Regio- and Stereoselectivity in the Reductions of Cyclic Enedione Systems

Chunjian Liu and D. Jean Burnell*

Department of Chemistry, Memorial University of Newfoundland, St. John's, Newfoundland A1B 3X7, Canada

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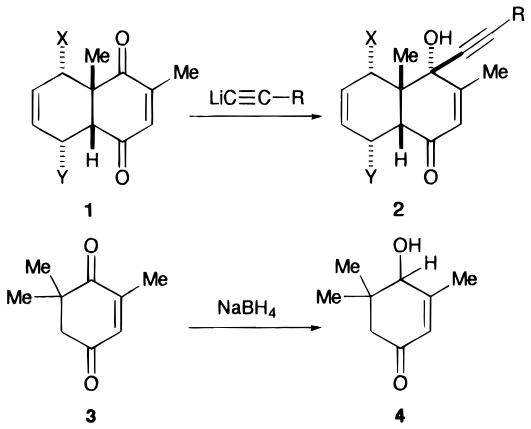
Reductions of cyclic enedione substrates by $NaBH_4$ and by $LiAl(O\text{-}t\text{-}Bu)_3H$ very predominantly gave monoreduction products with very high regio- and stereoselectivity. The reductions involved axial delivery of the hydride. The results indicated that electronic factors were dominated by steric considerations in the transition state of the reduction, even though the seemingly more encumbered carbonyl was reduced.

Introduction

The stereochemistry of additions to, and reductions of, carbonyl groups has been very extensively studied. The stereochemistry of ketone reduction, especially the issue of axial versus equatorial attack on cyclohexanones, appears to be the result of an interplay of torsional and hyperconjugative effects at the transition state.[1,2] However, relatively little attention has been paid to regioselectivity in molecules possessing two or more ketone functions. In cyclic anhydrides[3] and imides,[4] the carbonyl that seems more sterically hindered is often preferentially reduced. Kayser[3e] concluded that electronic, steric, and chelation effects can all be important in determining the regioselectivity of anhydride reduction. Liotta[5] found that additions of lithium acetylides to cyclohex-2-ene-1,4-dione derivatives **1** proceeded with excellent selectivity in favor of reaction at the seemingly more congested carbonyl to give **2**. Liotta pointed out that this regioselectivity could be explained by comparing the "accessibility" of the carbonyls, i.e., the relative amounts of steric hindrance between the nucleophile and the substrate, during axial attack by the nucleophile. Others have used Liotta's results to explain regioselectivities in similar molecules of synthetic interest.[6,7] In terms of ketone reductions, the reaction of 4-oxoisophorone **3** with $NaBH_4$ was reported to give **4**, but this outcome was not rationalized in any way.[6] A few similar observations have been made with more elaborate substrates.[7a,8] We present here the results of reductions of a number of bicyclic cyclohex-2-ene-1,4-dione derivatives. For the first time, the relative importance of accessibility compared to electronic differences between the carbonyls has been related to regioselectivity in the 1,2-reductions of enediones.



Results and Discussion

The cyclohex-2-ene-1,4-dione derivative **5** was available in very high yield by straightforward Diels−Alder reaction of 2,6-dimethyl-1,4-benzoquinone with 2,3-dimethyl-1,3-butadiene. Reduction of **5** with $NaBH_4$ in methanol at 0 °C led to nearly quantitative formation of a monoalcohol **6**. Chemical shift considerations and NOE experiments showed **6** was the product of attack onto the face of the apparently more congested ketone, syn to the methyl on the ring junction. Axial attack by hydride could be inferred by comparison with the reaction with $LiAl(O\text{-}t\text{-}Bu)_3H$. This reagent has long been known to give equatorial alcohols very stereoselectively from enones by axial attack on the carbonyl,[9] and in THF at 0 °C it also gave monoalcohol **6** from enedione **5** in an isolated

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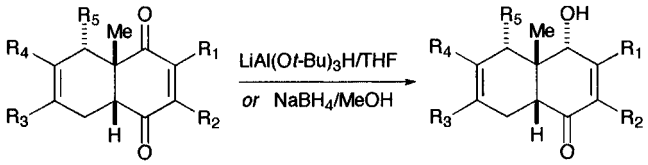
yield of 97%.[10] Liotta's substrates had shown analogous regioselectivity, but they had borne substituents in the second ring in positions that might have influenced this regioselectivity. Also, work with imides had demonstrated that conformation and thence regioselectivity could be influenced by distant substituents.[4] However, the reduction of **7** with LiAl(O-*t*-Bu)$_3$H yielded **8**, which suggested that a methyl group on the second ring had no adverse effect on the regioselectivity. A complete lack of regioselectivity in the Diels−Alder reaction of 2,6-dimethyl-1,4-benzoquinone with isoprene was exploited to yield a 1:1 mixture of enediones **9** and **10**. Reduction of these with LiAl(O-*t*-Bu)$_3$H led to the production of a mixture of monoalcohols for which the ^{1}H NMR spectrum revealed signals for only **11** and **12**, so neither of the remote methyls played a measurable role in determining the regio- or regioselectivity of reduction. A considerably more elaborate substrate **13** was also reduced both by $NaBH_4$ and by LiAl(O-*t*-Bu)$_3$H to give **14** as the only monoalcohol product.



