Articles

Regioselective Aryl Radical Cyclization. 1. Stereocontrolled Synthesis of Linearly Condensed Hydroaromatic Carbocyclic Systems through 6-*endo*-Ring Closures

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The stereocontrolled synthesis of *trans*-octahydroanthracenes **3**, **11a–c**, and **14a–c** and *trans*-octahydro-5a*H*-cyclohepta[*b*]naphthalene (**27**) through implementation of an efficient and highly regioselective 6-*endo-trig*-aryl radical cyclization of the respective 2-(*o*-bromoaryl)-1-methylenecyclohexanes **2**, **10a–c**, and **13a–c** and 2-(*o*-bromobenzyl)-1-methylenecycloheptane (**41**) with tri-*n*-butyltin hydride is described. The radical cyclization of 2-(*o*-bromobenzyl)-1-methylenecyclopentane (**43**), in contrast, produced a mixture of the *cis*- and *trans*-hexahydro-1*H*-benz[*f*]indenes (**38**) and (**37**).

Organotin hydride induced intramolecular radical cyclization reactions are now widely used for the construction of fused carbo- and heterocyclic ring systems.[1] With only a few exceptions, 5-*exo-trig* radical cyclizations are generally preferred over 6-*endo-trig* ring closures in substituted hexenyl systems. In contrast to the alkyl radical reactions in organic synthesis, only limited information is available on the rates and regiochemistry of aryl radical ring closures in tri-*n*-butyltin hydride mediated reactions.[2] Their synthetic applications have also been sparse in comparison to alkyl radical reactions. There are a few recent reports where aryl radicals, having *o*-cyclohexenyl or heteroenyl ring substituents with an *endo*-double bond in the 5,6-position relative to the radical center, have been shown to give regioselective ring closures in the *exo*-mode leading to the five-membered carbocyclic and heterocyclic ring annulated condensed cyclic compounds.[3] In recent years several 6-*endo*-ring closures of aryl radicals have been utilized[4] for the synthesis of a few natural products and six-membered heterocyclic ring annulated condensed cyclic compounds. An *o*-isoquinoline ring incorporating the C-1 *exo*-methylene group at the 5,6-position relative to the aryl radical center, however, was reported to give 6-*endo*-cyclization *exclusively*, leading to six-membered

condensed heterocyclic systems.[5] A similar 6-*endo* aryl radical cyclization involving a terminal olefin carbon atom has been reported recently in the formation of 1-(phenylsulfonyl)tetralin.[6] We envisaged that a tri-*n*-butyltin hydride induced aryl radical in a substrate such as **A** would readily undergo 6-*endo*-ring closure through the preferred attack[7] at the least substituted methylene center *via* the bridgehead radical **B** leading to exclusively or dominantly the respective *trans*-products **C**, thus providing a simple general route to hexaannulated linear polycyclic systems (eq 1).

In this paper, we report[8] details of our work on some scopes and feasibility of this strategy.

Results and Discussion

In order to validate the feasibility of our strategy and gain a better understanding of the regio- and stereochem-

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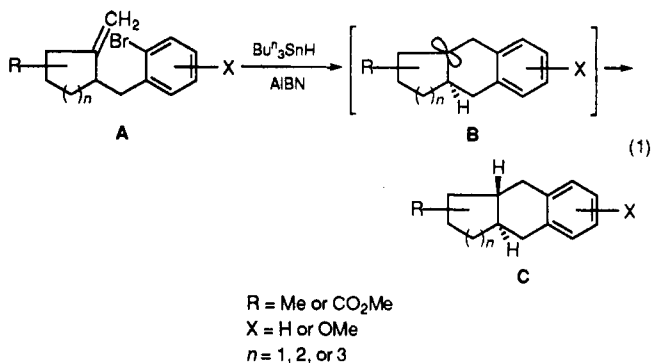
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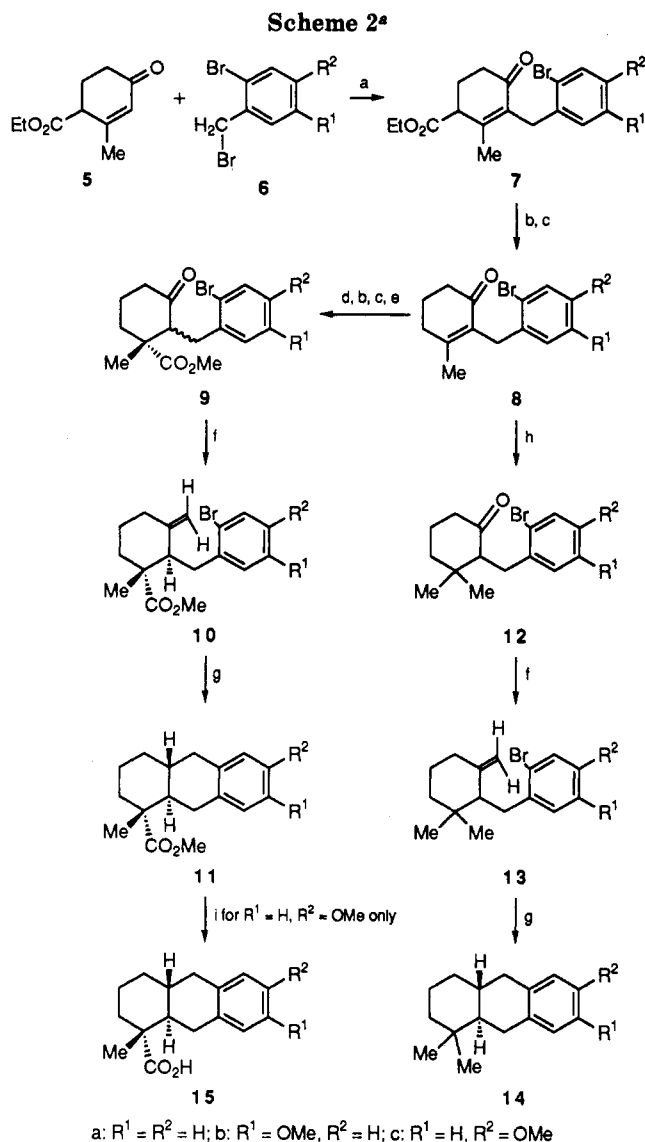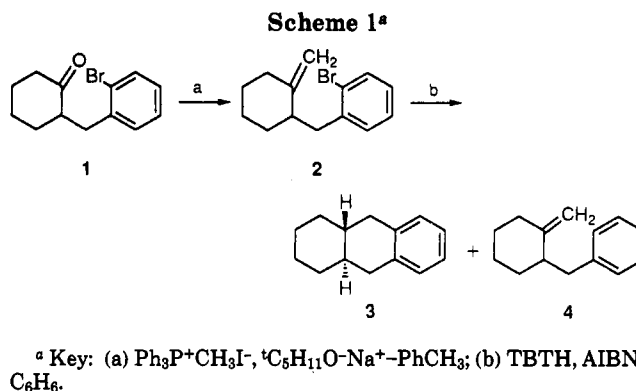
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(1)

R = Me or CO₂Me
X = H or OMe
n = 1, 2, or 3

Scheme 1[a]

[a] Key: (a) Ph₃P⁺CH₃I⁻, ᵗC₅H₁₁O⁻Na⁺–PhCH₃; (b) TBTH, AIBN, C₆H₆.

Scheme 2[a]

a: R¹ = R² = H; b: R¹ = OMe, R² = H; c: R¹ = H, R² = OMe

[a] Key: (a) BuᵗO⁻K⁺; BuᵗOH; (b) KOH–H₂O–EtOH; (c) HCl (6 N); (d) EtOH–KCN; (e) CH₂N₂–Et₂O; (f) Ph₃P⁺CH₃]⁻, ᵗC₅H₁₁O⁻Na⁺–PhCH₃; (g) AIBN, TBTH, C₆H₆; (h) LiMe₂Cu, BF₃·Et₂O, Et₂O; (i) BuᵗO⁻K⁺, DMSO.

ical factors governing the aryl radical cyclizations depicted in eq 1, we first examined in detail the behavior of the *exo*-olefins **2**, **10a–c**, and **13a–c** (Scheme 1 and 2). The alkene **2**, obtained in 90% yield from the ketone **1** by Wittig olefination,[9] on radical cyclization with tri-*n*-butyltin hydride and a catalytic amount of azoisobutyronitrile (AIBN) in refluxing benzene, furnished a 9:1 mixture (GLC and ¹H NMR analyses) of *trans*-octahydroanthracene (**3**) and the debrominated olefin **4** in 95% yield (Scheme 1).

