of concentrated hydrochloric acid, a new crystalline material **35** was formed in 80% yield. An X-ray structure (Fig. 1) of this compound confirmed that it was derived from the expected product of reaction at C-8 of **19**, and established the relative stereochemistry of **19** to be *cis* at C-2a and C-5a as surmised previously. The formation of **34** and **35** is rationalized in Scheme 3 as an acid-catalysed aldol condensation between the oxonium ion **36** and enol ether **37** produced from **32** and **19**, respectively, in the acidic conditions employed, followed by rearrangement to the benzoxepin.

At this stage it appeared that any transformation of **19** into a synthon useful for the natural products would require the elimination of the C-5 oxygen and the C_{8a}—C_{8b} double bond. This objective was achieved as follows: the alcohol **27** was generated (but not isolated) as before and then reduced further with

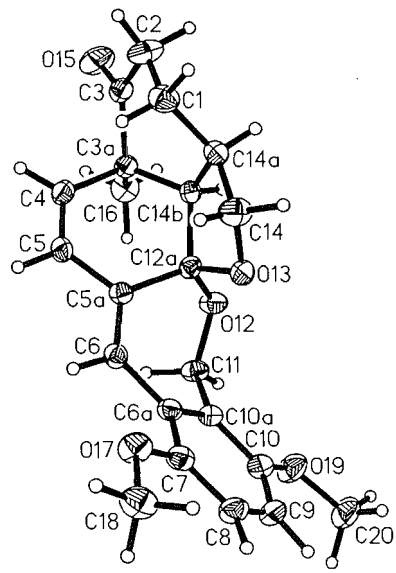
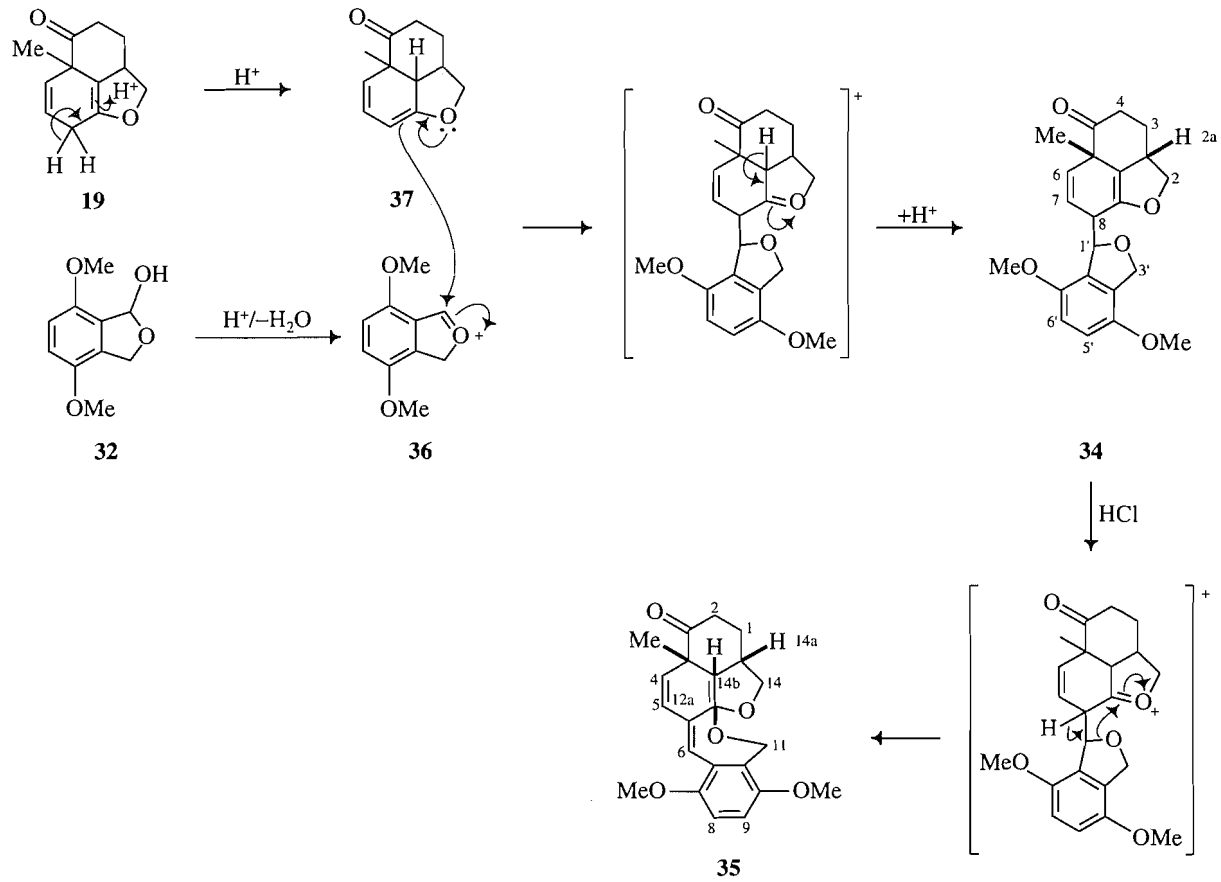


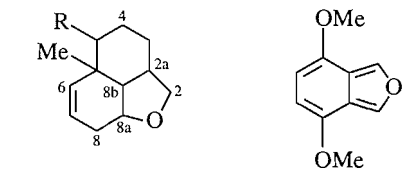
FIG. 1.Molecular plot of the X-ray crystallographic structure of **35**.

sodium cyanoborohydride in acidified solution to provide the alcohol **38** in 78% yield in a "one-pot" process. The relative stereochemistry of this alcohol is not evident from the ^{1}H NMR spectrum but it is assumed to be all *cis* at C-2a, 5a, 8a, and 8b from the X-ray structure of **35** and the well-known preference of 6/5 ring junctions for *cis* fusion. Deoxygenation of the alcohol could be achieved by radical procedures through several different intermediates. The imidazole thioester **29** could be obtained in 65% yield upon refluxing with thiocarbonyldiimidazole in benzene, the trichlorophenoxy thioester **39** in 23% yield by treatment with trichlorophenoxythiocarbonyl chloride in acetonitrile with a catalytic amount of dimethylaminopyridine, the xanthate **40** in 79% yield by reaction with *n*-butyl-



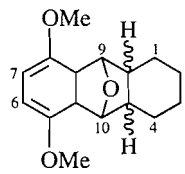
SCHEME 3. Aldol condensation of enol ether **37** with oxonium ion **36**

lithium at −78°C followed by carbon disulfide at 0°C and methyl iodide at 25°C. Preparation of the bromide, however, with CBr_4 and triphenylphosphine was unsuccessful. All three thio derivatives could be deoxygenated to **41** with tri-*n*-butyltin hydride and azobis isobutyro nitrile (AIBN) in refluxing toluene but the xanthate gave the best yield (69% in this step and 43% from **19**). Thus **41** is available from 2-methoxyphenol in 4.7% overall yield. No other diastereomer was detectable in the product but the *cis* stereochemistry at C-8a, 8b is to be expected for this 6/5 ring fusion. With the dihydro compound in hand, several attempts at allylic oxidation at C-8 were made. Various chromium(VI) reagents ($Cr(CO)_6$ and 90% *tert*-butyl hydroperoxide, dimethylpyrazole CrO_3, PCC), selenium dioxide with and without *tert*-butyl hydroperoxide, palladium(II) acetate and manganese dioxide, and DDQ all failed to oxidize the allylic methylene group. In many cases starting material was returned, but the PCC and DMP·CrO_3 oxidations of **41** gave 35% and 21% yields, respectively, of the γ-lactone **42**. Such oxidations of tetrahydrofurans to γ-lactones with Cr(VI) reagents are not unknown (19). Allylic bromination with NBS under various conditions was not successful and no method could be found to achieve allylic oxidation at C-8 of this tricyclic system. The final attempt to use **41** as a synthon depended on whether its unactivated double bond would undergo a Diels–Alder reaction with the reactive isobenzofuran **33**. This was tested by heating the precursor **32** in *p*-xylene with cyclohexene at 140°C with a catalytic amount of *p*-toluic acid for 36h. A 6:1 mixture of *endo*:*exo* adducts **43** was obtained in a total yield of 53%. The same conditions were then employed with **41** as the dienophile



29 (R = O-CS-Im)
38 (R = OH)
39 (R = O-CS-$C_6H_2Cl_3$)
40 (R = O-CS-SMe)
41 (R = H)

33



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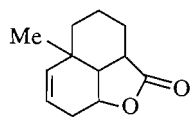

42

but no cycloaddition products could be found even when heating was conducted in a sealed tube placed in refluxing xylene for 5 days. The starting material **41** was recovered from these reactions, indicating the lower reactivity of its cyclohexene double bond towards cycloaddition. The isobenzofuran was produced as before, but polymerized in the absence of a sufficiently reactive dienophile. High pressure is perhaps one way of forcing this reaction to occur but, even if it does, a satisfactory yield cannot realistically be expected and the requirement for several further transformations detracts from the value of this route to the marine quinones. Other approaches to the natural products **2–6** are being explored at present. They show some

promise of success and these results will be reported in due course.