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9 R_1, R_3 = Me, R_2, R_4, R_5 = H
10 R_1, R_4 = Me, R_2, R_4, R_5 = H
17 R_1, R_5 = H, R_2, R_3, R_4 = Me

6 R_1, R_3, R_4 = Me, R_2, R_5 = H
8 R_1, R_5 = Me, R_2, R_3, R_4 = H
11 R_1, R_3 = Me, R_2, R_4, R_5 = H
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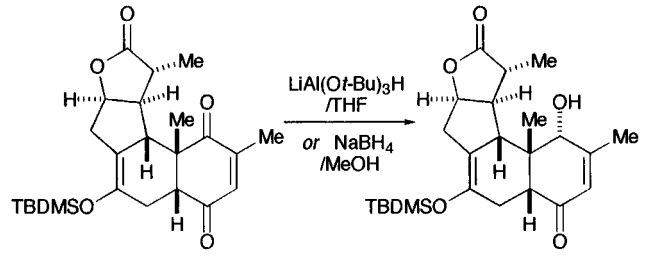
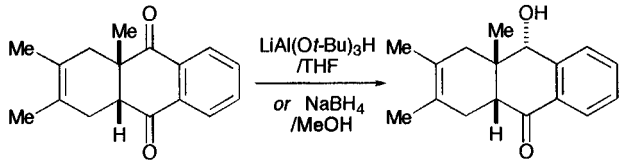
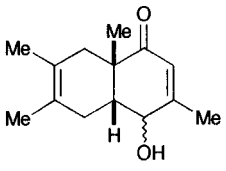


13 **14**



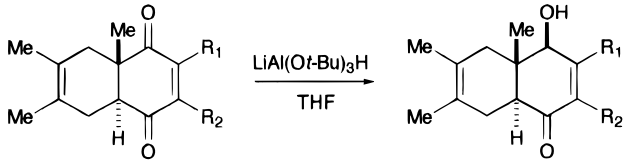
15 **16**



19

It is difficult to envision how a methyl group on the double bond of the enedione system could affect the stereochemistry of the reduction, but electron donation from this methyl might influence regioselectivity by reducing the reactivity of the β carbonyl. Liotta and coworkers[5] had dismissed such an electronic contribution because a Diels−Alder adduct of 2,5-dimethyl-1,4-benzoquinone still reacted with acetylide only at the carbonyl that would ostensibly have been electronically deactivated. In diketone **15**, no such bias was possible, and indeed, its reduction still provided a single keto alcohol **16**. On the other hand, electron donation from the vinyl methyl group in **17** should reduce the reactivity of the carbonyl next to the methyl on the ring junction, and a modest deterioration of regioselectivity was noted. Two reduction products, **18** and **19**, were detected by GC−MS analysis of the crude reaction mixture (15:1 with $NaBH_4$ and >25:1 with LiAl(O-*t*-Bu)$_3$H). The minor product was not isolated, so its structure was only tentatively assigned as **19**. It was clear that the methyl on the ring junction played a very dominant role in determining the regioselectivity of reduction with these cis-fused bicyclic enediones.

Warming **5**, **15**, and **17** in acetic acid gave the cis-fused and the trans-fused enediones **20**, **22**, and **24**, respectively, as inseparable mixtures. Nevertheless, the mixtures were reduced by LiAl(O-*t*-Bu)$_3$H, and the selectivities with the trans-fused substrates could be assessed without ambiguity by NMR. The results paralleled those with **5**, **15**, and **17**, except now the approach of the reducing agent was anti to the methyl on the ring junction even though all reductions proceeded by axial attack. Enediones **20** and **22** provided products **21** and **23**, respectively. Electron donation from the vinyl methyl group in **24** opposed the effect of the ring-junction-methyl, and there was a drop in the regioselectivity that led to the production of **25** and an unisolated isomer tentatively assigned structure **26**, in an 8:1 ratio by GC−MS. It should be pointed out that enedione **27** bears a much stronger carbonyl deactivating group than did any of our substrates, but Ishihara[6] reported that regioselectivity in its reaction with acetylide had no regioselectivity. Even a considerable electronic contribution had still not overcome the effect of the ring-junction-methyl.



