mmol) in buffer solution (25 mL, pH 7.3) was stirred at 40–41 °C. After 6 h of stirring, the whole solution was acidified to pH 2 by 1 N HCl solution, and then oily materials were extracted with ethyl acetate (30 mL × 3). Workup gave the corresponding monoester in a yield of 34% (0.55 g), $[\alpha]_D$ (MeOH) −4.88° (*c* 0.7), 24% ee.

(*S*)-(−)-Ethyl 3-Hydroxy-2-fluoro-2-methylbutyrate. After a mixture of *N*,*N*-dimethylformamide (3.4 mL) and oxalyl chloride (8 mL) in methylene chloride (40 mL) was stirred for 1 h at 0 °C, the solvent was removed under dynamic vacuum. Into the reaction vessel were added acetonitrile (30 mL) and tetrahydrofuran (100 mL) with a syringe under an atmosphere of nitrogen, and then (*S*)-(−)-2-fluoro-2-methylmalonic acid monoethyl ester (6.56 g, 40 mmol, 91% ee) was added at −30 °C. After 1 h of stirring at −30 °C, a solution of sodium borohydride (3.5 g, 93 mmol) in *N*,*N*-dimethylformamide (20 mL) was added slowly at −78 °C, cooling with the dry ice–acetone bath. After adding the above solution, the reaction mixture was stirred for 4 h at −20 °C, and the mixture was quenched with 3 N HCl (50 mL). Oily materials were extracted with ethyl acetate, and the organic layer was washed with 1 N HCl, 5% aqueous $NaHCO_3$, water, and brine. On removal of the solvent, distillation gave (*S*)-(−)-ethyl 3-hydroxy-2-fluoro-2-methylbutyrate (4.11 g, 27.4 mmol) in a yield of 69%, $[\alpha]_D$ (MeOH) −8.16° (*c* 1.81), bp 84–85 °C (8 mmHg), 91% ee: ^{19}F NMR ($CDCl_3$) δ 84.0 (ddq, J_{F-H_A} = 18 Hz, J_{F_A} = 21 Hz, J_{F-CH_3} = 23 Hz); ^1H NMR ($CDCl_3$) δ 1.33 (CH_3, t; $J_{CH_3-CH_2}$ = 7.1 Hz), 1.50 (CH_3, d), 2.67 (OH), 3.77 (H_A, d), 3.88 (H_B, d), 4.27 (CH_2, q).

(*S*)-(−)-Tosylate of 2. A mixture of (*S*)-(−)-ethyl 3-hydroxy-2-fluoromethylbutyrate (2.0 g, 13 mmol) and tosyl chloride (3.0 g, 16 mmol) in pyridine (20 mL) was stirred at room temperature. After 3 h of stirring, the mixture was poured into water and then oily materials were extracted with ethyl acetate. Tosylate was purified by column chromatography on silica gel using the *n*-hexane–diethyl ether (5:1) as an eluent, in 95% yield: $[\alpha]_D$ (MeOH) −1.79° (*c* 1.34); ^{19}F NMR ($CDCl_3$) δ 82.3 (ddq, J_{FCH_3} = 19.5 Hz, J_{FH_A} = 18.3 Hz, J_{FH_B} = 14.7 Hz); ^1H NMR ($CDCl_3$) δ 1.29 (CH_3, t; $J_{CH_3CH_2}$ = 7.4 Hz), 1.52 (CH_3, d), 2.46 (CH_3, s), 4.13 (H_B, d), 4.15 (H_A, d), 4.18 (CH_2, q), 7.30–7.75 (Ar H).

(*S*)-(−)-Ethyl 2-Fluoro-2-methylbutyrate. Into a solution of Me_2CuLi which was prepared from copper iodide (7.6 g, 40 mmol) and methyllithium (1.3 N, 80 mmol) in freshly dried diethyl ether (20 mL) at −20 °C was added (*S*)-(−)-tosylate (3)(5.8 g, 20 mmol) in diethyl ether (10 mL) slowly at 0–5 °C. After 10 h of stirring at 0–5 °C, the reaction mixture was worked up in the usual manner, giving the product in a 50% yield: $[\alpha]_D$ (MeOH) −4.99° (*c* 2.38); ^{19}F NMR ($CDCl_3$) δ 78.2 (ddq; J_{FH_A} = 20.7 Hz, J_{FCH_3} = 16.9 Hz, J_{FCH_3PW} = 17.9 Hz); ^1H NMR ($CDCl_3$) δ 0.94 (CH_3, t, $J_{CH_3CH_2}$ = 7.1 Hz), 1.32 (CH_3, t, $J_{CH_3CH_2}$ = 6.8 Hz), 1.49 (CH_3, d), 1.60–2.20 (m, 2 × H), 4.17 (CH_2, 2 × H).

(*R*)-(+)-Mesylate 6. A mixture solution of (*R*)-(−)-**5** (20 mmol), ethanol (3.8 mL), benzene (4.4 mL), and concentrated H_2SO_4 (4 drops) was refluxed. After 4 h, the reaction mixture was poured into water, and then oily materials were extracted with diethyl ether. After removing the solvent, crude hydroxy ester was obtained. Into the solution of crude hydroxy ester in pyridine (5 mL) was added methanesulfonyl chloride (1.8 g, 16 mmol), and then the whole solution was stirred for 1 day at room temperature. The reaction mixture was worked up in the usual manner. The mesylate was purified by column chromatography on silica gel using a mixture of *n*-hexane–diethyl ether (2:1) as an eluent, in 51% yield: $[\alpha]^{21}_D$ +9.06° (*c* 0.50, MeOH); ^1H NMR ($CDCl_3$) δ 0.97 (CH_3, t, $J_{CH_3CH_2}$ = 7.5 Hz), 1.30 (CH_3, t, $J_{CH_3CH_2}$ = 7.1 Hz), 1.70 (CH_3, s), 1.90 (CH_2, q), 3.03 (CH_3, s), 4.23 (CH_2, q); IR (C=O) 1740 cm^{-1}.

(*R*)-(+)-Mesylate 6 to (*S*)-(−)-2-Fluoro-2-methylbutyrate. To a solution of cesium fluoride (1.82 g, 12 mmol) and triethylene glycol (5 mL) heated at 110 °C was added (*R*)-(+)-mesylate **6** (10 mmol). The product was collected by the trap to trap distillation under dynamic vacuum: $[\alpha]^{21}_D$ −2.32° (*c* 3.00, MeOH).