Experimental

Melting points were determined on a Fischer Mel-Temp unit and are uncorrected. IR spectra were recorded on a Perkin Elmer 983 or a Bomem MB-100 Fourier Transform spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on Bruker AM-250, AC-200, or WP-80 spectrometers at the field strengths specified. Chemical shifts are reported in δ (ppm) and coupling constants (*J*) in hertz. Mass spectra were obtained on a Kratos MS 890 (at the Guelph MS Centre) or on a VG ZAB-E or VG 7070 spectrometer (at the S.W. Ontario Regional MS Centre at Hamilton). The EI and CI modes were used for ionization. Elemental analyses were performed by M-H-W Laboratories, Phoenix, Ariz.

*2-(2,3-Dihydro-7-methoxybenzo[*b*]furan-3-yl)acetic acid* ***14***

To a solution of ester **13** (5.50g, 23.3 mmol) in MeOH (100 mL) was added 50 mL of 10% NaOH and the resulting mixture was stirred for 5h at room temperature. The solution was cooled in ice and acidified with 2 N HCl. Extraction with EtOAc (3 × 50 mL) followed by washing the combined organic layers with water (2 × 50 mL) and drying (Na_2SO_4) provided 4.30g of crude product upon removal of the solvent under reduced pressure. The solid was recrystallized from Et_2O–hexane to give 4.00g (82%) of **14** as colourless plates; mp 99–100°C (lit. (20) mp 101–103°C); IR ($CHCl_3$): 3500–2500 (br), 3024, 1711, 1620, 1593, 1492, 1282, 723 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ: 2.77 (AB of an ABX system, J_{AB} = 17.0, J_{AX} = 5.1, J_{BX} = 9.6, $\Delta\nu$ = 50.7, 2H, $CHCH_2CO_2H$), 3.88 (s, 3H, OMe), 3.87–3.94 (m, 1H, H-3), 4.35 (dd, $J_{2\alpha,2\beta}$ = 9.3, $J_{3,2\beta}$ = 6.4, 1H, H-2β), 4.83 (t, $J_{2\beta,2\alpha} = J_{3,2\alpha}$ = 9.3, 1H, H-2α), 6.76–6.88 (m, 3H, H-4, H-5, and H-6), 11.05 (br s, exchanged with D_2O, 1H, OH); LRMS (EI) *m/e*: 208 (87, M^+), 190 (11), 177 (20), 161 (13), 149 (100), 131 (13), 121 (55), 103 (12), 91 (36), 77 (19), 68 (16), 51 (14). Anal. calcd. for $C_{11}H_{12}O_4$: C 63.45, H 5.81; found C 63.37, H 5.83.

*1-Diazo-3-(2,3-dihydro-7-methoxybenzo[*b*]furan-3-yl)-2-propanone* ***15***

To a solution of oxalyl chloride (1.42 mL, 16.3 mmol) in benzene (50 mL) at room temperature was added a mixture of acid **14** (2.00g, 9.61 mmol) and pyridine (0.85 mL, 11 mmol) in benzene (40 mL) dropwise over 30 min. The resulting solution was stirred an additional 30 min, then filtered to remove pyridinium hydrochloride. The filtrate was concentrated in vacuo with the aid of a drying tube on the aspirator to prevent the ingress of moisture. Any remaining solvent was removed under high vacuum. The acid chloride thus obtained was not purified but taken up in benzene (20 mL) and added dropwise to an ice-cold solution of diazomethane. The solution was stirred at 0°C for 2h and slowly allowed to warm to room temperature. The mixture was stirred for 15h to allow excess diazomethane to evaporate. The Et_2O was removed in vacuo and the resulting yellow solid was recrystallized from Et_2O to provide 1.93g (87%) of **15** as yellow needles; mp 96.5–97.5°C; IR ($CHCl_3$): 3007, 2961, 2111, 1732, 1640, 1492, 1283, 1196, 951 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ: 2.55–2.84 (m, 2H, $CHCH_2COCHN_2$), 3.86 (s, 3H, OMe), 3.90–4.00 (m, 1H, H-3), 4.28 (dd, $J_{2\alpha,2\beta}$ = 9.2, $J_{3,2\beta}$ = 6.1, 1H, H-2β), 4.80 (t, $J_{2\beta,2\alpha} = J_{3,2\alpha}$ = 9.2, 1H, H-2α), 5.26 (br s, 1H, $COCHN_2$), 6.73–6.85 (m, 3H, H-4, H-5, and H-6); LRMS (EI) *m/e*: 232 (19, M^+), 222 (13), 204 (15), 173 (12), 161 (34), 149 (55), 133 (9), 121 (100), 103 (10), 91 (56), 77 (32), 65 (16). Anal. calcd. for $C_{12}H_{12}N_2O_3$: C 62.06, H 5.21; found: C 62.28, H 5.34.

*Methyl 3-(2,3-dihydro-7-methoxybenzo[*b*]furan-3-yl)propionate* ***16***

Diazo ketone **15** (6.78 g, 29.6 mmol) was dissolved in MeOH (250 mL) and Ag_2O (7.54 g, 32.5 mmol) was added. The reaction mixture was stirred at room temperature for 2h, then filtered and concentrated. Flash chromatography of the crude oil on silica (40% EtOAc–hexanes eluent) afforded 6.49 g (93%) of **16** as a pale yellow oil. IR (neat): 2951, 1736, 1618, 1592, 1492, 1279, 1199, 773, 734 cm^{-1}, ^1H NMR (250 MHz, $CDCl_3$) δ: 1.88–2.15 (m, 2H, 2 × H-3′), 2.30–2.42 (m, 2H, 2 × H-2′), 3.44–3.56 (m, 1H, H-3), 3.67 (s, 3H, CO_2Me), 3.87 (s, 3H, ArOMe), 4.28 (dd, $J_{3,2\beta}$ = 5.8, $J_{2\alpha,2\beta}$ = 9.0, 1H, H-2β), 4.68 (t, $J_{3,2\alpha} = J_{2\beta,2\alpha}$ = 9.0, 1H, H-2α), 6.74–6.84 (m, 3H, H-4, H-5, H-6); LRMS (EI) *m/e*: 236 (78, M^+), 205 (18), 176 (15), 162 (100), 149 (97), 131 (13), 121 (59), 103 (11), 91 (77), 78 (20), 65 (17), 51 (16). Anal. calcd. for $C_{13}H_{16}O_4$: C 66.09, H 6.83; found: C 65.96, H 6.62.

*3-(2,3-Dihydro-7-methoxybenzo[*b*]furan-3-yl)propionic acid* ***17***

To ester **16** (3.03 g, 12.9 mmol) dissolved in THF (60 mL) was added 20 mL of 10% NaOH and the solution was stirred for 22h at room temperature. The solution was concentrated in vacuo and EtOAc (50 mL) was added. The solution was acidified with 2 N HCl and the layers separated. The aqueous layer was further extracted with EtOAc (2 × 50 mL). The organic extracts were combined, dried (Na_2SO_4), and the solvent removed under reduced pressure. Flash chromatography (silica, 50% Et_2O–hexanes eluent) followed by recrystallization from Et_2O – petroleum ether gave 2.5 g (87%) of **17** as colourless plates; mp 63–64°C; IR ($CHCl_3$): 3500–2500, 3023, 2942, 1708, 1618, 1491, 1278, 1197, 952 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 1.88–2.17 (m, 2H, 2 × H-3′), 2.38–2.48 (m, 2H, 2 × H-2′), 3.46–3.60 (m, 1H H-3), 3.87 (s, 3H, OMe), 4.30 (dd, $J_{3,2\beta}$ = 5.6, $J_{2\alpha,2\beta}$ = 9.1, 1H, H-2β), 4.69 (t, $J_{3,2\alpha} = J_{2\beta,2\alpha}$ = 9.1, 1H, H-2α), 6.74–6.88 (m, 3H, H-4, H-5, H-6), 10.75 (br s, exchanged with D_2O, 1H, OH); LRMS (EI) *m/e*: 222 (77, M^+), 208 (2), 189 (4), 176 (5), 162 (41), 149 (100), 131 (9), 121 (59), 103 (97), 91 (25), 77 (16), 65 (8). Anal. calcd. for $C_{12}H_{14}O_4$: C 64.85, H 6.35; found: C 65.00, H 6.37.

