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(±)-*trans*,*cis*-4-Hydroxy-5,6-di-*O*-isopropylidenecyclohex-2-ene-1-one: Synthesis and Facile Dimerization to Decahydrodibenzofurans

Victoria L. Paddock, Robert J. Phipps, Almudena Conde-Angulo, Araceli Blanco-Martin, Carles Giró-Mañas, Laetitia J. Martin, Andrew J. P. White, and Alan C. Spivey*

Department of Chemistry, Imperial College, London, SW7 2AY, U.K.

a.c.spivey@imperial.ac.uk

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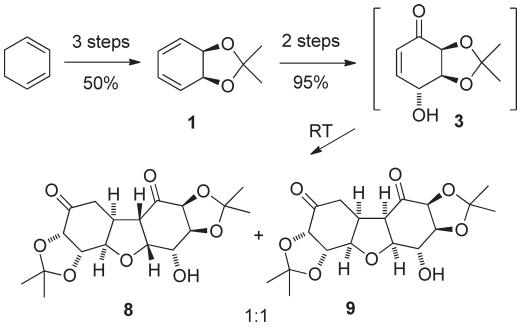

An efficient synthesis of (±)-*trans*,*cis*-4-hydroxy-5,6-di-*O*-isopropylidenecyclohex-2-ene-1-one (**3**) has been developed from acetonide-protected *meso*-1,2-dihydrocatechol derivative **1** via photooxygenation, then Kornblum−DeLaMare rearrangement. The product is unstable unless its 4-hydroxy group is protected, as it undergoes facile dimerization in solution to a 1:1 mixture of diastereoisomeric decahydrodibenzofurans **8** and **9**. A new synthesis of the dihydrocatechol **1** from 1,3-cyclohexadiene has also been developed.

During the course of ongoing studies toward the total asymmetric synthesis of the *Amaryllidaceae* alkaloid (-)-lycorine,[1,2] we required an efficient preparation of *racemic* 4-hydroxy enone **3** for development work. Syntheses of this versatile enone in an enantiomerically pure form, with various protecting groups (R) on the 4-hydroxy function, have been described previously from *meso*-1,2-dihydrocatechol derivative **1** via enzymatic acylative/deacylative desymmetrization [(-)-ent, R = Ac; (+)-ent, R = TBS),[3−5] from D-galactose [(+)-ent, R = Ac)[6] and from (-)-quinic acid [(-)-ent, R = TBS).[7−9] These routes employ either allylic alcohol oxidation or β-hydroxyketone elimination as the final step to establish the enone function and, therefore, do not provide enone **3** free of protection at the 4-OH group directly. By contrast, a shorter route pioneered by Hudlicky[10−13] from *Pseudomonas putida* chlorobenzene metabolite[14,15] (+)-*cis*-1-chloro-4,6-cyclohexadiene-2,3-diol via photooxygenation, then thiourea-mediated hydrogenolysis of the resulting endoperoxide, does provide the unprotected (-)-4-hydroxy enone **3** but has the drawback that this starting material is expensive (due to its nontrivial isolation from the fermentation broth). Vexed by the high cost and apparent instability[2] of (-)-4-hydroxy enone **3** obtained via this route, we sought to develop a new route to racemic enone **3**. Here, we describe these studies and also the structural elucidation of two diastereomeric dimers of this compound, the facile formation of which explains its instability in solution in the presence of base.