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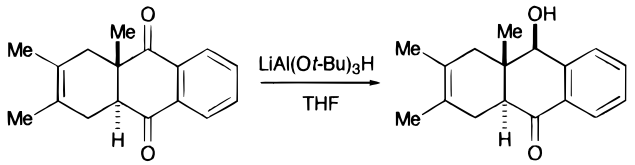
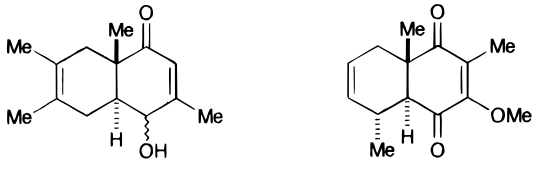
24 R_1 = H, R_2 = Me

21 R_1 = Me, R_2 = H
25 R_1 = H, R_2 = Me



22 **23**



26 **27**

The overwhelming preference for axial attack by nucleophiles onto conjugated cyclohexenones[2] has been

(10) Reaction of **5** with $LiBH_4$ in THF, which also reacts by axial attack on the carbonyl,[1a] gave **6**, but this product was contaminated by a significant amount of overreduced material. In contrast, treatment of **5** with L-Selectride, which reacts via equatorial attack,[1a] resulted in preferential reduction of the C-4 carbonyl.

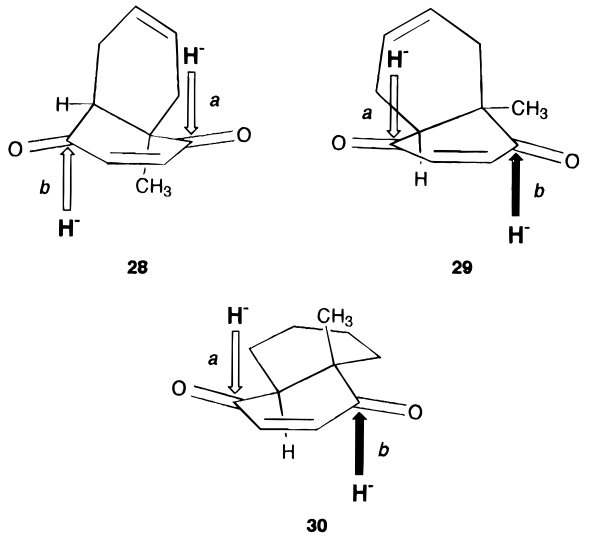


Figure 1. Regiochemical alternatives (*a* and *b*) for axial attack on cis and trans bicyclic enediones. The cis substrate has two conformers, **28** and **29**, of almost equal energy, whereas **30** is the only low-energy conformer for the trans enedione. The predominant modes of hydride addition are shown with the solid arrows, and the disfavored modes are the open arrows.

convincingly explained using ab initio transition structures. A pivotal difference between axial and equatorial attack resides in the interaction with the sp^3 center α to the carbonyl: the transition structure for axial attack is staggered, whereas for equatorial attack it is eclipsed. At the 6-31+G level of theory, equatorial attack was found to be 2.4 kcal/mol higher in energy than axial attack, but this difference also reflects better orbital overlap in the enone moiety of the axial transition state.[11] We propose that the stereochemical imperative for axial attack with $NaBH_4$ and $LiAl(O\text{-}t\text{-}Bu)_3H$ translates into the very high degree of regioselectivity in the reductions of the bicyclic enediones. AM-1[12] calculations indicated that there are two low-energy conformers for **5**, which are within 0.5 kcal/mol of each other in energy. These two conformers, **28** and **29**, are shown in Figure 1 using a simpler demethylated model. In conformer **28**, attack on the concave face (*a*) is hindered in its β position by the axial methylene from the second ring. On the convex face (*b*), an axial methyl, also β to the reacting carbonyl, must impede reduction. In conformer **29**, attack on the concave face (*a*) must contend with the β axial methylene, but axial approach to the convex face (*b*) is relatively unencumbered. The product of this final mode (*b*) of axial attack on **29** is the one that leads to all of the major reduction products (**6**, **8**, **11**, **12**, **14**, **16**, and **18**) from the cis substrates. AM-1 calculations indicated that the energy of **6** is only 0.45 kcal/mol more stable than the product of the other axial attack on the convex face of **28**, so the reason for the regioselectivity must be the result of a phenomenon that is considerably more regiochemically dissimilar at the transition states than in the products. This phenomenon might be simple steric hindrance between the reducing agent and the substrate or a torsional manifestation within the substrate molecule.

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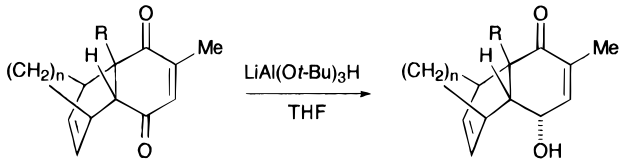
AM-1 calculations with the trans enediones confirmed that these substrates have one distinct conformational preference **30** with both rings twist-chair. In contrast with the cis substrates, there can be little facial shielding by the second ring. However, axial addition to one carbonyl (*a*) would be impeded by an axial methyl in the β position, whereas axial attack on the other carbonyl (*b*), which happens to have the same methyl in its α position, would be relatively unencumbered. The major products from the reductions of trans substrates **20**, **22**, and **24** were all consistent with the latter mode (*b*) of reaction.