The (*o*-bromobenzyl)cyclohexanones **9a–c** and **12a–c**, key intermediates for the olefins **10a–c** and **13a–c**, were prepared in good yields through the cyclohexenones **8a–c** by standard routes involving conjugate addition of a cyanide group[10] and a methyl group,[11] respectively. The cyclohexenones **8a–c** were obtained in good yields by alkylation of Hagemann's ester **5** with the appropriate benzyl bromides **6a–c** followed by alkaline hydrolytic decarboxylation of the corresponding C-3 alkylated products in over 90–95% purity (Scheme 2). The epimeric mixture of the enolizable keto esters **9a–c** (1:1 mixture by GLC and ¹H NMR analyses) on Wittig alkenation produced only a single epimer **10a–c** in each case, in 80–90% overall yields, by repeating the reaction twice with the recovered keto esters. The assigned stereochemistries of the alkenes **10a–c** have been based upon stereostructures of the corresponding cyclized products. Similarly, Wittig olefination of the ketones **12a–c** afforded the respective alkenes **13a–c** in excellent yields. The radical cyclization of **10a** afforded the crystalline *trans*-ester **11a** in 85% yield, as the only isolable product. An X-ray crystallographic determination[8] established the stereostructure of **11a**[12] and thereby the alkene **10a**.[12] The radical cyclizations of the methoxybenzyl substrates **10b** and **10c** under the same conditions afforded the respective *trans*-esters **11b** and **11c** in 67% and 85% isolable yields. The assigned stereochemistry to the methoxyoctahydroanthracene esters is based upon the analogy to the respective *des*-methoxy analog as well as the close similarity of their ¹H NMR spectral data (Experimental Section). The ester **11c** was further characterized through the respective crystalline acid **15c**. The radical cyclization of the alkene **13a** gave the *trans*-hydrocarbon **14a** in 95% yield. Similarly, the cyclizations of the methoxybenzyl olefin substrates **13b** and **13c** afforded the respective *trans*-

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(11) Banik, B. K.; Chakraborti, A. K.; Ghatak, U. R. *J. Chem. Res. Synop.* **1986**, 406; *J. Chem. Res. Miniprint* **1986**, 3391.

(12) The relative stereochemistry of the *gem*-carbomethoxy and methyl groups was erronously projected in the structures of these compounds in the preliminary communication (ref 8).

methoxyhydrocarbons **14b** and **14c** in 84% and 72% yields. The stereochemical assignments to **14a** and **14b** are based upon direct comparisons (GLC and ¹H NMR spectra) with the respective samples prepared from the esters **11a** and **11b** through the sequence **11a,b → 16a,b → 14a,b** (Scheme 3) using standard reactions.[13]

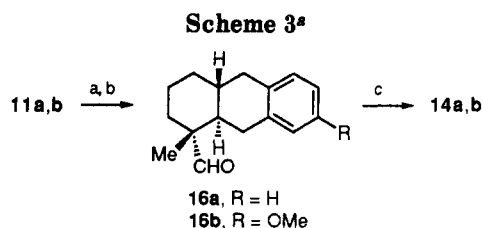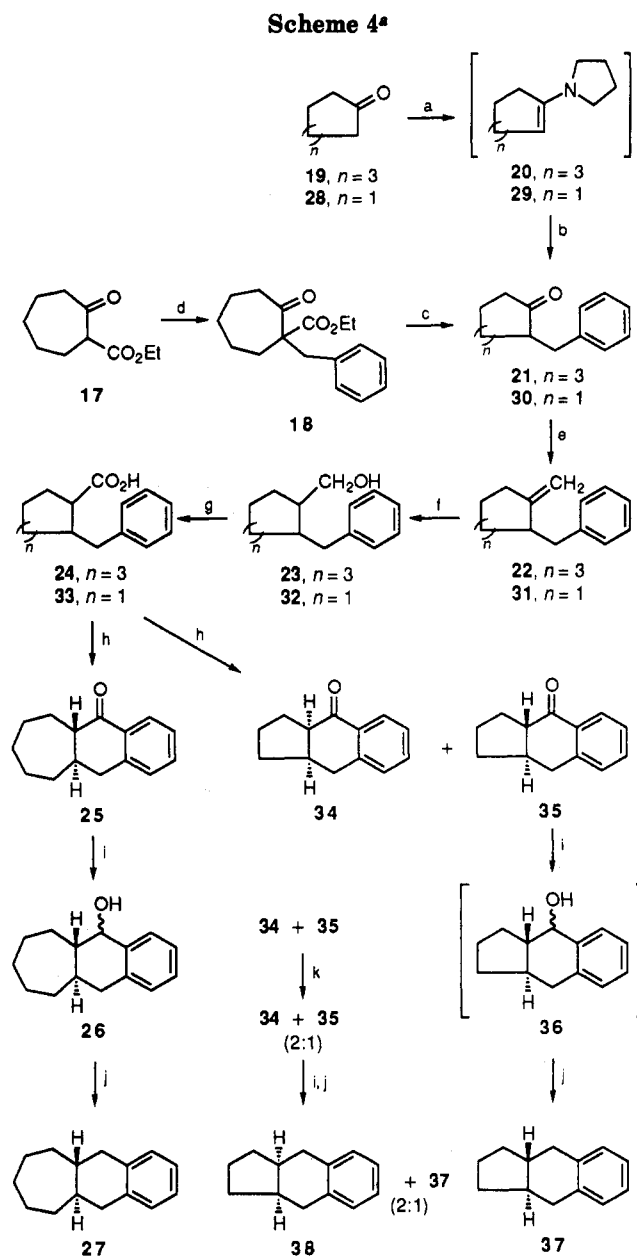The significant enhancement in the yields of the cyclized products with *gem* disubstitution at C-3 in the cyclohexane

Scheme 3ᵃ

16a, R = H
16b, R = OMe

ᵃ Key: (a) LiAlH₄–Et₂O; (b) PCC, CH₂Cl₂; (c) NH₂·NH₂·H₂O, (HOCH₂CH₂)₂, KOH.

ring in the alkene substrates **10a–c** and **13a–c** is in conformity with the *gem*-dimethyl effect[14] in facilitation of the ring-closure reaction of the intermediate open-chain aryl radical. Similar beneficial *gem*-substitution effects in ring closures involving alkyl radicals have been reported.[15]

With the successful development of a highly regio- and stereoselective hexannulation on cyclohexane ring substrates, attention was turned to the aryl radical cyclizations on the alkenes **41** and **43**, incorporating a seven- and a five-membered ring, respectively (Schemes 5 and 6). Realizing that structural and stereochemical elucidations of the linear hydrocarbons resulting from the radical cyclizations of these olefins could be quite difficult, we first synthesized the authentic samples of the cyclohepta-[*b*]naphthane **27** and the *trans*- and *cis*-benz[*f*]indenes **37** and **38** through the respective ketones **25, 35,**[16,17] and **34**[16] by an unequivocal general sequence (Scheme 4). The preparation of **21** was achieved in good yield by alkylation of the β-keto ester **17** followed by acidic hydrolytic decarboxylation of the alkylated product **18**. The desired compound **21** was obtained directly, albeit in 30% yield, by alkylation of the enamine **20**. Wittig olefination of **31** followed by hydroboration of the alkene **22** and oxidation with alkaline hydrogen peroxide gave the alcohol **23** in good yields. This on further oxidation with Jones reagent gave the acid **24**, which was cyclized with polyphosphoric acid to afford a sharp melting ketone **25**. This ketone was recovered unchanged on treatment with methanolic sodium methoxide solution. The *trans*-stereochemistry to this ketone has been assigned tentatively, from an examination of the molecular model (Drieding) and by analogy.[18] The reduction of **25** with sodium borohydride gave a mixture of the epimeric alcohols **26**, which on catalytic hydrogenolysis afforded the hydrocarbon **27**. Similarly, the benzylcyclopentanone **30**, prepared in excellent yield by alkylation of the enamine **29**, was smoothly transformed to the alkene **31**. The desired acid **33**, obtained through the alcohol **32**, on cyclization with polyphosphoric acid gave a mixture of the epimeric *cis*-and *trans*-ketones **34** and **35** in 77% overall yield from the alcohol. The pure *trans*-ketone **35**, partially separated from the mixture by column chromatography and recrys-

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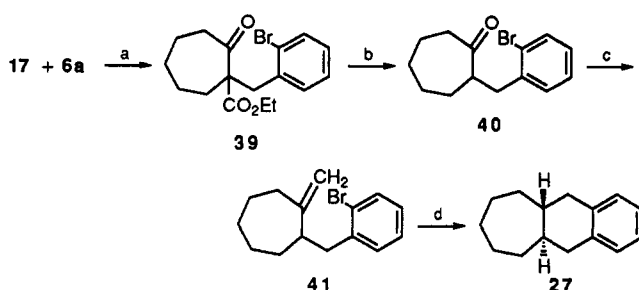
(14) Allinger, N. L.; Zalkow, V. *J. Org. Chem.* **1960**, *25*, 701. Capon, B.; McManus, S. P. *Neighboring Group Participation*; Plenum Press: New York, **1976**; Vol. 1.

(15) Della, E. W.; Knill, A. M.; Pigou, P. E. *J. Org. Chem.* **1993**, *58*, 2110.

(16) Synthesis of the ketone in a moderate yield by a cycloaddition reaction has been reported by: Moss, R. J.; White, R. O.; Rickborn, B. *J. Org. Chem.* **1985**, *50*, 5132.

