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Mohamed F. El-Mansy
Marquette University

Anobick Sar
Marquette University

Sergey Lindeman
Marquette University, sergey.lindeman@marquette.edu

William Donaldson
Marquette University, william.donaldson@marquette.edu

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Generation of molecular complexity from cyclooctatetraene: preparation of optically active protected aminocycloheptitols and bicyclo[4.4.1]undecatriene

Mohamed F. El-Mansy

*Department of Chemistry, Marquette University
Milwaukee, WI*

Anobick Sar

*Department of Chemistry, Marquette University
Milwaukee, WI*

Sergy Lindeman

*Department of Chemistry, Marquette University
Milwaukee, WI*

William A. Donaldson*^a

*Department of Chemistry, Marquette University
Milwaukee, WI*

Abstract: The racemic (6-cyclo-heptadienyl)Fe(CO)₃⁺ cation ((±)-**7**), prepared from cyclooctatetraene, was treated with a variety of carbon and heteroatom nucleophiles. Attack took place at the less hindered C¹ dienyl carbon and decomplexation of the (cycloheptadiene)Fe(CO)₃ complexes gave products rich in functionality for further synthetic manipulation. In particular, a seven-step route was developed from

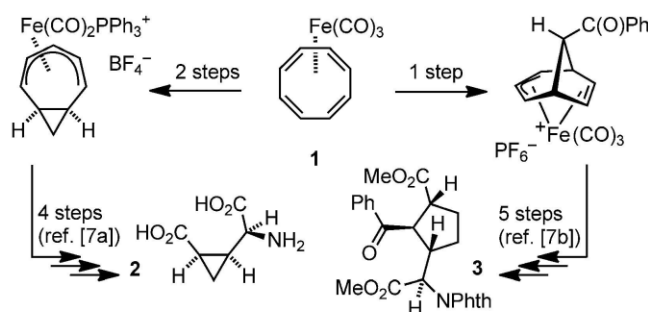
racemic (6-styryl-2,4-cycloheptadien-1-yl)phthalimide ((±)-**9d**) to afford the optically active aminocycloheptitols (–)-**20** and (+)-**20**.
Keywords: cyclitols, hydrocarbons, pi complexes, regioselectivity, synthetic methods

Introduction

The use of simple hydrocarbons as starting materials for the synthesis of complex molecules relies on efficient methods for oxidation, functionalization, or rearrangement. For example, various researchers have explored cyclopentadiene^[1] or cycloheptatriene^[2] as precursors for the preparation of a wide variety of drug candidates, natural products, and synthetic products. The simple hydrocarbon cyclooctatetraene (COT), prepared by the catalytic tetramerization of acetylene,^[3] has recently been used in the syntheses of minocyclitols,^[4a] bis-homoconduritols,^[4b] bis-homoinositol,^[4c] pentacycloanammoxic acid methyl ester,^[4d] the polyene segment of roxaticin,^[4e] and cyclooctitols.^[4f] Tricarbonyl(cyclooctatetraene) iron (**1**), which is readily prepared from COT,^[5] reacts with a variety of electrophiles to form (dienyl)iron cations.^[6] We have previously reported on the synthesis of 2-(2'-carboxycycloalkyl)glycines (**2** and **3**, Scheme 1) from cations derived from **1**.^[7]

Polyhydroxyl aminocyclohexanes ("aminocyclitols") and its derivatives are important biological entities. For example, certain 5-amino-1,2,3,4-cyclohexanetetraols are inhibitors of α -glucosidase and α -galactosidase.^[8] Although a variety of synthetic routes to aminocyclitols have been reported,^[8] there are considerably fewer syntheses of analogues with seven-membered-rings aminocycloheptitols, Figure 1).^[9] In general, these routes utilize chiral pool materials to generate the hydroxyl stereocenters. For example, Casiraghi and coworkers reported a 12-step synthesis of **4** that relied on a vinylogous aldol reaction between 2-(*tert*-butyldimethylsilyloxy)pyrrole and D-arabinose bis-acetonide,^[9a] and Yamada and co-workers prepared **5** from D-xylose by using an intramolecular nitron–alkene cycloaddition.^[9c] Similarly, the cycloheptane ring can be found in the unique bicyclic skeleton of ingenol (**6**). This diterpene has attracted considerable synthetic interest because various esters of ingenol act as activators of protein kinase (**PKC**).^[10] As part of our interest in the

generation of molecular complexity from simple hydrocarbons,^[7] we herein report on the reactivity of the (6-styrylcycloheptadienyl) iron cation **7** and transformation of these products into optically active aminocycloheptitols and the bicyclo[4.4.1]undecatriene skeleton.



Scheme 1. Preparation of 2-(2'-carboxycycloalkyl)glycines from (COT)-Fe(CO)₃.

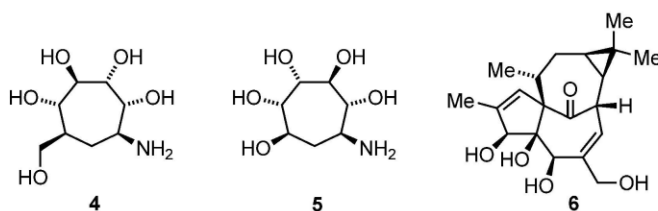
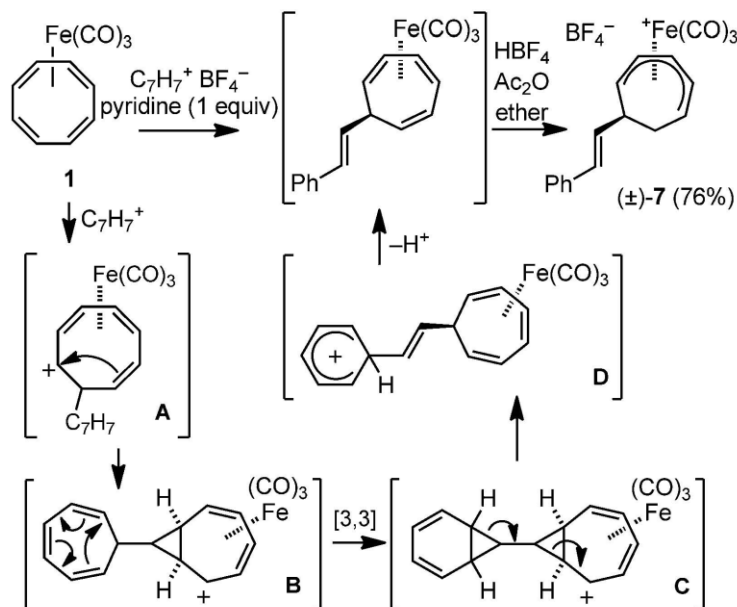


Figure 1. Structures of aminocycloheptitols and ingenol.

Results and Discussion

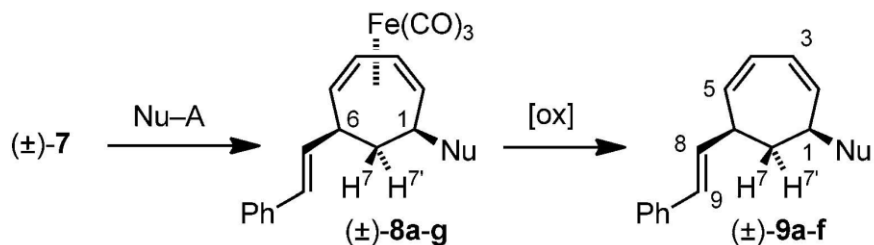
The literature procedure for the reaction of reaction of **1** with tropylium tetrafluoroborate in the presence of pyridine is reported to give (7-styryl-1,3,5-cycloheptatriene)iron in modest yield (41%).^[6d] The mechanistic rationale proposed by Connelly et al. begins with addition of the electrophile to a noncoordinated olefin to generate a homobutyl cation (Scheme 2, **A**). Rearrangement of the homobutyl cation to a cyclopropylcarbiny cation affords structure **B**, which undergoes a [3,3]-Cope rearrangement to generate the norcaradiene intermediate **C**. Opening of both of the cyclopropane rings gives the cyclohexadienyl cation **D**, which upon deprotonation gives the styrylcycloheptatriene complex. Protonation of this cycloheptatriene complex with HBF₄⁺ yields the cation (±)-**7** (67%). We were able to

improve the overall yield of **7** (76% from **1**) by i) using 1 equivalent of pyridine, ii) exhaustive extraction of the reaction mixture, and iii) use of the crude cycloheptatriene complex, without chromatographic purification, for protonation.