*8-Methoxy-2,2a,3,4,tetrahydronaphtho[1,8-*bc*]furan-5-one* ***18***

To acid **17** (4.00 g, 18.0 mmol) in CH_2Cl_2 (140 mL) was added trifluoroacetic acid (1.66 mL, 21.6 mmol) and trifluoracetic anhydride (3.05 mL, 21.6 mmol). The reaction mixture was stirred for 5 h. Water (75 mL) was added and the layers separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 75 mL) and the organic layers combined, dried (Na_2SO_4), and concentrated in vacuo to provide a solid that was recrystallized from EtOAc–hexane to give 3.21 g (87%) of **18** as colourless plates. The same compound was prepared utilizing PPA as follows: phosphorus pentoxide (20.83 g, 0.147 mol) was combined with 85% orthophosphoric acid (16.67 mL, 0.145 mol) and heated at 160–165°C for 5h. Acid **17** (0.50 g, 2.2 mmol) was added to the PPA at 90°C and heated for 1 h, then cooled and poured into ice. The mixture was extracted with CH_2Cl_2 (3 × 50 mL) and the organic layer was washed with 10% K_2CO_3 (75 mL) and water (2 × 75 mL), then dried (Na_2SO_4) and concentrated; 0.37 g (81%) of **18** was obtained after recrystallization from EtOAc–hexanes; mp 114–115°C; IR (neat): 2999, 2941, 1670, 1616, 1600, 1274, 1099, 914, 803cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 1.93 (qd, $J_{4\alpha,3\beta} = J_{2a,3\beta} = J_{3\alpha,3\beta}$ = 12.7, $J_{4\beta,3\beta}$ = 4.6, 1H, H3β), 2.37 (dtd, $J_{3\beta,3\alpha}$ = 12.7, $J_{2a,3\alpha} = J_{4\alpha,3\alpha}$ = 4.6, $J_{4\beta,3\alpha}$ = 2.6, 1H, H-3α), 2.65 (AB of an ABMX system, J_{AB} = 17.6 J_{AX} = 2.6, J_{AM} = 4.6, J_{BM} = 12.7, J_{BX} = 4.6, $\Delta\nu$ = 29, 2H, 2 × H-4), 3.64–3.83 (m, 1H, H-2a), 3.96 (s, 3H, OMe), 4.17 (dd, $J_{2a,2\beta}$ = 11.9, $J_{2\alpha,2\beta}$ = 8.6, 1H, H-2β), 4.95 (t, $J_{2a,2\alpha} = J_{2\beta,2\alpha}$ = 8.6, 1H, H-2α), 6.83 (d, *J* = 8.5, 1H, H-7), 7.42 (d, *J* = 8.5, 1H, H-6); LRMS (EI) *m/e*: 204 (100, M^+), 190 (15), 176 (72), 162 (29), 148 (32), 134 (28), 119 (46), 105 (26), 91 (34), 77 (21), 51 (13). Anal. calcd. for $C_{12}H_{12}O_3$: C 70.58, H 5.92; found: C 70.42, H 6.09.

*2,2a,3,4,5,5a-Hexahydro-5a-methyl-8*H*-naphtho[1,8-*bc*]furan-5-one* ***19***

To freshly distilled liquid ammonia (50 mL) at −78°C was slowly added a solution of **18** (0.500 g, 2.45 mmol) and *t*-BuOH (0.76 mL, 8.1 mmol) in THF (5 mL). Potassium metal (0.431 g, 11.0 mmol) was added in small pieces. The resulting dark blue solution was stirred for 30 min. A solution of LiBr (0.957 g, 11.0 mmol) in THF (3 mL) was added dropwise with stirring. The colourless mixture was stirred a further 30 min, then MeI (0.183 mL, 2.94 mmol) and aqueous THF (1:1, 2.1 mL) were added simultaneously. The cooling bath was removed and the ammonia allowed to evaporate. Water (75 mL) was added and

the mixture extracted with Et_2O (3 × 50 mL). The ether extracts were washed with water (75 mL) and brine (75 mL), dried (Na_2SO_4), and evaporated to dryness. The residue was purified by column chromatography (silica, 30% EtOAc–hexanes eluent) to give 354 mg (76%) of **19** as a colourless oil. IR (neat): 2957, 2925, 2886, 1705, 1450, 1389, 1329, 1201, 1069, 1010, 944, 934, 720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 1.36 (s, 3H, Me), 1.53–1.74 (m, 1H, H-3β), 2.07–2.20 (m, 1H, H-3α), 2.27–2.38 (ddd, $J_{4\alpha,4\beta}$ = 14.5, $J_{3\alpha,4\beta}$ = 3.0, $J_{3\beta,4\beta}$ = 4.0, 1H, H-4β), 2.56–2.66 (ddd, $J_{4\beta,4\alpha}$ = 14.5, $J_{3\beta,4\alpha}$ = 5.4, $J_{3\alpha,4\alpha}$ = 1.0, 1H, H-4α), 2.70–2.76 (m, 2H, 2 × H-8), 3.25–3.37 (m, 1H, H-2a), 4.08 (dd, $J_{2\alpha,2\beta}$ = 9.3, $J_{2a,2\beta}$ = 4.7, 1H, H-2β) 4.51 (t, $J_{2\beta,2\alpha}$ = $J_{2a,2\alpha}$ = 9.3, 1H, H-2α), 5.85 (AB of ABXX′, J_{AB} = 10.0, J_{AX} = 2.1, J_{BX} = 3.3, Δν = 42, 2H, H-6, H-7); LRMS (EI) *m/e*: 190 (28, M^+), 162 (61), 134 (78), 119 (100), 105 (27), 91 (47), 77 (18), 65 (11), 55 (11). Anal. calcd. for $C_{12}H_{14}O_2$: C 75.76, H 7.42; found: C 75.68, H 7.34.

*2-(2,3-Dihydrobenzo[*b*]-furan-3-yl)acetic acid*

To a solution of ester **20** (4.09, 19.8 mmol) in 60 mL THF and 30 mL MeOH was added 40 mL of 10% aqueous NaOH. The mixture was stirred at room temperature for 5h, then acidified with 2 N HCl and extracted with EtOAc (3 × 75 mL). The combined organics were washed with brine (75 mL) and dried (Na_2SO_4). Concentration in vacuo provided a yellow solid that was recrystallized from Et_2O–hexane to afford 3.00 g (91%) of the acid as colourless plates; mp 100–101°C; IR ($CHCl_3$): 3400–2500, 1709, 1596, 1481, 1217, 965 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 2.76 (AB of an ABX system, J_{AB} = 17.0, J_{AX} = 5.3, J_{BX} = 9.4, Δν = 40.7, $CHCH_2CO_2H$), 3.83–3.92 (m, 1H, H-3), 4.28 (dd, $J_{3,2\beta}$ = 6.3, $J_{2\alpha,2\beta}$ = 9.1, 1H, H-2β), 4.76 (t, $J_{3,2\alpha}$ = $J_{2\beta,2\alpha}$ = 9.1, 1H, H-2α), 6.79–6.91 (m, 2H, H-5, H-7), 7.12–7.20 (m, 2H, H-4, H-6), 10.20 (br s, exchanged with D_2O, 1H, OH); LRMS (EI) *m/e*: 178 (51, M^+), 147 (4), 131 (14), 119 (100), 91 (72), 77 (13), 65 (10), 51 (10). Anal. calcd. for $C_{10}H_{10}O_3$: C 67.41, H 5.66; found: C 67.30, H 5.60.