(17) This ketone of unspecified composition by Friedel–Crafts cyclization reaction has been reported by: Van der Heuvel, C. G.; Nibbering, N. M. M. *Org. Mass. Spectrum* **1978**, *13*, 584.

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Scheme 4ᵃ

19, n = 3
28, n = 1

20, n = 3
29, n = 1

17

18

21, n = 3
30, n = 1

24, n = 3
33, n = 1

23, n = 3
32, n = 1

22, n = 3
31, n = 1

25

34

35

26

34 + 35

36

34 + 35
(2:1)

27

38

+ 37
(2:1)

37

ᵃ Key: (a) C₄H₉N–C₆H₆; (b) C₆H₅CH₂Cl, NaI, EtOH; (c) HCl-AcOH–H₂O; (d) C₆H₆, molecular sodium, C₆H₅CH₂Cl; (e) Ph₃P⁺CH₃I⁻, ᵗC₅H₁₁O⁻Na⁺–PhCH₃; (f) THF–B₂H₆, OH⁻, H₂O₂; (g) Jones reagent; (h) PPA; (i) NaBH₄, EtOH; (j) Pd–C (10%) (H₂), EtOH; (k) MeONa, MeOH.

tallization, was converted to the *trans*-hydrocarbon **37** through the alcohols **36**. An inseparable *ca.* 2:1 mixture of the *cis*- and *trans*-ketones **34** and **35**, obtained by epimerization[16] of the residual mixture of the ketones, after separation of the *trans*-isomer, was directly converted to a mixture of the *cis*- and *trans*-hydrocarbons **38** and **37** (∼2:1 by GLC). Now with the authentic samples of the hydrocarbons **27** and **37** and **38** in hand we carried out the radical cyclizations of the alkenes **41** and **43**.

The alkene **41** was readily available by Wittig alkenation of the ketone **40**, which was prepared in good yield from the alkylated β-keto ester **39**. Treatment of **41** with tri-*n*-butyltin hydride and AIBN in refluxing benzene afforded the hydrocarbon **27** in 88% yield (GLC) by a 6-*endo-trig* mode, identified by coinjection with the sample of the hydrocarbon described earlier, along with three minor unidentified products. The pure hydrocarbon was separated by column chromatography.

Scheme 5[a]

17 + 6a   →(a)   **39** (O, Br, CO₂Et)   →(b)   **40** (O, Br)   →(c)

41 (CH₂, Br)   →(d)   **27** (H, H)

[a] Key: (a) molecular sodium, C_6H_6; (b) $HCl-AcOH-H_2O$; (c) $Ph_3P^+CH_3I^-$, $^tC_5H_{11}O^-Na^+$-$PhCH_3$; (d) TBTH, AIBN, C_6H_6.

Scheme 6[a]

29 + 6a   →(a)   **42** (O, Br)   →(b)   **43** (CH₂, Br)   →(c)

37   +   **38**   (2:1)
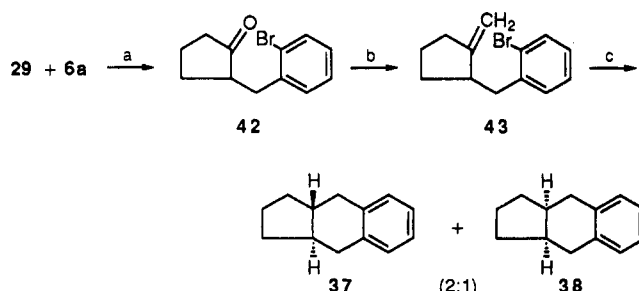
[a] Key: (a) EtOH, NaI; (b) $Ph_3P^+CH_3I^-$; $^tC_5H_{11}O^-Na^+$, $PhCH_3$; (c) TBTH, AIBN, C_6H_6.

Unlike the radical cyclization products from the aforementioned alkenes which gave both highly regio- and stereoselective ring closures leading only to the respective 6-*endo-trans*-products, the methylenecyclopentane **43** (prepared from the ketone **42**) on reaction with tri-*n*-butyltin hydride, under the usual conditions, gave a mixture of the *cis*- and *trans*-hydrocarbons **38** and **37** in a ratio of *ca.* 2:1 (97% by GLC) by coinjection with the authentic *trans*-compound **37** and the 2:1 mixture of **38** and **37**.

The *regio*- and *stereo*chemical outcome[19] of these radical cyclization reactions is remarkable. The intrinsic preference for a 6-*endo*-closure in the least substituted terminal carbon atom[20] of the *exo*-olefin is obviously controlled by favorable stereoelectronic factors. The *exclusive* formation of the respective *trans*-products **3, 11, 14,** and **27** in the radical cyclizations of the alkenes **2, 10, 13,** and **41** indicates the preferred trapping of the nearly planar[21] postcyclization bridged radical (e.g., **B** in eq 1) by hydrogen from the axial direction. Much lower *trans*-stereoselectivity in the transformation of the olefin **43** to a mixture of the *trans*- and *cis*-hydrocarbons **37** and **38** (*ca.* 1:2) possibly is due to the unfavorable transition states in the transfer of hydrogen from the axial phase in this intermediate radical. Interestingly, each of these products is the thermodynamically preferred stereoisomer.

(19) For a discussion on the stereochemical outcome of various radical reactions, see: Hart, D. J.; Wu, S. C. *Tetrahedron Lett.* 1991, 32, 4099. Ishibashi, H.; Nakamura, N.; Sato, T.; Takeuchi, M.; Ikeda, M. *Ibid.* 1991, 32, 1725. Takano, S.; Suzuki, M.; Kijima, A.; Ogasawara, K. *Ibid.* 1990, 31, 2315. Jones, K.; McCarthy, C. *Ibid.* 1989, 30, 2657. Jones, K.; Thompson, M.; Wright, C. *J. Chem. Soc., Chem. Commun.* 1986, 115.

(20) This preference has also been observed in a similar 7-*endo-trig*-aryl radical cyclization in our laboratories: Ghosh, A. K.; Ghosh, K.; Pal, S.; Ghatak, U. R. *J. Chem. Soc., Chem. Commun.* 1993, 809, 1176.

(21) (a) Some *trans*-fused N-heterocyclic products were obtained in 6-*endo*-aryl radical additions: Glover, S. A.; Warkentin, J. *J. Org. Chem.* 1993, 58, 2115. (b) An exclusive *trans*-N-heterocyclic product has been reported in a 7-*endo*-aryl radical cyclization by: Rigby, J. H.; Qabar, M. N. *J. Org. Chem.* 1993, 58, 4473.

Conclusion

A conceptually new general and convergent stereocontrolled synthetic route to linearly hexannulated condensed hydroaromatic systems has been developed using a highly regioselective 6-*endo*-aryl radical cyclization. The clean stereochemical outcome of the radical ring closure reaction generating only the *trans*-octahydroanthracenes and *trans*-octahydro-5a*H*-cyclohepta[*b*]naphthalene, in high yields, can be viewed as illustrations of the efficiency of our methodology. Further investigations are currently being undertaken in our laboratories to exploit this regio- and stereoselective aryl radical cyclization in the construction of more complex condensed carbocyclic systems and natural products.

Experimental Section

General Method. IR spectra were recorded on a Perkin-Elmer Model PE 298 spectrometer. ¹H NMR spectra were determined at 60, 100, and 200 MHz. Mass spectra were obtained by EI at 70 eV. Analytical GLC was performed on a Shimadzu GC 90 model. Petroleum ether refers to bp 60–80 °C. Elemental analyses were performed by S.K. Sarkar of this laboratory.

Ethyl 3-(*o*-Bromobenzyl)-2-methyl-4-oxocyclohex-2-ene-carboxylate (7a). The procedure described for the alkylation with benzyl chloride in our earlier report[10] was adopted. Hagemann's ester (5) (22 g, 120 mmol) was added to a thick suspension of t-BuOK [prepared from potassium (4.7 g, 120 mmol) and t-BuOH] and was shaken thoroughly. To this cold and straw yellow potassium salt was added the bromide **6a** (30 g, 120 mmol) with shaking, and the mixture was refluxed for 16 h. The cold reaction mixture was diluted with water, acidified with 6 N HCl, and extracted with benzene. The organic layer was washed with 5% $NaHCO_3$ solution followed by water and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded a pale yellow oil, which was distilled to give **7a** (26.11 g, 62%): bp 190–192 °C (0.1 mmHg); IR (neat) 1730 (–COOEt), 1670 (C=O) 1625 (C=C), 1600 cm⁻¹; ¹H NMR δ 1.30 (t, J = 8 Hz, 3H), 1.91 (s, 3H), 2.28–2.70 (m, 4H), 3.38–3.46 (m, 1H), 3.70 (δ_A) and 3.91 (δ_B) (AB_q, J = 14 Hz), 4.27 (q, J = 8 Hz), 6.98–7.26 (m, 3H), 7.58 (dd, J = 8 and 1 Hz, 1H). Anal. Calcd for $C_{17}H_{19}O_3Br$: C, 58.11; H, 5.45. Found: C, 57.89; H, 5.34.

