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A Rapid and Stereoselective Route to the *trans*-Hydrindane Ring System

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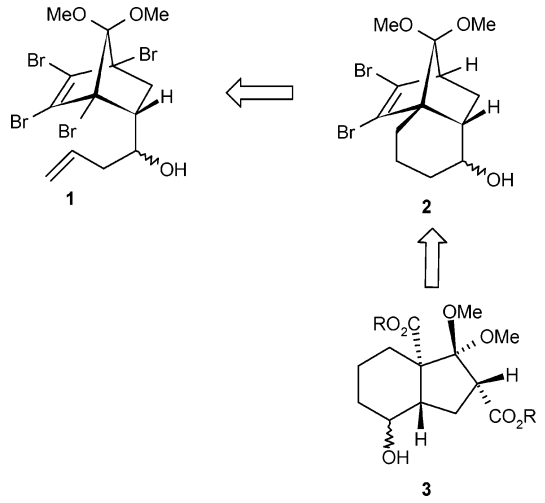
A short and stereoselective route to the *trans*-hydrindane derivative, a potential building block for the synthesis of steroidal and related molecules, was achieved by the operation of indium, tin, and ruthenium based reagents, starting from a tetrabromo norbornyl derivative.

Introduction

Stereoselective construction of trans-fused hydrindanes possessing suitable functional groups continues to be one of the challenging problems in natural product synthesis.[1,2] A large number of biologically active natural products contain the *trans*-hydrindane framework as the main structural unit or as part of a fused polycyclic structure, e.g., as in steroids, vitamin D, higher terpenes, and related natural products. Due to their widespread occurrence in nature, the synthesis of *trans*-hydrindane derivatives elicited extensive interest and various strategies have been reported as well as applied successfully to natural product synthesis. Many of the approaches toward this framework required several steps and also in the majority of cases there was a lack of selectivity where the formation of *cis*-hydrindane was also observed in considerable amount.[1,2] Since the *trans*-hydrindane ring system is the core skeleton of many biologically active natural products, there exists a need to innovate new strategies that are highly stereoselective and involve fewer steps.

A recent development of a promising methodology in our laboratory for the bridgehead functionalization[3] of tetrabromonorbornyl derivatives has led us to develop a new, flexible, and expeditious route to the functionalized *trans*-hydrindane ring system. The retrosynthetic plan for our approach is depicted in Scheme 1. We envisioned that the *trans*-hydrindane **3** could be stereoselectively obtained by intramolecular bridgehead C−C bond formation via radical cyclization[4] of **1** through a 6-*endo*-*trig* cyclization to generate a trans-fused six-membered ring

SCHEME 1. Retrosynthetic Scheme of Our Approach to *trans*-Hydrindane Derivative 3



leading to **2**. The 1,2-dibromoalkene moiety could be cleaved, via the intermediate α-diketone,[5] to obtain the much sought after *trans*-hydrindane **3**, constituting a concise synthetic strategy.

Results and Discussion

The precursor *endo*-homoallyl alcohol **1** could be easily prepared by allylation of aldehyde **4**[6] by any suitable allyl organometallic reagent. Attracted by indium-mediated reactions which have gained increasing importance recently due to their mild nature, functional group tolerance, high stereoselectivity, ease of handling, compat-

(1) Reviews: (a) Zhu, G.-D.; Okamura, W. H. *Chem. Rev.* **1995**, *95*, 1877. (b) Jankowski, P.; Marczak, S.; Wicha, J. *Tetrahedron* **1998**, *54*, 12071 and references therein.

(2) (a) Fall, Y.; Fernandez, C.; González, V.; Mouriño, A. *Tetrahedron Lett.* **2001**, *42*, 7815. (b) Daniewski, A. R.; Liu, W. *J. Org. Chem.* **2001**, *66*, 626. (c) Jones, D. N.; Maybury, M. W. J.; Swallow, S.; Tomkinson, N. C. O.; Wood, W. W. *Tetrahedron Lett.* **2001**, *42*, 2193. (d) Mitome, H.; Miyaoka, H.; Yamada, Y. *Tetrahedron Lett.* **2000**, *41*, 8107. (e) Couturier, M.; Deslongchamps, P. *Synlett* **1996**, 1140. (f) Sono, M.; Nakashiba, Y.; Nakashima, K.; Tori, M. *J. Org. Chem.* **2000**, *65*, 3099.

(3) Khan, F. A.; Prabhudas, B. *Tetrahedron Lett.* **1999**, *40*, 9289.

(4) For most recent books on radical chemistry, see: Renaud, P.; Sibi, M. P., Eds. *Radicals in Organic Synthesis*; Wiley-VCH Verlag GmbH: Weinheim, Germany, 2001; Vols. 1 and 2.

(5) For the preparation of α-diketones see: (a) Khan, F. A.; Prabhudas, B.; Dash, J.; Sahu, N. *J. Am. Chem. Soc.* **2000**, *122*, 9558. For some recent applications, see: (b) Khan, F. A.; Dash, J. *J. Am. Chem. Soc.* **2002**, *124*, 2424. (c) Khan, F. A.; Dash, J.; Sahu, N.; Sudheer, Ch. *J. Org. Chem.* **2002**, *67*, 3783. (d) Khan, F. A.; Dash, J. *J. Org. Chem.* **2003**, *68*, 4556.

(6) Substrates **4** and **12** were obtained via Diels−Alder reaction of 1,2,3,4-tetrabromo-5,5-dimethoxycyclopentadiene with acrolein and methyl acrylate, respectively, following literature procedure reported for related derivatives: Pews, R. G.; Roberts, C. W.; Hand, C. R. *Tetrahedron* **1970**, *26*, 1711.

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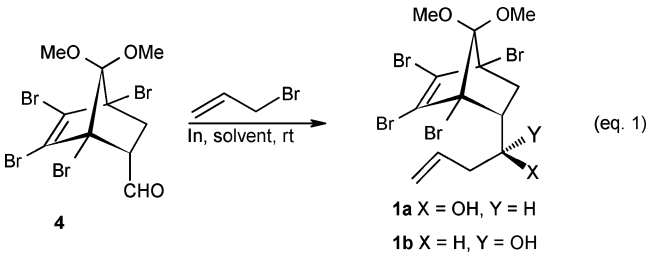
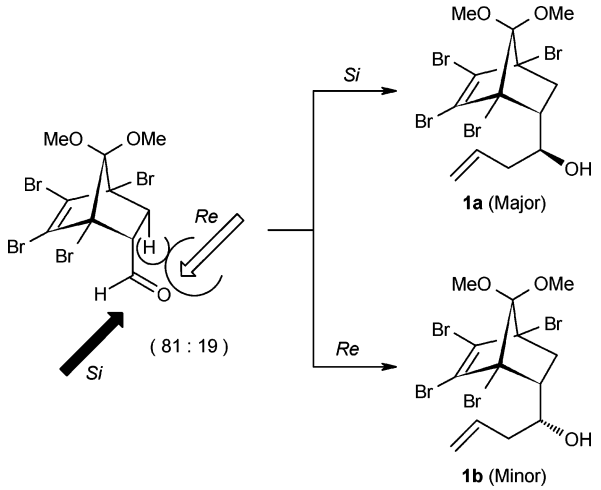
TABLE 1. Indium-Mediated Allylation of Aldehyde 4 in Different Solvents