*1-Diazo-3(2,3-dihydrobenzo[*b*]furan-3-yl)-2-propanone **23***

To a solution of oxalyl chloride (1.48 mL, 17.0 mmol) in benzene (50 mL) at room temperature was added a mixture of this acid (1.78 g, 10.0 mmol) and pyridine (0.89 mL, 11 mmol) in benzene (40 mL) dropwise over 30 min. The resulting solution was stirred an additional 30 min, then filtered to remove pyridine hydrochloride. The filtrate was concentrated to dryness while protecting from the entry of moisture by employing a drying tube on the aspirator. Any remaining solvent was removed under high vacuum. The acid chloride thus obtained was not purified but taken up in 20 mL of benzene and added dropwise at 0°C to the solution of diazomethane prepared previously. The solution was allowed to warm to room temperature and stirred for 15h to allow excess diazomethane to evaporate. The Et_2O was removed in vacuo and the resulting yellow solid was subjected to flash chromatography (silica, 40% EtOAc–hexanes eluent) to yield 1.69 g (84%) of **23** as a yellow oil. IR (neat): 3093, 2893, 2106, 1727, 1638, 1481, 1460, 1373, 1232, 1137, 962, 745 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ: 2.61–2.83 (m, 2H, $CHCH_2COCHN_2$), 3.90–397 (m, 1H, H-3), 4.21 (dd, $J_{2\alpha,2\beta}$ = 9.1, $J_{3,2\beta}$ = 6.0, 1H, H-2β), 4.74 (t, $J_{2\beta,2\alpha}$ = $J_{3,2\alpha}$ = 9.1, 1H, H-2α), 5.24 (br s, 1H, $COCHN_2$), 6.77–6.88 (m, 2H, H-5, H-7), 7.10–7.16 (m, 2H, H-4, H-6); LRMS (EI) *m/e*: 202 (2, M^+), 192 (4), 174 (19), 145 (7), 131 (51), 119 (60), 103 (7), 91 (100), 77 (12), 65 (18), 55 (13). Anal. calcd. for $C_{11}H_{10}N_2O_2$: C 65.34, H 4.98; found: C 65.53, H 5.00.

*Methyl 3-(2,3-dihydrobenzo[*b*]furan-3-yl)propionate **21***

Silver(I) oxide was prepared as follows: silver nitrate (4.50 g, 26.5 mmol) was dissolved in water (45 mL) and concentrated aqueous NaOH was added until the solution was basic. The brown precipitate of Ag_2O was filtered and rinsed with several portions of water (4 × 50 mL), then acetone (4 × 50 mL), then diethyl ether (4 × 50 mL). The solid was dried under high vacuum for several hours. Diazo ketone **23** (1.25 g, 6.18 mmol) was dissolved in MeOH (40 mL) and Ag_2O (1.58, 6.80 mmol) was added. The reaction mixture was stirred at room temperature for 2h, then was filtered and the filtrate was concentrated in vacuo. The resulting crude oil was chromatographed on silica (40% EtOAc/hexanes eluent) to provide 1.09 g (86%) of **21** as a colourless oil. IR (neat): 2950, 1734, 1609, 1481, 1229, 1170, 1017, 752 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 1.87–2.17 (m, 2H, 2 × H-3′), 2.34–2.43 (m, 2H, 2 × H-2′), 3.43–3.51 (m, 1H, H-3), 3.68 (s, 3H, OMe), 4.22 (dd, $J_{3,2\beta}$ = 5.8, $J_{2\alpha,2\beta}$ = 8.9, 1H, H-2β), 4.61 (t, $J_{2\beta,2\alpha}$ = $J_{3,2\alpha}$ = 8.9, 1H, H-2α), 6.77–6.90 (m, 2H, H-5, H-7), 7.09–7.20 (m, 2H, H-4, H-6); LRMS (EI) *m/e*: 206 (51, M^+), 175 (11), 146 (7), 132 (100), 131 (77), 119 (77), 91 (79), 77 (8), 65 (12), 51 (6), 45 (46). Anal. calcd. for $C_{12}H_{14}O_3$: C 69.89, H 6.84; found: C 69.64, H 6.67.

*3-(2,3-Dihydrobenzofuranyl) propionic acid **22***

This acid was prepared in 90% yield by the hydrolysis of ester **21** in THF–methanol (10:1) with 2 M sodium hydroxide for 3h at room temperature.[3]

*Methyl 3-(2,3-dihydrobeno[*b*]furan-3-yl)propioselenate **24***

In a dry box, $AlMe_3$ (12.5 mL of a 2 M solution in toluene, 25.0 mmol) was added to a flask containing selenium metal (2.05 g, 26.0 mmol). The mixture was refluxed for 2h, at which time it was cooled to room temperature and the unreacted Se was allowed to settle from the solution. A portion of this solution (1.34 mL, 2.67 mmol) was transferred to a solution of methyl ester **21** (0.500 g, 2.43 mmol) in 5 mL of argon-degassed CH_2Cl_2 at 0°C. The mixture was stirred at 0°C for 30 min, then allowed to warm to room temperature over 30 min. To the yellow solution was added sodium sulfate decahydrate (1 g) and the mixture was stirred for 20 min. The solution was extracted with Et_2O (3 × 20 mL) and the organic layer was dried (Na_2SO_4) and concentrated to provide 0.58 g (89%) of selenol ester **24** as a yellow oil. IR (neat): 3020, 2986, 1732, 1602, 1500, 1420, 1220, 1201, 1132, 1055, 906, 796 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ: 1.85–2.40 (m, 2H, 2 × H-3′), 2.25 (s, 3H, Me), 2.53–2.82 (m, 2H, 2 × H-2′), 3.28–3.71 (m, 1H, H-3), 4.21 (dd, $J_{2\alpha,2\beta}$ = 8.9, $J_{3,2\beta}$ = 6.1, 1H, H-2β), 4.61 (t, $J_{2\beta,2\alpha}$ = $J_{3,2\alpha}$ = 8.9, 1H, H-2α), 6.68–6.95 (m, 2H, H-5, H-7), 7.05–7.28 (m, 2H, H-4, H-6); LRMS (EI) *m/e*: 269 (75, M^+), 254 (10), 175 (15), 163 (100), 119 (16), 103 (11), 91 (77), 78 (16), 65 (12), 51 (18). Anal. calcd. for $C_{12}H_{14}O_2Se$: C 53.54, H 5.24; found: C 53.62, H 5.16.

*Methyl 3-benzo[*b*]furan-3-yl)propionate*

To ester **21** (1.00 g, 4.85 mmol) in dry dioxane (25 mL) was added a solution of DDQ (1.32 g, 5.82 mmol) in dioxane (15 mL). The mixture was refluxed for 4h, then cooled. The solid was filtered off and washed with benzene (20 mL), then chloroform (20 mL). The filtrate and washings were combined and concentrated under reduced pressure. The benzofuran ester (0.999 g, 100%) was obtained as a colourless oil after flash chromatography (silica, 30%, EtOAc–hexanes eluent). IR (neat): 2951, 1738, 1452, 1167, 1094, 857, 747 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 2.67–2.75 (m, 2H, 2 × H-3′), 2.98–3.06 (m, 2H, 2 × H-2′), 3.68 (s, 3H, OMe), 7.19–7.33 (m, 2H, H-5, H-7), 7.43–7.57 (m, 3H, H-2, H-4, H-6); LRMS (EI) *m/e*: 204 (61, M^+), 173 (6), 145 (55), 131 (100), 115 (24), 103 (9), 91 (9), 77 (14), 63 (9), 51 (7), 45 (12). Anal. calcd. for $C_{12}H_{12}O_3$: C 70.58, H 5.92; found: C 70.49, H 5.78.

*3-(Benzofuran-3-yl)propionic acid **25***

To the foregoing ester (0.999 g, 4.89 mmol) dissolved in THF (30 mL) with a few drops of MeOH was added 10 mL of 10% NaOH. The solution was stirred at room temperature for 22h. The mixture was concentrated in vacuo and EtOAc (50 mL) added. This was acidified with 2 N HCl and the layers were separated. The aqueous layer was further extracted with EtOAc (2 × 50 mL) and the combined organics were washed with brine and dried (Na_2SO_4). Evaporation of the solvent followed by recrystallization from ether–hexanes gave 0.77 g (83%) of **25** as a colourless solid; mp 106–108°C; IR ($CHCl_3$): 3400–2500, 1710, 1451, 1284, 1118, 858 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ: 2.75–2.81 (m, 2H, 2 × H-3′), 3.00–3.06 (m, 2H, 2 × H2′), 7.21–7.33 (m, 2H, H-5, H-7), 7.45 (s, 1H, H-2), 7.45–7.56 (m, 2H, H-4, H-6); LRMS (EI) *m/e*: 190 (58, M^+), 178 (7), 145 (29), 131 (100), 119 (15), 115 (14), 103 (9), 91 (14), 77 (14), 63 (6), 51 (5). Anal. calcd. for $C_{11}H_{10}O_3$: C 69.47, H 5.30; found: C 69.64, H 5.33.