Syntheses of Tetrahydrofuro[2,3-*b*]benzofurans: A Synthesis of (±)-Aflatoxin B_2

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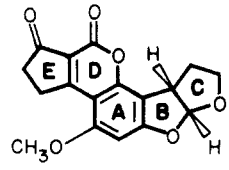
Aldehyde *O*-aryl oximes, on treatment with hydrogen chloride in tetrahydrofuran, are converted to 2-hydroxy-2,3-dihydrobenzofurans and their corresponding 4-chlorobutanol ketals. The major reaction pathway, a 3,4-oxaza Cope rearrangement, is accompanied by Beckmann fragmentation, the relative amount of which is sensitive to the stereochemistry of the oxime and the specific acid conditions. With appropriately substituted oximes, the 2,3,3a,8a-tetrahydrofuro[2,3-*b*]benzofuran ring system is efficiently prepared, as is demonstrated for the 4-hydroxy-6-methoxy derivative and its regioisomer. The former compound provides a total synthesis of aflatoxin B_2.

The aflatoxin are extremely toxic and carcinogenic fungal metabolites that frequently occur as contaminants in a large variety of foods. Their profound biological activity, wide distribution, and unusual structures have generated considerable synthetic activity and resulted in several total syntheses of the racemic mycotoxins, particularly aflatoxin B_2 (**1**).[1]



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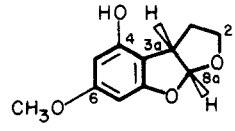

2

In general, the previous syntheses can be considered to consist of three stages: (1) preparation of an appropriately substituted ring A moiety with functionally differentiated phenolic groups, (2) elaboration of the ring A moiety, frequently a coumarin, into the tricyclic ABC ring system, and (3) annulation of the 2-pyran and its fused ring onto the tetrahydrofuro[2,3-*b*]benzfuran (**2**), to add rings D and E. The latter stage 3 (**2**→**1**) has been effectively accomplished.[2] Routes to furobenzofuran **2**, however, have been

(1) Recently reviewed by: Schuda, P. F. *Top. Curr. Chem.* **1980**, *91*, 75.

(2) (a) Roberts, J. C.; Sheppard, A. H.; Knight, J. A.; Roffey, P. *J. Chem. Soc. C* **1968**, 22. (b) Büchi, G.; Weinreb, S. M. *J. Am. Chem. Soc.* **1971**, *93*, 746.

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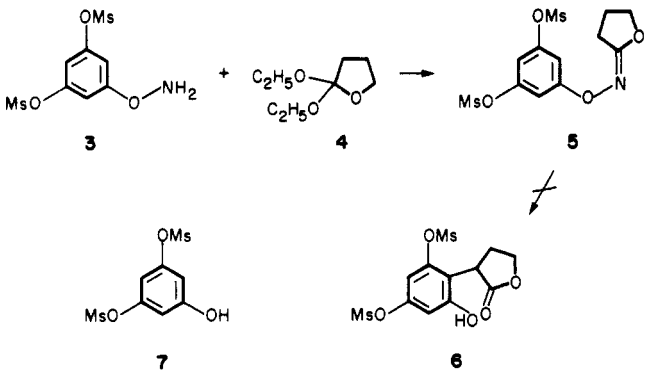
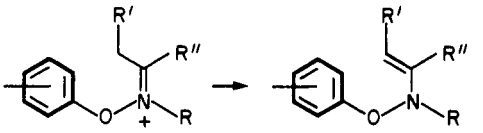
Scheme I. Aryloxyimidate and Attempted Rearrangement



Scheme II. 3,4-Oxaza Cope Rearrangement of Aldehyde *O*-Aryl Oximes



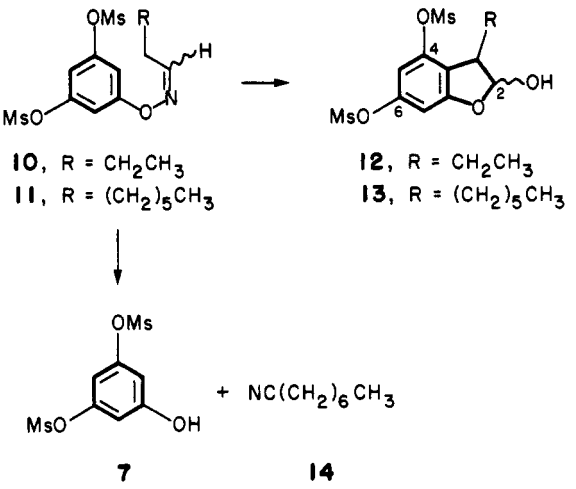
lengthy and complex.[3] We have addressed stages 1 and 2 and now report a straightforward and high-yielding sequence to **2** and its methyl ether regioisomer **30**. Our synthesis provides an example of the application of the benzofuranization of *O*-aryl oximes[4] to the construction of natural products.

Results and Discussion

Our initial route to tetrahydrofuro[2,3-*b*]benzofurans is outlined in Scheme I. The critical carbon–carbon bond formation (**5**→**6**) was to occur through a 3,4-oxaza Cope rearrangement, which is required for the benzofuranization of *O*-aryl oximes.[5] In the route planned, this rearrangement would involve a heteroatom at the 5-position of the 3,4-oxaza Cope system. Since no precedent exists for the application of this or the analogous 3,4-diaza Cope system in the Fischer indole synthesis, the requirements for rearrangement of the *N*-aryloxyimidate **5** are unknown. Should rearrangement be achieved, the synthesis would continue with adjustment in oxidation state of the anticipated lactone **6** to give the tetrahydrofurobenzofuran. The requisite *N*-aryloxyimidate **5** was readily prepared. Attempted rearrangement, however, under a variety of acid conditions led only to cleavage products 3,5-bis(mesyloxy)phenoxyamine (**3**) and 3,5-bis(mesyloxy)phenol (**7**).

The possibility was next explored of inducing rearrangement of the *N*-alkyl *O*-aryl oximes under neutral or alkaline conditions. Such variations of the Fischer indole synthesis have been successful.[6] The requisite intermediate would be an aryloxyiminium ion **8** that would allow the rate-determining tautomerization to the ene phenoxyamine to occur readily without the intervention of acidic conditions[5] (Scheme II). To prepare the aryloxyiminium ion, we attempted to alkylate an *O*-aryl oxime or to condense an alkyl(aryloxy)amine[7] with a carbonyl component. Both processes failed, and this approach was abandoned.

Scheme III. Synthesis of 2,3,3a,8a-Tetrahydro[2,3-*b*]benzofurans



Turning from the use of a preformed ring C, we adopted a plan for the formation of ring B followed by ring C. Butyraldehyde *O*-3,5-bis(mesyloxy)phenyl oxime (**10**) was chosen as a model for determining the acid conditions needed to induce 3,4-oxaza Cope rearrangements of aldehyde oximes. In the aqueous acid medium of phosphoric acid in formic acid, which gives excellent yields of benzofurans with ketone oximes,[4] the butyraldehyde oxime **10** gave only phenol **7** (95% yield). Beckmann rearrangement or fragmentation was considered a highly likely alternative reaction, causing nitrogen–oxygen bond cleavage and giving rise to phenol **7**. Missing was the carbonyl-derived portion of the oxime. To find and identify it, we used octanal oxime **11** to facilitate isolation of this fragment. When **11** was heated in the formic acid/phosphoric acid mixture,[4] we isolated *n*-heptyl cyanide in an amount (80% yield) commensurate with the production of phenol **7** (83% yield). These results clearly demonstrate that our previous aqueous acid conditions, successful with ketone oximes, could not be used with aldehyde oximes since they led to Beckmann fragmentation.[8]

As alternatives, various anhydrous acid systems that would minimize Beckmann rearrangement were explored. Effective conditions were found with 300 mol % of anhydrous HCl in refluxing THF, where the 3,4-oxaza Cope rearrangement was the major reaction pathway, affording dihydrobenzofuran **12** in 70% yield.