Scheme 2. Preparation of the (6-cycloheptadienyl)Fe(CO)₃⁺ cation and proposed mechanism for the formation of (7-styryl-1,3,5-cycloheptatriene)Fe(CO)₃.

The reaction of **7** with a variety of nucleophiles proceeded exclusively by attack at C¹ to afford the *cis*-1-substituted-6-styryl-2,4-heptadiene)iron complexes (±)-**8a-g** (Scheme 3, Table 1). The structures of **8a-g** were assigned on the basis of their NMR spectral data. In particular, two signals at approximately δ=87–91 ppm in the ¹³C NMR spectra and multiplets integrating to two protons at approximately δ=4.9–5.6 ppm in the ¹H NMR spectra are consistent with the two internal carbons (C³/C⁴) of an η⁴-bound cycloheptadiene and their attached protons.^[11]



Scheme 3. Reaction of the (6-cycloheptadienyl)Fe(CO)₃⁺ cation with nucleophiles.

In addition, an apparent quartet at approximately $\delta=0.9\text{--}2.0$ ppm ($J\approx 12$ Hz) in the ¹H NMR spectra for (±)-**8a**, **c**, **d**, and **f** was assigned to H⁷. The three large couplings are due to diaxial vicinal coupling of H⁷ with H¹ and H⁶, and a geminal coupling to H^{7'}. The regioselectivity for nucleophilic addition to **7** is similar to that observed for other 6-substituted (heptadienyl)Fe⁺ cations.^[11]

Table 1. Nucleophilic addition to (±)-**7** and decomplexation of (±)-**8**.

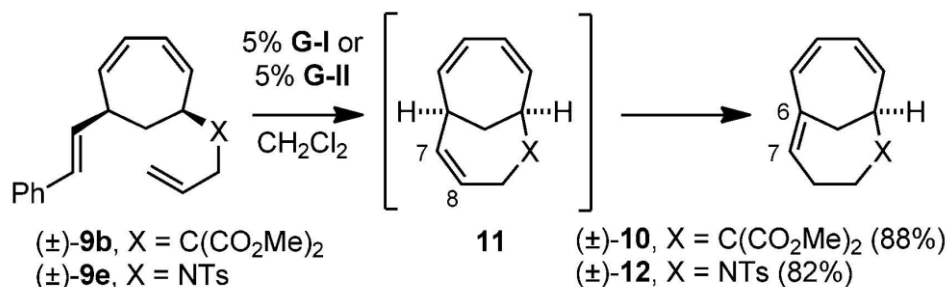
Nu-A	Nu	Complex ([%])	free diene ([%]) ^[a]
LiCH(CO ₂ Me) ₂	CH(CO ₂ Me) ₂	8a (46)	–
LiC(allyl)(CO ₂ Me) ₂	C(CO ₂ Me) ₂ allyl	8b (–) ^[b]	9b (67) ^[c]
LiC(propargyl)(CO ₂ Me) ₂	C(propargyl)(CO ₂ Me) ₂	8c (–) ^[b]	9c (33)
K ⁺ [–] NPhth	NPhth	8d (72)	9d (88)
		–	(81) ^[d]
Na ⁺ [–] N(allyl)SO ₂ Tol	(allyl)N(SO ₂ Tol)	8e (–) ^[e]	9e (51) ^[c]
H ₂ O/K ₂ CO ₃	OH	8f (70)	9f (50) ^[f]
PPh ₃	PPh ₃ ⁺ BF ₄ [–]	8g (83)	–

[a] Cerium ammonium nitrate (CAN) was used as the oxidant unless otherwise noted. [b] The product was an inseparable mixture of **8c** and unreacted nucleophile. [c] Yield of **9d** from **7** over two steps (nucleophilic addition/decomplexation). [d] Yield of **9d** from **7** with only one chromatographic purification. [e] Product was not isolated but used in the decomplexation step. [f] H₂O₂/NaOH was used as the oxidant instead of CAN.

Oxidative decomplexation of (±)-**8b–e** with cerium ammonium nitrate (CAN) in methanol gave the corresponding free ligands

(±)-**9b–e**, respectively (Table 1). In contrast, successful decomplexation of cycloheptadienol complex (±)-**8 f** required the use of basic decomplexation conditions (H₂O₂/NaOH/MeOH) to afford (±)-**9 f**. The structures of the products (±)-**9c, d**, and **f** were assigned based on their NMR spectral data. In particular, signals in the range of $\delta=5.5\text{--}6.0$ ppm that integrate to four protons correspond to the olefinic protons of the conjugated diene portion of the molecule. The structural assignment of (±)-**9d** was further corroborated by single-crystal X-ray diffraction analysis.^[12]

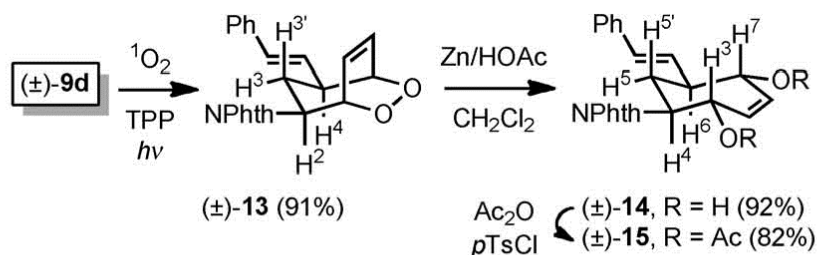
Treatment of (±)-**9b** with the Grubbs 1st generation catalyst (**G-I**) led to the ring-closed product (±)-**10** (Scheme 4).^[13] The structural assignment for **10** as the $\Delta^{6,7}$ isomer is based on its NMR spectral data. In particular, the ¹H NMR spectrum of **10** integrates to 18 H atoms, five of which are olefinic. Furthermore, the ¹³C NMR spectrum of **10** consisted of 15 signals with five olefinic methine carbons and one quaternary olefinic carbon. The reaction of (±)-**9e** with the Grubbs 1st generation catalyst led to a complex mixture of products; the use of the Grubbs 2nd generation catalyst (**G-II**) gave the 2-azabicyclo[4.4.1]undeca-5,7,9-triene **12**, which slowly underwent decomposition in solution. Olefin isomerization has previously been observed as a competitive side reaction of Ru-catalyzed olefin metathesis.^[14] Presumably, the thermodynamically more stable product **10/12** is formed by isomerization of the initially formed $\Delta^{7,8}$ isomer **11**.



Scheme 4. Ring-closing metathesis of **9b** and **9e**. Ts = tosyl.