Ethyl 3-(5-Methoxy-2-bromobenzyl)-2-methyl-4-oxocyclohex-2-enecarboxylate (7b) was prepared according to the procedure given for **7a** using **5** (21 g, 116 mmol), potassium (4.55 g, 116 mmol), and the bromide **6b** (32 g, 114 mmol). After workup **7b** (31.7 g, 73%), bp 210–220 °C (0.1 mmHg), was obtained as a thick oil: IR (neat) 1730 (COOEt), 1670 (=CC=O), 1625 cm⁻¹ (C=C); ¹H NMR δ 1.28 (t, J = 7 Hz, 3H), 1.92 (s, 3H), 2.26–2.72 (m, 4H), 3.44 (bs, 1H), 3.63 (δ_A) and 3.84 (δ_B) (ABq, J = 16 Hz, 2H), 3.76 (s, 3H), 4.27 (q, J = 7 Hz, 2H), 6.60–6.68 (m, 2H), 7.46 (d, J = 8 Hz, 1H); MS m/z (rel intensity) 301 (loss of Br, 71), 229 (loss of $CO_2CH_2CH_3$ from 301) (100), 199 (22), 135 (25), 128 (28), 115 (41), 109 (25), 91 (tropylium ion, 29), 77 ($C_6H_5^+$, 27). Anal. Calcd for $C_{18}H_{21}O_4Br$: C, 56.69; H, 5.55. Found: C, 56.39; H, 5.23.

Ethyl 3-(4-Methoxy-2-bromobenzyl)-2-methyl-4-oxocyclohex-2-enecarboxylate (7c) was prepared according to the procedure given for **7a** using **5** (18 g, 99 mmol), potassium (3.86 g, 99 mmol), and bromide **6c** (25 g, 89 mmol). After workup **7c** (24.38 g, 65%), bp 205–210 °C (0.1 mmHg), was obtained as a thick oil: IR (neat) 1730, 1665, 1625 cm⁻¹; ¹H NMR δ 1.27 (t, J = 7 Hz, 3H), 1.97 (s, 3H), 2.20–2.78 (m, 4H), 3.03 (bs, 1H), 3.60 (bs, 2H), 3.76 (s, 3H), 4.27 (m, 2H), 6.76–7.20 (m, 3H). Anal. Calcd for $C_{18}H_{21}O_4Br$: C, 56.69; H, 5.55. Found: C, 56.43; H, 5.32.

2-(*o*-Bromobenzyl)-3-methylcyclohex-2-en-1-one (8a). The keto ester **7a** (20 g, 56.98 mol) was refluxed under nitrogen for 14 h with an ethanolic KOH (26 g, in 25 mL of H_2O) solution. The mixture was diluted with water, and most of the alcohol was removed under reduced pressure. The mixture was cooled, decomposed with 6 N HCl until effervescence ceased, and then extracted with ether. The extracts were washed with brine and

dried over Na_2SO_4. Removal of the solvent under reduced pressure gave a yellowish oil, which was distilled to afford **8a** (11.28 g, 71%): bp 175–180 °C (0.1 mmHg); IR (neat) 1660 (=CC=O), 1605 cm^{-1}; ^{1}H NMR δ 1.94 (s, 3H), 1.98–2.54 (m, 6H), 3.78 (bs, 2H), 6.90 (dd, J = 7 and 1 Hz, 1H), 7.02–7.28 (m, 2H), 7.57 (dd, J = 7 and 1 Hz, 1H). Anal. Calcd for $C_{14}H_{15}OBr$: C, 60.21; H, 5.41. Found: C, 60.01; H, 5.36.

2-(5-Methoxy-2-bromobenzyl)-3-methylcyclohex-2-en-1-one (8b) was prepared following the same procedure as described for **8a** using keto ester **7b** (20 g, 52.4 mmol) and KOH (18 g, in 18 mL of H_2O). After workup the enone **8b** (10.7 g, 66%) was obtained as a light yellow oil: bp 195–200 °C (0.08 mmHg); IR (neat) 1665 (=CC=O), 1610 cm^{-1}; ^{1}H NMR δ 1.90 (s, 3H), 1.96–2.60 (m, 6H), 3.66–3.88 (m, 2H), 3.76 (s, 3H), 6.50 (bs, 1H), 7.48 (d, J = 6 Hz, 1H), 7.64 (bd, 1H); MS m/z (rel intensity) 229 (loss of Br, 100), 158 (11), 115 (25), 105 (12), 77 ($C_6H_5^+$, 15). Anal. Calcd for $C_{15}H_{17}O_2Br$: C, 58.25; H, 5.54. Found: C, 58.06; H, 5.32.

2-(4-Methoxy-2-bromobenzyl)-3-methylcyclohex-2-en-1-one (8c) was prepared according to the procedure described for **8a** using keto ester **7c** (20 g, 52.40 mmol) and KOH (18 g in 18 mL of H_2O). After workup **8c** (12.97 g, 80%) was obtained as a light yellow oil: bp 185–190 °C (0.06 mmHg); IR (neat) 1665 (=CC=O), 1610 cm^{-1}; ^{1}H NMR δ 1.92 (s, 3H), 1.20–2.76 (m, 6H), 3.72 (s, 2H), 3.80 (s, 3H), 6.76–7.20 (m, 3H). Anal. Calcd for $C_{15}H_{17}O_2Br$: C, 58.25; H, 5.54. Found: C, 58.53; H, 5.83.

Methyl 2-(o-Bromobenzyl)-3-methyl-1-oxocyclohexane-3-carboxylate (9a). A procedure described earlier[10] was adopted. A solution of the unsaturated ketone **8a** (6 g, 21.5 mmol) in 95% ethanol (150 mL) was heated under reflux with a solution of KCN (5 g, 76.92 mmol) in water (10 mL) for 14 h when the color turned to brown. The cyano derivative without isolation was hydrolyzed by refluxing with KOH (8 g) in water (60 mL) for 96 h. Most of the alcohol was then removed. The organic phase was acidified with 6 N HCl and repeatedly extracted with ether. The combined extracts were repeatedly washed with a solution of Na_2CO_3 (5%) until alkaline. The cooled basic washings after acidification with 6 N HCl were extracted with EtOAc. The extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude acid thus obtained was esterified with an excess of diazomethane in ether. The methyl esters were purified by chromatography over neutral alumina (50 g) and eluted with petroleum ether to afford a diastereometric mixture of keto esters **9a** (4.73 g, 65%): IR (neat) 1735 (CO_2Me), 1715, 1595 cm^{-1}; ^{1}H NMR δ 1.18 (s, CH$_3$ for minor isomer) 1.48 (s, CH$_3$, major isomer), 3.54 (s, COOCH$_3$, major isomer), 3.74 (s, COOCH$_3$, minor isomer). Anal. Calcd for $C_{16}H_{19}O_3Br$: C, 56.63; H, 5.64. Found: C, 56.31; H, 5.41.

Methyl 2-(5-methoxy-2-bromobenzyl)-3-methyl-1-oxocyclohexane-3-carboxylate (9b) was prepared following an identical procedure as described for **9a** using the unsaturated ketone **8b** (5 g, 16.18 mmol), KCN (3.5 g, 53.84 mmol) and KOH (7.2 g in water). The crude acid was esterified with an excess of ethereal diazomethane solutions and was purified by chromatography over neutral alumina (50 g) to afford a diastereomeric mixture of keto esters **9b** (3.86 g, 63%): IR (neat) 1730, 1715, 1600 cm^{-1}; ^{1}H NMR δ 1.13 (s, CH$_3$ for minor isomer), 1.50 (s, CH$_3$ for major isomer), 3.52 (s, COOMe, minor isomer), 3.66 (s, COOMe, major isomer), 3.76 (s, ArOCH$_3$, minor isomer), 3.79 (s, ArOCH$_3$, major isomer). Anal. Calcd for $C_{17}H_{21}O_4Br$: C, 55.28; H, 5.73. Found: C, 55.01; H, 5.62.

Methyl 2-(4-methoxy-2-bromobenzyl)-3-methyl-1-oxocyclohexane-3-carboxylate (9c) was prepared according to the procedure described for **9a** using the unsaturated ketone **8c** (4 g, 13.00 mmol) and KCN (3.5 g, 53.84 mmol), and after purification, **9c** (3.52 g, 72%) was obtained as a diastereomeric mixture: IR 1725, 1710 cm^{-1}; ^{1}H NMR δ 1.18 (s, Me, for major isomer), 1.48 (s, Me, for minor isomer), 1.60–3.52 (m), 3.60 (COOMe, major isomer), 3.72 (COOMe, minor isomer), 3.76 (ArOMe, both isomers), 6.68–7.48 (m, ArH). Anal. Calcd for $C_{17}H_{21}O_4Br$: C, 55.28; H, 5.73. Found: C, 55.38; H, 5.66.