Inspired by the syntheses of various conduritols by Balci,[16] we envisaged that (±)-4-hydroxy enone **3** could be prepared from *meso*-1,2-dihydrocatechol derivative **1** by photooxygenation[17,18] and then Kornblum−DeLaMare (KDLM)[19] rearrangement (Scheme 1).[20]

Although *meso*-1,2-dihydrocatechol (a *Pseudomonas putida* benzene metabolite[14,15]) is commercially available, it is expensive and prone to aromatization on storage, and so we required a more economic source of its acetonide derivative **1**. Nonenzymatic syntheses have been reported by Yang[21,22]

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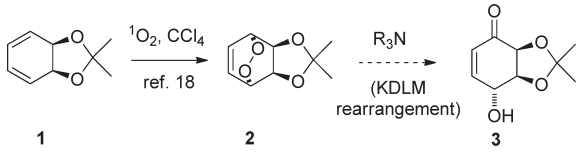
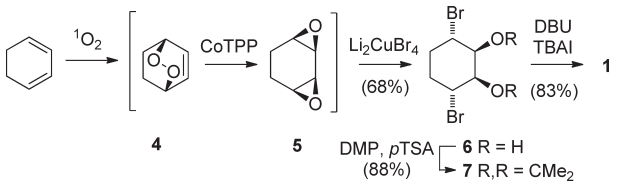
SCHEME 1. Envisaged Synthesis of 4-Hydroxy Enone 3



SCHEME 2. Synthesis of *meso*-1,2-Dihydrocatechol Derivative 1

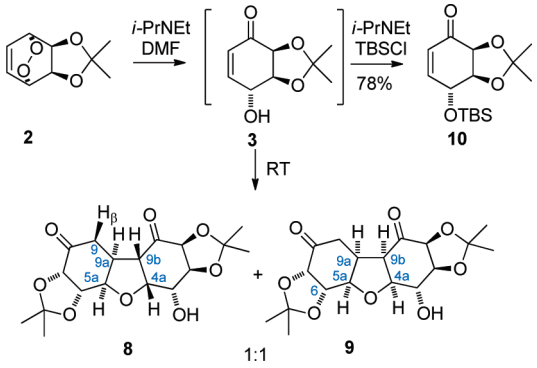


(four steps, 26% yield overall from 1,4-cyclohexadiene[23]) and by Fabris[24] (three steps, 36% yield overall from *myo*-inositol)[25], but these proved unsatisfactory in our hands. Consequently, we developed an alternative three-pot synthesis from 1,3-cyclohexadiene (Scheme 2).

Thus, photooxidation of 1,3-cyclohexadiene in CCl_4 at 0 °C (300 W sun lamp, 5.5 h) using tetraphenylphorphyrin (TPP, 2 mol %) as a photosensitizer gave endoperoxide **4**,[26,27] which was not isolated but treated directly with cobalt-TPP (2 mol %) to give bis-epoxide **5**.[28] Efficient isolation of bis-epoxide **5** is hampered by its low boiling point, but direct treatment of the crude reaction mixture with a solution of dilithium tetrabromocuprate (Li_2CuBr_4)[29] allows in situ bis-ring-opening to give *cis*-dibromide **6** in 68% overall yield from 1,3-cyclohexadiene.[30] Protection of the diol unit using DMP/*p*-TsOH gives acetonide **7** (88% yield); then, bis-elimination of HBr using DBU/TBAI in CH_2Cl_2 at reflux gives the desired diene **1** in 83% yield after distillation. The relative stereochemistry of compound **7** was confirmed by a single-crystal X-ray structure determination (see the Supporting Information). Overall, this three-pot sequence of reactions gives diene **1** in ~50% yield on a preparative scale from 1,3-cyclohexadiene.

Photooxygenation of diene **1** in CCl_4 at RT (300 W sun lamp, 7.5 h, TPP, 5 mol %)[17,18] gave the known endoperoxide **2** (95% yield). Pleasingly, treatment of this compound with