Reaction of (±)-**9d** with singlet oxygen gave (±)-**13** as a single diastereomer (Scheme 5). Cycloaddition occurs on the diene face opposite to the *syn*-C¹/C⁶ substituents. Similar facial selectivity was

also observed for substituted cycloheptadiene systems by the groups of Pearson and Seitz.^[15]

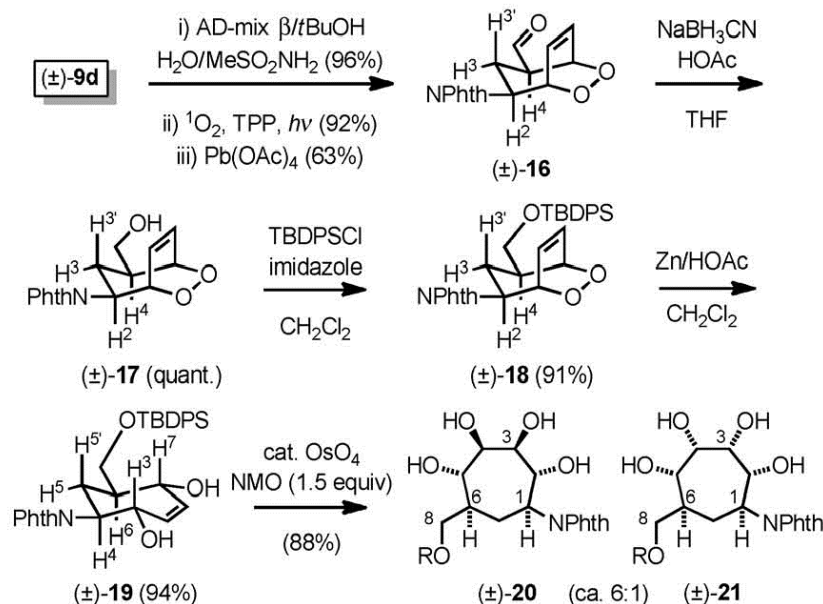


Scheme 5. Singlet oxygen cycloaddition to (±)-**9d**. TPP = tetraphenylporphorine.

Although the reduction of endoperoxide **13** with thiourea gave the diol (±)-**14**, these conditions proved to be low yielding and slow, giving only a 50% yield based on consumed starting material. Alternatively, the use of zinc and acetic acid to reduce **13** proceeded rapidly (<1 h) to afford **14** in excellent yield; the reaction of **14** with acetic anhydride gave the diacetate (±)-**15**. The relative stereochemistries of **13**, **14**, and **15** were assigned on the basis of their NMR spectral data; in particular, the signal for H^{3'} of **13** appears at δ=2.11 ppm, whereas the comparable signals for H^{5'} of **14** and **15** appear at δ=2.73 and 2.85 ppm, respectively. The relative upfield shift for H^{3'} of **13** (compared with H^{5'} of **14/15**) may be attributed to the anisotropic effects of the proximal C⁶–C⁷ olefin. In addition, the signal for H⁴ of **15** appears as a broad triplet at δ=4.42 ppm (*J*=10.8 Hz); these two large couplings are due to axial–axial couplings to both H^{5'} and H³, thus indicating that H³ occupies an axial orientation in **15**.

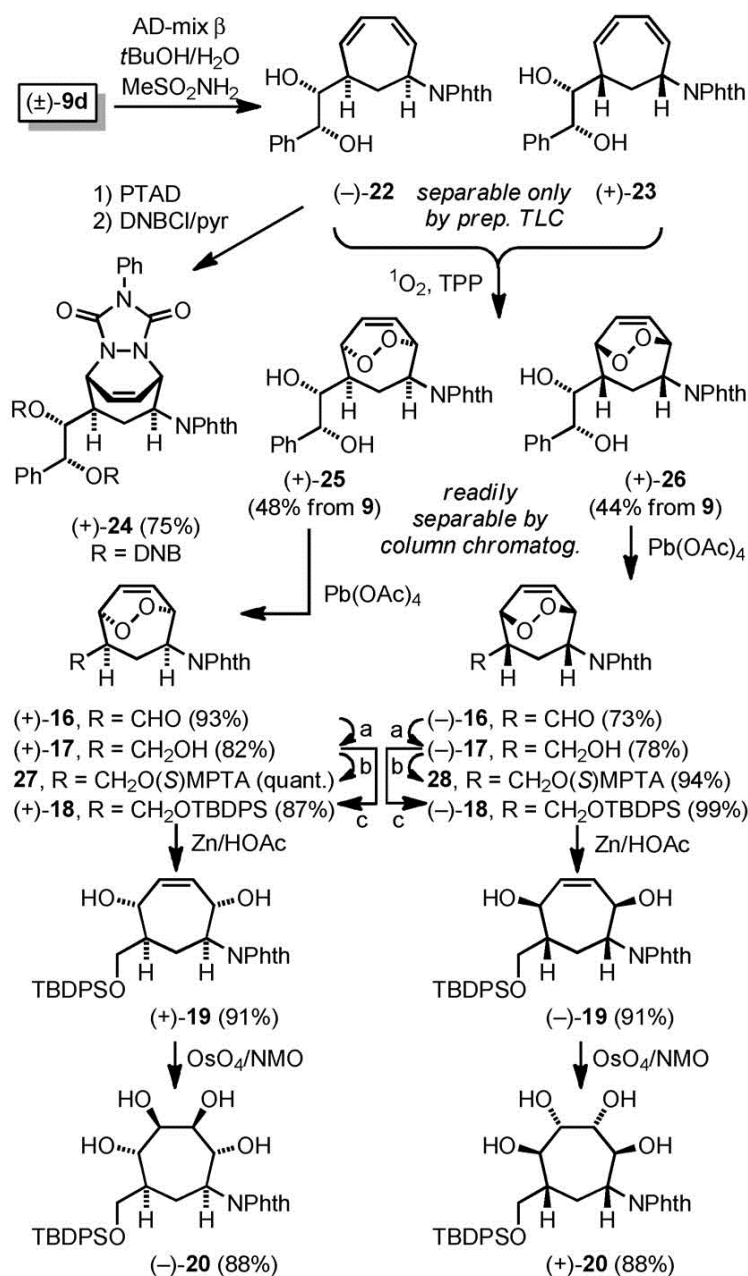
Truncation of the styryl group present in **9d** into a hydroxymethyl substituent was done in the following fashion. Dihydroxylation of (±)-**7d** with commercially available AD-mix β gave a mixture of diastereomeric diols. Singlet oxygen cycloaddition to the mixture of diols gave a mixture of diastereomeric endoperoxide diols, which undergo cleavage with Pb(OAc)₄ to give a single, racemic aldehyde endoperoxide (±)-**16** (Scheme 6). This three-step process could be conducted with only a single chromatographic purification of the aldehyde (±)-**16**. Reduction of the aldehyde functionality in the presence of the endoperoxide proved challenging; however, this was

eventually accomplished by using $\text{NaBH}_3\text{CN}/\text{AcOH}$ to afford (\pm)-**17** in quantitative yield. Reaction of **17** with *tert*-butylchlorodiphenylsilane (TBDPSCI) gave the silyl ether (\pm)-**18**. Reduction of the endoperoxide moiety with Zn/HOAc gave the diol (\pm)-**19**. The relative stereochemistries of **16**–**19** were assigned by comparison of their ^1H NMR spectral data with those for **13**–**15**. In particular, the signals for $\text{H}^{3'}$ of **16**, **17**, and **18** appear relatively upfield at $\delta=2.11$, 1.84, and 1.78 ppm respectively. The signal for H^4 of **19** appears as a doublet of doublets at $\delta=4.14$ ppm ($J=2.4, 10.0, 12.4$ Hz); the two larger couplings are due to axial–axial couplings to $\text{H}^{5'}$ and H^3 . Dihydroxylation of **19** with catalytic OsO_4 gave a mixture of diastereomeric tetraols (\pm)-**20** and (\pm)-**21** (ca. 6:1), from which the major diastereomer can be isolated by careful chromatography. The relative stereochemistry of **20** was tentatively assigned on the basis of the facial selectivity noted by Kishi et al.^[16] for dihydroxylation on the face of an allylic alcohol opposite to the adjacent hydroxyl groups. In this fashion, the racemic protected cycloheptitol (\pm)-**20** was prepared from (cyclooctatetraene) $\text{Fe}(\text{CO})_3$ (**1**) in 11 steps and six chromatographic purifications in 22% overall yield.



Scheme 6. Synthesis of protected aminocycloheptitol (\pm)-**20**. NMO = *N*-methylmorpholine *N*-oxide.