entry	solvent	time	yield[a] (%)	ratio (**1a**:**1b**)
1	THF:H_2O (1:1)	10 h	97	81:19
2	THF:H_2O (1:3)	16 h	95	79:21
3	H_2O	12 d	75	81:19
4	THF	6 h	70	77:23
5	DMF	12 h	95	69:31
6	DMSO	12 h	94	86:14

[a] Isolated yields of products.

SCHEME 2. Preferential Formation of the Major Isomer 1a



ibility with water as a solvent, and insensitivity to air,[7] and also due to our own interest in indium chemistry,[8] we decided to use allylindium reagent for this purpose. Indium-mediated allylation of the aldehyde **4** was performed with different solvent systems (eq 1, Table 1). The homoallylic alcohols **1a** and **1b** were formed in excellent yield with high diastereoselectivity. The highest diastereoselectivity (86:14) was observed in DMSO with 94% yield (entry 6). The best solvent system in terms of yield and diastereoselectivity was found to be THF:H_2O (1:1) where 97% of the products **1a**,**b** in a 81:19 ratio were obtained (entry 1). The diastereomeric ratio in all the cases was determined by ^{1}H NMR analysis of the unpurified reaction mixtures. The carbinol-H of the major diastereomer **1a** shows a multiplet at 3.86 ppm, while in the minor isomer **1b** it is shielded showing a multiplet at 3.37 ppm in the ^{1}H NMR (300 MHz) spectrum.

A likely model to explain the observed diastereoselectivity is depicted in Scheme 2. The preferential formation of the major diastereomer **1a** may be rationalized by the favored attack of the allyl nucleophile from the less hindered *Si*-face of the presumed conformer of aldehyde **4**. The *Re*-face attack, on the other hand, encounters steric obstruction due to the presence of an adjacent *endo*-H (Scheme 2), resulting in the formation of a minor isomer.

Having prepared the separable diastereomers **1** in high yield, we executed the tributyltin hydride mediated intramolecular bridgehead cyclization on the major isomer **1a** (Scheme 3). Tributyltin hydride was added slowly to a dilute (0.007 M) solution of the substrate **1a** in benzene. Within 4 h the starting material was completely consumed and chromatographic separation resulted in the isolation of **6** (20%) and **7** (24%) along with 25% of a tribromo derivative **5a** in an overall yield of 69%. The structural assignment of **5a** was made on the basis of ^{1}H NMR, where the bridgehead proton at C_4 coupled with the *exo*-H at C_3, J = 4.1 Hz. The yield of the cyclized product **7** was substantially improved (53%) by the slow addition and prolonged reaction time of 12 h (Scheme 3). The bridgehead-reduced product **5b** was formed in 17% yield under these conditions. Compound **6** was converted to **7** by separate treatment with tributyltin hydride, thereby increasing the yield of the cyclized product **7** to 63%.

The cyclized product **7** was formed via a 6-*endo*-*trig* mode of ring closure (structure and stereochemistry was proved by a single-crystal X-ray analysis).[9] A 5-hexenyl radical normally undergoes 5-*exo*-*trig* cyclization (due to kinetic preference) to form a five-membered ring, but it is interesting to note that a radical centered at the bridgehead position of the rigid bicyclic system is directing a 6-*endo*-*trig* pathway leading to a six-membered ring. Examples of 6-*endo*-*trig* ring closures for 5-hexenyl radicals are scarce in the literature.[10] We presume that the p-orbital of the bridgehead radical, because of rigid conformational constraints, is unable to attain the Burgi−Dunitz angle (109°)[11] for attack at the internal olefinic carbon. Furthermore, a 5-*exo*-*trig* cyclization would lead to an unfavorable *trans*-fused 5-5-ring junction.

The minor diastereomer **1b** was also subjected to tributyltin hydride mediated radical cyclization conditions, with longer reaction time. After 14 h, only two products **8** (20%) and **9** (42%) were isolated in 62% overall yield (Scheme 4). A single X-ray crystal structure of compound **9** was also obtained to unambiguously confirm the structure.[9]

At this stage, we thought of examining the intramolecular bridgehead cyclization of homopropargyl derivatives **10**, which were easily prepared in high yield via indium-mediated propargylation of aldehyde **4** (Scheme 5). The two diastereomers **10a** and **10b** were formed in 94% yield in a ratio of 60:40 and were separated with silica gel column chromatography. The major isomer **10a**

(7) (a) Cintas, P. *Synlett* **1995**, 1087. (b) Chan, T.-H.; Isaac, M. B. *Pure Appl. Chem.* **1996**, *68*, 919. (c) Marshall, J. A. *Chemtracts* **1997**, *10*, 481. (d) Hashmi, A. S. K. *J. Pract. Chem.* **1998**, *349*, 84. (e) Li, C.-J.; Chan, T.-H. *Tetrahedron* **1999**, *55*, 11149.

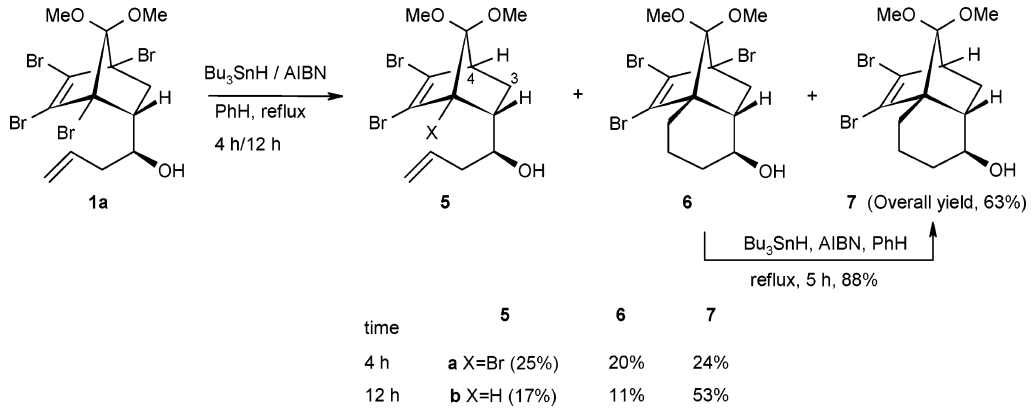
(8) (a) Khan, F. A.; Prabhudas, B. *Tetrahedron* **2000**, *56*, 7595. (b) Khan, F. A.; Dash, J.; Sahu, N.; Gupta, S. *Org. Lett.* **2002**, *4*, 1015. (c) Khan, F. A.; Dash, J.; Sudheer, Ch. *Chem. Eur. J.* **2004**, *10*, 2507.