SCHEME 3. Synthesis of 4-Hydroxy Enone 3



Hunig's base (1 equiv) in either CH_2Cl_2 or DMF (~0.4 M) effected KDLM rearrangement to give 4-hydroxyenone **3** essentially quantitatively within 40 min, as judged by ^1H NMR and TLC. However, if left for longer, a new substance started to form, which was slightly less polar than enone **3** and non-UV-active by TLC. This substance also formed during solvent evaporation and significantly impaired isolation of enone **3** (66% yield). It displays a m/z (MNH_4^+) of 386 Da, which corresponds to a dimer of enone **3**, but the complexity of the ^1H NMR fingerprint was suggestive of more than one isomer. A single-crystal X-ray structure determination on a crystalline component of this product (see the Supporting Information) revealed it to be the pentacyclic *cis*,*trans*,*cis*-decahydrodibenzofuran derivative **8** (Scheme 3). This compound accounts for exactly half of the ^1H NMR signals in the crude spectrum; the remaining signals are those of the diastereomeric *cis*,*cis*,*cis*-decahydrodibenzofuran **9**, which is noncrystalline, is chromatographically inseparable from *cis*,*trans*,*cis*-decahydrodibenzofuran **8**, and is formed in a close to equal amount (i.e., **8**/**9** 1:1).[31] The stereochemical assignments for dimers **8** and **9** were confirmed by NOESY NMR: dimer **8** shows nOe crosspeaks for $H_{4a} \leftrightarrow H_{9b}$, $H_{5a} \leftrightarrow H_{9a}$, and $H_{9b} \leftrightarrow H_{9\beta}$, whereas dimer **9** shows them for $H_{4a} \leftrightarrow H_{9b}$, $H_{4a} \leftrightarrow H_{5a}$, $H_{5a} \leftrightarrow H_{9a}$, $H_{5a} \leftrightarrow H_{9b}$, $H_{5a} \leftrightarrow H_6$, and $H_{9a} \leftrightarrow H_{9b}$. These are consistent with the crystal structure of dimer **8** and a MMFF94 minimized structure for dimer **9** (Scheme 3).

Formation of these dimers probably results from a double Michael addition cascade: first, *inter*molecular addition of the alcohol/alkoxide to the enone, then *intra*molecular addition of the resulting enol/enolate to the remaining enone, effecting 5-*exo*-trig cyclization to give the central THF ring. There appears to be no preference for which face of the enone is attacked in the initial conjugate addition step to form the C_{4a} stereocenter, but the enol/enolate reacts with complete facial selectivity for the formation of the C_{8a} and C_{8b} stereocenters. An analogous dimerization process has previously been reported by Carreño and Ribagorda[32] for a 4-substituted-4-hydroxycyclohexen-2-one using NaH in CH_2Cl_2, which was reported to give a *cis*,*trans*,*cis*-decahydrodibenzofuran exclusively.

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(23) The Chan sequence of reactions (ref 21) has been reported by Johnson et al. to proceed in 87% overall yield. In our hands, however, the original yields are reproduced; see: Johnson, C. R.; Ple, P. A.; Adams, J. P. *J. Chem. Soc., Chem. Commun.* **1991**, 1006.
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(25) The Fabris route (ref 24) is based on one developed by Mereyala for the synthesis of the cyclohexylidene analogue; see: Mereyala, H. B.; Pannala, M. *Tetrahedron Lett.* **1995**, *36*, 2121.
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(30) $CuBr_2$ can also be employed to affect this transformation, but the yield is slightly lower. Interestingly, if any 1,3-cyclohexadiene is carried through into this step (due to incomplete photooxygenation), $CuBr_2$ affects efficient conversion of this compound to 1,4-dibromocyclohex-2-ene, predominantly as the crystalline *trans* isomer. This compound has been prepared previously by treatment of 1,3-cyclohexadiene with Br_2 at −70 °C and a crystal structure reported; see: Han, X.; Khedekar, R. N.; Masnovi, J.; Baker, R. J. *J. Org. Chem.* **1999**, *64*, 5245–5250.
(31) Dimers **8** and **9** are also formed as an ~1:1 mixture from the decomposition of the enantiomerially pure (-)-**3** formed by the Hudlicky route (ref 2), as judged by ^1H NMR following attempted isolation. However, this is only a minor component of the decomposition pathway in those reactions; the major decomposition product is highly polar and results from reaction of the enone **3** with the thiourea (or derived carbodiimide) employed to affect the final endoperoxide hydrogenolysis.
(32) Carreno, M. C.; Ribagorda, M. *Org. Lett.* **2003**, *5*, 2425–2428.