The mixture of diastereomeric diols (–)-**22** and (+)-**23** resulting from the asymmetric dihydroxylation of (±)-**9d** was separable only by preparative thin layer chromatography (Scheme 7). The absolute configuration of the 1',2'-dihydroxy-2'-phenylethyl side chain for each was assigned based on the Sharpless mnemonic device.^[17] Cycloaddition of the less polar cycloheptadiene diastereomer, (–)-**22**, with *N*-phenyl-1,3,5-triaza-2,4-dione (PTAD), followed by reaction with 3,5-dinitrobenzoylchloride gave (+)-**24**. Assignment of the relative stereochemistry of (+)-**24** was accomplished by single-crystal X-ray diffraction analysis (Figure 2),^[18] which also allowed assignment of the configurations of (–)-**22** and (+)-**23** as indicated. Separation of diastereomeric endoperoxide diols (+)-**25** and (+)-**26** proved more facile and could be accomplished by column chromatography on a >1 g scale. Separate singlet oxygen cycloaddition of (–)-**22** gave (+)-**25**, thus allowing the configurational assignments for (+)-**25** and (+)-**26**. Separate glycol cleavage of (+)-**25** and (+)-**26** gave the optically active aldehyde endoperoxides (+)-**16** and (–)-**16**, which, upon reduction with NaBH₃CN, gave the primary alcohols (+)-**17** and (–)-**17**, respectively. Analysis of the ¹H NMR spectra ([D₆]acetone) of the diastereomeric (*S*)-MTPA (α -methoxy- α -trifluoromethylphenylacetate) esters^[16] of (+)-**17** and (–)-**17** (esters **27** and **28**, respectively) indicated clear separation in one of the olefinic signals (**27**, δ =6.22 ppm; **28**, δ =6.31 ppm). With this method, both **27** and **28** were determined to have a >94% diastereomeric excess (*de*). Separate protection of the alcohol (+)-**17** gave the silyl ether (+)-**18**; reduction of the endoperoxide functionality in (+)-**18** gave diol (+)-**19**, and dihydroxylation afforded (–)-**20** after chromatographic purification. In a similar fashion, (–)-**17** was successively transformed into (–)-**18**, (–)-**19**, and (+)-**20**, respectively. The overall yield of the optically active protected cycloheptitols (–)-**20** and (+)-**20**, based on **1**, is 15.7 and 12.2%, respectively.



Scheme 7. Separation of the diastereomeric pairs **22/23** and **25/26**, and preparation of the optically active aminocycloheptitols **(-)-20** and **(+)-20** (DNB = 3,5-dinitrobenzoyl, pyr = pyridine; reagents: a) NaBH₃CN/HOAc/THF; b) (*S*)-MPTA/*N,N'*-dicyclohexylcarbodiimide (DCC)/4-dimethylaminopyridine (DMAP); c) TBDPSCI/imidazole).

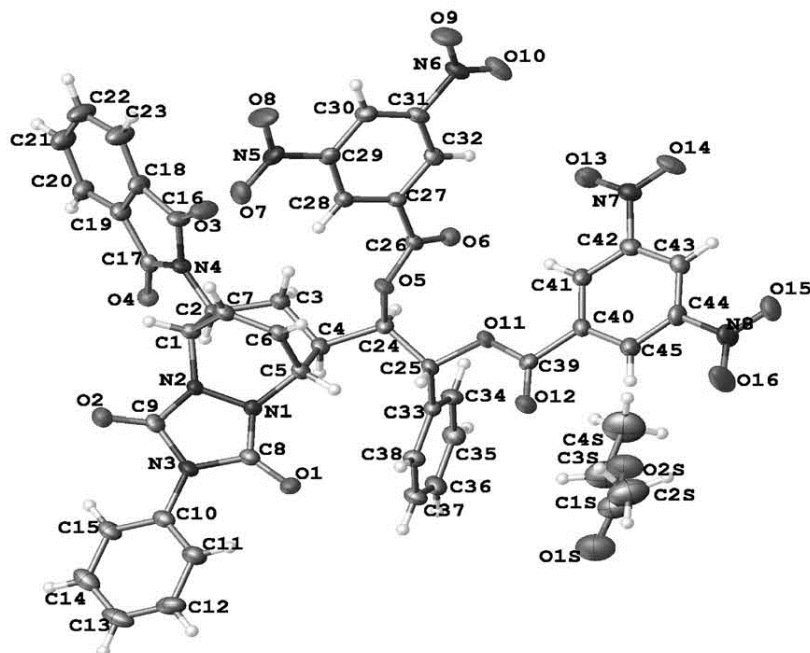


Figure 2. Molecular structure of (+)-**24**-ethyl acetate.

Conclusion

An improved preparation of (6-cycloheptadienyl)Fe(CO)₃⁺ ((±)-**7**) was developed and the reactions of this cation with a variety of carbon and heteroatom nucleophiles were examined. Nucleophilic attack occurs preferentially at the less hindered C¹ dienyl terminus. Decomplexation of these complexes gave *cis*-1,6-disubstituted 2,4-cycloheptadienes. The racemic free ligand (6-styryl-2,4-cycloheptadien-1-yl)phthalimide ((±)-**9d**) was transformed into the racemic and optically active, protected aminocycloheptitols (±)-, (–)-, and (+)-**20**.

Experimental Section

General methods: All reactions involving moisture- or air-sensitive reagents were carried out under a nitrogen atmosphere in oven-dried glassware with anhydrous solvents. THF and diethyl ether were distilled from sodium/benzophenone. Purifications by chromatography were carried out by using flash silica gel (32–63 μ). NMR spectra were recorded on either a Varian Mercury+ 300 MHz or a

Varian UnityInova 400 MHz instrument. CDCl_3 , CD_3OD , and $[\text{D}_6]$ acetone were purchased from Cambridge Isotope Laboratories. ^1H NMR spectra were calibrated to $\delta=7.27$ ppm for residual CHCl_3 , $\delta=3.31$ ppm for CD_2HOD , or $\delta=2.05$ ppm for $[\text{D}_5]$ acetone. ^{13}C NMR spectra were calibrated from the central peak at $\delta=77.23$ ppm for CDCl_3 , $\delta=49.15$ ppm for CD_3OD , or $\delta=29.92$ ppm for $[\text{D}_6]$ acetone. Coupling constants are reported in Hz. The procedures for preparation of compounds **8 f**, **8g**, **9b**, **9c**, **9e**, **9 f**, **12**, **13**, **15b**, (+)-**24**, and the (S)-Mosher esters of (+)-**17** and (–)-**17** can be found in the Supporting Information.

Tricarbonyl(η^5 -6-cyclohepta-2,4-dien-1-yl)iron(+1)

tetrafluoroborate ((\pm)-7): Dry pyridine (1.6 mL, 20 mmol) was added to a solution of **1** (5.00 g, 20.5 mmol) in dry acetone (25 mL) at -23°C under N_2 and the mixture was stirred for 5 min. A solution/suspension of tropylium tetrafluoroborate (4.00 g, 22.5 mmol) in dry acetone (300 mL) was slowly added. The reaction mixture was stirred for 6 h at -23°C , and then for 2 h at room temperature. The clear reddish solution was concentrated to dryness under reduced pressure. Ether (100 mL) was added to the solid residue and the slurry was stirred for 2 h and filtered. This extraction process was repeated three times. The combined ethereal extracts were concentrated. The residue was dissolved in acetic anhydride (30 mL) and cooled to 0°C . A solution of tetrafluoroboric acid (30 mL, 50% in H_2O) and acetic anhydride (30 mL) was added dropwise to the cooled solution. After stirring for 30 min, the slurry was poured into ether (2 L). The yellow precipitate was collected by vacuum filtration and the filtrate was washed several times with dry ether to afford (\pm)-**7** (6.63 g, 76%) as a bright yellow solid. The ^1H NMR spectral data for this cation was identical to the literature values.^[6d]