With extension of the benzofuranization to aldehyde *O*-aryl oximes assured, we proceeded directly to the synthesis of (±)-aflatoxin B_2 intermediate **2** as given in Scheme III. The requisite aldehyde, 4-(benzoyloxy)-butyraldehyde (**15**) was prepared in 89% yield by oxidation[9] of 4-(benzoyloxy)butanol. This monobenzoylated 1,4-butanediol was in turn produced in 82% yield by a significant improvement over previous procedures.[10]

When aldehyde **15** and 3,5-bis(mesyloxy)phenoxyamine (**3**)[11] were condensed in equimolar amounts, oxime **16** was

(3) (a) Büchi, G.; Foulkes, D. M.; Kurono, M.; Mitchell, G. F.; Schneider, R. S. *J. Am. Chem. Soc.* **1967**, *89*, 6745. (b) Knight, J. A.; Roberts, J. C.; Roffey, P. *J. Chem. Soc. C* **1966**, 1308.

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(5) Comprehensively reviewed by: Robinson, B. "The Fischer Indole Synthesis"; Wiley: New York, 1982; pp 709–729.

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(7) Sheradsky, T.; Nov, E. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2781.

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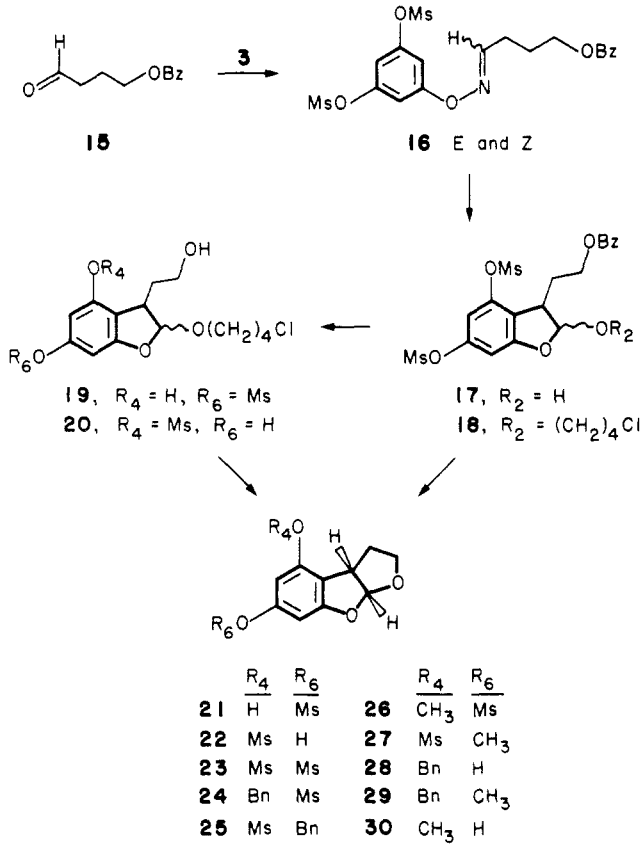
(9) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480.

(10) (a) Wolf, K.-H.; Herlinger, H. *Angew. Makromol. Chem.* **1977**, *65*, 133. (b) Frecht, J. M.; Nuyens, L. J. *Can. J. Chem.* **1976**, *54*, 926. (c) Mitsunobu, O.; Kimura, J.; Iiizumi, K.; Yanagida, N. *Bull. Chem. Soc. Jpn* **1976**, *49*, 510.

(11) Castellino, A. J.; Rapoport, H. *J. Org. Chem.* **1984**, *49*, 1348.

Scheme IV



	R_4	R_6		R_4	R_6
21	H	Ms	**26**	CH_3	Ms
22	Ms	H	**27**	Ms	CH_3
23	Ms	Ms	**28**	Bn	H
24	Bn	Ms	**29**	Bn	CH_3
25	Ms	Bn	**30**	CH_3	H

obtained as an *E* and *Z* mixture in a 2.4/1 ratio, separable by preparative LC. The structural assignments of the oxime isomers are based on the positions in the ^1H NMR spectra of the aldehyde proton absorptions. This absorption is expected to be farther downfield in the *E* isomer, where the proton is in closer proximity to the aromatic residue than it is in the *Z* isomer.

Although oxime **16** could be converted to 2-hydroxy-3-[2-(benzoyloxy)ethyl]-4,6-bis(mesyloxy)dihydrobenzofuran (**17**), the yields and consumption of starting material were erratic, probably because HCl was being lost during the reflux. By increasing the acid stoichiometry to 1000 mol % (1.0 M) and conducting the reaction in a sealed tube at 65–70 °C, we were able to consistently consume all of educt **16**. However, instead of just obtaining hemiacetal **17** (17% yield) we also isolated 2-(4-chlorobutoxy)-3-[2-(benzoyloxy)ethyl]-4,6-bis(mesyloxy)dihydrobenzofuran (**18**) in 59% yield. This acetal results from subsequent reaction of intermediate hemiacetal **17** with 4-chlorobutanol derived from acid cleavage of solvent THF. Such an outcome was clearly advantageous, because it provided a free protection step and gave a reaction product that was readily purified by column chromatography. Therefore, acetalization was forced to completion by simply extending the reaction time and gave **18** in 76% yield as a 3.1/1 mixture of trans and cis isomers, as determined by HPLC. The structural assignment for each isomer is based on the coupling constant between the proton of the acetal functionality and the benzylic proton at C-3. For *trans*-**18** and *cis*-**18** these coupling constants are 2 and 6 Hz, respectively, as expected for a rigid five-membered ring system.

Some phenol **7** was also being formed in these reactions. Because the source of **7** is a Beckmann rearrangement, the *Z* isomer of **16** was expected to give a lower yield of dihydrobenzofuran **18** than the *E* isomer, since the former has the hydrogen and the departing phenoxy residue in a transperiplanar relationship. This expectation was confirmed when *Z*-**16** gave **18** and **7** in 61% and 36% yields, respectively, whereas *E*-**16** provided corresponding yields of 83% and 13%. With the stereochemistry of the oxime playing such an important role, we attempted to isomerize *Z*-**16** to the more stable *E*-**16**. Separation of the *E* and *Z* oxime isomer mixture followed by such an isomerization would effectively increase the yield of conversion from **16** to **18**. However, stirring the oxime isomers (*E*/*Z* 1/1) as a chloroform solution or a suspension over silica led, after 48 h, to a thermodynamic mixture (*E*/*Z* 1.8/1) that was not preparatively practical for the above purpose. In the hope that the kinetic ratio would be more favorable, we increased the relative amount of aldehyde **15** to 150 mol % in the synthesis of **16** and obtained an oxime mixture in 83% yield with an *E*/*Z* ratio of 18/1. Unreacted **15** can be recovered quantitatively. Conversion of **16**, acquired in this fashion, gave **18** in 87% yield.