Because 4-hydroxyenone **3** is prone to dimerization, particularly during solvent evaporation, in situ protection proved to be the preferred method for obtaining its O-protected derivatives. For example, if further Hunig's base (1 equiv) and TBSCl (2 equiv) are added immediately after the disappearance of endoperoxide **2** in the KDLM rearrangement reaction and the solution is left to stir overnight, the TBS ether **10** is isolated in 78% yield (Scheme 3).

In conclusion, a new synthesis of (±)-4-hydroxyenone **3** has been developed utilizing a KDLM rearrangement. The reason for its known, but previously unexplained, instability in solution has been shown to be at least partly due to the facile formation of a pair of diastereoisomeric decahydrodibenzofurans **8** and **9** in the presence of base. In situ hydroxyl protection, however, allows for efficient preparation of protected derivatives (e.g., **10**) that are established synthetic intermediates en route to *Amaryllidaceae* alkaloids,[2,11,12] conduritols,[4−6,10] shikimate derivatives,[3] scyphostatin analogues,[7,8] and aldopentoses.[13]

Experimental Section

(1*R,2*R**,3*S**,4*S**)-3,6-Dibromocyclohexane-1,2-diol 6.** A solution of TPP (65 mg, 0.11 mmol) in CCl_4 (20 mL) was purged with O_2 and 1,3-cyclohexadiene (0.5 mL, 5.25 mmol) added. The solution was cooled to 0 °C and irradiated with a 300 W lamp at this temperature under an atmosphere of O_2 for 5.5 h. After this time, full conversion to endoperoxide **4**[2] was observed by ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.46 (2H, dm, J = 9.4), 2.27 (2H, dm, J = 9.4), 4.63 (2H, m), 6.66 (2H, dd, J = 4.4, 3.3). CoTPP (71 mg, 0.11 mmol) was added to the solution, and the reaction mixture was stirred at 25 °C under an inert atmosphere. After 2.5 h, full conversion to bis-epoxide **5** was observed by TLC. This solution of crude bis-epoxide was used directly in the next step. An aliquot of the solution was taken and purified by FC (SiO_2, 100% hexane → 95:5 hexane/Et_2O → 2:1 hexane/Et_2O) to give an analytical sample of bis-epoxide **5**[33] as a yellow oil. R_f = 0.28 (Et_2O/hexane, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.77−1.79 (4H, m), 3.04−3.05 (2H, m), 3.31 (2H, dm, J = 4.3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 19.65 (×2), 47.30 (×2), 47.94 (×2); IR ν_{max} (neat): 761, 779, 796, 888, 917, 938, 1267, 1415, 1440, 2935, 3004 cm^{-1}; m/z (CI^+) 130 (MNH_4^+, 100%) 52 (10); HRMS (CI^+) m/z calcd for $C_6H_{12}NO_2$ [MNH_4^+] 130.0868, found 130.0870 (Δ = 1.5 ppm). A solution of dilithium tetrabromocuprate (Li_2CuBr_4) was prepared according to the method of Ciaccio[29] by dissolving $CuBr_2$ (1.88 g, 8.4 mmol) and LiBr (1.46 g, 16.8 mmol) in MeCN (10 mL) at 0 °C and warming to 25 °C. To this dark purple solution was added a solution of the crude bis-epoxide **5** (~5.25 mmol) in CCl_4 (~20 mL) via cannular. The bis-epoxide containing flask was washed with MeCN (10 mL) and cannulated likewise and the reaction mixture allowed to stir at 25 °C for 1 h. The solvent was then removed in vacuo and the crude mixture partitioned between H_2O (20 mL) and Et_2O (20 mL). The phases were separated and the aqueous phase extracted further with Et_2O (2 × 60 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by FC (SiO_2, 100% hexane → hexane/Et_2O, 99:1 → hexane/Et_2O, 97:3 → hexane/Et_2O, 95:5 → hexane/Et_2O, 2:1→ hexane/Et_2O, 1:1 → hexane/Et_2O, 1:2) to give diol **6** as a white crystalline solid (983 mg, 68% from cyclohexadiene). mp 80−82 °C; R_f = 0.42 (Et_2O/hexane, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.10 (2H, m), 2.21−2.27 (2H, m), 3.06 (2H, s), 4.21 (2H, m), 4.28 (2H, m); ^{13}C (100 MHz, $CDCl_3$): δ_C 29.9 (×2), 52.6 (×2, broad), 72.9 (×2); IR ν_{max} (neat): 675, 1040, 1077, 2946, 3395 cm^{-1}; m/z (EI^+) 276 [{M(^{81}Br, ^{81}Br)}$^{+\bullet}$, 21%], 274 [{M(^{81}Br, ^{79}Br)}$^{+\bullet}$, 45%)], 272 [{M(^{79}Br, ^{79}Br)}$^{+\bullet}$, 22%], 256 (30), 175 (39), 113 (51), 84 (77), 67 (100); HRMS (EI^+) m/z calcd for $C_6H_{10}O_2{}^{79}Br_2$ [$M^{+\bullet}$] 271.9048, found 271.9042 (Δ = −2.0 ppm).