Tricarbonyl[*dimethyl 2-(6-styryl-2,4-cycloheptadien-*

1yl)propanedioate]iron ((\pm)-8 a): A solution of *n*BuLi (0.20 mL, 1.6M in hexane, 0.43 mmol) was added to a stirred solution of dimethyl malonate (0.060 mL, 0.43 mmol) in THF (6 mL) at 0°C under nitrogen and then stirred for 30 min. Cation (\pm)-**7** (100 mg, 0.24 mmol) was added to the stirring mixture and the mixture was stirred for additional 45 min and gradually warmed to room temperature. The reaction was quenched with water and extracted several times with

ether, washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (SiO_2 , hexanes/ethyl acetate 7:3) to afford (\pm)-**8a** (50 mg, 46%) as a yellow oil. ^1H NMR (400 MHz, CDCl_3): δ =7.35–7.17 (m, 5H; Ar-H), 6.32 (d, J =16.0 Hz, 1H; H^9), 6.01–5.92 (dd, J =8.4, 15.6 Hz, 1H; H^8), 5.33–5.26 (m, 2H; H^3 , H^4), 3.74 (s, 3H; OCH_3), 3.72 (s, 3H; OCH_3), 3.28 (d, J =6.4 Hz, 1H; CHE_2), 2.91–2.72 (m, 4H; H^1 , H^2 , H^5 , H^6), 1.05 (q, J =12.6 Hz, 1H; H^7), 0.90–0.80 ppm (m, 1H; $\text{H}^{7'}$); ^{13}C NMR (100 MHz, CDCl_3): δ =210.9 (M–C=O), 167.6 (CO_2Me), 137.3, 136.3, 128.8, 128.7, 127.4, 126.2, 88.3, 88.0, 61.8, 61.6, 59.8, 58.6, 52.7, 43.0, 39.1, 33.5 ppm; HRMS (FAB) m/z calcd for $\text{C}_{23}\text{H}_{22}\text{O}_7\text{Fe}$: 466.0715 [M^+]; found: 466.0707.

Tricarbonyl[(6-styryl-2,4-cycloheptadien-1-yl)phthalimide]iron

((\pm)-8 d**):** Solid potassium phthalimide (0.659 g, 3.56 mmol) was added to a stirred suspension of (\pm)-**7** (1.00 g, 2.37 mmol) in dry CH_2Cl_2 (100 mL) under N_2 at room temperature. The reaction mixture was stirred for 12 h and then quenched with water. The reaction mixture was extracted several times with CH_2Cl_2 , dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (SiO_2 , hexanes/ethyl acetate 4:1) to afford (\pm)-**8d** (820 mg, 72%) as a light-yellow solid. M.p. 185–188°C; ^1H NMR (400 MHz, CDCl_3): δ =7.88–7.80 and 7.78–7.70 (m, 4H; Phth), 7.20–7.35 (m, 5H; C_6H_5), 6.38 (d, J =15.6 Hz, 1H; H^9), 6.01 (dd, J =8.2, 15.8 Hz, 1H; H^8), 5.57 (dd, J =5.2, 7.2 Hz, 1H; H^3 or H^4), 5.44 (dd, J =5.2, 7.4 Hz, 1H; H^3 or H^4), 4.76 (dd, J =4.0, 12.4 Hz, 1H; H^1), 3.03–2.95 (m, 2H; H^2 , H^6), 2.75 (d, J =6.8 Hz, 1H; H^5), 2.01 (q, J =12.9 Hz, 1H; $\text{H}^{7'}$), 1.59–1.48 ppm (br d, J =12.9 Hz, 1H; H^7); ^{13}C NMR (100 MHz, CDCl_3): δ =210.1 (M–C=O), 167.9 (N–C=O), 137.3, 135.4, 134.2, 132.0, 129.1, 128.8, 127.6, 126.3, 123.4, 89.5, 88.5, 61.8, 56.4, 50.7, 43.6, 33.7 ppm; elemental analysis calcd (%) for $\text{C}_{26}\text{H}_{19}\text{NO}_5\text{Fe}$: C 64.88, H 3.98; found: C 64.85, H 3.97.

(6-Styryl-2,4-cycloheptadien-1-yl)phthalimide ((\pm)-9 d**):** The decomplexation of (\pm)-**8d** (500 mg, 1.04 mmol) in methanol with ceric ammonium nitrate (1.71 g, 3.12 mmol) was carried out in a similar fashion to the decomplexation of (\pm)-**8 c**. Purification of the residue by column chromatography (SiO_2 , hexanes/ethyl acetate 3:1) gave (\pm)-**8d** (315 mg, 88%) as a light-yellow solid. M.p. 107–108°C; ^1H NMR (400 MHz, CDCl_3): δ =7.88–7.80 and 7.75–7.56 (ABq, 4H; Phth), 7.35–

7.17 (m, 5H; C₆H₅), 6.45 (d, *J*=16.0 Hz, 1H; H⁹), 6.16 (dd, *J*=8.2, 15.9 Hz, 1H; H⁸), 5.88–5.75 (m, 4H; CH=CH–CH=CH), 5.25 (br d, *J*=11.2 Hz, 1H; H¹), 3.60–3.50 (m, 1H; H⁶), 2.84 (dt, *J*=11.2, 12.8 Hz, 1H; H⁷), 2.06–2.00 ppm (m, 1H; H^{7'}); ¹³C NMR (100 MHz, CDCl₃): δ=167.7 (CO), 137.2, 136.9, 134.1, 133.6, 132.2, 132.0, 129.8, 128.6, 127.3, 126.2, 124.0, 123.9, 123.3, 50.5 (C¹), 44.0 (C⁶), 38.2 ppm (C⁷); elemental analysis calcd (%) for C₂₃H₁₉NO₂: C 80.92, H 5.61; found: C 80.61, H 5.67.

rac-2-Formyl-4-phthalimido-6,7-dioxabicyclo[3.2.2]non-8-ene ((±)-16): Methane sulfonamide (60 mg, 0.59 mmol) was added at room temperature to a mixture of (±)-**9d** (1.00 g, 2.93 mmol) in a mixture of *t*BuOH (20 mL), ethyl acetate (5 mL), and water (25 mL). The mixture was cooled to 0°C with an ice bath and then solid AD-mix β (4.325 g) was added. The reaction mixture was stirred for 34 h at 0°C, after which time, monitoring by TLC indicated the disappearance of starting material. The reaction was quenched with water (20 mL). The mixture was transferred to a separatory funnel and the top, organic layer was decanted. The aqueous layer was extracted several times with ethyl acetate and the combined organic layers were dried (NaSO₄), concentrated, and the residue was purified by column chromatography (SiO₂, hexanes/ethyl acetate=2:3) to afford a 1:1 mixture of diastereomeric diols (1.050 g, 96%) as a colorless foam. This material was used in the next step without further characterization. Tetraphenylporphyrine (15 mg) was added to a solution of the diol mixture (1.00 g, 2.67 mmol) in CHCl₃ (30 mL). The darkpurple solution was irradiated for a 5 h period with a commercially available 100W halogen lamp while ultra-pure O₂ was bubbled through the solution. The organic solvent was removed to afford a mixture of diastereomeric endoperoxide diols (1.00 g, 92%) that were used in the next step without further purification. Solid Pb(OAc)₄ (544 mg, 1.23 mmol) was added to a solution of the endoperoxide diols (500 mg, 1.29 mmol) in dry CH₂Cl₂ (25 mL) at -78°C. The mixture was stirred for 30 min, and then quenched with water. The mixture was extracted several times with CH₂Cl₂, and the combined extracts were dried (Na₂SO₄) and concentrated. Purification of the residue by column chromatography (SiO₂, hexanes/ethyl acetate 3:2) gave (±)-**16** (244 mg, 63%) as a colorless solid. M.p. 179–180°C; ¹H NMR (400 MHz, CDCl₃): δ=9.65 (s, 1H; CHO), 7.88–7.78 (m, 4H; Phth), 6.77 (dd,

$J=7.2, 9.3$ Hz, 1H; CH=CH), 6.43 (dd, $J=7.2, 9.3$ Hz, 1H; CH=CH), 5.26 (d, $J=7.2$ Hz, 1H; H¹), 4.86–4.80 (m, 2H; H², H⁵), 3.16 (dd, $J=5.0, 13.0$ Hz, 1H; H⁴), 2.11 (q, $J=13.0$ Hz, 1H; H³), 2.05–1.97 ppm (m, 1H; H³); ¹³C NMR (100 MHz, CDCl₃): $\delta=199.0$ (CHO), 167.7 (N-C=O), 134.6, 131.7, 129.8, 124.6, 123.7, 80.0, 75.4, 54.3, 52.1, 23.9 ppm; HRMS (ESI): m/z calcd for C₁₆H₁₃NO₅+Na⁺:322.0686 [$M+Na^+$]; found: 322.0685.