To complete C-ring formation, alkaline hydrolysis of the benzoate was required, but this could not be done selectively for **18**, since a mesyl substituent was also hydrolyzed. For **17**, however, this selectivity was achieved due to base-promoted ring opening of the hemiacetal to a phenoxide whose negative charge protected the mesylate from hydrolysis.[12] Upon neutralization to pH 7.00, closure of ring C was spontaneous and afforded **23**; however, the isolated yield (39%) was poor.

Because a preference was evident for cleavage of one of the mesyl substituents along with the benzoate, we proceeded with the bis hydrolysis of **18**. Thus a solution of **18** and 300 mol % $LiOH{\cdot}H_2O$ in a mixture of THF and water (3/1) was heated to 40 °C for 1 day to give a mixture of **19** and **20** in 95% yield. At this time, **20** was assumed to be the major isomer based on the rationale that the less sterically hindered 6-mesylate would be more labile to alkaline hydrolysis.

Because attempted purification of the phenolic product (**19**/**20**) by either silica or alumina chromatography led to its complete destruction, the crude product was directly subjected to ring closure by heating at 40 °C for 45 min with *p*-toluenesulfonic acid in acetonitrile in the presence of 4-Å sieves. To realize a 95% yield of ring-closed product (**21**/**22**), the reaction mixture was filtered directly into aqueous sodium bicarbonate before extractive isolation. Purification was further delayed until after formation of the methyl ethers, which was accomplished by stirring a solution of **21**/**22** and 400 mol % dimethyl sulfate in acetonitrile in the presence of 200 mol % potassium carbonate. After silica chromatography, **26**/**27** was obtained in 71% overall yield from **18**. This mixture was then hydrolyzed to **30**/**2** in quantitative yield with 400 mol % tetraethylammonium hydroxide in a refluxing solution of THF and water. Analysis (HPLC) indicated a 16/1 regioisomer ratio. Definitive structural assignments were not possible until **2** and **30** were preparatively separated and their spectral data compared to that reported for **2**.[3b] Thus, we identified the minor isomer in the mixture to be **2**, and the assumption that the 6-mesylate of **18** would be preferentially hydrolyzed is incorrect. That this unexpected selective hydrolysis of the 4-mesylate of **18** was proceeding by the normal sulfur–oxygen bond cleavage anticipated for aryl sulfonates was demonstrated by an hydrolysis in an $H_2{}^{18}O$-enriched system. No ^{18}O was incorporated into the phenolic product.

To determine more accurately the degree of preference for 4-mesylate hydrolysis, analysis of a product mixture

(12) This effect has been exploited in the partial hydrolysis of benzenesulfonyl esters of phloroglucinol: Kampouris, E. M. *J. Chem. Soc.* **1965**, 2651.

closer to the hydrolysis was needed. The most accurate determination would come from an analysis of the **19/20** mixture; however, this is precluded by its instability to chromatography and our inability to derivatize it efficiently. Although product mixture **21/22**, formed in the next step, is also unstable, it can be quantitatively benzylated. The benzyl ethers **24/25** are stable to silica and HPLC analysis showed **24/25** to be present in the ratio 8.1/1, thus reflecting the degree of preference for 4-mesylate hydrolysis in **18** to give **19** as the major isomer. The structural identities of **24** and **25** were confirmed by converting the former compound to **2** as described below.

One possible reason for the preponderance of 7-mesylate hydrolysis in **19** may reside in the participation of the neighboring 2-hydroxyethyl side chain in the subsequent hydrolysis. This possibility was explored when the ring-closed compound **23** was hydrolyzed under identical conditions. The phenols formed were then benzylated, and analysis by HPLC revealed a **24/25** ratio of 6.6/1. Thus, with no internal assistance possible, the preference for 4-mesylate hydrolysis still persisted.

Although this preference poses some interesting mechanistic questions and leads to a high-yielding synthesis of **30**, which might be annulated to give a linear aflatoxin B_2 analogue, it does not give the proper regiochemistry in the A-ring that would lead to the natural product. However, from the benzyl ether mixture **24/25**, this regiochemistry can be easily established. Separation of the mixture required a simple fractional crystallization from the ethyl acetate/hexanes to give **24** free of its regioisomer. Transfer hydrogenolysis with Pd on carbon in refluxing ethyl acetate and 1,4-cyclohexadiene gives, in quantitative yield, phenol **21** free of **22**. The phenolic mesylate **21** is of some interest in that introduction of the coumarin ring system could be possible at this stage.

For the formal total synthesis of (±)-aflatoxin B_2, however, we proceeded from **24** to **2** by hydrolyzing **24** in a refluxing 25% aqueous solution of tetraethylammonium hydroxide. Crude **28** (91% yield) was methylated with dimethyl sulfate in acetonitrile and gave, after chromatography, **29** in 84% overall yield from **24**. Transfer hydrolysis of **29** then gave a quantitative yield of tricycle **2** whose physical and spectral properties are identical with those reported.[3b] The overall yield of **2** from **3** and **15** is 47%. Since the conversion **2** → **1** is well in hand,[2] this completes a synthesis of (±)-aflatoxin B_2.

Experimental Section

General Methods. All melting points were taken on a hot-stage microscope and are uncorrected. ^1H NMR chemical shifts in $CDCl_3$ (unless otherwise specified) are expressed (in ppm) downfield from internal Me_4Si. Elemental analyses were performed by the Analytical Laboratory, College of Chemistry, University of California, Berkeley. Preparative chromatography was done on 230–400-mesh SiO_2 (E. Merck). Thin-layer chromatography (TLC) was done on precoated silica G-60/F-254 aluminum-backed plates (E. Merck). Gas chromatography (GC) was performed with a 4 mm × 1.5 m 10% OV-17 chrom W AW-DMCS glass column at 125 °C with He as the carrier gas at 100 mL/min. Preparative and analytical high-pressure liquid chromtography (HPLC) was performed on the following columns: 4.6 × 250 mm 5 μm Partisil analytical metal column (A); Whatman M-9 50 cm preparative metal column (B); Whatman M-20 ODS-3 preparative metal column (C); 4.6 × 250 cm Ultrasphere ODS analytical metal column (D); IBM 4.5 × 250 cm, 5 μm SiO_2 analytical metal column (E); IBM 4.5 × 250 cm, 5 μm C_{18}-SiO_2 analytical metal column (F). TLC and HPLC were performed with the following solvent system: CH_2Cl_2/hexanes (a); ethyl ether/hexanes (b); water/CH_3CN (c); ethyl acetate/hexanes (d). THF was distilled from $LiAlH_4$. Solutions of HCl in THF were prepared by passing HCl gas through anhydrous THF and titrated immediately prior to use. CH_3CN, CH_3OH, and triethylamine (TEA) were distilled from CaH_2. Dimethyl sulfoxide (Me_2SO) was distilled under reduced pressure from CaH_2. Dimethylformamide (DMF) was distilled under reduced pressure from CaH_2 and then from Al_2O_3. Hexanes were distilled from sodium benzophenone. CH_2Cl_2 was distilled from P_2O_5. All solvents and liquid reagents were stored over 4-Å sieves, except TEA which was stored over CaH_2. Oxalyl chloride was distilled and stored over 3-Å sieves. Benzoyl chloride (BzCl) and benzyl bromide (BnBr) were distilled from $CaCl_2$. All organic layers were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. All reactions requiring an anhydrous atmosphere were performed under N_2.