2-(o-Bromobenzyl)-3,3-dimethylcyclohexan-1-one (12a). The procedure described earlier[11] was adopted. To a stirred suspension of CuI (8.2 g, 43.15 mmol) in dry ether (30 mL) under nitrogen at –25 °C (bath temperature) was added MeLi in ether (58 mL, 1.5 M, 87 mmol). The resulting yellow suspension was

cooled to –50 °C, and $BF_3\cdot Et_2O$ (6.1 g, 43.26 mmol) was added. After 5 min, unsaturated ketone **8a** (4 g, 14.33 mmol) in ether was added dropwise during 15 min and stirring at –30 °C was continued for 15 min. An additional lot of $BF_3\cdot Et_2O$ (6.1 g, 43.26 mmol) was added, stirring was continued for 1 h, and the mixture was finally allowed to warm to 0 °C. The reaction mixture was carefully quenched by dropwise addition of saturated NH$_4$Cl solution, extracted with ether, washed with $Na_2S_2O_3$, and dried over Na_2SO_4. After removal of solvent the crude product was purified by column chromatography on neutral alumina (110 g) using petroleum ether as eluant to afford pure solid **12a** (3.84 g, 91%): mp 61 °C (ether–petroleum ether); IR (KBr) 1705 (C=O), 1590 cm^{-1}; ^{1}H NMR δ 0.88 (s, 3H), 1.29 (s, 3H), 1.60–1.98 (m, 6H), 2.20–2.30 (m, 1H), 2.72–3.20 (m, 2H), 7.02–7.54 (m, 4H). Anal. Calcd for $C_{15}H_{19}OBr$: C, 61.05; H, 6.48. Found: C, 61.29; H, 6.34.

2-(5-Methoxy-2-bromobenzyl)-3,3-dimethylcyclohexan-1-one (12b) was prepared according to the procedure described for **12a** using the unsaturated ketone **8b** (5 g, 16.18 mmol). After workup and purification, **12b** (4.62 g, 88%) was obtained as a colorless solid: mp 72 °C; IR (KBr) 1700 (C=O), 1605 cm^{-1}; ^{1}H NMR δ 0.86 (s, 3H), 1.27 (s, 3H), 1.58–2.38 (m, 6H), 2.66–2.84 (m, 2H), 3.00–3.10 (m, 1H), 3.80 (s, 3H), 6.64 (dd, J = 8 and 2 Hz, 1H), 7.05 (d, J = 2 Hz, 1H), 7.39 (d, J = 8 Hz, 1H). Anal. Calcd for $C_{16}H_{21}O_2Br$: C, 59.06; H, 6.51. Found: C, 58.92; H, 6.31.

2-(4-Methoxy-2-bromobenzyl)-3,3-dimethylcyclohexan-1-one (12c) was prepared according to the procedure described for **12a** using the unsaturated ketone **8c** (5g, 16.2 mmol). After workup and purification by chromatography on neutral alumina, using petroleum ether as eluent, **12c** (3.8 g, 72%) was obtained as a thick oil: IR (neat) 1700 cm^{-1}; ^{1}H NMR δ 0.76 (s, 3H), 1.23 (s, 3H), 1.90–3.06 (m, 9H), 3.63 (s, 3H), 6.57 (dd, J = 8 and 2 Hz, 1H), 6.86 (d, J = 2 Hz, 1H), 7.23 (d, J = 8 Hz, 1H). Anal. Calcd for $C_{16}H_{21}O_2Br$: C, 59.06; H, 6.51. Found C, 59.02; H, 6.21.

Synthesis of 1-Methylenecyclohexanes. General Procedure. The procedure described earlier[9b] was adopted. To a stirred suspension of methyl(triphenyl)phosphonium iodide (4.5 g, 11.6 mmol) and freshly prepared sodium *tert*-pentoxide (7 mL, 1.5 M) in toluene at room temperature was added the ketone in toluene dropwise, and the mixture was heated to 80 °C. The reaction mixture after quenching with saturated NH$_4$Cl solution was extracted with ether and dried over Na_2SO_4. After removal of the solvent the residue was dissolved in petroleum ether (100 mL) and immediately filtered through a short-wide column of silica gel (30 g). MeI was added to the filtrate and the resulting mixture left for 1 h at room temperature. The precipitated methyltriphenylphosphonium iodide was filtered off, and the filtrate was concentrated in vacuo to give the pure alkene.

2-(o-Bromobenzyl)-1-methylenecyclohexane (2). Ketone 1[22] (1 g, 3.74 mmol) gave 890 mg (90%) of **2**: IR (neat) 1635 (C=C) 1600 cm^{-1}; ^{1}H NMR δ 1.19–1.82 (m, 5H), 2.02–2.55 (m, 5H), 3.10 (dd, J = 14 and 2 Hz, 1H), 4.22 (m, 1H), 4.74 (m, 1H), 7.04–7.61 (m, 4H). Anal. Calcd for $C_{14}H_{17}Br$: C, 63.38; H, 6.45. Found C, 63.16; H, 6.53.

Methyl 2-(o-Bromobenzyl)-3-methyl-1-methylenecyclohexane-3-carboxylate (10a). The diastereomeric mixture of the keto esters **9a** (1.2g, 3.54 mmol) gave **10a** (1.05 g, 88%) as a single isomer, as revealed from ^{1}H NMR and GLC: IR (neat) 1730, 1600 cm^{-1}; ^{1}H NMR δ 1.45 (s, 3H), 1.54–2.36 (m, 6H), 2.70–3.28 (m, 3H), 3.60 (s, 3H), 4.45 (brs, 1H), 4.72 (brs, 1H), 7.06–7.32 (m, 3H), 7.56 (d, J = 8 Hz, 1H). Anal. Calcd for $C_{17}H_{21}O_2Br$: C, 60.52; H, 6.28. Found: C, 60.81; H, 6.18.

Methyl 2-(5-Methoxy-2-bromobenzyl)-3-methyl-1-methylenecyclohexane-3-carboxylate (10b). Ketone **9b** (1.3 g, 3.52 mmol) gave **10b** (1.06 g, 82%): IR (neat) 1730, 1630 cm^{-1}; ^{1}H NMR δ 1.21 (s, 3H), 1.41–2.36 (m, 7H), 2.62–3.19 (m, 2H), 3.53 (s, 3H), 3.66 (s, 3H), 4.46 (bs, 1H), 4.68 (bs, 1H), 6.52 (dd, J = 8.2 Hz, 1H), 7.06 (d, J = 2 Hz, 1H), 7.23 (d, J = 8 Hz, 1H). Anal. Calcd For $C_{18}H_{23}O_3Br$: C, 58.85; H, 6.31. Found: C, 58.49; H, 6.42.

Methyl 2-(4-Methoxy-2-bromobenzyl)-3-methyl-1-methylenecyclohexane-3-carboxylate (10c). Ketone **9c** (1 g, 2.7 mmol) gave 796 mg (80%) of **10c**: IR (neat) 1725, 1645 cm^{-1}; ^{1}H

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NMR δ 1.24 (s, 3H), 1.39–3.24 (m, 9H), 3.60 (s, 3H), 3.78 (s, 3H), 4.46 (bs, 1H), 4.74 (bs, 1H), 6.76 (dd, J = 8.2 Hz, 1H), 7.04–7.20 (m, 2H). Anal. Calcd for $C_{18}H_{23}O_3Br$: C, 58.85; H, 6.31. Found: C, 58.61; H, 6.45.

2-(o-Bromobenzyl)-3,3-dimethyl-1-methylenecyclohexane (13a). Ketone **12a** (1.5 g, 5.08 mmol) gave 1.37 g (92%) of **13a**: IR (neat) 1640, 1590 cm⁻¹; ¹H NMR δ 0.98 (s, 3H), 1.06 (s, 3H), 1.26–2.36 (m, 3H), 2.78 (t, J = 12 Hz, 1H), 3.08 (bd, 1H), 4.20 (brs, 1H), 4.60 (brs, 1H), 7.00–7.26 (m, 3H), 7.55 (dd, J = 8 and 1 Hz, 1H). Anal. Calcd for $C_{16}H_{21}Br$: C, 65.53; H, 7.22. Found: C, 65.59; H, 7.18.

2-(5-Methoxy-2-bromobenzyl)-3,3-dimethyl-1-methylenecyclohexane (13b). Ketone **12b** (1.2 g, 3.7 mmol) gave 1.03 g (86%) of **13b**: IR (neat) 1635, 1610; ¹H NMR δ 0.98 (s, 3H), 1.04 (s, 3H), 1.26–2.34 (m, 7H), 2.76 (t, J = 12 Hz, 1H), 3.02 (dd, J = 12 and 2 Hz, 1H), 3.76 (s, 3H), 4.24 (bs, 1H), 4.61 (bs, 1H), 6.61 (dd, J = 8 and 1 Hz, 1H), 6.68 (d, J = 1 Hz, 1H), 7.40 (d, J = 8 Hz, 1H). Anal. Calcd for $C_{17}H_{23}OBr$: C, 63.14; H, 7.17. Found: C, 63.02; H, 7.23.