2,3-Dihydro-1H-cyclopenta[b]benzofuran-3-one ***26***

Polyphosphoric acid was prepared by combining phosphorus pentoxide (0.85 g, 6.0 mmol) with 85% orthophosphoric acid (0.559 mL, 8.17 mmol) and heating at 85°C for 30 min. The acid **25** (0.100 g, 0.526 mmol) was added to the PPA and the mixture was heated at 90°C for 1h. The dark purple solution was cooled to 60°C and poured into ice water. Extraction with Et_2O (3 × 25 mL) was followed by washing the ether extracts with 20% NaOH (50 mL) and water (2 × 25 mL). The organic layer was dried (Na_2SO_4) and concentrated to give 13 mg (14%) of **26** after flash chromatography (silica, 10% EtOAc–hexanes eluent). The basic layer was acidified with 2 N HCl and extracted with EtOAc (2 × 25 mL). The organics were washed with brine (50 mL), dried (Na_2SO_4), and the solvent was removed to provide 76 mg of an orange polymeric material that was not characterized. **26** could be recrystallized from Et_2O–hexanes to afford colourless needles; mp 145–146°C; IR ($CHCl_3$): 3003, 2929, 1688, 1590, 1442, 1394, 1043, 820 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ: 3.00–3.09 (m, 4H, 2 × H-2, 2 × H-1), 7.35 (td, J = 7.9, J = 1.1, 1H, H-7), 7.48–7.61 (m, 2H, H-5, H-6), 7.71 (d, J = 7.9, 1H, H-8); LRMS (EI) *m/e*: 172 (100, M^+), 144 (28), 115 (68), 89 (8), 63 (10); HRMS calcd. for $C_{11}H_8O_2$: 172.05242; found: 172.05240.

2,2a,3,4,5,5a-Hexahydro-5-hydroxy-5a-methyl-8H-naphtho[1,8-bc]furan ***27***

To **19** (450 mg, 2.37 mmol) in EtOH (20 mL) at 0°C was added $NaBH_4$ (24.2 mg, 0.639 mmol). After stirring for 1h at 0°C, water (10 mL) was added and the EtOH was removed under reduced pressure. The aqueous residue was extracted with EtOAc (3 × 20 mL) and the organic extracts were washed with water (50 mL), dried (Na_2SO_4), and concentrated in vacuo. The pale yellow oil was chromatographed (silica, 30% Et_2O–hexanes) to afford 424 mg (93%) of **27** as a colourless oil. IR (neat): 3439 (br), 2931, 1633, 1443, 1389, 1330, 1197, 1062, 1028, 1002, 948, 917, 729 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 1.11 (s, 3H, Me), 1.14–1.32 (m, 1H, H-3β), 1.47–1.79 (m, 2H, H-3α and H-4β), 1.83–1.95 (m, 1H, H-4α), 2.70–2.75 (m, 2H, 2 × H-8), 2.84–2.98 (m, 1H, H-2a), 3.46 (dd, $J_{4\alpha,5}$ = 4.4, $J_{4\beta,5}$ = 11.1, 1H, H-5), 3.96 (dd, $J_{2\alpha,2\beta}$ = 9.1, $J_{2a,2\beta}$ = 5.2, 1H, H-2β), 4.42 (t, $J_{2a,2\alpha} = J_{2\beta,2\alpha}$ = 9.1, 1H, H-2α), 5.75 (AB of ABXX′, J_{AB} = 9.9, J_{AX} = 2.1, J_{BX} = 3.3, Δν = 42, 2H, H-6, H-7); LRMS (EI) *m/e*: 192 (52, M^+), 177 (5), 159 (18), 148 (8), 133 (100), 119 (11), 105 (31), 91 (22), 77 (15), 65 (7). Anal. calcd. for $C_{12}H_{16}O_2$: C 74.96, H 8.39; found: C 74.88, H 8.41.

2a,3,4,8b-Tetrahydro-5-methyl-2H-azuleno[8,1-bc]furan ***28***

To a solution of **27** (70 mg, 0.36 mmol) in THF (2 mL) was added 1,1′-thiocarbonyldiimidazole (0.144 g of 90% technical grade, 0.728 mmol) and the mixture was stirred at 70°C for 3h. The solution was cooled to 25°C and water (10 mL) added. The mixture was extracted with CH_2Cl_2 (3 × 10 mL) and the organic extracts were combined and washed sequentially with 2 N HCl (10 mL), saturated $NaHCO_3$ (10 mL), and water (10 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure to provide an oil, which was subjected to flash chromatography (silica, 20% Et_2O–hexanes eluent) to give 30 mg (48%) of **28** as a pale yellow oil. IR (neat): 2952, 2883, 1640, 1534, 1450, 1368, 1178, 777, 744 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 1.39–1.60 (m, 1H, H-3), 1.84 (s, 3H, Me), 2.11–2.24 (m, 1H, H-3), 2.39–2.53 (m, 1H, H-4), 2.61–2.70 (dd, $J_{3,4}$ = 7.4, $J_{4\alpha,4\beta}$ = 15.5, 1H, H-4), 2.91 (d, $J_{2a,8b}$ = 8.6, 1H, H-8b), 3.01–3.14 (m, 1H, H-2a), 4.08 (dd, $J2a,2\beta$ = 1.3, $J_{2\alpha,2\beta}$ = 8.8, 1H, H-2β), 4.36 (dd, $J_{2a,2\alpha}$ = 5.7, $J_{2\beta,2\alpha}$ = 8.8, 1H, H-2α), 5.53 (dd, $J_{8b,8}$ = 1.4, $J_{7,8}$ = 6.2, 1H, H-8), 6.14 (AB of an ABX system, J_{AB} = 11.3, J_{AX} = 6.1, Δν = 19.7, 2H, H-6, H-7); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 19.89, 31.99, 33.05, 43.96, 49.61, 76.42, 94.43, 125.67, 127.21, 128.25, 132.10, 155.28; LRMS (EI) *m/e*: 174 (91, M^+), 159 (7), 146 (85), 145 (100), 131 (23), 115 (16), 105 (16), 91 (22), 77 (17), 62 (18); HRMS calcd. for $C_{12}H_{14}O$: 174.1044; found 174.1041. Anal. calcd. for $C_{12}H_{14}O$: C 82.72, H 8.10; found: C 82.51, H 7.97.

Attempted dehydrogenation of ***19****, synthesis of 3-(2,3-dihydro-4-methylbenzol[b]furan-3-yl)propanoic acid* ***(30)***

To ketone **19** (118 mg, 0.621 mmol) in dry dioxane (3.5 mL) was added DDQ (0.141 g, 0.621 mmol) and the mixture refluxed for 7h. The solution was cooled and the solid was filtered off. The solid was washed with benzene and the filtrate was concentrated. Flash chromatography (silica, 40% Et_2O–hexanes eluent) afforded an orange oil that appeared as several spots on TLC. NMR analysis of this material revealed the absence of any vinylic protons and the presence of aromatic protons. This material was rechromatographed to furnish 40 mg (31%) of **30** as a colourless solid that could be recrystallized from Et_2O–hexanes.

Attempted bromination of ***19****, synthesis of* ***30***

To **19** (50 mg, 0.26 mmol) in CCl_4 (3 mL) was added freshly recrystallized NBS (50 mg, 0.27 mmol) and the mixture was heated at 60°C for 20 min. The succinimide was seen floating on top of the solution. The flask was cooled in ice and the solution was filtered. The filtrate was concentrated in vacuo. Flash chromatography (silica, 30% EtOAc–hexanes) provided 40 mg (74%) of **30**; mp 85.5–86°C; IR ($CHCl_3$): 3400–2500, 2931, 1709, 1596, 1453, 1244, 710, 649 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ: 1.82–2.11 (m, 2H, 2 × H-3′), 2.31 (s, 3H, Me), 2.28–2.47 (m, 2H, 2 × H-2′), 3.47 (m, 1H, H-3), 4.33 (dd, $J_{2\alpha,2\beta}$ = 9.1, $J_{3,2\beta}$ = 3.1, 1H, H-2β), 4.49 (t, $J_{2\beta,2\alpha} = J_{3,2\alpha}$ = 9.1, 1H, H-2α), 6.63 (d, J = 7.8, 1H, H-5 or H-7), 6.67 (d, J = 7.8, 1H, H-5 or H-7), 7.04 (t, J = 7.8, 1H, H-6); LRMS (EI) *m/e*: 206 (36, M^+), 146 (15), 133 (100), 105 (46), 84 (25), 49 (38). Anal. calcd. for $C_{12}H_{14}O_3$: C 69.89, H 6.84; found: C 69.95, H 6.91.