***N*-[3,5-Bis(mesyloxy)phenoxy]-2-iminotetrahydrofuran (5).** To a melt of 2,2-diethoxytetrahydrofuran (**4**; 135 mg, 0.84 mmol)[13] and aryloxyamine **3** (223 mg, 0.75 mmol)[11] at 100 °C was added one drop of glacial acetic acid. After 15 min the reaction was allowed to cool to room temperature, whereupon the mixture solidified. After trituration with cold ethanol, the resulting solids were purified by chromatography on neutral Al_2O_3 (activity II) using CH_2Cl_2 and recrystallized from absolute ethanol to give 184 mg, 67% yield, of **5** as colorless needles: mp 110–120 °C; TLC (a) R_f 0.32; ^1H NMR δ 2.26 (quin, 2 H, J = 7 Hz), 2.79 (t, 2 H, J = 7), 3.16 (s, 6 H), 4.48 (t, 2 H, J = 7), 6.86 (t, 1 H, J = 2), 7.14 (d, 2 H, J = 2); HRMS, calcd for $C_{12}H_{15}NO_8S_2$ m/e 365.0240, found m/e 365.0255.

Butyraldehyde and octanal *O*-3,5-bis(mesyloxy)phenyl oximes (10, 11) were prepared by the following general procedure:[4] A solution of equimolar amounts of the carbonyl compound and aryloxyamine **3** in absolute EtOH (5 mL/mmol) containing a catalytic amount of concentrated HCl was heated to reflux, whereupon the heat source was immediately removed. Water was added to induce precipiration and give *E* and *Z* mixtures of the oximes.

10: TLC (CH_2Cl_2) R_f 0.29; ^1H NMR δ 1.01 (t, 3 H, J = 7 Hz), 1.6–1.7 (m, 2 H), 2.31 (m, $^6/_5$ H), 2.44 (m, $^4/_5$ H), 2.44 (m, $^4/_5$ H), 3.18 (s, 6 H), 6.89 (m, 1 H), 7.02 (t, $^2/_5$ H, J = 6), 7.09 (d, $^6/_5$ H, J = 2), 7.13 (d, $^4/_5$ H, J = 2), 7.75 (t, $^3/_5$ H, J = 6). Anal. Calcd for $C_{12}H_{17}NO_7S_2$: C, 41.0; H, 4.9; N, 4.0. Found: C, 41.0; H, 4.9; N, 3.9.

11: TLC (CH_2Cl) R_f 0.36; ^1H NMR δ 0.8–0.9 (m, 3 H), 1.3–1.6 (m, 10 H), 2.3–2.4 (m, $^5/_3$ H), 2.5–2.6 (m, $^1/_3$ H, 3.18 (s, 6 H), 6.89 (m, 1 H), 7.01 (t, $^1/_6$ H, J = 6 Hz), 7.08 (d, $^5/_3$ H, J = 2), 7.13 (d, $^1/_3$ H, J = 2), 7.74 (t, $^5/_6$ H, J = 6). Anal. Calcd for $C_{16}H_{25}NO_7S_2$: C, 47.1; H, 6.2; N, 3.4. Found: C, 47.4; H, 6.3; N, 3.3.

***n*-Heptyl Cyanide from 7b.** A solution of **11** (1.06 g 2.5 mmol) in 75 mL of HCO_2H (95–97%) and 7.5 mL of H_3PO_4 (85%) was heated at 60 °C for 90 min and then refluxed for 1 h. After cooling to room temperature, the reaction mixture was poured into 500 mL of cold water and extracted with Et_2O (1 × 400, 3 × 200 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$, extracted with 0.5 N NaOH (1 × 400, 3 × 200 mL), dried, and evaporated to give a residue that was Kugelrohr distilled. From the distillate was obtained 250 mg (80% yield) of *n*-heptyl cyanide, identical with an authentic sample: GC t_R 2.7 min; IR (thin film) 2270 cm^{-1}.

***cis*- and *trans*-2-Hydroxy-3-ethyl-4,6-bis(mesyloxy)dihydrobenzofuran (12).** To oxime **10** (255 mg, 0.73 mmol) in 7 mL of THF was added 0.63 mL of 3.5 M HCl in THF. The resulting solution was refluxed for 1 day, and then solvent was evaporated, the residue was partitioned between 70 mL of water and $CHCl_3$/*i*-PrOH (3/1, 2 × 70 mL), and the combined organic layers were evaporated. The resulting residue was purified by preparative reversed phase HPLC (column C, solvent c) to give after lyophilization 180 mg (71% yield) of **12** as an oil: HPLC (column D; solvent c, 1.0 mL/min) t_R 8.6 min; ^1H NMR (acetonitrile-d_3) δ 0.93 (t, 3 H, J = 7 Hz), 1.6–1.7 (m, 1 H), 1.8–1.9 (m, 1 H), 3.21 (s, 3 H), 3.28 (m + s, 4 H), 5.8 (bs, 1 H), 6.77 (d, 1 H, J = 7), 6.86 (d, 1 H, J = 2). Anal. Calcd for $C_{12}H_{16}O_8S_2$: C, 40.9; H, 4.6. Found: C, 41.1; H, 4.6.

4-(Benzoyloxy)butanol. To 1,4-butanediol (0.88 mL, 10 mmol) in 100 mL of THF at −78 °C was added *n*-BuLi (2.3 M, 4.35 mL, 10 mmol). After stirring for 0.5 h, the solution was

(13) Deslongchamps, P.; Chenevert, R.; Taillefer, R. J.; Moreau, C.; Saunders, J. K. *Can. J. Chem.* **1975**, *53*, 1601.

transferred over a 5-min period to a solution of BzCl (2.4 mL, 20 mmol) in 100 mL of THF at 0 °C. After stirring for 3 h, 100 mL of 10% Na_2CO_3 was added, and the resulting two-phase mixture was stirred at 20 °C for 1 h. The THF was evaporated, and the resulting aqueous solution was diluted with 100 mL of water and extracted with Et_2O (2 × 150 mL). The combined organic layers were dried and concentrated to give a residue that was chromatographed (solvent d, 50/50). Obtained was 1.56 g (82% yield) of the monobenzoate as an oil: TLC R_f 0.40; ^1H NMR δ 1.8–1.9 (m, 4 H), 3.73 (t, 2 H, J = 6 Hz), 4.37 (t, 2 H, J = 6), 7.4–7.6 (m, 3 H), 8.04 (dd, 2 H, J = 1 8) (reported[11b] absorptions at δ 1.6–2.0, 3.72, 4.37).