2-(4-Methoxy-2-bromobenzyl)-3,3-dimethyl-1-methylenecyclohexane (13c). Ketone **12c** (1.2 g, 3.7 mmol) gave 880 mg (74%) of **13c**: IR (neat) 1640, 1610 cm⁻¹; ¹H NMR δ 0.96 (s, 3H), 1.04 (s, 3H), 1.20–2.40 (m, 6H), 2.52–3.16 (m, 3H), 3.78 (s, 3H), 4.22 (m, 1H), 4.60 (m, 1H), 6.76 (dd, J = 8 and 2 Hz, 1H), 7.00 (d, J = 8 Hz, 1H), 7.08 (d, J = 2 Hz, 1H). Anal. Calcd for $C_{17}H_{23}OBr$: C, 63.14; H, 7.17. Found: C, 63.22; H, 7.35.

Radical Cyclization: Typical Procedure. The olefin was refluxed with 1.1 equiv of Buⁿ₃SnH and a catalytic amount of AIBN (20 mg) in dry benzene for 6 h. The concentration of Buⁿ₃SnH in benzene was maintained at 0.02–0.007 M. After removal of the benzene under reduced pressure the crude product was stirred with 15 mL of a saturated solution of KF[23] and white precipitate filtered off. The filtrate was extracted with ether and dried (Na₂SO₄). The product obtained, after removal of the solvent, was purified by column chromatography on neutral alumina using petroleum ether as eluent. The product was analyzed by GLC and ¹H NMR.

trans-1,2,3,4,4a,9,9a,10-Octahydroanthracene (3). Olefin **2** (200 mg, 0.75 mmol) on radical cyclization gave over 90% of the product which on GLC analysis was revealed to be a mixture of **3** and **4** in a ratio of 9:1 by coinjection with the known samples. Careful chromatography of the mixture on neutral alumina (7 g), using petroleum ether as eluent, gave **3** (110 mg, 79%), mp 53 °C (lit.[24] mp 53.4–54.5 °C).

(±)-trans-Methyl 1β-Methyl-1,2,3,4,4a,9,9aα,10-octahydroanthracene-1α-carboxylate (11a). The olefin **10a** (500 mg, 1.48 mmol) on radical cyclization gave **11a** (325 mg (85%) as a colorless crystalline solid, mp 92 °C (methanol): IR (KBr) 1730 (COOMe), 1590 cm⁻¹; ¹H NMR δ 1.22 (s, 3H), 1.62–2.15 (m, 8H), 2.48–2.92 (m, 4H), 3.68 (s, 3H), 7.00–7.10 (m, 4H). Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.53. Found: C, 78.92; H, 8.70.

(±)-trans-Methyl-1β-Methyl-1,2,3,4,4a,9,9aα,10-octahydro-7-methoxyanthracene-1α-carboxylate (11b). The olefin **10b** (500 mg, 1.36 mmol) on radical cyclization gave **11b** (262 mg, 67%) as a colorless viscous oil after chromatography on neutral alumina (15 g), using ether–petroleum ether (1:19) as eluent: IR (neat) 1730, 1615, 1595 cm⁻¹; ¹H NMR δ 1.20 (s, 3H), 1.26 (m, 6H), 2.20–2.84 (m, 6H), 3.70 (s, 3H), 3.76 (s, 3H), 6.60 (bd, 1H), 6.68 (bd, 1H), 6.98 (d, J = 8 Hz, 1H). Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.86; H, 8.39. Found: C, 74.72; H, 8.25.

(±)-trans-Methyl-1β-Methyl-1,2,3,4,4a,9,9aα,10-octahydro-6-methoxyanthracene-1α-carboxylate (11c). The olefin **10c** (250 mg, 0.7 mmol) on radical cyclization gave **11c** (170 mg, 87%) as a colorless crystalline solid: mp 111–112 °C (ether–petroleum ether); IR (neat) 1720, 1610 cm⁻¹; ¹H NMR δ 1.22 (s, 3H), 1.46–2.98 (m, 12H), 3.68 (s, 3H), 3.78 (s, 3H), 6.56–6.76 (m, 2H), 6.96 (d, J = 8 Hz, 1H). Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.86; H, 8.39. Found: C, 74.82; H, 8.55.

(±)-trans-1β-Methyl-1,2,3,4,4a,9,9aα,10-octahydro-6-methoxyanthracene-1α-carboxylic Acid (15c). The procedure reported by Chang et al.[25] was adopted. The ester **11c** (100 mg, 0.34 mmol) was stirred with K⁺BuᵗO⁻ (380 mg, 3.4 mmol) in dry

DMSO (10 mL) at room temperature for 4 h. The reaction mixture was poured onto water and acidified with 6 N HCl. The liberated acid was extracted with ether, and the crude solid acid thus obtained was recrystallized from ether–petroleum ether to afford the acid **15c** (90 mg, 96%): mp 173–174 °C; IR (neat) 1685 cm⁻¹. Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.40; H, 8.05.

trans-1,1-Dimethyl-1,2,3,4,4a,9,9a,10-octahydroanthracene (14a). The olefin **13a** (500 mg, 1.69 mmol) on radical cyclization gave **14a** (347 mg, 95%) as a thick colorless liquid: IR (neat) 1600 cm⁻¹; ¹H NMR δ 0.80 (s, 3H), 1.05 (s, 3H), 1.08–1.96 (m, 8H), 2.34–2.90 (m, 4H), 7.12 (bs, 4H). Anal. Calcd for $C_{16}H_{22}$: C, 89.65; H, 10.35. Found: C, 89.55; H, 10.45.

trans-1,1-Dimethyl-1,2,3,4,4a,9,9a,10-octahydro-7-methoxyanthracene (14b). The olefin **13b** (500 mg, 1.54 mmol) on radical cyclization gave **14b** (245 mg, 65%) as a thick colorless liquid after chromatography on neutral alumina (15 g) using ether–petroleum ether (1:19) as the eluent: IR (neat) 1600 cm⁻¹; ¹H NMR δ 0.88 (s, 3H), 1.0 (s, 3H), 1.07–1.72 (m, 7H), 1.80–2.91 (m, 5H), 3.78 (s, 3H), 6.65 (bs, 1H), 6.72 (bs, 1H), 6.97 (d, J = 8 Hz, 1H), MS m/z (rel intensity), 244 (M⁺, 90), 229 (21), 171 (48), 150 (54), 144 (27), 134 (100), 121 (29), 109 (28), 91 (22). Anal. Calcd for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.61; H, 9.75.

trans-1,1-Dimethyl-1,2,3,4,4a,9,9a,10-octahydro-6-methoxyanthracene (14c). The olefin **13c** (250 mg, 0.77 mmol) on radical cyclization gave **14c** (135 mg, 72%) as a thick colorless liquid after chromatography on neutral alumina (15 g) using ether–petroluem ether (1:19); ¹H NMR δ 0.88 (s, 3H), 0.98 (s, 3H), 1.00–1.88 (m, 8H), 2.35–2.80 (m, 4H), 3.75 (s, 3H), 6.58 (d, J = 2 Hz, 1H), 6.67 (dd, J = 8 and 2 Hz, 1H), 6.98 (d, J = 8 Hz, 1H). Anal. Calcd: C, 83.55; H, 9.90. Found: C, 83.55; H, 9.77.

Conversion of 11a,b to 16a,b: (±)-trans-1β-Methyl-1,2,3,4,-4a,9,9aα,10-octahydroanthracene-1α-carbaldehyde (16a). The ethereal solution of the ester **11a** (300 mg, 1.16 mmol) was added to a stirred suspension of LiAlH₄ in ether (30 mL) and the resulting mixture refluxed for 5 h. After being cooled to 0 °C, the excess LiAlH₄ was decomposed by slow addition of saturated Na₂SO₄ solution. The ethereal layer was filtered, and the slurry mass was washed well with ether. The combined ether layers were evaporated to yield the respective alcohol. The crude alcohol (256 mg) in CH₂Cl₂ (5 mL) was added to a magnetically stirred suspension of PCC (300 mg) in CH₂Cl₂ (10 mL) at 0 °C and the stirring continued for 4 h. After usual workup the product was chromatographed over silica gel (6 g) using ether–petroleum ether (1:8) as the eluent to afford the pure aldehyde **16a** (218 mg, 86%) as a colorless viscous oil: IR (neat) 1715, 1590 cm⁻¹; ¹H NMR δ 0.79 (s, 3H), 1.24–1.87 (m, 8H), 2.33–2.96 (m, 4H), 6.91 (bs, 4H), 9.31 (s, 1H). Anal. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 84.02; H, 8.99.

Anthracene 14a. The aldehyde **16a** (100 mg, 0.43 mmol) in diethylene glycol (7 mL) and hydrazine hydrate (4 mL) was heated at 120–130 °C (graphite bath for 1.5 h under dry nitrogen atmosphere) with a continuous distillation system. The reaction mixture was cooled, KOH (50 mg, 1 mmol) was added, and the temperature was raised to 210–220 °C. After 2.5 h at that temperature, the reaction mixture and the distillate were poured into water and extracted with ether. The combined ether extracts were washed with water and dried over Na₂SO₄. Removal of solvent gave a gummy mass which was purified by chromatography on neutral alumina (4 g) using petroleum ether as the eluent afford the hydrocarbon **14a**, identical in all respects (¹H NMR, GLC) with the sample described before above.