The regioselectivity in the reductions of the bicyclic enediones was consistent with axial attack, presumably by virtue of interactions with α substituents, onto the carbonyl that was less hindered, by interactions with a β substituent. In the more rigid bridged systems, accessibility was defined by an α methyl. With $LiAl(O\text{-}t\text{-}Bu)_3H$, enedione **31** was reduced relatively slowly (2 h versus minutes for the bicyclic enediones) to give three products, but only the major one was a monoalcohol. This was **32**, the product of reduction from the convex side of the electronically deactivated, but nevertheless less hindered, ketone. The minor compounds proved to be a mixture (2.5:1) of epimers **33** and **34**, products of 1,4-reduction. Enedione **35** was slightly more flexible than **31**, and its reduction, which was also slow, yielded two monoalcohols **36** and **37** in a 10:1 ratio, respectively. Finally, the ring-junction-methyl was absent in **38**, and it reacted rapidly with $LiAl(O\text{-}t\text{-}Bu)_3H$. With **38**, electron donation from the vinyl methyl at last played a dominant role in determining regiochemistry, with **39** and **40** being produced in a 1:5 ratio, respectively.



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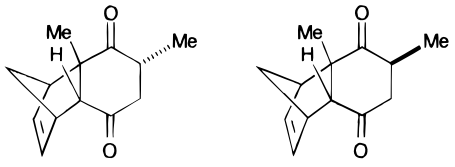
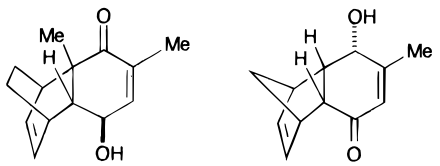
38 n = 1, R = H

32 n = 1, R = Me
36 n = 2, R = Me
39 n = 1, R = H



33 **34**



37 **40**

In conclusion, regioselectivity in the reduction of these cyclohexenediones by $NaBH_4$ or $LiAl(O\text{-}t\text{-}Bu)_3H$) can be predicted by first assuming a predilection for axial attack on carbonyl and then by assessing the hindrance in the possible modes of axial addition. The electronic effect of alkyl substitution on the conjugated double bond is subservient to the steric or torsional one, and in "mis-

matched" pairs the electronic contribution reduced the regioselectivity, but it did not reverse the regiochemical preference.

Experimental Section

General Methods. Enedione substrates with *cis* ring junctions were synthesized by Diels−Alder cycloaddition of a quinone with an excess of the appropriate diene.[13] Following the reaction, solvent and excess diene were removed under reduced pressure, and the enedione was purified by flash chromatography. Enedione substrates with *trans* ring junctions were obtained by epimerization of the corresponding *cis* compound, but this only provided inseparable mixtures of roughly 1:1 of the *cis* and the *trans* compounds. Product ratios were determined by careful integration of the ^{1}H NMR spectra of the crude product mixtures and by GC−MS.[14] (The chemical shift of the vinyl proton of the enedione moiety after reduction was indicative of the regiochemistry of the reduction.) With the *trans* substrates, the determination of product ratios was only slightly complicated by the presence of the known products derived from the epimeric *cis* substrates. Flash chromatography was over silica gel with elution by hexane containing an increasing proportion of EtOAc. IR data include the following descriptors: s, strong; m, medium; w, weak; br, broad. ^{1}H NMR spectra were obtained at 300 MHz in $CDCl_3$ solution unless otherwise noted; chemical shifts are relative to internal TMS. NOE measurements were made with difference spectra, using previously described parameters.[15] NOE data take this form: saturated signal (enhanced signal, enhancement). ^{13}C NMR spectra are at 75 MHz in $CDCl_3$ unless otherwise noted; chemical shifts are relative to a solvent resonance.

Reductions with $NaBH_4$. To a solution of the enedione (0.60 mmol) in MeOH (5.0 mL) at 0 °C was added solid $NaBH_4$ (0.48 mmol) over 5 min. The mixture was stirred for 5 min before a dilute, aqueous NH_4Cl solution (40 mL) was added. This was extracted with EtOAc (4 × 25 mL), and the combined organic solutions were washed with H_2O (2 × 25 mL) and brine (25 mL). The solution was dried ($MgSO_4$) and concentrated under vacuum. Flash chromatography provided the monoreduction product.

Reductions with LiAl(O-*t*-Bu)$_3$H. To a solution of enedione (1.0 mmol) in dry THF (8.0 mL) at a 0 °C was added LiAl(O-*t*-Bu)$_3$H (1.2 mmol) dropwise over 5 min. The mixture was stirred for 15−20 min (for **31** and **35** 2 h was required). The mixture was poured into H_2O (50 mL). This was extracted with EtOAc (4 × 25 mL), and the combined organic solutions were washed with H_2O (2 × 25 mL) and brine (25 mL). The solution was dried ($MgSO_4$) and concentrated under vacuum. When necessary, flash chromatography was used to purify the monoreduction product.