(9) See the Supporting Information for single-crystal X-ray data as well as CIF files for **7** and **9**.

(10) For a few examples of 6-*endo*-*trig* cyclizations, see: (a) Ward, D. E.; Gai, Y.; Kaller, B. F. *J. Org. Chem.* **1995**, *60*, 7830. (b) Porter, N. A.; Chang, V. H.-T.; Magnin, D. R.; Wright, B. T. *J. Am. Chem. Soc.* **1988**, *110*, 3554. (c) Wilt, J. W. *Tetrahedron* **1985**, *41*, 3979.

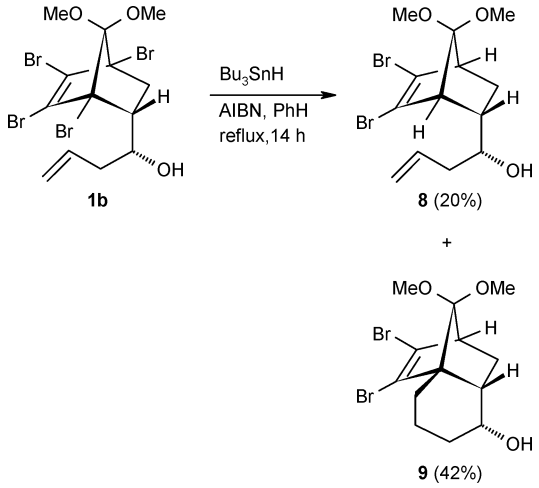
(11) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

SCHEME 3. 6-*endo-trig*-Radical Cyclization of 1a[9]

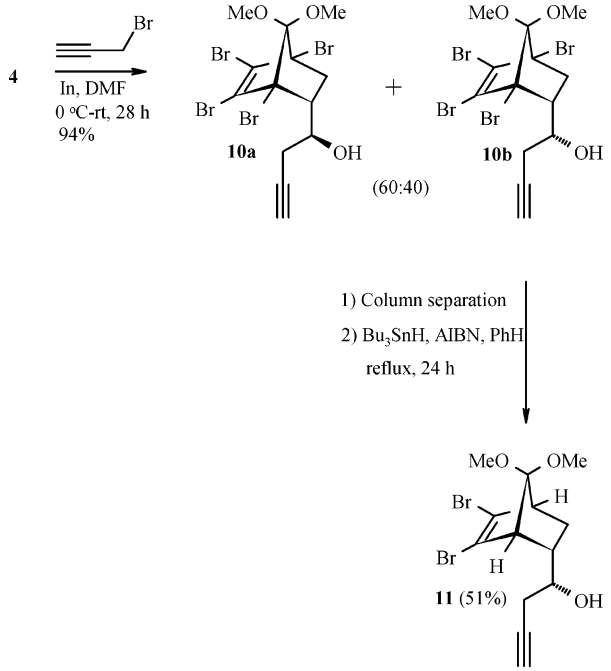


time	5	6	7
4 h	**a** X=Br (25%)	20%	24%
12 h	**b** X=H (17%)	11%	53%

SCHEME 4. 6-*endo-trig*-Radical Cyclization of 1b[9]



SCHEME 5. Reaction of Homopropargyl Derivative 10 with Bu_3SnH

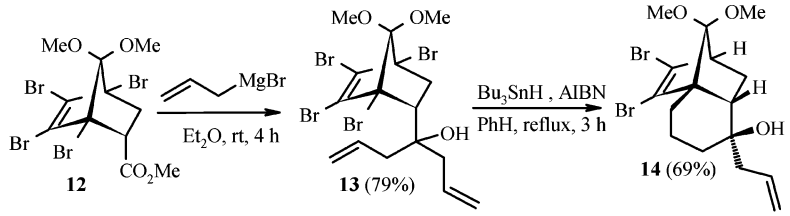


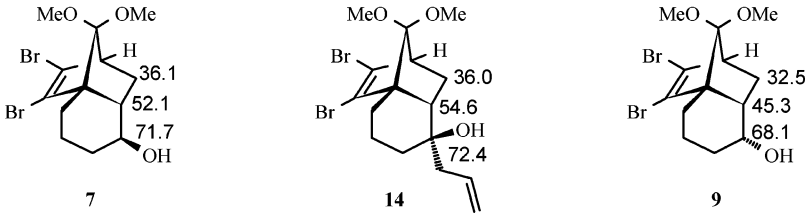
was assigned the stereochemistry based on comparison of the ^{1}H NMR value of the carbinol hydrogen with that of homoallyl alcohol **1a**. The carbinol-H for homoallyl alcohol **1a** appears at 3.86 ppm while homopropargyl alcohol **10a** shows a multiplet at 3.83 ppm. Similar analogy was applied for minor isomer **10b** where the minor homoallyl alcohol **1b** shows a multiplet at 3.37 ppm, while the minor homopropargyl alcohol **10b** shows a multiplet at 3.41 ppm. The isomer **10b** was subjected to tributyltin hydride mediated cyclization under identical conditions as for **1** (Scheme 5). As anticipated (on account of further deviation to attain the Burgi−Dunitz angle in **10**), no cyclized product could be detected, only 51% of the bridgehead reduced compound **11** was isolated.

After successfully achieving bridgehead cyclization of **1**, we drew our attention toward a possible cascade cyclization employing a bisallyl derivative **13**. The bisallyl carbinol **13** was prepared in 79% yield by treating the ester **12**[6] with allyl Grignard reagent (Scheme 6). Radical cyclization of **13** under the usual high dilution conditions (0.007 M) resulted in the formation of **14** in 69% yield. Only one double bond was involved in 6-*endo-trig* cyclization while the other double bond did not participate. The β-stereochemistry of the hydroxyl group was assigned based on comparison of the ^{13}C NMR values with those of related compound **7**. The carbinol carbon for **7** appeared at 71.7 ppm while the carbinol carbon for allyl carbinol **14** appeared at 72.4 ppm. In the case of **9**, where the carbinol carbon has an α-stereochemistry for the hydroxyl group, ^{13}C NMR showed a peak at 68.1 ppm. Also, the ^{13}C NMR values for adjacent methine (54.6 ppm) and methylene (36.0 ppm) carbons in **14** are in very close range with those for **7** (52.1 and 36.1 ppm, Scheme 6). On the other hand, for diastereomer **9** both these values are comparably shielded, appearing at 45.3 and 32.5 ppm, respectively, as shown in Scheme 6.