4-(Benzoyloxy)butyraldehyde (15). To a stirred solution of oxalyl chloride (2.8 mL, 30.8 mmol) in 70 mL of CH_2Cl_2 at −60 °C was added Me_2SO (4.8 mL, 62.0 mmol) in 14 mL of CH_2Cl_2 over a 5-min period. Two min later, 4-(benzoyloxy)butanol (5.50 g, 28.3 mmol) in 28 mL of CH_2Cl_2 was added over a 5-min period. After an additional 15 min, 20 mL of TEA (0.14 mmol) was added to the stirred mixture at −60 °C and this was continued for 15 more min. After reaching room temperature, the reaction mixture was diluted with 150 mL of water and extracted with CH_2Cl_2 (2 × 150 mL). The combined organic layers were washed sequentially with 150 mL each of 1% HCl, water, 5% Na_2CO_3, and water and then dried and concentrated. The resulting residue was Kugelrohr distilled (0.1 torr, 110 °C) and then chromatographed with solvent d to give 5.32 g (98% yield) of **15**: TLC (d, 50/50) R_f 0.49; ^1H NMR δ 2.13 (quin, 2 H, J = 6 Hz), 2.65 (t, 2 H, J = 6), 4.37 (t, 2 H, J = 6), 7.5–7.6 (m, 3 H), 8.03 (dd, 2 H, J = 8), 9.84 (s, 1 H); IR (thin film) 1720 cm^{-1}. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.7; H, 6.3. Found: C, 68.9; H, 6.2.

(*E*)- and (*Z*)-4-(Benzoyloxy)butyraldehyde *O*-3,5-Bis(mesyloxy)phenyl Oxime (16). A solution of aryloxyamine **3** (5.43 g, 18.3 mmol) and aldehyde **15** (5.32 g, 27.7 mmol) in 90 mL of absolute EtOH containing four drops of concentrated HCl was heated to reflux whereupon the heat source was immediately removed. The cooled reaction mixture was diluted with 1 L of Et_2O and washed with 0.5 N NaOH (1 × 500 mL), 20% $NaHSO_3$ (2 × 500 mL),[14] and water (1 × 500 mL). The organic layer was dried and concentrated to give a residue that was chromatographed (solvent d, 50/50). Separation of the E and Z isomers was performed by preparative HPLC (column B; solvent d, 35/65). Oxime **16** was obtained as an oil in 83% yield (7.16 %): TLC (d, 50/50) R_f 0.28.

***Z*-Oxime**: oil; HPLC (column a) eluting with solvent d, 35/65 at 1.0 mL/min, t_R 14.3 min; ^1H NMR ($CDCl_3$) δ 2.10 (quin, 2 H, J = 6 Hz), 2.27 (q, 2 H, J = 6), 3.17 (s, 6 H), 4.41 (t, 2 H, J = 6), 6.90 (t, 1 H, J = 2), 7.10 (m, 3 H), 7.5–7.6 (m, 3 H), 8.04 (dd, 2 H, J = 8).

***E*-Oxime**: mp 79.0–79.5 °C; HPLC (column A; solvent d, 35/65, 1.0 mL/min) t_R 12.8 min; ^1H NMR δ 2.11 (quin, 2 H, J = 6 Hz), 2.56 (q, 2 H, J = 6), 3.17 (s, 6 H), 4.43 (t, 2 H, J = 6), 6.90 (t, 1 H, J = 2), 7.07 (d, 2 H, J = 2), 7.4–7.6 (m, 3 H), 7.84 (t, 1 H, J = 6), 8.83 (dd, 2 H, J = 1, 8). Anal. Calcd for $C_{19}H_{21}NO_9S_2$: C, 48.3; H, 4.3. Found: C, 48.1; H, 4.3.

***cis*- and *trans*-2-(4-Chlorobutoxy)-3-[2-(benzoyloxy)ethyl]-4,6-bis(mesyloxy)dihydrobenzofuran (18b).** To oxime **16** (3.38 g, 7.16 mmol) with E/Z 18/1 in 70 mL of THF was added 18.1 mL of 3.90 M HCl in THF, and the resulting solution was heated at 65 °C for 24 h in thick-walled glass tubes. After being cooled to 20 °C, the contents were evaporated, and the residue was partitioned between 700 mL of water and 700 mL of Et_2O. The aqueous layer was extracted with 350 mL of Et_2O, and the combined organic layers were dried and concentrated. Chromatography of the residue (SiO_2, CH_2Cl_2) gave a mixture of cis and trans isomers of **18** (3.51 g, 87% yield) that were separated by preparative HPLC (column B, solvent d, 65/35).

***cis*-18**: oil; HPLC (column B; solvent d, 50/50, 6.0 mL/min) t_R 25.7 min; ^1H NMR ($CDCl_3$) δ 1.7–1.8 (m, 2 H), 2.1–2.4 (m, 2 H), 3.18 (s, 3 H), 3.22 (s, 3 H), 3.5–3.9 (m, 5 H), 4.4–4.5 (m, 2 H), 5.61 (d, 1 H, J = 2 Hz), 6.78 (d, 1 H, J = 2), 6.85 (d, 1 H, J = 2), 7.4–7.6 (m, 3 H), 8.05 (dd, 2 H, J = 1.8).

***trans*-18**: oil; HPLC (column B; solvent d, 50/50, 6.0 mL/min) t_R 24.2 min; ^1H NMR δ 1.8–1.9 (m, 2 H), 2.2–2.7 (m, 2 H), 3.17 (s, 3 H), 3.22 (s, 3 H), 3.5 4.0 (m, 5 H), 4.4–4.8 (m, 2 H), 5.97 (d, 1 H, J = 6 Hz), 6.76 (d, 1 H, J = 2), 6.78 (d, 1 H, J = 2), 7.4–7.6 (m, 3 H), 8.07 (dd, 2 H, J = 1, 8). Anal. Calcd for $C_{23}H_{27}O_{10}S_2Cl$: C, 49.1; H, 4.8; Cl, 6.3. Found: C, 49.0; H, 5.0; Cl, 6.3.