(3a*R,4*R**,7*S**,7a*S**)-4,7-Dibromo-2,2-dimethylhexahydro-1,3-benzodioxole 7.** To a solution of diol **6** (1.52 g, 5.55 mmol) in CH_2Cl_2 (60 mL) was added a solution of DMP (4.10 mL, 33.30 mmol) and p-TsOH·H_2O (211 mg, 1.11 mmol) in CH_2Cl_2 (5 mL) at 0 °C, and the resultant solution was allowed to stir at this temperature for 2 h. After this time, the reaction mixture was quenched with aqueous NaOH (100 mL, 1 M). The phases were separated and the aqueous phase extracted further with CH_2Cl_2 (2 × 50 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by FC (SiO_2, 100% hexane → hexane/Et_2O, 99:1 → hexane/Et_2O, 98:2 → hexane/Et_2O, 97:3 → hexane/Et_2O, 9:1) to give acetonide **7** as a white crystalline solid, which was recrystallized from n-hexane to give colorless blocks (1.53 g, 88%). mp 74−77 °C; R_f = 0.42 (hexane/Et_2O, 9:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.34 (3H, s), 1.47 (3H, s), 2.07−2.22 (4H, m), 4.18−4.26 (2H, m), 4.40−4.44 (2H, m); ^{13}C (125 MHz, $CDCl_3$): δ_C 26.3, 28.6, 30.0 (×2), 50.0 (×2), 79.3 (×2), 110.1; IR ν_{max} (neat): 864, 1050, 1063, 1220, 1211, 1382, 2986 cm^{-1}; m/z (CI^+) 334 [M(^{81}Br, ^{81}Br)NH_4^+, 23%], 332 [M(^{81}Br, ^{79}Br)NH_4^+, 46%], 330 [M(^{79}Br, ^{79}Br)NH_4^+, 24%], 317 [M(^{81}Br, ^{81}Br)H^+, 48%], 315 [M(^{81}Br, ^{79}Br)H^+, 100%], 313 [M(^{79}Br, ^{79}Br)H^+, 50%]; HRMS (CI^+) m/z calcd for $C_9H_{15}O_2Br_2$ [MH^+] 312.9439, found 312.9449 (Δ = 3.3 ppm). A single-crystal X-ray structure determination was performed on this product (see the Supporting Information).