2,2a,3,4,5,5a-Hexahydro-5-methoxy-5a-methyl-8H-naphtho[1,8-bc]furan ***(31)***

To a solution of **27** (172 mg, 0.895 mmol) and HMPA (171 μL, 0.980 mmol) in dry THF (4 mL) at −78°C was added *n*-BuLi (0.615 mL of a 1.6 M solution in hexanes, 0.98 mmol) dropwise. The solution was stirred at −78°C for 1h. MeI (0.111 mL, 1.77 mmol) was added and the solution allowed to warm to 25°C and stirred for 1h. Water (10 mL) was added and the organic solvents evaporated off under reduced pressure. The aqueous residue was extracted with EtOAc (3 × 10 mL). The organic extracts were combined, washed with brine (20 mL), dried (Na_2SO_4), and concentrated in vacuo. Flash chromatography (silica, 10% EtOAc–hexanes eluent) afforded 152 mg (82%) of methyl ether **31** as a colourless oil. IR (neat): 2933, 2885, 1668, 1582, 1202, 1098, 1000, 955, 932, 729 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 1.09 (s, 3H, Me), 1.15–1.50 (m, 2H, 2 × H-3), 1.84–1.97 (m, 2H, 2 × H-4), 2.70–2.74 (m, 2H, 2 × H-8), 2.84–3.01 (m, 1H, H-2a), 2.94 (dd, $J_{4\beta,5\beta}$ = 3.7, $J_{4\alpha,5\beta}$ = 7.4, 1H, H-5), 3.96 (dd, $J_{2\alpha,2\beta}$ = 9.1, $J_{2a,2\beta}$ = 5.4, 1H, H-2β), 4.42 (t, $J_{2a,2\alpha} = J_{2\beta,2\alpha}$ = 9.1, 1H, H-2α), 5.60 (dt, $J_{8,7}$ = 3.3, $J_{6,7}$ = 9.9, 1H, H-7), 5.88 (dt, $J_{7,6}$ = 9.9, $J_{8,6}$ = 2.1, 1H, H-6); LRMS (EI) *m/e*: 206 (45, M^+), 189 (16), 173 (19), 159 (23), 145 (36), 133 (100), 119 (12), 105 (34), 91 (22), 77 (14), 65 (7). Anal. calcd. for $C_{13}H_{18}O_2$: C 75.71, H 8.80; found: C 75.52, H 8.65.

8-(4′,7′-Dimethoxy-1′,3′-dihydro-1′-benzo[c]furanyl)-2,2a,3,4,5,5a-hexahydro-5a-methyl-8H-naphtho[1,8-bc]furan-5-one ***34***

To a solution of **19** (200 mg, 1.05 mmol) and **32** (103 mg, 0.525 mmol) in CCl_4 (3 mL) was added AcOH (30 μL, 0.53 mmol) and the solution was refluxed for 2h. Saturated aqueous $NaHCO_3$ (5 mL) was added and the mixture was extracted with CCl_4 (3 × 5 mL). The organic extracts were combined, washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude material was subjected to flash chromatography (silica, 10% EtOAc–hexanes eluent) to afford 90 mg (50%) of **34**, which was recrystallized from Et_2O as colourless plates; mp 177–179° C; IR ($CHCl_3$): 3001, 2929, 1702, 1500, 1310, 1258, 1090, 1049, 953, 796, 713 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 1.41 (s, 3H, Me), 1.57–1.75 (m, 1H, H-3β), 2.09–2.22 (m, 1H, H-3α), 2.33 (dt, $J_{4\alpha,4\beta}$ = 14.7, $J_{3\beta,4\beta} \approx J_{3\alpha,4\beta}$ = 3.4, 1H, H-4β), 2.65 (td, $J_{4\beta,4\alpha} = J_{3\beta,4\alpha}$ = 14.7, $J_{3\alpha,4,\alpha}$ = 5.4, 1H, H-4α), 3.36–3.51 (m, 1H, H-2a), 3.59–3.60 (m, 1H, H-8), 3.77 (s, 3H, OMe), 3.78 (s, 3H, OMe), 4.13 (dd, $J_{2\alpha,2\beta}$ = 9.2, $J_{2a,2\beta}$ = 5.2, 1H, H-2β), 4.66 (t, $J_{2a,2\alpha} = J_{2\beta,2\alpha}$ = 9.2, 1H, H-2α), 5.00–5.01 (m, 2H, 2 × H3′), 5.19 (dd, $J_{6,7}$ = 10.0, $J_{8,7}$ = 3.65, 1H, H-7), 5.61–5.63 (m, 1H, H-1′), 5.98 (dd, $J_{7,6}$ = 10.0, $J_{8,6}$ = 1.7, 1H, H-6), 6.71 (s, 2H, H-6′, H-5′); ^{13}C NMR (50

MHz, $CDCl_3$) δ: 25.71, 33.51, 37.79, 39.40, 39.82, 41.41, 50.65, 55.61, 72.95, 75.03, 82.73, 109.93, 110.32, 113.05, 122.79, 128.36, 129.53, 132.01, 148.01, 148.47, 150.01, 211.75; LRMS (EI) *m/e*: 368 (21, M^+), 340 (2), 179 (100), 145 (10), 121 (4), 91 (5), 77 (2); HRMS calcd. for $C_{22}H_{24}O_5$: 368.1623; found: 368.1620.

(3aα,12aS, 14aα,* 14bα)-(±)-*1,2,3a,14,14a,14b-Hexahydro-7,10-dimethoxy-3a-methyl-3*H,*11*H-*benz[*c*]*isobenzofuro[7,1*-ij*][1]-benzoxepin-3-one **35***

To a solution of **34** (50 mg, 0.14 mmol) in EtOH (2 mL) was added 1 drop of concentrated HCl and the solution was stirred at room temperature for 20 min. Water (5 mL) was added and the solution was extracted with $CHCl_3$ (3 × 10 mL). The organic extracts were combined, dried, and concentrated in vacuo. The crude solid was recrystallized from Et_2O to provide 40 mg of **35** as yellow prisms; mp 139.5–140.5° C; IR ($CHCl_3$): 3002, 2937, 1705, 1481, 1461, 1262, 1090, 1046, 953, 798, 715 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 1.28 (s, 3H, Me), 1.81–2.14 (m, 2H, 2 × H-1), 2.26–2.79 (m, 4H, 2 × H-2, H-14a, H-14b), 3.46 (dd, $J_{14\alpha,14\beta}$ = 8.9, $J_{14a,14\beta}$ = 5.4, 1H, H-14β), 4.27 (s, 3H, OMe), 4.32 (s, 3H, OMe), 4.01 (dd, $J_{14\alpha,14\beta}$ = 8.9, $J_{14a,14\alpha}$ = 7.6, 1H, H-14α), 4.88 (AB q, J_{AB} = 13.9, Δν = 65, 2H, 2 × H-11), 5.62 (d, $J_{4,5}$ = 9.8, 1H, H-5), 6.47 (dd, $J_{4,5}$ = 9.8, *J4,14b* = 0.7, 1H, H-4), 6.78 (s, 2H, H-8 and H-9), 7.01 (s, 1H, H-6); LRMS (EI) *m/e*: 368 (44, M^+), 340 (6), 297 (8), 269 (100), 226 (10), 179 (30), 149 (21), 115 (19), 91 (31), 77 (31), 55 (56), 44 (52), 41 (70). HRMS calcd. for $C_{22}H_{24}O_5$: 368.1623; found: 368.1618.

*X-ray structure determination summary of **35***

Crystals of **35** ($C_{22}H_{24}O_5$) are triclinic, space-group $P\bar{1}$ with *a* = 9.411 (2), *b* = 9.694 (2), *c* = 11.478(3) Å, α = 99.92 (2)°, β = 113.50 (2)°, γ = 97.88 (2)° , *V* = 921.1 (4) $Å^3$; Mol. Wt. 368.4, *Z* = 2, D_c = 1.328 g/ cm^3, *F*(000) = 392, μ (MoKα) = 0.93 cm^{-1}.

Data were collected on a colourless prism of dimensions 0.42 × 0.40 × 0.32mm mounted on a Nicolet–Siemens P3m/V diffractometer at 295 K. Data were collected by the ω -scan method to a 2θ-maximum of 50° . From a total of 3265 absorption corrected (ψ-scan) independent reflections measured, 2439 with $F > 6\sigma(F)$ were considered observed and used in the structure solution and refinement. The structure was solved by direct methods (Siemens SHELXTL PLUS) and refined by full-matrix least-squares methods to *R* and *wR* values of 4.24 and 4.04%; the weighting scheme used was $w^{-1} = \sigma^2(F)$. Full details have been deposited as supplementary material.[5]

*5-Hydroxy-5a-methyl-2,2a,3,4,5,5a,8,8a-octahydro-2*H*-naphtho-[1,8-*bc*]furan **38***

To a solution of **27** (80 mg, 0.42 mmol) and $NaBH_3CN$ (27 mg of a 95.7% grade, 0.42 mmol) in EtOH (2 mL) was added one drop of bromocresol green – methyl red indicator. The solution was cooled to 0° C. One drop of concentrated HCl was added to maintain the yellow colour of the solution. The solution was warmed to 25°C and HCl was added a drop at a time as the solution turned blue. The mixture was stirred for 3.5h. Water (10 mL) was added and the EtOH was removed by evaporation under reduced pressure. The aqueous residue was extracted with EtOAc (3 × 10 mL). The organic extracts were combined, washed with water (25 mL), dried (Na_2SO_4), and concentrated in vacuo. Flash chromatography on silica (30% Et_2O–hexanes eluent) afforded 66 mg (82%) of **38** as a colourless oil.