***cis*- and *trans*-2-Hydroxy-3-[2-(benzoyloxy)ethyl]-4,6-bis(mesyloxy)dihydrobenzofuran (17).** To oxime **16** (1.89 g, 4.0 mmol; E/Z 18/1) in 40 mL of THF was added 6.5 mL of 6.19 M HCl in THF, and the resulting solution was heated at 65 °C in a sealed glass tube. After 16 h, the reaction mixture was treated as above to give 1.10 g (48% yield) of **18**. The flash column was then eluted with CH_3OH to give a mixture of **17** and phenol **7**. Preparative reversed-phase HPLC (column E, solvent c) and lyophilization afforded a 420-mg (22% yield) mixture of *cis*- and *trans*-**17**: oil; HPLC (column E; solvent c, 1.0 mL/min) t_R 16.2 min; ^1H NMR δ 2.1–2.4 (m, 2 H), 3.16 (s, 3 H), 3.20 (s, 3 H), 3.6–3.7 (m, 1 H), 4.44 (t, 2 H, J = 6 Hz), 5.93 (bs, 1 H), 6.80 (bs, 1 H), 6.83 (bs, 1 H), 7.4–7.6 (m, 3 H), 8.0–8.1 (m, 2 H). Anal. Calcd for $C_{19}H_{20}O_{10}S_2$: C, 48.3; H, 4.3. Found: C, 48.1; H, 4.3.

4,6-Bis(mesyloxy)-2,3,3a,8a-tetrahydro[2,3-*b*]benzofuran (23). A two-phase mixture consisting of **17** (410 mg, 0.87 mmol) in 50 mL of Et_2O and 50 mL of 0.5 N NaOH was vigorously stirred at 20 °C for 1 h. The aqueous layer was cooled to 0 °C, neutralized to pH 7.0 with dilute HOAc, and then extracted with Et_2O (1 × 50, 2 × 25 mL). The combined organic layers were dried and concentrated, and the residue was chromatographed (solvent d, 50/50) to give 120 mg (39% yield) of **23**: mp 125–126 °C; TLC (d, 50/50) R_f 0.21; ^1H NMR δ 2.2–2.3 (m, 2 H), 3.18 (s, 3 H), 3.27 (s, 3 H), 3.6–3.7 (m, 1 H), 4.1–4.2 (m, 2 H), 6.41 (d, 1 H, J = 6 Hz), 6.71 (d, 1 H), J = 2), 6.81 (d, 1 H, J = 2). Anal. Calcd for $C_{12}H_{14}O_8S_2$: C, 41.1; H, 4.0. Found: C, 41.1, H, 4.1.

***cis*- and *trans*-2-(4-Chlorobutoxy)-3-(2-hydroxyethyl)-4-hydroxy-6-(mesyloxy)dihydrobenzofuran (19).** A solution of **18** (3.51 g, 6.23 mmol) and $LiOH·H_2O$ (784 mg, 18.7 mmol) in 114 mL of THF and 38 mL of water was heated at 40 °C for 1 day. After cooling to 20 °C, the reaction mixture was poured into 1.5 L of cold 0.5 N NaOH and extracted with Et_2O (2 × 750 mL). The aqueous layer was neutralized to pH 7.0 with dilute HOAc and extracted with Et_2O (3 × 750 mL). Concentrating the combined organic layers gave 2.24 g (95% crude yield) of **19** contaminated with **20**.

19: TLC (d, 50/50) R_f 0.14; ^1H NMR δ 1.6–2.1 (m, 6 H), 3.14 (s, 3 H), 3.3–4.0 (m, 7 H), 5.34 (d, $^2/_3$ H, J = 1 Hz), 5.68 (d, $^1/_3$ H, J = 7), 6.3–6.4 (m, 2 H); HRMS,[15] calcd for $C_{15}H_{19}O_6S^{35}Cl$ m/e 362.0592, found m/e 362.0587; calcd for $C_{15}H_{19}O_6S^{37}Cl$ m/e 364.0562, found m/e 364.0567.

4-Hydroxy-6-(mesyloxy)-2,3,3a,8a-tetrahydrofuro[2,3-*b*]benzofuran (21). To a stirred suspension at 20 °C of 2 g of 4-Å activated sieves in 25 mL of CH_3CN containing **19**/**20** (344 mg, 0.90 mmol) was added 70 mg of *p*-toluenesulfonic acid monohydrate. After 45 min, the reaction mixture was filtered into 250 mL of aqueous $NaHCO_3$ (20% saturated) and extracted with Et_2O (3 × 150 mL). The combined organic layers were dried and concentrated to give 233 mg (95% crude yield) of **21**/**22**. Pure **21** was prepared (described below) by converting the phenols to benzyl ethers, separated the isomers, and hydrogenolyzing benzyl ether **24**.

21: mp 163–164 °C; TLC (d, 50/50) R_f 0.25; ^1H NMR δ 2.2–2.3 (m, 2 H), 3.14 (s, 3 H), 3.6–4.2 (m, 3 H), 6.32 (d, 1 H, J = 2 Hz), 6.35 (d, 1 H, J = 2), 6.36 (d, 1 H, J = 6). Anal. Calcd for $C_{11}H_{12}O_6S$: C, 48.5; H, 4.4. Found: C, 48.5; H, 4.4.

4-(Benzyloxy)-6-(mesyloxy)- and 4-(Mesyloxy)-6-(benzyloxy)-2,3,3a,8a-tetrahydrofuro[2,3-*b*]benzofuran (24, 25). Potassium hydride (118 mg of a 35 wt % dispersion in oil) was washed with hexanes (2 × 2 mL) and suspended in 10 mL of DMF. To the stirred suspension at 0 °C was added **21**/**22** (272 mg, 1.0 mmol) in 8 mL of DMF over 5 min. The reaction mixture was allowed to reach 20 °C, (30 min), BnBr (119 μL, 1.0 mmol) in 8 mL of DMF was added, and stirring was continued for 1 day. The DMF solution was poured into 200 mL of 0.5 N NaOH and extracted with CH_2Cl_2 (1 × 200, 2 × 100 mL); the organic layers were dried and concentrated, and the residual DMF was removed by Kugelrohr distillation. The resulting residue was passed

(14) This step is omitted if the intention is to recover unreacted aldehyde **15** in the subsequent chromatography.

(15) These values are for $M^+ - 18$. A molecular ion could not be observed in the HRMS; however, low-resolution gave the M^+ m/z 380 peak.

through a plug of silica with EtOAc to give 336 mg of **24/25** (93% yield). The isomers are separated by fractional crystallization from EtOAc/hexane and chromatography (solvent d, 50/50).

25: mp 125–127 °C; TLC (d, 50/50) R_f 0.35; HPLC (column F) eluting with solvent d, 40/60, at 1.0 mL/min, t_R 5.7 min; ^{1}H NMR δ 2.2–2.3 (m, 2 H), 3.18 (s, 3 H), 3.6–3.7 (m, 1 H), 4.1–4.2 (m, 2 H), 5.01 (s, 2 H), 6.34 (d, 1 H, J = 6 Hz), 6.43 (d, 1 H, J 2), 6.45 (d, 1 H, J 2), 7.3 (m, 5 H).