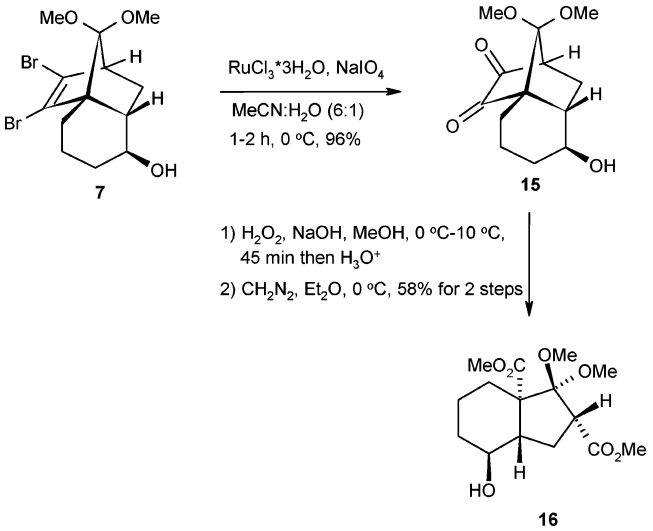
Our next task was to cleave the sturdy bromine bearing double bond of the cyclized product **7** to disclose the *trans*-hydrindane **3**. Treatment of compound **7** with 8% $RuCl_3 \cdot 3H_2O$ and 1.6 equiv of $NaIO_4$ at 0 °C smoothly gave the α-diketone **15**. The secondary hydroxyl group remained intact and did not get oxidized under the reaction conditions. The yield of the α-diketone wavered between 68 and 96% depending on the reaction time. The cleavage of the α-diketone **15**, using alkaline H_2O_2 in MeOH, followed by treatment with an ethereal solution of diazomethane at 0 °C furnished the highly functionalized *trans*-hydrindane diester **16** (Scheme 7). Since varied reaction time and temperature altered the yield of the

SCHEME 6. Radical Cyclization of 13

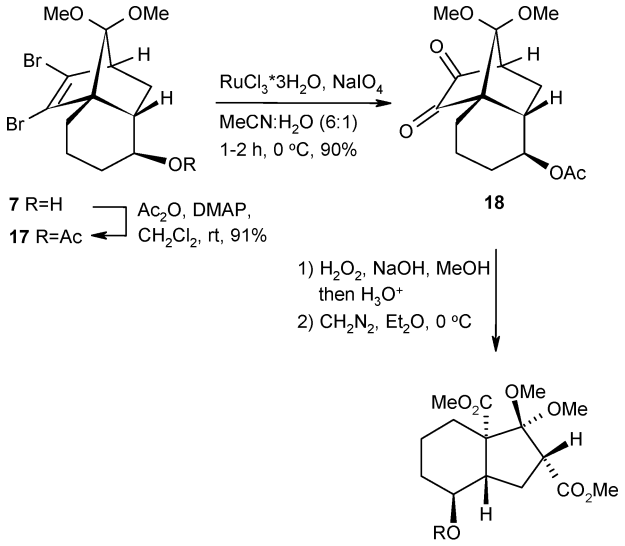




SCHEME 7. Conversion of 7 into *trans*-Hydrindane Derivative



SCHEME 8. Conversion of 7 into *trans*-Hydrindane Derivatives



Time/temp. at step 1	**16** R=H	**19** R=Ac
2 h, 0 °C-rt	61%	15%
20 min., 0 °C	--	92%

diketone **15**, we decided to carry out the oxidation and cleavage reaction sequence after protecting the secondary alcohol group in both the major and minor alcohols, **7** and **9**. The major cyclized alcohol **7** was converted to acetate **17** and subsequent ruthenium oxidation furnished the diketone **18** in excellent yields (Scheme 8). The *trans*-hydrindane derivative **19** was obtained in 92% yield from acetate **18** by successive treatment with alkaline hydrogen peroxide at 0 °C for 20 min and diazomethane. Allowing the reaction to warm to room temperature in 2 h furnished 61% of alcohol **16**, due to hydrolysis of the acetate group, along with 15% of **19** (Scheme 8). Similarly the minor alcohol **9** was transformed into diketone **21** via the acetate **20**, eventually to reveal exclusively *trans*-hydrindane derivative **23** or a mixture of the *trans*-hydrindane derivatives **22** and **23**, depending on the reaction time (Scheme 9).

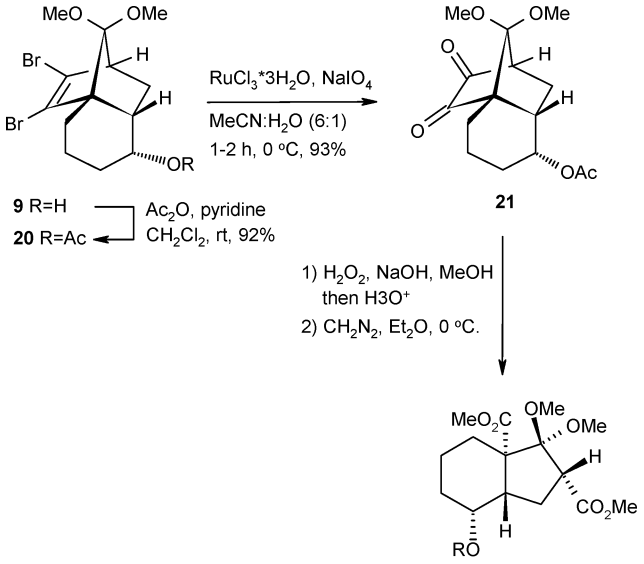
Our approach to the *trans*-hydrindane derivatives **16**,**19** and **22**,**23** establishes a four-step sequence from the Diels−Alder adduct **4** invoving indium-mediated allylation, 6-*endo*-*trig* radical cyclization at the bridgehead, catalytic ruthenium oxidation, and finally alkaline hydrogen peroxide cleavage of the resulting α-diketone. We have exploited the intrinsic geometric constraint of tetrabromonorbornyl derivatives **1** leading to six-membered-ring annulation through a C−C bond formation at the bridgehead as the key step in achieving *trans*-hydrindanes.