(3a*R,7a*S**)-2,2-Dimethyl-3a,7a-dihydro-1,3-benzodioxole 1**[34]**.** Into a dry two-neck flask containing TBAI (3.87 g, 9.76 mmol) was cannulated a solution of acetonide **7** (1.53 g, 4.87 mmol) in CH_2Cl_2 (10 mL); the flask was washed with CH_2Cl_2 (3.6 mL) and cannulated likewise. To this solution was added DBU (7.28 mL, 48.73 mmol), and the solution was heated to reflux. After 2 h, the reaction mixture was quenched with a citric acid monohydrate solution (15.40 g, 73.05 mmol in 20 mL of H_2O) and allowed to stir for 10 min. The phases were separated and the aqueous phase extracted further with CH_2Cl_2 (3 × 15 mL). The combined organic phases were washed with brine (3 × 50 mL) and H_2O (2 × 50 mL), dried over Na_2SO_4, and filtered. The crude product was isolated by distillation at 55 °C to give diene **1** as a yellow oil (617 mg, 83%). R_f = 0.83 (petrol/EtOAc, 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 1.38 (3H, s), 1.40 (3H, s), 4.63−4.64 (2H, m), 5.85−5.90 (2H, m), 5.96−6.00 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 23.7, 25.7, 69.3 (×2), 103.5, 122.7 (×2), 122.2 (×2); IR ν_{max} (neat): 694, 872, 1027, 1045, 1159, 1208, 1238, 1370, 1381, 2886, 2935, 2986, 3045 cm^{-1}; m/z (CI^+) 322 (2M + NH_4^+, 25%), 305 (2M + H^+, 10%), 264 (100), 247 (58), 170 (MNH_4^+, 85%); HRMS (CI^+) m/z calcd for $C_{18}H_{25}O_4$ [2M + H^+] 305.1753, found 305.1751 (Δ = −0.6 ppm).

(1*R,2*S**,6*R**,7*R**)-4,4-Dimethyl-3,5,8,9-tetraoxa-tricyclo-[5.2.2.0^{2,6}]undec-10-ene 2**[17,18]**.** A solution of diene **1** (2.74 g, 18 mmol) and TPP (221 mg, 0.36 mmol) in CCl_4 (73 mL) was irradiated with light from a 300 W lamp for 5.5 h while oxygen was bubbled through the solution. TTP (300 mg, 0.49 mmol) and CCl_4 (40 mL) were added, and the reaction mixture was irradiated with light from a 300 W lamp for an extra 2 h while oxygen was bubbled through the solution. The reaction mixture was concentrated in vacuo. The residue was dissolved in ice-cold EtOAc/hexane (2:8) and was stirred with activated carbon. The mixture was filtered through a pad of Celite and then concentrated

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(34) Ramesh, K.; Wolfe, M. S.; Lee, Y.; Velde, D. V.; Borchardt, R. T. *J. Org. Chem.* **1992**, *57*, 5861–5868.

in vacuo to give endoperoxide **2** as white/light pink needles (3.05 g, 95%). R_f = 0.30 (EtOAc/petrol 1:9); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.36 (6H, s), 4.59 (2H, m), 4.91 (2H, m), 6.58 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 25.4, 25.7, 71.5 (×2), 71.9 (×2), 110.3, 130.6 (×2); *m*/*z* (CI^+) 202 (MNH_4^+, 100%).