(±)-trans-1β-Methyl-1,2,3,4,4a,9,9aα,10-octahydro-7-methoxyanthracene-1α-carbaldehyde (16b). The ester **11b** (300 mg, 1.04 mmol) was converted to the aldehyde **16b** (190 mg, 79%) following the same procedure as described for **16a**: IR (neat) 1715, 1610 cm⁻¹; ¹H NMR δ 0.81 (s, 3H), 1.51 (m, 12 H), 3.77 (s, 3H), 6.65–6.76 (m, 2H), 6.92 (bd, 1H), 9.33 (s, 1H). Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.02; H, 8.58. Found: C, 78.89; H, 8.63.

Methoxyanthracene 14b. The aldehyde **16b** (100 mg, 0.38 mmol) was transformed to the hydrocarbon **14b** (77 mg, 82%) according to the procedure described for **16a**. This was found to be identical (¹H NMR, GLC) with the sample described above.

Ethyl 2-Benzyl-1-oxocycloheptane-2-carboxylate (18). To an ice-cold suspension of molecular sodium (2.3 g, 100 mmol) in dry benzene (150 mL) was added the β-keto ester **17** (17 g, 92.39

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mmol) dropwise over a period of 1 h. The next day the sodio salt was refluxed with benzyl chloride (16.2 g, 128 mmol) for 10 h. The cooled reaction mixture was diluted with water, the organic layer was separated, and the aqueous layer was extracted with benzene. Combined organic layers were thoroughly washed with water and dried over Na_2SO_4. Removal of the solvent afforded a pale yellow oil which was distilled to give 18 (16.45 g, 65%): bp 168–172 °C (0.2 mmHg); IR (neat) 1735 (CO_2Et), 1700, 1600 cm^{-1}; ^1H NMR δ 1.13 (t, 3H), 1.33–2.67 (m, 10H), 2.83 (δ_A) and 3.26 (δ_B) (ABq, J = 11 Hz, 2H), 4.06 (q, 2H), 7.13 (bs, 5H). Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.18; H, 8.21.

2-Benzylcycloheptanone (21): Method A. The keto ester 18 (10 g, 36.49 mmol) was refluxed for 24 h with a mixture of CH_3CO_2H (110 mL), concentrated HCl (60 mL), and water (30 mL). The CH_3CO_2H was removed under reduced pressure, diluted with water, and extracted with ether. The organic layer was thoroughly washed with brine and dried over Na_2SO_4. Removal of the solvent under reduce pressure gave a viscous oil, which was purified by evaporative distillation to give 21 (4.57 g, 62%): bp 158–162 °C (2 mmHg); IR (neat) 1695 (C=O), 1600 cm^{-1}; ^1H NMR δ 1.03–3.33 (m, 13H), 7.27 (bs, 5H). Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.89; H, 9.06.

Method B. Cycloheptanone (19) (7 g, 62.5 mmoL) in benzene (100 mL) was refluxed with pyrrolidine (15 mL, 168 mmol) for 3 h. Benzene and the excess of pyrrolidine were then removed completely under reduced pressure. The crude enamine was refluxed with benzyl chloride (17 g, 135 mmol) in dry ethanol and a catalytic amount of anhydrous NaI for 4 h. The alcohol was removed under reduced pressure, and the residue was treated with water. The organic material was extracted with ether and washed with HCl (3 N) and then with water. Removal of the solvent and purification of the crude product, as mentioned above, gave 21 (4 g, 34%).

2-Benzyl-1-methylenecycloheptane (22) was obtained using the ketone 21 (5 g, 24.75 mol) according to the standard alkenation procedure as described before. After workup 22 (4.2 g, 85%) was obtained as an oil: bp 150 °C (2 mmHg); IR (neat) 1628, 1600 cm^{-1}; ^1H NMR δ 0.96–2.33 (m, 11H), 2.50–2.82 (m, 2H), 4.60 (bs, 1H), 4.80 (bs, 1H), 7.29 (bs, 5H). Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.87; H, 10.26.

2-Benzyl-1-(hydroxymethyl)cycloheptane (23). This transformation was carried out according to the procedure described earlier.[9b] Diborane gas (prepared from 3 g, $NaBH_4$, 9.9 mL, $BF_3·Et_2O$ in diglyme 15 mL) was passed through a cold (0 °C) solution of the olefin 22 (4.8 g, 24 mmol) in dry THF (15 mL) for 2 h under a continuous stream of nitrogen. The reaction mixture was then carefully decomposed with water and was transferred into a 3 N solution of NaOH (65 mL). To this well-stirred cold alkaline mixture was added 30% (v/v) H_2O_2 (50 mL) dropwise during 15 min. Stirring at a cold temperature was continued for 30 min, and then an additional lot of H_2O_2 (25 mL) was added in the same way. The mixture was allowed to sit overnight. It was extracted with ether, washed with water, and dried over Na_2SO_4. Removal of the solvent gave a crude mass which was purified by evaporative distillation, bp 170–172 °C (1 mmHg) to obtained the alcohol 23 (3.22 g, 62%): IR (neat) 3425, 1600 cm^{-1}; ^1H NMR δ 1.06–2.01 (m, 12H), 2.07–2.85 (m, 3H), 3.39 (bs, 2H), 7.09 (bs, 5H). Anal. Calcd for $C_{15}H_{22}O$: C, 82.51; H, 10.16. Found: C, 82.36; H, 10.02.

***trans*-1,2,3,4,5a,6,11,11a-Octahydrocyclohepta[*b*]naphthalen-6(5a*H*)-one (25).** To a magnetically stirred cold solution of the alcohol 23 (3 g, 13.7 mmol) in dry acetone (30 mL) was added Jones reagent[26] (5.5 mL, 15 mmol) dropwise until the reagent color persisted. Stirring at a cold temperature was continued for 45 min, and then the solution was diluted with water and extracted with ether. The ether layer was washed with 2% NaOH solution and then with water. The aqueous portion was acidified with 6 N HCl, extracted with ether, and washed with water. Evaporation of the solvent afforded the acid 24 (2.4 g) as a thick liquid, IR (neat) 1705, 1600 cm^{-1}, which was used directly for the PPA cyclization. To a well stirred homogeneous solution of PPA [prepared from P_2O_5 (40 g) and H_3PO_4 (20 mL)] was added the acid 24 (2.2 g) in ether (10 mL)

at 80–85 °C. Stirring at that temperature was continued for 2 h, and the mixture was cooled, poured onto crushed ice, and extracted with ether. The ether extracts were washed with 5% Na_2CO_3 solution and then with water and dried over Na_2SO_4. After removal of solvent the product was chromatographed on silica gel (20 g), using ether–petroleum ether as the eluent, to afford the ketone 25 (1.85 g, 63%) as a colorless solid: mp 53 °C (ether–petroleum ether); IR (KBr) 1675, 1600 cm^{-1}; ^1H NMR δ 1.20–2.33 (m, 12H), 2.67–3.0 (m, 2H), 7.08–7.33 (m, 3H), 7.68–8.00 (m, 1H). Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.44. Found: C, 84.12; H, 8.33.

***trans*-1,2,3,4,5a,6,11,11a-Octahydrocyclohepta[*b*]naphthalene-6(5*H*)-ol (26).** Sodium borohydride (320 mg, 8.42 mmol) was added to a magnetically stirred solution of the ketone 25 (600 mg, 2.8 mmol) in 95% ethanol (40 mL). It was left overnight, and excess borohydride was decomposed with water and extracted with ether. The ethereal layer was washed with brine, dried over Na_2SO_4, and evaporated to give a mixture of two epimeric alcohols 26 (500 mg, 83%) (87:13 from ^1H NMR): mp 125–130 °C; IR (KBr) 3375, 1595 cm^{-1}; ^1H NMR δ 1.20–2.00 (m), 2.21–2.92 (m), 4.18–4.37 (m), 7.00–7.67 (m). Anal. Calcd for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.01; H, 9.46.

***trans*-1,2,3,4,5,6,11,11a-Octahydro-5a*H*-cyclohepta[*b*]naphthalene (27).** The epimeric mixture of the alcohols 26 (200 mg, 0.92 mmol) was hydrogenated in dry ethanol (30 mL) using 10% Pd–C (30 mg) and two drops of 70% aqueous $HClO_4$ for 3 h at room temperature and atmospheric pressure. After neutralization with solid Na_2CO_3 the catalyst was filtered off. Removal of the solvent under reduced pressure followed by chromatography on neutral alumina (15 g), using petroleum ether as eluent, gave 27 (168 mg, 91%) as a colorless oil: IR (neat) 1590 cm^{-1}; ^1H NMR δ 1.20–2.10 (m, 12H), 2.46–2.86 (m, 4H), 7.05 (bs, 4H); MS m/z (relative intensity) 200 (M^+, 16), 158 (18), 141 (30), 128 (50), 117 (67), 91 (100), 77 (60). Anal. Calcd for $C_{15}H_{20}$: C, 89.94; H, 10.06. Found: C, 89.87; H, 10.13.