Experimental Section

Allyindium Addition to Aldehyde 4. A mixture of aldehyde **4**[6] (2.81 g, 5.64 mmol), allyl bromide (0.77 mL, 9.0 mmol), and indium (1 g, 8.7 mmol) in THF (28.6 mL) and H_2O (28.6 mL) was stirred at room temperature for 16 h. Dilute HCl (15 mL) was added and extracted with ethyl acetate (3 × 15 mL). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. Removal of solvent and purification of the crude over silica gel column chromatography afforded the diastereomeric homoallylic alcohols **1a** and **1b** in 97% yield and (81:19) ratio.

Homoallyl alcohol 1a: yield 2.4 g, 79%; colorless solid; mp 78−79 °C; ^{1}H NMR (300 MHz) δ 5.86−5.73 (m, 1H), 5.18−5.12 (m, 2H), 3.88−3.85 (m, 1H), 3.63 (s, 3H), 3.59 (s, 3H), 2.66−2.62 (m, 1H), 2.40−2.34 (m, 2H), 2.22−2.12 (m, 2H); ^{13}C NMR (75 MHz) δ 134.0, 125.5, 124.3, 119.0, 112.2, 72.5, 68.3, 67.1, 53.2, 52.5, 51.6, 41.4, 38.0; IR (KBr) 3450, 2950, 1625,

SCHEME 9. Conversion of 9 into *trans*-Hydrindane Derivatives



Time/temp. at step 1	**22** R=H	**23** R=Ac
45 min., 0 °C	14%	71%
20 min., 0 °C	--	92%

1560, 1440 cm^{-1}. Anal. Calcd for $C_{13}H_{16}Br_4O_3$: C 28.92, H 2.99. Found: C 29.31, H 2.90.

Homoallyl alcohol 1b: yield 550 mg, 18%; mp 112−114 °C; ^{1}H NMR (300 MHz) δ 5.93−5.79 (m, 1H), 5.17−5.11 (m, 2H), 3.63 (s, 3H), 3.60 (s, 3H), 3.37 (m, 1H), 2.75 (dt, 1H, J = 9.5, 4.1 Hz), 2.50 (dd, 1H, J = 11.7, 8.9 Hz), 2.29−2.02 (m, 2H), 1.45 (dd, 1H, J = 11.7, 4.1 Hz); ^{13}C NMR (75 MHz) δ 133.8, 126.1, 124.3, 118.5, 111.6, 71.9, 71.2, 67.4, 53.2, 51.9, 51.8, 42.0, 39.0; IR (KBr) 3500, 2950, 1625, 1550, 1430, 1170 cm^{-1}. Anal. Calcd for $C_{13}H_{16}Br_4O_3$: C 28.92, H 2.99. Found: C 28.85, H 2.92.

Typical Procedure for Tributyltin Hydride Mediated Cyclization of Homoallylic Alcohols. To a solution of **1a** (1.5 gm, 2.77 mmol) in benzene (275 mL) at reflux temperature was added a solution of Bu_3SnH (1.9 mL, 7 mmol) and AIBN (45 mg, 0.27 mmol) in benzene (90 mL) over a period of 8 h. The reaction mixture was refluxed for an additional 4 h. Solvent was distilled off and the crude mixture was directly purified with silica gel column chromatography. First 100-mL fractions were collected with hexane as eluent to remove tin impurities and later on the polarity was increased from 5% to 25% ethyl acetate−hexane to afford **5b** (180 mg, 17%), **6** (140 mg, 11%), and **7** (561 mg, 53%). When the reaction was carried out for 4 h (instead of 12 h, as above), **5a** (25%), **6** (20%), and **7** (24%) were obtained after chromatographic separation.

Alcohol 5a: obtained as a viscous liquid; ^{1}H NMR δ 5.86−5.80 (m, 1H), 5.17−5.14 (m, 2H), 3.87−3.84 (m, 1H), 3.45 (s, 3H), 3.36 (s, 3H), 3.04 (d, 1H, J = 4.1 Hz), 2.57−2.53 (m, 1H), 2.40 (m, 1H), 2.27−2.21 (m, 1H), 2.10 (ddd, 1H, J = 11.8, 8.8, 4.1 Hz), 1.65 (dd, 1H, J = 11.8, 4.9 Hz); ^{13}C NMR δ 134.4, 124.3, 120.9, 118.5, 114.2, 74.7, 67.9, 53.0, 52.4, 50.8, 50.5, 41.4, 26.7; IR (neat) 3450, 2950, 1630, 1560, 1440, 1180 cm^{-1}. Anal. Calcd for $C_{13}H_{17}Br_3O_3$: C 33.87, H 3.72. Found: C 33.81, H 3.71.

Alcohol 5b: obtained as a viscous liquid; ^{1}H NMR (300 MHz) δ 5.93−5.79 (m, 1H), 5.21−5.16 (m, 2H), 3.32−3.25 (m, 1H), 3.21 (s, 3H), 3.18 (s, 3H), 3.01−2.99 (m, 2H), 2.63−2.57 (m, 1H), 2.38 (m, 1H), 2.18−2.07 (m, 1H), 1.84−1.72 (m, 1H), 1.31 (dd, 1H, J = 12.3, 4.0 Hz); ^{13}C NMR (75 MHz) δ 134.1, 123.3, 118.9, 118.7, 116.3, 72.5, 56.1, 54.7, 52.3, 49.6, 44.7, 40.8, 28.6; IR (neat) 3450, 2956, 1630, 1565, 1430 cm^{-1}. Anal. Calcd for $C_{13}H_{18}Br_2O_3$: C 40.87, H 4.75. Found: C 40.96, H 4.81.

Tribromo compound 6: colorless solid; mp 115−117 °C; ^{1}H NMR δ 3.55 (s, 3H), 3.34 (s, 3H), 3.27 (dt, 1H, J = 10.9, 3.9 Hz), 2.51 (ddd, 1H, J = 11.2, 9.3, 5.4 Hz), 2.37−2.32 (m, 2H), 2.02−1.97 (m, 2H), 1.83−1.71 (m, 3H), 1.32−1.22 (m, 1H); ^{13}C NMR δ 129.7, 123.4, 114.2, 71.8, 70.6, 62.2, 52.7, 51.3, 38.3, 35.7, 25.0, 21.3; IR (KBr) 3480, 2950, 1560, 1130 cm^{-1}. Anal. Calcd for $C_{13}H_{17}Br_3O_3$: C 33.87, H 3.72. Found: C 33.92; H 3.79.