(4α,4a*β*,8a*β*)-4,4a,5,8,8a-Pentahydro-4-hydroxy-3,4a,6,7-tetramethylnaphthalen-1-one (6): yields, $NaBH_4$ 96% (by GC−MS >50:1), LiAl(O-*t*-Bu)$_3$H 97% (by GC−MS >50:1); white solid; mp 129.0−131.0 °C; IR (Nujol) 3451 (s), 1659 (s) cm^{-1}; ^{1}H NMR δ 5.87 (1H, s), 4.27 (1H, d, J = 6.8 Hz), 2.69 (1H, d, J = 16.1 Hz), 2.23−2.02 (7H, m), 1.64−1.55 (7H, m), 1.20 (3H, s); NOE data 4.27 (1.20, 1%), 1.20 (4.27, 9%); ^{13}C NMR: δ 198.7 (0), 160.1 (0), 125.9 (1), 123.5 (0), 122.8 (0), 78.0 (1), 50.4 (1), 41.0 (0), 33.9 (2), 27.5 (2), 23.7 (3), 20.3 (3), 19.4 (3), 18.8 (3); HRMS calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1450.

(4α,4a*β*,5α,8a*β*)-4,4a,5,8,8a-Pentahydro-4-hydroxy-3,4a,5-trimethylnaphthalen-1-one (8): yield, LiAl(O-*t*-Bu)$_3$H 89%; colorless crystals; mp 111.5−112.5 °C; IR (CCl_4) 3503, 1644 cm^{-1}; ^{1}H NMR ($C_6D_5CD_3$ at 100 °C[16]) δ 5.66 (1H, q, J = 1.3 Hz), 5.41 (2H, m), 3.74 (1H, m), 2.55 (1H, m), 2.13−1.77 (4H, m), 1.72 (3H, nar m), 0.94 (3H, d, J = 7.4 Hz), 0.88 (3H, s); ^{13}C NMR (CD_2Cl_2 at −85 °C[16]) δ 203.6, 199.6, 163.9, 157.3, 133.6, 131.0, 125.8, 124.3, 122.3, 121.9, 76.7, 72.8, 49.6, 48.3, 45.1, 38.0, 37.6, 35.5, 27.8, 26.5, 25.0, 22.3, 20.9, 20.3, 19.8, 13.2; HRMS calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1306.

(4α,4a*β*,8a*β*)-4,4a,5,8,8a-Pentahydro-4-hydroxy-3,4a,7-tetramethylnaphthalen-1-one (11) and (4α,4a*β*,8a*β*)-4,4a,5,8,8a-pentahydro-4-hydroxy-3,4a,6-tetramethylnaphthalen-1-one (12): yield of **11** and **12** (1:1), LiAl(O-*t*-Bu)$_3$H 92%. NMR data for the mixture of **11** and **12**: ^{1}H NMR (partial) δ 5.88 (2H, overlapped narrow signals), 5.36 (1H, m), 5.25 (1H, m), 4.30 (2H, nar m), 2.81 (1H, br d, $J \approx$ 17 Hz), 2.70 (1H, d, J = 17.1 Hz), 2.02 (6H, nar m), 1.69 (3H, br s), 1.59 (3H, br s), 1.22 (6H, s); ^{13}C NMR (some signals overlapped) δ 198.7, 198.6, 160.3, 132.0, 131.4, 125.9, 118.7, 118.4, 78.1, 78.0, 50.5, 49.7, 41.2, 40.4, 32.3, 27.7, 25.9, 23.9, 23.6, 23.5, 23.4, 21.3, 20.3.

(1α,4a*β*,7aα,10α,10aα,10b*β*,10c*β*)-6-((*tert*-Butyldimethylsilyl)oxy)-4a,5,7,7a,10,10a,10b,10c-octahydro-1-hydroxy-2,10,10c-trimethyl-1*H*-benz[6,7]indeno[2,1-*b*]furan-4,9-dione (14): yields, $NaBH_4$ 82%, LiAl(O-*t*-Bu)$_3$H 90%; white solid; mp 171.0−172.0 °C; IR (Nujol) 3448, 1740, 1666 cm^{-1}; ^{1}H NMR δ 5.83 (1H, s), 5.02 (1H, br m), 3.91 (1H, d, J = 7.8 Hz), 3.08 (1H, ddd, J = 1.6, 7.2, 17.4 Hz), 2.78−2.17 (7H, m), 2.08 (3H, s), 1.40 (3H, d, J = 7.5 Hz), 1.10 (3H, s), 0.91 (9H, s), 0.11 (3H, s), 0.089 (3H, s); NOE data 3.91 (2.08, 2%; 1.10, 2%); ^{13}C NMR δ 200.3, 179.7, 155.9, 140.3, 123.3, 118.3, 82.2, 74.2, 53.3, 51.5, 47.7, 43.0, 38.7, 33.7, 32.0, 27.0, 25.6, 18.0, 16.2, −3.8, −3.9; HRMS calcd for $C_{24}H_{36}O_5Si$ 432.2330, found 432.2351.