*Direct reduction of **19** to **38***

Compound **19** (1.13 g, 5.94 mmol) and $NaBH_4$ (60.7 mg, 1.61 mmol) were allowed to react according to the procedure given above except that after 1h at 0°C the bromocresol green – methyl red indicator was added and the previous procedure was followed. After flash chromatography on silica (10% Et_2O–hexanes eluent), 0.886 g (78%) of **38** was obtained. IR (neat): 3415 (br), 2934, 2872, 1455, 1060, 1002, 941, 909, 732 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ : 1.13 (s, 3H, Me), 1.44–1.83 (m, 5H, 2 × H-3, 2 × H-4, H-8b), 1.95–2.09 (m, 1H, H-8α), 2.25–2.45 (m, 1H, H-2a), 2.51 (dtd, $J_{8\alpha,8\beta}$ = 15.7, $J_{8a,8\beta}$ = $J_{7,8\beta}$ = 5.7, $J_{6,8\beta}$ = 0.9, 1H, H-8β), 3.61 (dd, $J_{2\alpha,2\beta}$ = 8.4, $J_{2a,2\beta}$ = 1.2, 1H, H-2β), 3.69–3.72 (q, 1H, $J_{4,5}$ = 11.1, 4.4, H-5), 3.89 (ddd, $J_{8b,8a}$ = 9.9, $J_{8\alpha,8a}$ = 11.4, $J_{8\beta,8a}$ = 5.6, 1H, H-8a), 4.03 (dd, $J_{2\beta,2\alpha}$ = 8.4, $J_{2a,2\alpha}$ = 6.1, 1H, H-2α), 5.70 (AB of an ABMX system, J_{AB} = 9.8, J_{BX} = 5.7, J_{BM} = 1.8, J_{AX} = 2.8, J_{AM} = 0.9, Δν = 39.6, 2H, H-6, H-7); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 19.65, 28.20, 30.11, 32.60, 34.63, 41.60, 53.28, 73.08, 73.81, 74.90, 123.12, 136.54; LRMS (EI) *m/e*: 194 (27, M^+), 176 (38), 161 (22), 145 (31), 135 (38), 119 (24), 108 (54), 93 (100), 79 (59), 69 (47). Anal. calcd. for $C_{12}H_{18}O_2$: C 74.19, H 9.34; found: C 74.39, H 9.08.

*5a-Methyl-2a,3,4,5,5a,8,8a,8b-octahydro-2*H*-naphtho[1,8-*bc*]-furanyloxythiocarbonyl-1-imidazole **29***

Alcohol **38** (200 mg, 1.03 mmol) and 1,1′-thiocarbonyldiimidazole (408 mg, 2.06 mmol) were refluxed in benzene (8 mL) for 5h. The solution was cooled to 25°C and the benzene removed under reduced pressure. Water (20 mL) was added to the residue and the mixture extracted with CH_2Cl_2 (3 × 20 mL). The organic layer was washed with 2 N HCl (25 mL), saturated aqueous $NaHCO_3$ (25 mL), and water (50 mL), then dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (silica, 50% Et_2O–hexanes eluent) provided a pale yellow solid, which was recrystallized from $CHCl_3$–hexanes to give 202 mg (65%) of **29** as colourless cubes; mp 152–154° C; IR (neat): 2934, 2879, 1458, 1380, 1330, 1319, 1277, 1233, 979, 738 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ: 1.34 (s, 3H, Me), 1.60–1.81 (m, 3H, 2 × H-3, H-8b), 1.85–2.15 (m, 3H, 2 × H-4, H-8α), 2.39–2.51 (m, 1H, H-2a), 2.58 (dt, $J_{8\alpha,8\beta}$ = 16.2, $J_{7,8\beta}$ = $J_{8a,8\beta}$ = 5.3, 1H, H-8β), 3.67 (dd, $J_{2a,2\beta}$ = 1.3, $J_{2\alpha,2\beta}$ = 8.6, 1H, H-2β), 3.98 (ddd, $J_{8\alpha,8a}$ = 11.5, $J_{8b,8a}$ = 10.0, $J_{8\beta,8a}$ = 5.3, 1H, H-8a), 4.08 (dd, $J_{2\beta,2\alpha}$ = 8.6, $J_{2a,2\alpha}$ = 6.1, 1H, H-2α), 5.53–5.64 (m, 3H, H-5, H-6, H-7), 7.05 (dd, *J* = 1.0, 1H, H-4′ or 5′), 7.63 (dd, *J* = 1.5, *J* = 1.0, 1H, H-4′ or 5′), 8.34 (t, *J* = 1.0, 1H, H-2′); LRMS (EI) *m/e*: 304 (32, M^+), 271 (7), 177 (100), 159 (8), 147 (10, 131 (9), 117 (11), 105 (20), 95 (21), 91 (24), 81 (34), 67 (35). HRMS calcd. for $C_{16}H_{20}N_2O_2S$: 304.1245; found: 304.1235.

*5a-Methyl-2a,3,4,5,5a,8,8a,8b-octahydro-2*H*-naphtho[1,8-*bc*]-furanyl-5-oxy-2,4,6-trichlorophenoxythiocarbonate **39***

To a solution of alcohol **38** (100 mg, 0.515 mmol) in benzene (2.5 mL) was added pyridine (42μ L, 0.52 mmol) and *N*-hydroxysuccinimide (12 mg, 0.10 mmol). Trichlorophenoxythiocarbonyl chloride (156 mg, 0.566 mmol) in benzene (2.5 mL) was added to the solution and the mixture was refluxed for 20h. The solution was filtered to remove any pyridine hydrochloride and the solvent was evaporated under reduced pressure. Water (10 mL) was added to the residue and this was extracted with EtOAc (3 × 10 mL). The organic layer was washed with water (25 mL), dried (Na_2SO_4), and concentrated in vacuo. Flash chromatography (silica, 20% EtOAc–hexane eluent) provided 48 mg (48%) of alcohol starting material and 49 mg (22%, 42% based on recovered starting material) of **39**. This was recrystallized from Et_2O–hexanes; mp 102–103° C; IR ($CHCl_3$): 2938, 2875, 1773, 1568, 1451, 1330, 1233, 1176, 1130, 1054, 1004, 820, 804, 756 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ: 1.24 (s, 3H, Me), 1.53–2.16 (m, 6H, 2 × H-3, 2 × H-4, H-8b, H-8α), 2.32–2.50 (m, 1H, H-2a), 2.51–2.62 (m, 1H, H-8β), 3.65 (dd, $J_{2\alpha,2\beta}$ = 8.5, $J_{2a,2\beta}$ = 1.0, 1H, H-2β), 3.95 (ddd, $J_{8\alpha,8a}$ = 11.5, $J_{8b,8a}$ = 9.9, $J_{8\beta,8a}$ = 5.2, 1H, H-8a), 4.06 (dd, $J_{2\beta,2\alpha}$ = 8.5, $J_{2a,2\alpha}$ = 6.2, 1H, H-2α), 5.30 (dd, $J_{4,5}$ = 4.1, $J_{4,5}$ = 11.5, 1H, H-5), 5.60–5.70 (m, 2H, H-6, H-7), 7.39 (s, 2H, 2 × ArH); LRMS (EI) *m/e*: 434 (17, M^+), 194 (11), 178 (17), 177 (100), 147 (12), 105 (20), 81 (36), 67 (44), 45 (26). Anal. calcd. for $C_{19}H_{19}Cl_3O_3S$: C 52.61, H 4.41; found: C 52.88, H 4.78.

[5]Tables of crystal data, atomic coordinates, bond lengths and angles, anisotropic displacement factors, and observed and calculated structure factors can be purchased from: The Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0S2, Canada.

Tables of crystal data, atomic coordinates, and bond lengths and angles have also been deposited with the Cambridge Crystallographic Data Centre, and can be obtained on request from The Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, 12 Union Road, Cambridge, CB2 1EZ, U.K.