Dibromo compound 7: Colorless solid; mp 128−130 °C; ^{1}H NMR (300 MHz) δ 3.31−3.23 (m, 1H), 3.25 (s, 3H), 3.23 (s, 3H), 2.95 (d, 1H, J = 4.2 Hz), 2.38−2.29 (m, 2H), 2.06−1.97 (m, 3H), 1.78−1.69 (m, 2H), 1.28−1.22 (m, 2H); ^{13}C NMR (75 MHz) δ 125.5, 123.9, 116.6, 71.7, 64.0, 55.3, 52.1, 50.5, 50.3, 36.1, 27.2, 24.9, 21.4; IR (KBr) 3400, 2920, 1580, 1430, 1050 cm^{-1}. Anal. Calcd for $C_{13}H_{18}Br_2O_3$: C 40.87, H 4.75. Found: C 40.82, H 4.72.

Application of the general procedure (**1b** (1.5 g, 2.77 mmol), Bu_3SnH (1.9 mL, 7 mmol), AIBN (45 mg, 0.27 mmol)) afforded **8** (215 mg, 20%) and **9** (445 mg, 42%).

Alcohol 8: yield 215 mg, 20%; obtained as a viscous liquid; ^{1}H NMR δ 5.84 (m, 1H), 5.17−5.13 (m, 2H), 3.28−3.26 (m, 1H), 3.21 (s, 3H), 3.18 (s, 3H), 3.18 (m, 1H, merged with OMe peak), 2.98 (m, 1H), 2.43 (m, 1H), 2.32 (m, 1H), 2.07−1.97 (m, 2H), 1.84 (d, 1H, J = 4.2 Hz, OH), 0.85 (dd, 1H, J = 12.0, 4.4 Hz); ^{13}C NMR δ 134.6, 122.6, 120.0, 118.5, 116.0, 71.8, 56.5, 54.8, 52.2, 49.6, 44.7, 39.5, 28.1; IR (neat) 3450, 2950, 1625, 1575, 1450 cm^{-1}. Anal. Calcd for $C_{13}H_{18}Br_2O_3$: C 40.87, H 4.75. Found: C 40.93, H 4.80.

Dibromo compound 9: yield 445 mg, 42%; mp 103−104 °C; ^{1}H NMR δ 4.02 (m, 1H), 3.25 (s, 3H), 3.23 (s, 3H), 2.92 (d, 1H, J = 4.3 Hz), 2.52−2.45 (m, 1H), 2.38−2.23 (m, 1H), 2.10 (m, 1H), 1.97 (ddd, 1H, J = 12.0, 9.3, 4.4 Hz), 1.88−1.73 (m, 2H), 1.56−1.47 (m, 2H), 1.28 (dd, 1H, J = 12.0, 6.8 Hz), 1.10 (d, 1H, J = 6.0 Hz); ^{13}C NMR δ 125.6, 123.3, 117.4, 68.1, 60.7, 54.8, 52.2, 50.3, 45.3, 32.5, 27.1, 26.1, 16.4; IR (KBr) 3480, 2940, 1580 cm^{-1}. Anal. Calcd for $C_{13}H_{18}Br_2O_3$: C 40.87, H 4.75. Found: C 40.94, H 4.79.

Homopropargyl Derivatives 10. To a suspension of indium metal (132 mg, 1.15 mmol) in DMF (0.2 mL) was added propargyl bromide (0.2 mL, 2.2 mmol) at 0 °C. After indium metal has dissolved, a solution of aldehyde **4** (498 mg, 1 mmol) in DMF (2.5 mL) was added to the mixture. After the solution was stirred for 28 h at room temperature, cold dilute HCl (10 mL) was added and extracted with ether. The combined ether layers were washed with brine and dried over anhydrous Na_2SO_4. The crude product obtained after evaporation of ether layer was purified on a silica gel column to afford of **10a** (303 mg, 56%) and **10b** (207 mg, 38%).

10a: obtained as a viscous liquid; ^{1}H NMR δ 3.85−3.80 (m, 1H), 3.58 (s, 3H), 3.54 (s, 3H), 2.76−2.71 (m, 1H), 2.46−2.35 (m, 2H), 2.11−2.00 (m, 2H), 0.83−0.81 (m, 1H); ^{13}C NMR δ 125.8, 124.0, 112.0, 94.3, 80.1, 71.7, 68.0, 66.9, 53.2, 51.9, 51.7, 38.4, 27.2; IR (neat) 3500, 3200, 1560 cm^{-1}. Anal. Calcd for $C_{13}H_{14}Br_4O_3$: C 29.03, H 2.62. Found: C 29.12, H 2.56.

10b: obtained as a viscous liquid; ^{1}H NMR δ 3.59 (s, 3H), 3.54 (s, 3H), 3.41 (m, 1H), 2.86 (dt, 1H, J = 9.0, 4.1 Hz), 2.49 (dd, 1H, J = 11.7, 9.0 Hz), 2.43−2.37 (m, 2H), 2.27−2.20 (m, 1H), 2.06 (t, 1H, J = 2.6 Hz), 1.38 (dd, 1H, J = 11.7, 4.1 Hz); ^{13}C NMR δ 126.2, 124.2, 111.5, 79.6, 71.5, 70.7, 69.7, 67.2, 53.2, 51.8, 51.3, 41.7, 25.1; IR (neat) 3440, 3200, 1540 cm^{-1}. Anal. Calcd for $C_{13}H_{14}Br_4O_3$: C 29.03, H 2.62. Found: C 29.12, H 2.59.

Homopropargyl Alcohol 11. The reaction was carried out as described in the typical procedure above for **1a**. Yield 53 mg (51%) from **10b** (148 mg, 0.28 mmol); obtained as a viscous liquid; ^{1}H NMR δ 3.30−3.29 (m, 2H), 3.21 (s, 3H), 3.19 (s, 3H), 2.99 (m, 1H), 2.57−2.45 (m, 2H), 2.30−2.23 (m, 2H), 2.09 (t, 1H, J = 2.6 Hz), 2.05−1.98 (m, 1H), 0.82 (dd, 1H, J = 11.9, 4.1 Hz); ^{13}C NMR δ 122.8, 119.9, 116.0, 80.5, 71.1, 56.4, 54.8, 52.3, 49.7, 44.2, 28.0, 25.3; IR (neat) 3500, 3190, 1550 cm^{-1}. Anal. Calcd for $C_{13}H_{16}Br_2O_3$: C 41.08, H 4.24. Found: C 41.16, H 4.29.