(7*R)-Hydroxy-2,2-dimethyl-(7,7a*S**)-dihydro-(3a*R**)*H*-benzo-[1,3]dioxol-4-one 3,**[11] **(4*R**)-Hydroxy-(2*S**,3*R**,6*S**,7*S**)-bis-[di-*O*-isopropylidene]deca-[4a*R**,5a*R**,9a*S**,9b*S**]hydrodibenzofuran-1,8-dione 8, and (4*R**)-Hydroxy-(2*S**,3*R**,6*S**,7*S**)-bis-[di-*O*-isopropylidene]deca-[4a*S**,5a*R**,9a*S**,9b*R**]hydrodibenzofuran-1,8-dione 9.** To a stirred solution of endoperoxide **2** (400 mg, 2.17 mmol) in CH_2Cl_2 (10 mL) was added triethylamine (304 μL, 2.71 mmol), and the resulting solution was stirred for 2 h at 25 °C. The reaction mixture was then washed with water (2 × 20 mL) and the aqueous washings extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by FC (SiO_2, EtOAc/hexane, 1:9 → 1:1) to give the following:

Enone **3** as a colorless oil (265 mg, 1.80 mmol, 66%). R_f = 0.4 (EtOAc/hexane 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.46 (3H, s), 1.47 (3H, s), 4.51 (2H, m), 4.63 (1H, m), 6.17 (1H, dd, *J* = 10.3, 1.5), 6.92 (1H, dd, *J* = 10.3, 3.3, CH) (OH absent), [lit.[11]]; ^{1}H NMR (270 MHz, $CDCl_3$): δ_H 6.87 (1H, dd, *J* = 10.3, 3.2), 6.11 (1H, dd, *J* = 10.3, 1.6), 4.58 (1H, br s), 4.46 (2H, m), 1.40 (6H, s)]; *m*/*z* (CI^+) 202 (MNH_4^+, 100%), 185 (MH^+, 47%), 162 (16), 146 (9), 129 (5); HRMS (CI^+) *m*/*z* calcd for $C_9H_{16}NO_4$ [MNH_4^+] 202.1079, found 202.1079 (Δ = 0.0 ppm).

Decahydrodibenzofurans **8** and **9** as a colorless oil (105 mg, 0.28 mmol, 26%, **8**/**9**, 1:1 as determined by NMR). R_f = 0.45 (EtOAc/hexane 2:1); ν_{max} (thin film): 734, 863, 909, 1062, 1087, 1161, 1212, 1384, 1732, 2935, 2989, 3452 cm^{-1}; *m*/*z* (CI^+) 386 (MNH_4^+, 25%), 202 (100), 185 (45); HRMS (CI^+) *m*/*z* calcd for $C_{18}H_{28}NO_4$ (MNH_4^+) 386.1815, found 386.1811 (Δ = 1.1 ppm.). *cis*,*trans*,*cis*-Decahydrodibenzofuran **8** was isolated by crystallization from CH_2Cl_2/pentane as colorless prisms. mp 184.6−186.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.36 (3H, s), 1.38 (3H, s), 1.51 (3H, s), 1.57 (3H, s), 2.23 (1H, dd, *J* = 13.3, 8.8), 2.31 (1H, d, *J* = 2.2), 2.75 (1H, dd, *J* = 13.3, 7.2), 3.26 (1H, dd, *J* = 9.5, 3.3), 3.33 (1H, m), 4.29 (1H, dd, *J* = 5.4, 3.7), 4.34 (1H, d, *J* = 7.5), 4.37 (1H, m), 4.43 (1H, d, *J* = 6.7), 4.70 (1H, dd, *J* = 7.5, 3.9), 4.73 (1H, dd, *J* = 6.7, 3.7), 4.87 (1H, dd, *J* = 9.5, 3.4); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 23.6, 25.1, 26.1, 26.9, 37.5, 39.0, 51.3, 67.4, 76.3, 77.3, 77.4, 78.0, 78.4, 78.4, 110.7, 112.1, 202.4, 205.9. A single-crystal X-ray structure determination was performed on this product (see the Supporting Information). The noncrystalline *cis*,*cis*,*cis*-decahydrodibenzofuran **9** was not obtained pure, but its ^{1}H and ^{13}C NMR characteristics can be deduced by comparison of data for that of isolated **8** with that of the mixture of **8** and **9**. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.39 (6H, s), 1.53 (6H, s), 2.49 (1H, dd, *J* = 14.0, 8.8), 2.70 (1H, bs), 3.04 (1H, dd, *J* = 14.0, 8.2), 3.16 (1H, m), 3.57 (1H, dd, *J* = 10.9, 7.2), 4.01 (1H, dd, *J* = 3.6, 2.2), 4.30 (1H, d, *J* = 7.5), 4.32 (1H, d, *J* = 7.5), 4.40 (1H, d, *J* = 6.6), 4.63 (1H, dd, *J* = 7.5, 3.7), 4.70 (1H, dd, *J* = 6.6, 2.2), 4.79 (1H, dd, q*J* = 10.9, 2.1); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 23.5, 25.1, 26.0, 26.7, 33.7, 38.5, 48.6, 66.4, 76.9, 77.0, 77.2, 77.3, 77.5, 77.8, 110.8, 111.6, 202.6, 210.7.