Asymmetric dihydroxylation of (±)-9d: A 25 mL round-bottomed flask was charged with a mixture of *t*BuOH (3 mL) and water (3 mL) and stirred for 5 min at room temperature. Solid AD-mix β (0.826 g) was added to the stirring solution followed by the addition of methane sulfonamide (60 mg, 0.59 mmol). The mixture was stirred until the two layers were separated. The mixture was cooled to 0°C, at which point an inorganic salt was precipitated. Alkene (200 mg, 0.59 mmol) was added in one portion and the mixture was stirred for 72 h while maintaining the temperature at 0°C. The reaction mixture was quenched with water, extracted several times with ethyl acetate, and the combined extracts were washed with brine. The organic layer was concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂, hexanes/ethyl acetate=1:1) to give a mixture of diastereomers as a colorless oily liquid (149 mg, 71%). The diastereomers could be separated by preparative TLC (SiO₂, hexanes/ethyl ether 1:1) to afford a less polar fraction (–)-**22** and a more polar fraction (+)-**23**.

6R-(1'R,2'R-Dihydroxy-2'-phenylethyl)-2,4-cycloheptadien-1S-yl)phthalimide((–)-22): $[\alpha]_D^{23}=-5.1$ ($c=0.500$ in CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃): $\delta=7.80-7.72$ (m, 2H; Phth), 7.68–7.60 (m, 2H; Phth), 7.35–7.29 (m, 5H; C₆H₅), 5.90–5.77 (m, 3H; olefinic H), 5.57 (dd, $J=1.5, 11.1$ Hz, 1H; olefinic H), 4.99 (qd, $J=2.8, 11.1$ Hz, 1H; H¹), 4.65 (d, $J=6.9$ Hz, 1H; H⁹), 3.68–3.60 (m, 1H; H⁸), 2.95 (br s, 1H; OH), 2.86 (q, $J=11.4$ Hz, 1H; H⁷), 2.71 (d, $J=4.2$ Hz, 1H; OH), 2.60 (br d, $J=11.1$ Hz, 1H; H⁶), 1.82 ppm (br d, $J=12.9$ Hz, 1H; H⁷); ¹³C NMR (75 MHz, CDCl₃): $\delta=167.9, 140.9, 134.2, 133.1, 132.9, 132.1, 128.9, 128.5, 126.9, 125.8, 124.6, 123.4, 79.2, 75.1, 50.9, 41.5, 35.4$ ppm; elemental analysis calcd (%) for C₂₃H₂₁O₄N•3/4H₂O: C 71.02, H 5.83; found: C 71.19, H 5.83.

6S-(1'R,2'R-Dihydroxy-2'-phenylethyl)-2,4-cycloheptadien-1R-yl)phthalimide ((+)-23): $[\alpha]_{\text{D}}^{23} = +74.1$ ($c=0.486$ in CH_2Cl_2); ^1H NMR

(300 MHz, CDCl_3): $\delta=7.90\text{--}7.80$ (m, 2H; Phth), 7.78–7.70 (m, 2H; Phth), 7.41–7.25 (m, 5H; C_6H_5), 5.90–5.76 (m, 3H; olefinic H), 5.67 (br d, $J=11.7$ Hz, 1H; olefinic H), 5.05 (br d, $J=9.6$ Hz, 1H; H^1), 4.68 (d, $J=6.9$ Hz, 1H; H^9), 3.84–3.77 (m, 1H; H^8), 3.12 (br s, 1H; OH), 2.91 (br s, 1H; OH), 2.71 (td, $J=11.1, 12.9$ Hz, 1H; H^7), 2.58 (br d, $J=10.8$ Hz, 1H; H^6), 1.98 ppm (br s, 1H; H^7); ^{13}C NMR (75 MHz, CDCl_3): $\delta=167.9$ (N–C=O), 141.0, 136.5, 134.2, 132.9, 132.2, 128.9, 128.5, 126.7, 125.4, 124.5, 123.5, 79.3, 75.3, 51.2, 41.2, 31.6 ppm.

Singlet oxygen cycloaddition of diastereomeric diol mixture: A 50 mL two-necked round-bottomed flask, equipped with a condenser, was charged with dienediol (1.30 g, 3.46 mmol), dry CHCl_3 (30 mL), and tetraphenylporphorine (25 mg, 0.041 mmol). The dark-purple solution was irradiated with a 100 W tungsten-halogen lamp for 6 h while ultra-pure O_2 was bubbled through the solution. The reaction mixture was concentrated under vacuum and the residue was purified by column chromatography (SiO_2 , hexanes/ethyl acetate 3:2) to give a less polar endoperoxide (+)-**25** (671 mg, 48%) and a more polar endoperoxide (+)-**26** (626 mg, 44%) as foamy compounds.

4-(1'R,2'R-Dihydroxy-2'-phenylethyl)-2-phthalimido-6S,7R-

dioxabicyclo-[3.2.2]non-8-ene ((+)-25): M.p. 97–98°C; $[\alpha]_{\text{D}}^{23} = +41.0$ ($c=0.0011$ in CH_2Cl_2); ^1H NMR (300 MHz, CDCl_3): $\delta=7.85\text{--}7.71$ (m, 4H; Phth), 7.39–7.26 (m, 5H; C_6H_5), 6.71 (dd, $J=7.2, 9.1$ Hz, 1H; CH=CH), 6.41 (dd, $J=7.5, 8.4$ Hz, 1H; CH=CH), 5.18 (d, $J=7.2$ Hz, 1H; H^1), 4.73–4.68 (m, 3H; $\text{H}^2, \text{H}^5, \text{H}^{10}$), 3.43–3.39 (narrow m, 1H; H^9), 2.68 (d, $J=3.9$ Hz, 1H; OH), 2.48 (d, $J=4.8$ Hz, 1H; OH), 2.29 (dd, $J=5.7, 12.6$ Hz, 1H; H^3), 2.10–2.03 (m, 1H; H^4), 1.60 ppm (br d, $J=12.6$ Hz, 1H; H^3); ^{13}C NMR (75 MHz, CDCl_3): $\delta=167.8, 141.0, 134.5, 131.8, 128.9, 128.8, 128.4, 126.5, 125.8, 123.6, 79.8, 78.1, 76.9, 74.0, 52.2, 43.8, 27.6$ ppm; HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{21}\text{NO}_6 + \text{Na}^+$: 430.1261 [M+Na⁺]; found: 430.1254.

4-(1'R,2'R-Dihydroxy-2'-phenylethyl)-2-phthalimido-6R,7S-

dioxabicyclo-[3.2.2]non-8-ene ((+)-26): $[\alpha]_{\text{D}}^{23} = +33$ ($c=0.0011$ in CH_2Cl_2); ^1H NMR (300 MHz, CDCl_3): $\delta=7.90\text{--}7.70$ (m, 4H; Phth), 7.40–7.25 (m, 5H; C_6H_5), 6.65 (dd, $J=7.6, 8.8$ Hz, 1H; CH=CH), 6.47 (dd,

$J=8.0, 8.8$ Hz, 1H; CH=CH), 4.73–4.65 (m, 2H), 4.58 (dd, $J=4.4, 12.8$ Hz, 1H; H^2), 4.49 (dd, $J=2.4, 6.9$ Hz, 1 H), 3.80–3.75 (narrow m, 1H; H^9), 3.25–3.10 (br s, 2H; 2OH), 2.23 (q, $J=12.6$ Hz, 1H; $H^{3'}$), 2.07–1.98 (m, 1H; H^4), 1.65 ppm (td, $J=4.0, 12.8$ Hz, 1H; H^3); ^{13}C NMR (75 MHz, CDCl_3): $\delta=167.8, 140.7, 134.4, 131.8, 129.0, 128.7, 127.3, 126.6, 126.5, 123.5, 81.4, 79.7, 77.0, 75.1, 52.4, 44.0, 23.4$ ppm. HRMS (ESI): m/z calcd for $\text{C}_{23}\text{H}_{21}\text{NO}_6+\text{Na}^+$: 430.1261 [$\text{M}+\text{Na}^+$]; found: 430.1252.