(4aα,9aα,10*β*)-1,4,4a,9a,10-Pentahydro-10-hydroxy-2,3,-4a-trimethylanthracen-9-one (16): yields, $NaBH_4$ 97% (by GC−MS >60:1), LiAl(O-*t*-Bu)$_3$H 98% (by GC−MS >100:1); white solid; mp 119.0−120.5 °C; IR (Nujol) 3466, 1664 cm^{-1}; ^{1}H NMR δ 8.00 (1H, d, J = 7.8 Hz), 7.98 (1H, d, J = 7.8 Hz), 7.62 (1H, br m), 7.38 (1H, br m), 4.83 (1H, d, J = 8.0 Hz), 2.89 (1H, d, J = 17.4 Hz), 2.44 (1H, m), 2.23−2.21 (2H, m), 1.87 (1H, d, J = 17.4 Hz), 1.68 (3H, s), 1.60 (1H, d, J = 17.4 Hz), 1.49 (3H, s), 1.31 (3H, s); NOE data 4.83 (7.98, 2%; 2.44, 5%; 1.31, 1%), 1.31 (4.83, 9%; 2.44, 6%; 2.23−2.21, 4%); ^{13}C NMR δ 197.5 (0), 143.7 (0), 134.1 (1), 130.5 (0), 127.7 (1), 126.8 (1), 126.5 (1), 123.7 (0), 122.6 (0), 76.2 (1), 50.9 (1), 41.0 (0), 33.7 (2), 28.0 (2), 23.6 (3), 19.4 (3), 18.9 (3); HRMS calcd for $C_{17}H_{20}O_2$ 256.1463, found 256.1478.

(4α,4a*β*,8a*β*)-4,4a,5,8,8a-Pentahydro-4-hydroxy-2,4a,6,7-tetramethylnaphthalen-1-one (18): yields, $NaBH_4$ 96% (by GC−MS **18**:tentative **19** = 15:1), LiAl(O-*t*-Bu)$_3$H 98% (by GC−MS **18**:tentative **19** = >25:1). For **18**: white solid; mp 99.0−101.5 °C; IR (Nujol) 3460, 1658 cm^{-1}; ^{1}H NMR δ 6.46 (1H, m), 4.38 (1H, m), 2.71 (1H, d, J = 17.6 Hz), 2.20 (1H, m), 2.13−2.07 (3H, m), 1.78−1.77 (3H, m), 1.65 (3H, s), 1.57 (1H, d, J = 15.1 Hz), 1.55 (3H, s), 1.19 (3H, s); NOE data 4.38 (6.46, 4%; 2.20, 4%; 1.19, 1%), 1.19 (4.38, 8%; 2.20, 5%); ^{13}C NMR δ 199.4 (0), 144.8 (1), 134.6 (0), 123.4 (0), 122.6 (0), 75.1 (1), 50.1 (1), 42.1 (1), 33.3 (2), 27.3 (2), 23.5 (3), 19.4 (3), 18.8 (3), 15.6 (3); HRMS calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1488.

For tentative **19**: ^{1}H NMR (from the spectrum of the crude product mixture) δ 5.78; MS (from GC−MS) 220 (M^+).

Epimerization of 5, 15, and 17. A solution of the *cis* isomer (1.5 mmol) in glacial acetic acid (10 mL) was heated at reflux for 12 h. Acetic acid was removed under reduced pressure, and the residue was redissolved in Et_2O and washed with aqueous $NaHCO_3$, water, and brine. After being dried over anhydrous Na_2SO_4, the solution was concentrated under vacuum, and flash chromatography provided a 1:1 mixture of the *cis* and *trans* isomers. These were inseparable by flash chromatography, so assessment of the reductions of the *trans* isomers were made with these epimeric mixtures.

(13) Compound **13** was prepared in conjunction with an ongoing synthetic effort. Details will be presented in a forthcoming manuscript.

(14) For many reductions, signals attributable to a minor product were not detected by ^{1}H NMR, so the products were also examined by GC−MS. However, by this technique it was not possible to identify minor components with any certainty, other than they had the correct mass. GC−MS ratios may underestimate the selectivity of the 1,2-reduction process because in at least one instance the minor components proved to be 1,4-reduction products.

(15) Gillard, J. R.; Newlands, M. J.; Bridson, J. N.; Burnell, D. J. *Can. J. Chem.* **1991**, *69*, 1337−1343.

(16) The NMR spectra for **8** at ambient temperature showed very broad peaks. At −85 °C signals for two conformers (roughly 1:1) were evident.

(4α,4aα,8aβ)-4,4a,5,8,8a-Pentahydro-4-hydroxy-3,4a,6,7-tetramethylnaphthalen-1-one (21): yield, LiAl(O-*t*-Bu)$_3$H 97% (by GC−MS 30:1); ^{1}H NMR (clearly discernable signals from a mixture of **21** and **6**) δ 5.87 (1H, s), 4.33 (1H, d, J = 6.2 Hz), 2.36 (1H, dd, J = 11.2, 5.8 Hz), 2.03 (3H, s), 0.80 (3H, s); NOE data 4.33 (2.36, 5%); ^{13}C NMR δ 199.9, 161.6, 126.0, 123.4, 122.5, 79.4, 49.8, 44.4, 42.3, 28.2, 20.0, 19.0, 18.7, 11.5; MS (from GC−MS) 220 (M^+).