(7*R)-(*tert*-Butyldimethylsilanyloxy)-2,2-dimethyl-(7,7a*S**)-dihydro-(3a*R**)*H*-benzo[1,3]dioxol-4-one 10**[11]**.** To a solution of endoperoxide **2** (0.5 g, 2.71 mmol) in DMF (7.5 mL) was added diisopropylethylamine (470 μL, 2.71 mmol), and this solution was stirred for 40 min at 25 °C. During this time, a solution of TBSCl (813 mg, 5.42 mmol) in DMF (2.5 mL) was degassed to remove HCl by bubbling through with N_2 for 10 min prior to addition of diisopropylethylamine (470 μL, 2.71 mmol) and a further 10 min degassing. This TBSCl solution was then added to the first solution after the aforementioned 40 min, and the reaction was stirred for 14 h. EtOAc (30 mL) and brine (30 mL) were added, the layers were separated, and the aqueous phase was extracted with further EtOAc (2 × 30 mL). The combined organic extracts were washed with brine (2 × 50 mL), dried over Na_2SO_4, and concentrated in vacuo to give a yellow oil. This was initially purified by FC (SiO_2, EtOAc/pentane, 0:100 → 5:95 → 10:90) to give a mixture of 4-silyloxy enone **10** and TBSOH, which was removed by heating to 70 °C for 1 h under high vacuum to leave 4-silyloxy enone **10** as a waxy solid upon storage at −20 °C (630 mg, 78%). R_f = 0.85 (EtOAc/hexane 2:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.16 (3H, s), 0.19 (3H, s) 0.93 (9H, s), 1.42 (3H, s), 1.43 (3H, s), 4.45 (2H, m), 4.55 (1H, dt, *J* = 3.5, 1.0), 6.10 (1H, dd, *J* = 0.8, 10.3), 6.78 (1H, ddd, *J* = 10.3, 3.8, 1.1); ^{13}C NMR (400 MHz, $CDCl_3$): δ_C −4.7 (×2), 18.08, 25.7 (×3), 25.9, 27.4, 67.0, 74.3, 79.6, 110.17, 127.9, 148.5, 194.6; IR ν_{max} (thin film): 515, 669, 727, 779, 838, 891, 1075, 1220, 1252, 1383, 1472, 1694, 2858, 2932 cm^{-1}; *m*/*z* (CI^+) 316 ($M-NH_4^+$, 100%), 299 (MH^+, 20), 241 (7), 186 (8), 145 (15), 132 (15), 126 (32); HRMS (CI^+) *m*/*z* calcd for $C_{15}H_{27}O_4Si$ [MH^+] 299.1679, found 299.1676 (Δ = 1.0 ppm.).

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Supporting Information Available: General experimental directions, NMR spectra for compounds **1**−**3** and **6**−**9**, and details of the crystallographic analyses, including CIF files for structures **7** and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.