Methyl-5a-methyl-2a,3,4,5,5a,8,8a,8b-octahydro-2H-naphtho[1,8-bc]furanyl-5-xanthate ***40***

Compound **38** (564 mg, 2.90 mmol) was dissolved in dry THF (15 mL) and cooled to −78° C. *n*-BuLi (2.37 mL of a 1.6 M solution in hexanes, 3.80 mmol) was added dropwise to this solution and the mixture stirred at −78°C for 30 min, then at 0°C for 20 min. Dry carbon disulfide (0.263 mL, 4.37 mmol) was added dropwise and the reactin mixture was stirred at 0°C for 40 min. Iodomethane (0.727 mL, 11.6 mmol) was added and the solution stirred at 0°C for 20 min, then at 25°C for 30 min. The solution was poured into ice water (50 mL) and extracted with EtOAc (3 × 40 mL). The EtOAc layer was washed with saturated aqueous NH_4Cl (75 mL), and brine (75 mL), then dried (Na_2SO_4). Concentration in vacuo followed by flash chromatography (silica, 10% EtOAc–hexanes) afforded 0.652 g (79%) of **40** as a colourless oil. IR (neat): 2932, 2870, 1452, 1369, 1216, 1055, 1010, 968, 728 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ: 1.29 (s, 3H, Me), 1.55–2.08 (m, 6H, 2 × H-3, 2 × H-4, H-8b, H-8α), 2.33–2.52 (m, 2H, H-2a, H-8β), 2.56 (s, 3H, SMe), 3.64 (dd, $J_{2\alpha,2\beta}$ = 8.6, $J_{2a,2\beta}$ = 1.4, 1H, H-2β), 3.96 (ddd, $J_{8\alpha,8a}$ = 11.5, $J_{8b,8a}$ = 9.9, $J_{8\beta,8a}$ = 5.3, 1H, H-8a), 4.06 (dd, $J_{2\beta,2\alpha}$ = 8.6, $J_{2a,2\alpha}$ = 6.1, 1H, H-2α), 5.58–5.68 (m, 3H, H-5, H-6, H-7); LRMS (EI) *m/e*: 284 (20, M^+), 251 (5), 237 (5), 177 (100), 159 (20), 133 (14), 117 (19), 105 (29), 91 (36), 81 (36), 79 (20), 67 (37), 55 (16), 41 (20). Anal. calcd. for $C_{14}H_{20}O_2S_2$: C 59.12, H 7.09; found: C 59.01, H 7.01.

5a-Methyl-2a,3,4,5,5a,8,8a,8b-octahydro-2H-naphtho[1,8-bc]furan ***41***

To a solution of xanthate **40** (620 mg, 2.18 mmol) in dry toluene (15 mL) at 90°C was added a solution of *n*-Bu_3SnH (1.99 mL, 7.19 mmol) and AIBN (221 mg) dropwise over 30 min. The solution was stirred an additional 30 min at 90° C, then cooled to 25° C. The solvent was removed by concentrating in vacuo and the residue chromatographed (silica, 100% hexane then 50% CH_2Cl_2–hexanes eluent) to provide 268 mg (69%) of **41**. IR (neat): 2927, 2868, 1459, 1365, 1060, 1006, 938, 724 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 1.11 (s, 3H, Me), 1.31–1.72 (m, 7H, 2 × H-3, 2 × H-4, 2 × H-5, H-8b), 2.00 (ddd, $J_{8\alpha,8\beta}$ = 15.3, $J_{8a,8\alpha}$ = 10.1, $J_{7,8\alpha}$ = 1.5, 1H, H-8α), 2.26–2.39 (m, 1H, H-2a), 2.42–2.55 (m, 1H, H-8β), 3.62 (dd, $J_{2\alpha,2\beta}$ = 8.3, $J_{2a,2\beta}$ = 1.3, 1H, H-2β), 3.89 (ddd, $J_{8\alpha,8a}$ = 11.1, $J_{8a,8b}$ = 10.1, $J_{8\beta,8a}$ = 5.2, 1H, H-8a), 4.04 (dd, $J_{2\beta,2\alpha}$ = 8.3, $J_{2a,2\alpha}$ = 6.1, 1H, H-2α), 5.45–5.46 (m, 2H, H-6, H-7); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 20.99, 26.82, 28.51, 32.64, 34.48, 35.12, 50.80, 65.92, 73.60, 74.41, 121.30, 139.54; LRMS (EI) *m/e*: 178 (68, M^+), 163 (20), 147 (34), 134 (36), 119 (27), 105 (43), 91 (66), 82 (100), 69 (65), 55 (32), 41 (72); HRMS calcd. for $C_{12}H_{18}O$: 178.1358; found: 178.1347.

5a-Methyl-2a,3,4,5,5a,8,8a,8b-octahydro-2H-naphtho[1,8-bc]furan-2-one ***42***

Chromium trioxide (438 mg, 4.38 mmol) was suspended in 5 mL of dry CH_2Cl_2 at −20°C and 3,5-dimethylpyrazole (421 mg 4.36 mmol) was added in one portion. After stirring at −20°C for 15 min, **41** (65 mg, 0.36 mmol) in CH_2Cl_2 (1 mL) was added and the mixture was stirred for 4h at −23°C. NaOH (3 mL of a 5 M solution) was added and the mixture was stirred at 0°C for 1 h. The layers were separated and the organic layer was washed with 0.5 N HCl (10 mL) to remove the DMP. The CH_2Cl_2 layer was subsequently washed with water (2 × 10 mL), and brine (10 mL). After drying (Na_2SO_4) and concentrating in vacuo, flash chromatography (silica, ether–hexane 1:1) provided 40 mg (62%) of starting material and 15 mg of **42** as a colourless oil. IR (neat): 2933, 2862, 1780, 1449, 1196, 1160, 1037, 1010, 967, 726 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ: 1.09 (s, 3H, Me), 1.39–1.71 (m, 6H, 2 × H-3, 2 × H-4, 2 × H-5), 1.88–2.04 (m, 2H, H-8, H-8b), 2.23 (ddd, $J_{8,8}$ = 14.9, $J_{8a,8}$ = 10.4, $J_{7,8}$ = 0.9, 1H, H-8), 2.71–2.52 (m, 2H, H-8, H-2a), 4.53 (td, $J_{8a,8\alpha} \approx J_{8a,8b} \approx$ 11.0, $J_{8a,8\beta}$ = 5.3, 1H, H-8a), 5.50–5.51 (m, 2H, H-6, H-7); LRMS (EI) *m/e*: 192 (42, M^+), 177 (5), 164 (12), 148 (33), 133 (100), 119 (31), 106 (68), 91 (96), 79 (63), 67 (34), 55 (29), 41 (58).

5,8-Dimethoxy-1,2,3,4,4a,9,9a,10-octahydro-9,10-epoxyanthracene ***43***

To a solution of **32** (150 mg, 0.765 mmol) in dry *p*-xylene (1.5 mL) was added dry cyclohexene (387μ L, 3.82 mmol) and toluic acid (11 mg, 0.076 mmol). The mixture was heated at 140°C for 36h. The solvent was removed under reduced pressure and the residue was subjected to flash chromatography (neutral alumina, 50% CH_2Cl_2–hexanes eluent) to provide 105 mg (53%) of a 6:1 mixture of *endo* and *exo* isomers of **43**. This mixture was recrystallized from Et_2O to provide colourless needles; mp 75–76° C; IR ($CHCl_3$): 3106, 2937, 2864, 1500, 1461, 1297, 1256, 1091, 985, 894, 846, 797 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ, *exo* isomer: 1.18–1.70 (m, 10H, 2 × H-1, 2 × H-2, 2 × H-3, 2 × H-4, H-4a, H-9a), 3.79 (s, 6H, 2 × OMe), 5.10 (s, 2H, H-9, H-10), 6.63 (s, 2H, 2 × ArH); *endo* isomer: 0.20–0.38 (m, 2H, H-4a, H-9a), 1.18–1.70 (m, 6H, 2 × H-2, 2 × H-3, H-4, H-1), 2.33–2.48 (m, 2H, H-1, H-4), 3.78 (s, 6H, 2 × OMe), 5.42 (d, *J* = 4.8, 2H, H-9, H-10), 6.65 (s, 2H, 2 × ArH); LRMS (EI) *m/e*: 260 (4, M^+), 242 (4) 227 (3), 201 (1), 178 (100), 163, (54), 135 (4), 115 (3), 92 (3), 77 (3), 67 (2), 41 (2). Anal. calcd. for $C_{16}H_{20}O_3$: C 73.82, H 7.74; found: C 73.61, H 7.73.

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