(4aα,9aβ,10α)-1,4,4a,9a,10-Pentahydro-10-hydroxy-2,3,4a-trimethylanthracen-9-one (23): yields, $NaBH_4$ 96% (by GC−MS 33:1), LiAl(O-*t*-Bu)$_3$H 95% (by GC−MS 48:1); ^{1}H NMR (clearly discernable signals from a mixture of **23** and **16**) δ 4.84 (1H, d, J = 7.6 Hz), 2.58 (1H, dd, J = 6.0, 11.0 Hz), 0.72 (3H, s); NOE data 4.84 (2.58, 8%); ^{13}C NMR δ 198.7, 144.0, 134.0, 130.9, 127.4, 126.4, 125.6, 123.5, 122.6, 77.6, 50.2, 44.5, 41.9, 28.5, 19.1, 18.7, 11.2; MS (from GC−MS) 256 (M^+).

(4α,4aα,8aβ)-4,4a,5,8,8a-Pentahydro-4-hydroxy-2,4a,6,7-tertramethylnaphthalen-1-one (25): yield, LiAl(O-*t*-Bu)$_3$H 97% (by GC−MS **25**: tentative **26** = 8:1). For **25**: ^{1}H NMR δ 6.49 (1H, s), 4.40 (1H, m), 2.34 (1H, dd, J = 5.9, 11.1 Hz), 1.78 (3H, s), 0.80 (3H, s); ^{13}C NMR δ 200.5, 145.6, 134.9, 123.4, 122.4, 77.1, 49.1, 44.5, 43.2, 28.2, 19.0, 18.6, 15.3, 11.5; NOE data 4.40 (2.34, 7%); MS (from GC−MS) 220 (M^+).

For tentative **26**: ^{1}H NMR (from the spectrum of the crude product mixture) δ 5.85; MS (from GC−MS) 220 (M^+).

(4α,4aβ,5β,8β,8aβ)-4,4a,5,8,8a-Pentahydro-4-hydroxy-2,8a-dimethyl-5,8-methanonaphthalen-1-one (32). Ratio of products by ^{1}H NMR **32**:**33**:**34** = 23.5:2.5:1. Isolated yield for **32** as a white solid (77%): mp 53.0−54.5 °C; IR 3435 (br), 1641 cm^{-1}; ^{1}H NMR δ 6.28 (1H, m), 6.10 (1H, dd, J = 2.8, 5.6 Hz), 5.82 (1H, dd, J = 2.9, 5.6 Hz), 4.83 (1H, m), 3.16 (1H, br s), 2.89 (1H, br s), 2.67 (1H, m), 2.13 (1H, br s), 1.66 (3H, dd, J = 1.4, 2.4 Hz), 1.57 (1H, d, J = 8.8 Hz), 1.45−1.41 (4H, m); NOE data 4.83 (2.67, 5%), 2.67 (4.83, 6%; 1.57, 3%), 1.57 (2.67, 4%); ^{13}C NMR δ 203.8 (0), 144.8 (0), 144.8 (1), 135.7 (1), 135.4 (1), 65.2 (1), 56.6 (1), 51.0 (0), 50.4 (1), 47.1 (2), 45.8 (1), 25.3 (3), 15.6 (3); HRMS calcd for $C_{13}H_{16}O_2$ 204.1149, found 204.1132.

For **33** (from an inseparable mixture of **33** and **34**): ^{1}H NMR δ 6.30 (1H, dd, J = 3.0, 5.7 Hz), 6.04 (1H, dd, J = 2.9, 5.7 Hz), 3.24 (1H, m), 3.08 (1H, m), 2.88 (1H, br m), 2.80 (1H, dd, J = 1.7, 3.8 Hz), 2.54 (1H, ddd, J = 1.7, 5.2, 16.0 Hz), 2.04 (1H, br dd, J = 14.2, 16.0 Hz), 1.61 (1H, br d, $J \approx$ 8.5 Hz), 1.50 (1H, overlapped d), 1.43 (3H, s), 1.01 (3H, d, J = 6.6 Hz); NOE data 1.43 (3.08, 5%; 2.88, 4%; 2.80, 8%; 1.61, 4%), 1.01 (2.88, 3%; 2.54, 0.8%; 2.04, 0.5%); ^{13}C NMR δ 213.5, 210.4, 140.5, 134.3, 60.8, 57.1, 51.5, 49.2, 46.4, 45.9, 39.4, 28.0, 14.1. For **34** (from the mixture of **33** and **34**): ^{1}H NMR δ 6.19 (1H, dd, J = 2.9, 5.7 Hz), 6.11 (1H, dd, J = 2.9, 5.7 Hz), 3.38 (1H, m), 2.99 (1H, m), 2.75 (1H, br d, J = 3.7 Hz), 2.55 (1H, overlapped), 2.43 (1H, dd, J = 4.9, 13.7 Hz), 2.23 (1H, br m), 1.65−1.50 (2H, overlapped), 1.52 (3H, s), 1.16 (3H, d, J = 7.0 Hz); NOE data 1.52 (2.75, 8%); ^{13}C NMR δ 215.1, 208.9, 137.8, 136.8, 60.7, 57.8, 55.7, 46.6, 46.2, 45.0, 43.1, 27.9, 16.6.