2-Benzylcyclopentanone (30) was prepared according to the procedure described for 21 (method B) using ketone 28 (7 g, 83.33 mmol), pyrrolidine (18 mL, 216 mmol), and benzyl chloride (17 g, 134 mmol). After workup, the alkylated product 30 (12.3 g, 85%), bp 120–129 °C (3 mmHg) (lit.[27] bp 120–121 °C (3 mmHg)), was obtained as colorless oil: IR (neat) 1714, 1590 cm^{-1}; ^1H NMR δ 1.29–3.32 (m, 9H), 7.21 (bs, 5H).

2-Benzyl-1-methylenecyclopentane (31) was prepared following the standard alkenation procedure using the ketone 30 (4 g, 22.9 mmol). After workup, the olefin 31 (3.75 g, 95%), bp 135–140 °C (3 mmHg), was obtained as a colorless oil: IR (neat) 1635 (C=C), 1600 cm^{-1}; ^1H NMR δ 1.00–2.42 (m, 7H), 2.56–2.81 (m, 2H), 4.52 (bs, 1H), 4.82 (bs, 1H), 7.22 (bs, 5H). Anal. Calcd for $C_{13}H_{16}$: C, 90.64; H, 9.36. Found: C, 90.53; H, 9.59.

2-Benzyl-1-(hydroxymethyl)cyclopentane (32) was prepared according to the procedure described for 24 using the olefin 31 (3.5 g, 20.34 mmol). After workup and purification, 32 (3.22 g, 83%) was obtained as colorless oil: bp 134–139 °C (1 mmHg); IR (neat) 3425, 1600 cm^{-1}; ^1H NMR δ 1.20–3.02 (m, 11H), 3.37 (m, 2H), 7.16 (bs, 5H). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 82.16; H, 9.44.

***trans*-2,3,3a,4,9,9a-Hexahydro-1*H*-benz[*f*]inden-4-one (35) and *cis*- and *trans*-2,3,3a,4,9,9a-Hexahydro-1*H*-benz[*f*]inden-4-one (34) and (35).** The alcohol 32 (3 g, 15.8 mmol) was converted to the tricyclic ketones according to the procedure described for 23. The product obtained (1.79 g, 61%), on column chromatography over silica gel (30 g), gave the pure *trans*-isomer 35 (440 mL, 15%) as a crystalline solid, mp 62 °C (lit.[16] mp 62–63 °C), recrystallization from ether–petroleum ether. The thick liquid and semisolid fractions were mixed together and epimerized by treatment with 10% methanolic NaOMe (30 mL) for 2 h at room temperature. It was diluted with water, acidified with 6 N HCl, and extracted with ether. Removal of solvent gave the semisolid 2:1[16] mixture of *cis*- and *trans*-ketones: IR (KBr) (*trans*-isomer) 1670, 1600 cm^{-1}; ^1H NMR δ (*trans*-isomer) 1.02–2.40 (m, 6H), 2.42–3.10 (m, 4H), 7.00–7.17 (m, 3H), 7.38–8.08 (m, 1H).

***trans*-2,3,3a,4,9,9a-Hexahydro-1*H*-benz[*f*]inden-4-ol (36)** was prepared according to the procedure described for 26 using

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35 (400 mg, 2.15 mmol). After workup and purification the epimeric alcohol **36** (350 mg, 85%) was obtained as thick oil: IR (neat) 3370, 1600 cm^{-1}; ^{1}H NMR δ 1.18–2.00 (m, 6H), 2.06–2.96 (m, 5H), 4.16–4.50 (m, 1H), 6.82–7.10 (m, 4H). Anal. Calcd for C$_{13}$H$_{16}$O: C, 82.93; H, 8.57. Found: C, 82.71; H, 8.77.

***trans*-2,3,3a,4,9,9a-Hexahydro-1*H*-benz[*f*]indene (37)** was prepared according to the procedure described for **27** using **36** (180 mg, 0.95 mmol). After workup and purification the *trans*-hydrocarbon **37** (150 mg, 92%) was obtained as a colorless oil: ^{1}H NMR δ 1.06–2.98 (m, 12H), 7.04 (m, 4H). Anal. Calcd for C$_{13}$H$_{16}$: C, 90.64; H, 9.36. Found: C, 90.52; H, 9.48.

***cis*- and *trans*-2,3,3a,4,9,9a-Hexahydro-1*H*-benz[*f*]indan (38 and 37)** was prepared from the *cis*- and *trans*-ketone mixture **34** and **35** (180 mg, 0.95 mmol) following the same procedure as described for **25**. After workup and purification it was obtained as inseparable mixture of (ca. 2:1) *cis*- and *trans*-hydrocarbons **38** and **37** (153 mg, 93%).

Ethyl 2-Bromo-1-oxobenzylcycloheptanecarboxylate (39) was prepared according to the procedure described for its debromo analogue **18** using β-keto ester **17** (17 g, 92 mmol) and benzyl bromide **6a** (32 g, 128 mmol). After workup and purification, **39** (23 g, 69%), bp 143–147 °C (0.2 mmHg), was obtained as a viscous oil: IR (neat) 1735, 1700, 1605 cm^{-1}; ^{1}H NMR δ 1.31 (t, J = 7 Hz, 3H), 1.39–3.72 (m, 12H), 4.11 (q, J = 7 Hz, 2H), 6.98–7.67 (m, 4H). Anal. Calcd for C$_{17}$H$_{21}$O$_3$Br: C, 57.77; H, 5.52. Found: C, 57.92; H, 5.21.

2-(*o*-Bromobenzyl)cycloheptanone (40) was prepared according to the procedure described for **21** (method A), using keto ester **39** (15 g, 42 mmol). After workup and purification, **40** (7.5 g, 63%), bp 138–143 °C (0.4 mmHg), was obtained as a colorless oil: IR (neat) 1700, 1590 cm^{-1}; ^{1}H NMR δ 1.10–3.0 (m, 13H), 6.98–7.61 (m, 4H). Anal. Calcd for C$_{14}$H$_{17}$OBr: C, 59.79; H, 6.09. Found: C, 59.39; H, 6.18.

2-(*o*-Bromobenzyl)-1-methylenecycloheptane (41) was prepared using ketone **40** (1.2 g, 4.2 mmol) following the standard alkenation procedure as a colorless oil (940 mg, 79%): IR (neat) 1630, 1600 cm^{-1}; ^{1}H NMR δ 1.18–2.20 (m, 10H), 2.60–2.84 (m,

3H), 4.52 (bs, 1H), 4.76 (bs, 1H), 7.09–7.40 (m, 3H), 7.58 (dd, J = 8 and 1 Hz, 1H). Anal. Calcd for C$_{15}$H$_{19}$Br: C, 64.50; H, 6.85. Found: C, 64.11; H, 6.92.

***trans*-1,2,3,4,5,6,11,11a-Octahydro-5a*H*-cyclohepta[*b*]naphthalene (27).** The olefin **41** (500 mg, 1.79 mmol) on radical cyclization gave the product as a gummy oil which on careful chromatography over silica gel (20 g), using petroleum ether as eluent, afforded **27** (240 mg, 67%) as the only isolable product, which was identical (^{1}H NMR, GLC) with the sample described earlier.

2-(*o*-Bromobenzyl)cyclopentanone (42) was prepared following the procedure described for **21** (method B) using ketone **28** (7 g, 83.3 mmol) and bromide **6a** (33 g, 132 mmol). After workup and purification **42** (18.3 g, 87%), bp 132–135 (0.4 mmHg), was obtained as a viscous liquid: IR (neat) 1735, 1590 cm^{-1}; ^{1}H NMR δ 1.54–2.72 (m, 8H), 3.36 (dd, J = 11 and 4 Hz, 1H), 7.06–7.32 (m, 3H), 7.56 (bd, 1H). Anal. Calcd for C$_{12}$H$_{13}$OBr: C, 56.41; H, 5.17. Found: C, 56.21; H, 5.29.

2-(*o*-Bromobenzyl)-1-methylenecyclopentane (43). The Wittig alkenation of the ketone **42** (1 g, 3.95 mmol) was carried out following the standard method described before. The olefin **43** (922 mg, 93%) was obtained as a viscous liquid: IR (neat) 1635, 1605 cm^{-1}; ^{1}H NMR δ 1.26–2.50 (m, 6H), 2.52–2.86 (m, 2H), 3.07 (dd, J = 15 and 4 Hz, 1H), 4.90 (bs, 1H), 4.98 (bs, 1H), 7.03–7.34 (m, 3H), 7.58 (d, J = 8 Hz, 1H). Anal. Calcd for C$_{13}$H$_{15}$Br: C, 62.14; H, 6.01. Found: C, 62.01; H, 5.82.

***trans*- and *cis*-2,3,3a,4,9,9a-Hexahydro-1*H*-benz[*f*]indene 37 and 38.** The olefin **43** (500 mg, 1.99 mmol) on radical cyclization gave the product as a gummy oil, which on careful chromatography over silica gel (20 g), using petroleum ether as eluent, gave a 67:33 mixture of **38** and **37** (294 mg, 86%) as revealed by coinjection with an authentic sample of the *trans*- and *cis*-hydrocarbon mixture described above.