24: mp 191–193 °C; TLC (d, 50/50) R_f 0.43; HPLC (column F; solvent d, 40/60, 1.0 mL/min) t_R 4.8 min; ^{1}H NMR δ 2.2–2.3 (m, 2 H), 3.09 (s, 3 H), 3.6–3.8 (m, 1 H), 4.0–4.1 (m, 2 H), 5.09 (s, 2 H), 6.35 (d, 1 H, J = 2 Hz), 6.39 (d, 1 H, J = 2), 6.47 (d, 1 H, j = 2), 7.4 (m, 5 H). Anal. Calcd for $C_{18}H_{18}O_6S$: C, 59.7; H, 5.0. Found: C, 59.7; H, 5.0.

4-Methoxy-6-(mesyloxy)-2,3,3a,8a-tetrahydro[2,3-*b*]benzofuran (26). To a stirred suspension of K_2CO_3 (233 mg, 1.7 mmol) in 8.5 mL of CH_3CN at 20 °C containing **21/22** (233 mg, 0.85 mmol) was added Me_2SO_4 (320 μL, 3.4 mmol). After 1.75 h, the solvent was evaporated and the residue was shaken for 5 h with excess 2.8 M glycine. The mixture was diluted with 100 mL of water and extracted with CH_2Cl_2 (3 × 75 mL), and the combined organic layer was washed with 0.5 N NaOH (2 × 75 mL), dried, and concentrated. The resulting residue was chromatographed (solvent d, 35/65) to give 226 mg (93% yield) of **26/27**. Fractional crystallization from EtOAc/hexanes gave pure **26**: mp 118–119 °C; TLC (d, 50/50) R_f 0.38; ^{1}H NMR δ 2.2 (m, 2 H), 3.15 (s, 3 H), 3.6–3.8 (m, 1 H), 3.84 (s, 3 H), 4.0–4.1 (m, 2 H), 6.35 (d, 1 H, J = 6 Hz), 6.38 (d, 1 H, 2), 6.40 (d, 1 H, J = 2). Anal. Calcd for $C_{12}H_{14}O_6S$: C, 50.3; H, 4.9. Found: C, 50.5; H, 5.1.

4-Methoxy-6-hydroxy-2,3,3a,8a-tetrahydrofuro[2,3-*b*]benzofuran (30). A solution of **26/27** (147 mg, 0.51 mmol) and 300 mg of $Et_4N^+OH^-$ in 7.6 mL of THF and 0.9 mL of H_2O was heated at reflux for 5 h. After cooling to 20 °C, the reaction mixture was poured into 85 mL of cold 0.5 N NaOH and extracted with CH_2Cl_2 (2 × 40 mL). The aqueous layer was neutralized to pH 7.0 with dilute HOAc and extracted with Et_2O (1 × 80, 2 × 40 mL). Evaporating the combined organic layers gave 106 mg (100% yield) of **30/2**, which required no further purification. Preparative HPLC (column B, solvent d, 50/50) and sublimation (0.15 torr, 150 °C) gave pure **30**: mp 170–171 °C; TLC (d, 30/70) R_f 0.18; HPLC (column B; solvent d, 5.6 mL/min, t_R 8.2 min); ^{1}H NMR δ 2.1–2.2 (m, 2 H), 3.6–3.7 (m, 1 H), 3.79 (s, 3 H), 3.9–4.1 (m, 2 H), 5.08 (bs, 1 H) 6.0 (m, 2 H), 6.29 (d, 1 H, J = 6 Hz). Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.5; H, 5.8. Found: C, 63.5; H, 5.7.

4-(Benzyloxy)-6-hydroxy-2,3,3a,8a-tetrahydrofuro[2,3-*b*]benzofuran (28). A suspension of **24** (100 mg, 0.28 mmol) in 6 mL of 25% aqueous $Et_4N^+OH^-$ was heated to reflux for 4 h. After cooling to 20 °C, the homogeneous solution was poured into 60 mL of cold 0.5 N NaOH, neutralized to pH 7.0 with dilute HOAc, and extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were evaporated to give 71 mg of **28**: TLC (d, 30/70) R_f 0.23; ^{1}H NMR δ 1.6 (bs, 1 H), 2.1–2.2 (m, 2 H), 3.6–3.7 (m, 1 H), 4.0–4.1 (m, 2 H), 5.05 (s, 2 H), 5.98 (d, 1 H, J = 2 Hz), 6.03 (d, 1 H, J = 2), 6.30 (d, 1 H, J = 6), 7.3–7.4 (m, 5 H).

4-(Benzyloxy)-6-methoxy-2,3,3a,8a-tetrahydrofuro[2,3-*b*]benzofuran (29). To a stirred suspension of K_2CO_3 (69 mg, 0.5 mmol) in 2.5 mL of CH_3CN at 20 °C containing 71 mg of crude **28** (0.25 mmol) was added Me_2SO_4 (95 μL, 1.0 mmol). After 5 h the solvent was evaporated, and the residue was shaken for 5 h with excess 2.8 M glycine. After dilution with 30 mL of water, the mixture was extracted with CH_2Cl_2 (1 × 30, 2 × 15 mL), the combined organic layers were extracted with 0.5 N NaOH (2 × 15 mL) and evaporated, and the residue was chromatographed (solvent d, 30/70) to give 69 mg (84% overall yield from **24**) of **29**: mp 93.0–93.5 °C; TLC (d, 30/70) R_f 0.43; ^{1}H NMR δ 2.1–2.2 (m, 2 H), 3.6–3.7 (m, 1 H), 3.74 (s, 3 H), 4.0–4.1 (m, 2 H), 5.06 (s, 2 H), 6.06 (d, 1 H, J = 2 Hz), 6.09 (d, 1 H, J = 2), 6.30 (d, 1 H, J = 6). Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.5; H, 6.1. Found: C, 72.4; H, 6.2.

4-Hydroxy-6-methoxy-2,3,3a,8a-tetrahydrofuro[2,3-*b*]benzofuran (2). To a solution of **29** (20 mg, 67 μmol) in 2 mL of EtOAc and 0.5 mL of 1,4-cyclohexadiene at reflux was added 15 mg of 30% Pd on carbon. After 5 h, the suspension was filtered hot through celite and the filtrate was evaporated, leaving 14 mg (100% yield) of pure **2**: mp 152–154 °C (lit.[3b] mp 153–154 °C); HPLC (column B; solvent d, 50/50, 5.6 mL/min) t_R 9.6 min; ^{1}H NMR δ 2.1–2.2 (m, 2 H), 3.6–3.7 (m + s, 4 H), 5.1 (bs, 1 H), 5.92 (d, 1 H, J = 2 Hz), 6.03 (d, 1 H, J = 2), 6.32 (d, 1 H, J = 6).

Under identical reaction conditions, **24** was converted to **21** in quantitative yield.

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