Bisallyl Alcohol 13. To a suspension of Mg (178 mg, 7.43 mmol) and a crystal of iodine in dry ether (1 mL) was added a solution of allyl bromide (0.32 mL, 3.85 mmol) in ether (4 mL). After the metal has reacted, a solution of the *endo*-ester **12**[6] (500 mg, 0.95 mmol) in ether (3 mL) was added and allowed to stir at room temperature for 4 h. Cold dilute HCl (5 mL) was added and the aqueous layer was extracted with ether (3 × 5 mL). The combined ether layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified on a silica gel column with 0.5% ethyl acetate−hexane as eluant to obtain 433 mg (79%) of **13** as a colorless solid; mp 85−87 °C; ^{1}H NMR δ 5.97−5.86 (m, 1H), 5.81−5.70 (m, 1H), 5.21−5.10 (m, 4H), 3.63 (s, 3H), 3.59 (s, 3H), 2.82 (dd, 1H, J = 9.1, 5.0 Hz), 2.75−2.62 (m, 2H), 2.43 (dd, 1H, J = 11.2, 9.1 Hz), 2.26 (dd, 1H, J = 11.2, 5.0 Hz), 2.17−2.03 (m, 2H), 1.55 (br s, 1H, OH); ^{13}C NMR δ 133.3, 132.7, 125.0, 124.6, 119.5, 119.3, 112.5, 74.7, 71.7, 67.6, 53.4, 52.5, 51.8, 43.0, 42.4, 40.0; IR (KBr) 3500, 2950, 1620, 1560 cm^{-1}. Anal. Calcd for $C_{16}H_{20}Br_4O_3$: C 33.14, H 3.48. Found: C 33.23, H 3.39.

Alcohol 14. The reaction was carried out as described in the typical procedure above for **1a**. Yield 76 mg (69%) from **13** (150 mg, 0.26 mmol); obtained as a viscous liquid; ^{1}H NMR δ 5.89−5.79 (m, 1H), 5.13−5.06 (m, 2H), 3.28 (s, 3H), 3.23 (s, 3H), 2.92 (d, 1H, J = 4.4 Hz), 2.34 (dd, 1H, J = 9.1, 6.8 Hz), 2.30−2.05 (m, 4H), 1.91 (ddd, 1H, J = 12.1, 9.1, 4.4 Hz), 1.73−1.55 (m, 3H), 1.35 (dt, 1H, J = 13.9, 4.6 Hz), 1.26 (dd, 1H, J = 12.1, 6.8 Hz), 1.18 (br s, 1H, OH); ^{13}C NMR δ 133.4, 125.8, 122.8, 118.6, 117.4, 72.4, 61.9, 54.6, 52.2, 50.3, 48.5, 46.0, 36.0, 25.8, 25.6, 18.2; IR (neat) 3450, 3080, 2950, 1630, 1590, 1450, 1080 cm^{-1}. Anal. Calcd for $C_{16}H_{22}Br_2O_3$: C 45.52, H 5.25. Found: C 45.65, H 5.18.

Tricyclic Diketone 15. To a stirred solution of **7** (48 mg, 0.125 mmol) in acetonitrile (1.5 mL) at 0 °C was added a solution of $RuCl_3 \cdot 3H_2O$ (3 mg, 0.01 mmol) and $NaIO_4$ (45 mg, 0.212 mmol) in water (0.25 mL). The mixture was stirred for 30 min at 0 °C. The resulting suspension was filtered through a thin pad of silica gel, which was then washed with ethyl acetate (15 mL). Concentration of the filtrate followed by silica gel column chromatography (35% ethyl acetate−hexane) gave the diketone **15**. Yield 31 mg, 96%; obtained as a viscous liquid; ^{1}H NMR δ 3.42 (s, 3H), 3.29 (s, 3H), 3.28−3.22 (m, 1H), 3.20 (d, 1H, J = 6.0 Hz), 2.46−2.38 (m, 1H), 2.34−2.27 (m, 1H), 2.18−1.99 (m, 3H), 1.85−1.75 (m, 2H), 1.67−1.59 (m, 1H), 1.27−1.17 (m, 1H); ^{13}C NMR δ 201.6, 196.4, 107.4, 71.6, 64.8, 53.0, 51.5, 50.8, 47.6, 36.0, 24.7, 23.8, 20.9; IR (neat) 3250, 2800, 1740, 1420, 1210 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_5$: C 61.41, H 7.13. Found: C 61.83, H 7.09.

***trans*-Hydrindane Derivative 16.** To a stirred solution of diketone **15** (46 mg, 0.18 mmol) in methanol (2 mL) was added 30% H_2O_2 (0.13 mL) followed by slow addition of 6 N NaOH solution (0.05 mL). After the mixture was stirred at room temperature (∼20 °C) for 45 min, a few drops of 5% HCl was added along with cold water and extracted with ethyl acetate (3 × 5 mL). The combined ethyl acetate layer was washed once with brine and dried over Na_2SO_4. The crude carboxylic acid obtained after concentration of the ethyl acetate layer was treated with excess diazomethane in ether:methanol (1:1) at 0 °C. After excess diazomethane was quenched with acetic acid, the solution was concentrated and silica gel column chromatography afforded the pure *trans*-hydrindane **16**. Yield 33 mg, 58%; colorless solid; mp 126−127 °C; ^{1}H NMR δ 3.90 (dt, 1H, J = 10.8, 4.6 Hz), 3.72 (s, 3H), 3.66 (s, 3H), 3.35 (s, 3H), 3.29 (s, 3H), 3.17 (t, 1H, J = 9.3 Hz), 2.88 (ddd, 1H, J = 13.6, 12.2, 9.3 Hz), 2.25−2.19 (m, 1H), 2.03 (ddd, 1H, J = 12.0, 9.3, 6.6 Hz), 1.99−1.95 (m, 1H), 1.87−1.72 (m, 3H), 1.67 (dd, 1H, J = 13.1, 3.9 Hz), 1.34−1.26 (m, 1H), 1.18−1.08 (m, 1H); ^{13}C NMR δ 172.1, 171.6, 110.9, 70.1, 62.7, 52.0, 51.7, 51.4, 51.1, 50.1, 49.5, 35.2, 31.3, 27.8, 22.5; IR (KBr) 3320, 2900, 1710, 1420, 1200, 1150 cm^{-1}. Anal. Calcd for $C_{15}H_{24}O_7$: C 56.95, H 7.65. Found: C 57.04, H 7.95.

Tricyclic Diketone 18. To a solution of dibromo alcohol **7** (536 mg, 1.40 mmol) in dichloromethane (3 mL) were added acetic anhydride (4.8 mL) and DMAP (464 mg, 3.8 mmol). The mixture was stirred at room temperature for 4 h and then cold water was added. The separated aqueous layer was extracted with dichloromethane (3 × 4 mL) and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel with 5% ethyl acetate−hexane to furnish the corresponding acetate derivative **17** (545 mg, 91%) as a colorless solid, mp 72−74 °C.