2R-Formyl-4S-phthalimido-6S,7R-dioxabicyclo[3.2.2]non-8-ene ((+)-16): solid $\text{Pb}(\text{OAc})_4$ (1.061 g, 2.396 mmol) was added to a solution of less polar endoperoxide diol (+)-**25** (650 mg, 1.60 mmol) dissolved in dry CH_2Cl_2 (30 mL). The reaction mixture was stirred for 15 min and then quenched with water, and the mixture was extracted several times with CH_2Cl_2 . The combined organic extracts were dried (Na_2SO_4) and concentrated, and the residue was purified by column chromatography (SiO_2 , hexanes/ethyl acetate 3:2) to afford (+)-**16** (439 mg, 93%) as a colorless solid. M.p. 55–57°C; $[\alpha]_{\text{D}}^{20}=+88$ ($c=0.0011$ in CH_2Cl_2); the NMR spectral data for (+)-**16** was identical to that for the racemic material (\pm)-**16**.

2S-Formyl-4R-phthalimido-6R,7S-dioxabicyclo[3.2.2]non-8-ene ((-)-16): The glycol cleavage of endoperoxide diol (+)-**26** (46 mg, 0.11 mmol) was carried out in a similar fashion to the glycol cleavage of (+)-**25** to afford (–)-**16** (23 mg, 73%). M.p. 55–57°C; $[\alpha]_{\text{D}}^{20}=-100$ ($c=0.287$ in CH_2Cl_2). The NMR spectral data for (–)-**16** was identical to that for the racemic material (\pm)-**16**.

4-Hydroxymethyl-2-phthalimido-8,9-dioxabicyclo[3.2.2]non-6-ene ((±)-17): Compound (\pm)-**16** (50.0 mg, 0.167 mmol) was added to a solution of THF (10 mL) and glacial acetic acid (2 mL) and the mixture was stirred for 5 min. Solid NaBH_3CN (16 mg, 0.254 mmol) was added, and monitoring of the reaction by TLC indicated complete disappearance of starting material after 1 h. The solvent was evaporated and the residue was purified by column chromatography (SiO_2 , hexanes/ethyl acetate 2:3) to afford (\pm)-**17** (51 mg, quant.) as a colorless solid. M.p. 139–141°C; ^1H NMR (400 MHz, CDCl_3): $\delta=7.90-7.72$ (m, 4H; Phth), 6.77 (dd, $J=7.2, 9.8$ Hz, 1H; CH=CH), 6.45 (dd, $J=6.8, 9.8$ Hz, 1H; CH=CH), 4.98 (d, $J=7.2$ Hz, 1H; H^1), 4.81–4.73

(m, 2H; H², H⁵), 3.66–3.60 (m, 1H; CH₂O), 3.47–3.38 (m, 1H; CH₂O), 2.40–2.31 (m, 1H; H⁴), 1.84 (q, *J*=12.8 Hz, 1H; H³), 1.61 (td, *J*=4.4, 12.8 Hz, 1H; H³), 1.53 ppm (br s, 1H; OH); ¹³C NMR (100 MHz, [D₆]acetone): δ=167.8, 134.5, 131.9, 129.7, 124.9, 123.6, 80.0, 78.3, 64.2, 52.3, 44.7, 26.6 ppm; HRMS (ESI): *m/z* calcd for C₁₆H₁₅NO₅+Na⁺: 324.0842 [M+Na⁺]; found: 324.0839.

4S-Hydroxymethyl-2S-phthalimido-8,9-dioxabicyclo[3.2.2]non-6-ene ((+)-17): The reduction of (+)-**16** (400 mg, 1.34 mmol) was carried out in a similar fashion to the reduction of (±)-**16** to afford the optically active primary alcohol (+)-**17** (329 mg, 82%). M.p. 163–166°C; [α]_D²⁰ = +119 (*c*=0.00176 in CH₂Cl₂). The NMR spectral data for (+)-**17** was identical to that for the racemic compound (±)-**17**.

4R-Hydroxymethyl-2R-phthalimido-8,9-dioxabicyclo[3.2.2]non-6-ene ((±)-17): The reduction of (–)-**16** (360 mg, 1.204 mmol) was carried out in a similar fashion to the reduction of (±)-**16**, to afford the optically active primary alcohol (–)-**17** (281 mg, 78%). M.p. 167–169°C; [α]_D²⁰ = –95 (*c*=0.00082 in CH₂Cl₂). The NMR spectral data for (–)-**17** was identical to that for the racemic compound (±)-**17**.

4-(tert-Butyldiphenylsilyloxy)methyl-2-phthalimido-8,9-dioxabicyclo-[3.2.2]non-6-ene ((±)-18): Imidazole (18 mg, 0.266 mmol) was added to a solution of (±)-**17** (40.0 mg, 0.133 mmol) in freshly distilled CH₂Cl₂ (5 mL) cooled to 0°C, and was followed by the dropwise addition of *tert*-butylchlorodiphenylsilane (44 mg, 0.159 mmol) over a period of 15 min at 0°C. After stirring at room temperature for 3 h, monitoring of the reaction mixture by TLC indicated the complete disappearance of starting material. The mixture was quenched with water and extracted several times with CH₂Cl₂. The combined extracts were concentrated and the residue was purified by column chromatography (SiO₂, hexanes/ethyl acetate 4:1) to give (±)-**18** (65 mg, 91%) as a colorless foam. M.p. 44–46°C; ¹H NMR (400 MHz, CDCl₃): δ=7.87–7.70 (m, 4H; Phth), 7.65–7.60 (m, 4H; Ar-H), 7.48–7.37 (m, 6H; Ar-H), 6.71 (ddd, *J*=1.2, 7.2, 9.6 Hz, 1H; CH=CH), 6.25 (ddd, 0.8, 7.2, 9.2 Hz, 1H; CH=CH), 5.01 (d, *J*=7.2 Hz, 1H; H¹), 4.75 (dd, *J*=4.8, 12.8 Hz, 1H; H²), 4.72 (d, *J*=6.8 Hz, 1H; H⁵), 3.60 (dd, *J*=5.0, 10.4 Hz, 1H; CH₂OSi), 3.36 (dd, *J*=8.6, 10.6, 1H; CH₂OSi), 2.50–2.38 (m, 1H; H⁴), 1.78 (q, *J*=12.7 Hz, 1H; H³), 1.47 (td, *J*=4.8,

12.8 Hz, 1H; H³), 1.07 ppm (s, 9H; *t*Bu); ¹³C NMR (100 MHz, CDCl₃): δ=167.7, 135.7, 134.4, 133.3, 131.9, 130.0, 129.4, 128.0, 125.0, 123.5, 80.0, 78.6, 65.0, 52.4, 44.5, 27.0, 26.3, 19.4 ppm. HRMS (ESI): *m/z* calcd for C₃₂H₃₃NO₅Si+Na⁺: 562.2020 [M+Na⁺]; found: 562.2010.

4S-(*tert*-Butyldiphenylsilyloxy)methyl-2S-phthalimido-8,9-dioxabicyclo-[3.2.2]non-6-ene ((+)-18): Protection of (+)-**17** (200 mg, 0.664 mmol) with *tert*-butyldiphenylsilyl chloride was carried out in a similar fashion to the reaction of (±)-**17** to afford (+)-**18** (311 mg, 87%). M.p. 44–47°C; [α]_D²⁰ = +48 (*c*=0.0013 in CH₂Cl₂). The NMR spectral data for (+)-**18** was identical to that for the racemic compound (±)-**18**.