(4α,4aβ,5β,8β,8aβ)-4,4a,5,8,8a-Pentahydro-4-hydroxy-2,8a-dimethyl-5,8-ethanonaphthalen-1-one (36): yield, LiAl(O-*t*-Bu)$_3$H 75% (by ^{1}H NMR **36**:**37** = 10:1). For **36**: IR 3444 (s), 3044 (w), 1658 (s) cm^{-1}; ^{1}H NMR δ 6.30 (1H, m), 6.24 (1H, m), 5.96 (1H, m), 4.74 (1H, m), 2.90 (1H, m), 2.70 (1H, m), 2.36 (1H, br s), 2.09 (1H, d, J = 7.1 Hz), 1.78 (1H, m), 1.66 (3H, dd, J = 1.5, 2.2 Hz), 1.56 (1H, m), 1.28 (3H, s), 1.22−1.18 (2H, m); NOE data 4.74 (6.30, 3%; 2.09, 4%), 1.28 (4.74, 3%; 2.09, 7%; 1.78, 4%); ^{13}C NMR δ 204.0 (0), 143.3 (1), 137.5 (0), 135.8 (1), 131.4 (1), 65.2 (1), 50.2 (1), 49.9 (0), 41.4 (1), 29.1 (2), 29.0 (1), 21.8 (3), 18.4 (2), 15.6 (3); HRMS calcd for $C_{14}H_{18}O_2$ 218.1307, found 218.1318.

For **37**: (from the NMR spectra of the product mixture) ^{1}H NMR δ 6.38; ^{13}C NMR (unoverlapped signals) δ 144.9, 142.8, 137.0, 132.5, 68.4, 54.0, 37.2, 35.5, 29.2, 25.0, 20.2, 16.6; MS (from GC−MS) 218 (M^+).

(4α,4aβ,5β,8β,8aβ)-4,4a,5,8,8a-Pentahydro-4-hydroxy-2-methyl-5,8-methanonaphthalen-1-one (39) and (4α,4aβ,5β,8β,8aβ)-4,4a,5,8,8a-pentahydro-4-hydroxy-3-methyl-5,8-methanonaphthalen-1-one (40): yield, LiAl(O-*t*-Bu)$_3$H 73% (by ^{1}H NMR **39**:**40** = 1:5). For **39**: colorless viscous oil; ^{1}H NMR δ 6.27 (1H, br s), 6.16 (1H, dd, J = 2.9, 5.6 Hz), 5.78 (1H, dd, J = 2.9, 5.6 Hz), 4.76 (1H, m), 3.38 (1H, m), 3.22 (1H, br s), 3.06−2.99 (2H, m), 1.92 (3H, br s), 1.66−1.65 (3H, m), 1.42 (1H, m), 1.33 (1H, d, J = 8.5 Hz); NOE data 4.76 (6.27, 3%; 3.06−2.99, 2%), 3.06−2.99 (4.76, 4%; 1.33, 4%); ^{13}C NMR δ 201.0 (0), 145.6 (1), 136.5 (0), 135.7 (1), 134.1 (1), 65.4 (1), 51.2 (1), 48.9 (2), 47.9 (1), 45.8 (1), 40.9 (1), 15.6 (3).

For **40**: white solid; mp 93.0−94.5 °C; IR (Nujol) 3380, 1618 cm^{-1}; ^{1}H NMR δ 6.14 (1H, dd, J = 2.9, 5.6 Hz), 5.83 (1H, dd, J = 2.9, 5.6 Hz), 5.68 (1H, br s), 4.66 (1H, m), 3.39 (1H, br s), 3.24 (1H, br s), 3.04−3.01 (2H, m), 2.36 (1H, d, J = 6.6 Hz), 1.96 (3H, s), 1.46 (1H, m), 1.34 (1H, m); NOE data 4.66 (3.04−3.01, 3%), 3.04−3.01 (4.66, 7%; 1.34, 5%); ^{13}C NMR δ 200.3 (0), 161.9 (0), 135.6 (1), 134.7 (1), 127.5 (1), 68.2 (1), 50.5 (1), 48.9 (2), 48.6 (1), 45.9 (1), 41.0 (1), 20.4 (3); HRMS calcd for $C_{12}H_{14}O_2$ 190.0993, found 190.0999.

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Supporting Information Available: Preparation and characterization for enediones **5**, **7**, **9** + **10**, **15**, **17**, **20**, **22, 24**, **31**, **35**, and **38**; MS fragmentation data for the reduction products; ^{1}H NMR spectrum of **8** (at 100 °C); ^{13}C NMR spectra of **5**−**7**, **8** (two conformers at −85 °C), **9** + **10**, **11** + **12**, **14**−**18**, **20** + **5**, **21** + **6**, **22** + **15**, **23** + **16**, **24** + **17**, **25** + **18**, **31**, **32**, **35**, **36**, **38**−**40** (32 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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