The dibromo acetate derivative **17** (120 mg, 0.28 mmol) was dissolved in acetonitrile (7.2 mL). A solution of $RuCl_3 \cdot 3H_2O$ (5.7 mg, 0.022 mmol) and $NaIO_4$ (96 mg, 0.45 mmol) in water (1.2 mL) was added at 0 °C and the reaction mixture was stirred for 45 min. The resulting suspension was filtered through a thin pad of silica gel, which was then washed with ethyl acetate (15 mL). Concentration of the filtrate followed by silica gel column chromatography (30% ethyl acetate−hexane) gave the diketone **18** (74 mg, 90%). Yellow solid; mp 98−100 °C; ^{1}H NMR δ 4.47−4.40 (m, 1H), 3.43 (s, 3H), 3.30 (s, 3H), 3.18 (d, 1H, J = 5.9 Hz), 2.56−2.49 (m, 1H), 2.39−2.31 (m, 1H), 2.21−2.08 (m, 3H), 2.01 (s, 3H), 1.81−1.78 (m, 1H), 1.70−1.62 (m, 1H), 1.53−1.48 (m, 1H), 1.29−1.19 (m, 1H); ^{13}C NMR δ 201.0, 195.7, 170.2, 107.2, 73.6, 64.6, 52.8, 51.5, 50.8, 45.0, 32.1, 24.4, 23.7, 21.0, 20.6; IR (neat) 2900, 1750, 1720, 1440, 1360 cm^{-1}. Anal. Calcd for $C_{15}H_{20}O_6$: C 60.80, H 6.80. Found C 60.85, H 6.83.

Tricyclic Diketone 21. To a solution of dibromo alcohol **9** (80 mg, 0.20 mmol) in dichloromethane (2 mL) were added acetic anhydride (0.4 mL) and pyridine (0.7 mL). The mixture was stirred at room temperature for 8 h and then cold water was added along with a few drops of 10% HCl. The separated aqueous layer was extracted with dichloromethane (3 × 4 mL) and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel with 10% ethyl acetate−hexane to furnish the corresponding acetate derivative **20** (78 mg, 92%).

The dibromo acetate derivative **20** (70 mg, 0.16 mmol) was dissolved in acetonitrile (3.6 mL). A solution of $RuCl_3 \cdot 3H_2O$ (3.3 mg, 0.013 mmol) and $NaIO_4$ (56 mg, 0.26 mmol) in water (0.6 mL) was added at 0 °C and the mixture was stirred for 3 h. The resulting suspension was filtered through a thin pad of silica gel, which was then washed with ethyl acetate (15 mL). Concentration of the filtrate followed by silica gel column chromatography (30% ethyl acetate−hexane) furnished the diketone **21** (44 mg, 93%). Yellow solid; mp 112−114 °C; ^{1}H NMR δ 5.03−5.02 (m, 1H), 3.39 (s, 3H), 3.29 (s, 3H), 3.12 (d, 1H, J = 6.4 Hz), 2.63 (ddd, 1H, J = 11.1, 7.0, 2.0 Hz), 2.33−2.24 (m, 2H), 2.13 (tq, 1H, J = 13.7, 4.4 Hz), 2.00−1.96 (m, 1H), 1.91 (s, 3H), 1.73 (dt, 1H, J = 12.7, 6.7 Hz), 1.64−1.60 (m, 1H), 1.52−1.44 (m, 2H); ^{13}C NMR δ 200.0, 198.2, 170.2, 107.0, 70.2, 61.7, 52.7, 51.5, 50.5, 45.0, 29.2, 24.3, 24.0, 20.4, 16.9; IR (neat) 2950, 1750, 1700 cm^{-1}. Anal. Calcd for $C_{15}H_{20}O_6$: C 60.80, H 6.80. Found C 60.84, H 6.82.

***trans*-Hydrindane Derivative 19.** To a stirred solution of diketone **18** (48 mg, 0.16 mmol) in methanol (2 mL) was added 30% H_2O_2 (0.16 mL) followed by slow addition of 6 N NaOH solution (0.07 mL). After the mixture was stirred at 0 °C for 20 min, a few drops of 5% HCl was added along with 2 mL of cold water and extracted with ethyl acetate (3 × 4 mL). The combined ethyl acetate layer was washed once with brine and dried over Na_2SO_4. The crude carboxylic acid obtained after concentration of the ethyl acetate layer was treated with excess diazomethane in ether:methanol (1:1) at 0 °C. After excess diazomethane was quenched with acetic acid, the solution was concentrated and silica gel column chromatography afforded the *trans*-hydrindane derivative **19** (53 mg, 92%). ^{1}H NMR δ 5.07 (dt, 1H, J = 10.8, 4.6 Hz), 3.75 (s, 3H), 3.65 (s, 3H), 3.35 (s, 3H), 3.30 (s, 3H), 3.15 (t, 1H, J = 9.5 Hz), 2.90−2.77 (m, 1H), 2.29−2.24 (m, 1H), 2.12−2.05 (m, 1H), 2.05 (s, 3H), 2.01−1.85 (m, 2H), 1.76−1.68 (m, 2H), 1.39−1.31 (m,

1H), 1.20−1.10 (m, 1H); ^{13}C NMR δ 171.8, 171.5, 170.5, 110.7, 73.0, 62.9, 51.8, 51.6, 51.2, 49.9, 49.4, 48.8, 31.7, 31.4, 28.0, 22.2, 21.2; IR (KBr) 2900, 1720, 1430 cm^{-1}. Anal. Calcd for $C_{17}H_{26}O_8$: C 56.97, H 7.31. Found: C 57.05, H 7.34.

***trans*-Hydrindane Derivative 23. 23** was prepared following the same procedure as above. Yield 33 mg, 92% from **21** (30 mg, 0.1 mmol); colorless solid; ^{1}H NMR δ 5.18 (d, 1H, J = 2.2 Hz), 3.70 (s, 3H), 3.68 (s, 3H), 3.35 (s, 3H), 3.17 (s, 3H), 3.10 (t, 1H, J = 9.3 Hz), 3.02−2.93 (m, 1H), 2.38−2.34 (m, 1H), 2.09−2.04 (m, 1H), 2.02 (s, 3H), 1.90−1.69 (m, 4H), 1.64−1.55 (m, 1H), 1.50−1.45 (m, 1H); ^{13}C NMR δ 172.9, 170.8, 170.5, 110.8, 70.3, 58.1, 51.7, 51.0, 50.9, 50.5, 49 3, 47.9, 30.9, 30.6, 28.5, 21.1, 18.6; IR (KBr) 2927, 1733, 1640, 1265 cm^{-1}. Anal. Calcd for $C_{17}H_{26}O_8$: C 56.97, H 7.31. Found: C 57.03, H 7.35.

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Supporting Information Available: X-ray crystal structures and crystallographic data for **7** and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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