4R-(*tert*-Butyldiphenylsilyloxy)methyl-2S-phthalimido-8,9-dioxabicyclo-[3.2.2]non-6-ene ((-)-18): Protection of (-)-**17** (200 mg, 0.664 mmol) with *tert*-butyldiphenylsilyl chloride was carried out in a fashion similar to the reaction of (±)-**17**, except that the reaction time was extended to 15 h, to afford (-)-**18** (358 mg, 99%). M.p. 45–47°C; [α]_D²⁰ = -48 (*c*=0.0012 in CH₂Cl₂). The NMR spectral data for (-)-**18** was identical to that for the racemic compound (±)-**18**.

6-(*tert*-Butyldiphenylsilyloxy)methyl-3,7-dihydroxy-4-phthalimido-cycloheptene ((±)-19): Activated zinc dust (55 mg) was added to a solution of (±)-**18** (55.0 mg, 0.102 mmol) in CH₂Cl₂ (5 mL). Acetic acid (61 mg, 1.020 mmol) dissolved in CH₂Cl₂ (3 mL) was added dropwise over a 10 min period to this suspension. The reaction mixture was stirred for 15 min at room temperature, the solvent was evaporated, and the residue was purified by column chromatography (SiO₂, hexanes/ethyl acetate 2:3) to afford (±)-**19** (52 mg, 94%) as a colorless foam. M.p. 51–53°C; ¹H NMR (400 MHz, CDCl₃): δ=7.85–7.63 (m, 8H; Phth, Ar-H), 7.45–7.34 (m, 6H; Ar-H), 5.80 (td, *J*=2.8, 12.8 Hz, 1H; CH=CH), 5.68 (td, *J*=2.6, 12.8 Hz, 1H; CH=CH), 4.93–4.87 (m, 1H; H³), 4.45 (br d, *J*=9.6 Hz, 1H; H⁷), 4.14 (ddd, *J*=2.4, 10.0, 12.4 Hz, 1H; H⁴), 4.07 (d, *J*=2.4 Hz, 1H; OH), 3.75 (dd, *J*=4.0, 10.2 Hz, 1H; CH₂OSi), 3.69 (dd, *J*=7.2, 10.2 Hz, 1H; CH₂OSi), 2.38 (td, *J*=12.0, 14.8 Hz, 1H; H⁵), 2.00–1.90 (brm, 1H; H⁶), 1.87 (d, *J*=6.8 Hz, 1H; OH), 1.56 (td, *J*=2.4, 14.4 Hz, 1H; H⁵), 1.07 ppm (s,

9H; *t*Bu); ^{13}C NMR (100 MHz, CDCl_3): δ =168.7, 136.3, 135.8, 135.7, 134.2, 132.7, 132.07, 132.02, 130.23, 130.17, 128.11, 128.06, 123.4, 74.1, 70.2, 68.7, 55.0, 44.8, 33.1, 27.0, 19.3 ppm; elemental analysis calcd (%) for $\text{C}_{32}\text{H}_{35}\text{NO}_5\text{Si}$: C 70.95, H 6.51; found: C 70.66, H 6.60.

6S-(*tert*-Butyldiphenylsilyloxy)methyl-3S,7R-dihydroxy-4S-phthalimidocycloheptene ((+)-19): The reduction of endoperoxide (+)-**18** (80 mg, 0.15 mmol) with Zn and acetic acid was carried out in a similar fashion to the reduction of the racemic endoperoxide (\pm)-**18** to afford (+)-**19** (73 mg, 91%). M.p. 53–55°C; $[\alpha]_{\text{D}}^{20} = +17$ ($c=0.0011$ in CH_2Cl_2). The NMR spectral data for (+)-**19** was identical to that for the racemic compound (\pm)-**19**.

6R-(*tert*-Butyldiphenylsilyloxy)methyl-3R,7S-dihydroxy-4S-phthalimidocycloheptene ((\pm)-19): The reduction of endoperoxide (–)-**18** (80 mg, 0.15 mmol) with Zn and acetic acid was carried out in a similar fashion to the reduction of the racemic endoperoxide (\pm)-**18** to afford (–)-**19** (80 mg, 91%). M.p. 57–59°C; $[\alpha]_{\text{D}}^{20} = -11$ ($c=0.00062$ in CH_2Cl_2). The NMR spectral data for (–)-**19** was identical to that for the racemic compound (\pm)-**19**.

6-(*tert*-Butyldiphenylsilyloxy)methyl-2,3,4,5-tetrahydroxy-1-phthalimidocycloheptane ((\pm)-20): A solution of *N*-methylmorpholine *N*-oxide (14 mg, 0.122 mmol) in water (1 mL) was added to a solution of (\pm)-**19** (44 mg, 0.081 mmol) in acetone (5 mL), followed by the addition of a solution of OsO_4 (0.05 mL, 0.2M in toluene, 0.01 mol). The reaction mixture was stirred for 2 h at room temperature under N_2 . The solvent was evaporated and the residue was purified by column chromatography (SiO_2 , hexanes/ethyl acetate 1:4) to afford (\pm)-**20** (41 mg, 88%) as a colorless foam. M.p. 86–87°C; ^1H NMR (400 MHz, CD_3OD): δ =7.90–7.78 (m, 4H; Phth), 7.65–7.55 (m, 4H; Ar-H), 7.35–7.22 (m, 6H; Ar-H), 4.50 (dd, $J=7.0, 10.2$ Hz, 1H; H^2), 4.11 (dt, $J=1.6, 11.0$ Hz, 1H; H^1), 3.97 (d, $J=4.8$ Hz, 1H; H^4), 3.89 (dd, $J=4.2, 9.8$ Hz, 1H; H^5), 3.83 (d, $J=6.8$ Hz, 1H; H^3), 3.68–3.58 (m, 2H; H^8, H^8), 2.60 (td, $J=11.2, 14.4$ Hz, 1H; H^7), 1.76–1.67 (m, 1H; H^6), 1.55 (d, $J=14.0$ Hz, 1H; H^7); 0.99 ppm (s, 9H; *t*Bu); ^{13}C NMR (100 MHz, CD_3OD): δ =169.8, 136.9, 136.8, 135.4, 133.5, 130.93, 130.88, 128.88, 128.84, 124.2, 78.5, 75.8, 73.6, 72.1,

67.9, 58.5, 29.4, 27.5, 20.2 ppm; HRMS (ESI): m/z calcd for $C_{32}H_{37}NO_7Si+Na^+$: 598.2232 $[M+Na^+]$; found: 598.2219.

6S-(tert-Butyldiphenylsilyloxy)methyl-2R,3S,4R,5S-tetrahydroxy-1Sphthalimido-cycloheptane (–)-20: The dihydroxylation of (+)-**19** (65 mg, 0.12 mmol) with catalytic OsO_4 was carried out in a fashion to the dihydroxylation of (\pm)-**19**, to afford (–)-**20** (61 mg, 88%). M.p. 86–88°C; $[\alpha]_D^{20} = -17$ ($c=0.0010$ in MeOH). The NMR spectral data for (–)-**20** was identical to that for the racemic compound (\pm)-**20**.

6R-(tert-Butyldiphenylsilyloxy)methyl-2S,3R,4S,5R-tetrahydroxy-1Rphthalimido-cycloheptane ((+)-20): The dihydroxylation of (–)-**19** (75 mg, 0.138 mmol) with catalytic OsO_4 was carried out in a similar fashion to the dihydroxylation of (\pm)-**19** to afford (+)-**20** (70 mg, 88%). M.p. 74–76°C; $[\alpha]_D^{20} = +14$ ($c=0.00090$ in MeOH). The NMR spectral data for (+)-**20** was identical to that for the racemic compound (\pm)-**20**.

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Notes: [a] M. F. El-Mansy, Dr. A. Sar, Dr. S. Lindeman, Dr. W. A. Donaldson, Department of Chemistry, Marquette University, P.O. Box 1881, Milwaukee, Wisconsin 53201-1881 (USA)
Fax: (+1) 414-288-7066
E-mail: william.donaldson@marquette.edu
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