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Bridged aromatic alkenes for the study of carbocation–π interaction

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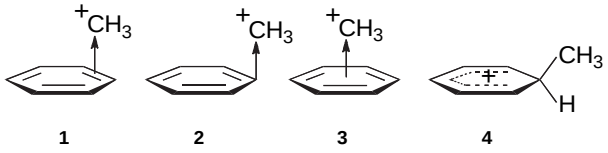
ABSTRACT

Toward the goal of gaining further insight into carbocation–π interactions, bridged-ring aromatic alkene model systems are being investigated in which one isomer will permit π complexation of an intramolecular tertiary carbocation with a benzene ring, but the other isomer will not. The syntheses of three sets of such isomers, having, respectively, benzobicyclo[3.2.1]octene, benzobicyclo[2.2.1]heptene, and benzobicyclo[4.2.1]nonene structures, are described.

1. Introduction

Cation–π interaction between positively charged species and aromatic amino acids has become recognized as an important contributor to binding in proteins.[1–3] Ample convincing evidence for this type of binding has emerged for ammonium, metal, and carbon cations. It was originally considered in all cases to have the cation in an η^6 complex with an aromatic ring, having 'electrostatic attraction between a positive charge and the quadrupole moment of the aromatic' as the dominant defining feature.[1] However, we have suggested[4] that complexes of aromatic rings with carbocations might well be expected to be fundamentally different in geometry and energy from those of ammonium or metal ions, with the carbocationic center located over the edge of the aromatic ring (η^2 complex) in order to maximize orbital interaction. This idea was supported by our computational study of the complexation of methyl cation with benzene.[4] In this study we found that, although they were not energy minima, both the η^2 complex **1** and the η^1 complex **2**, with the cation located above the periphery of the aromatic ring, were significantly more stable than the η^6 complex **3**, and had approximately 80% of the binding energy in stable σ complex **4**.[4] A recent additional computational study of complexation between methyl cation and benzene by Zheng et al.[5] confirmed and extended our results. Heidrich[6] has reported computations demonstrating that there is an energy minimum π complex between the *tert*-butyl cation and benzene in which the carbocation likewise is located peripherally over the aromatic ring, in agreement with similar unpublished results obtained in our laboratory.[7] More recently, it has been recognized [3] that orbital as well as electrostatic interactions contribute significantly to the cation-π binding of divalent metal ions. And Sherrill et al.[8] have very recently demonstrated computationally that cation–π interactions of metal and ammonium ions are significantly stabilizing even when the geometry varies so far from the η^6 model as to put the cation on the side of the aromatic ring.



In continuation of our efforts to better understand carbocation–π interactions, we have been seeking experimental information about their geometries and energies. This is obviously more difficult than investigating the cation–π interactions of ammonium or metal ions, because carbocations are unstable, highly reactive species. Our strategy has been to try to design intramolecular model systems in which one isomer will permit π complexation of a generated tertiary carbocation with a benzene ring, while the other isomer will not permit such complexation. This approach is generically illustrated in isomeric carbocationic structures **5** and **6**. Specific structural examples of **5** were selected for experimental investigation which molecular modeling indicated to have geometry appropriate for intramolecular carbocation–π interaction over the periphery of the benzene ring. These examples of **5** should also make intramolecular electrophilic aromatic substitution to form σ complexes of type **7** relatively unfavorable, because of the additional strain that would thereby

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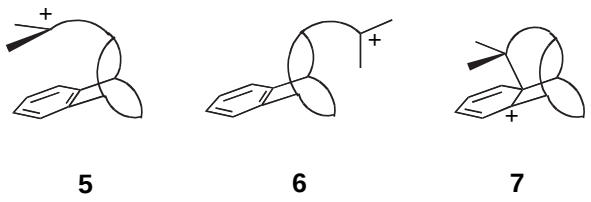


be introduced. Complexes between aromatic amino acids of proteins and biochemical carbocation intermediates presumably must avoid such σ complex formation.

This paper describes the syntheses of three sets of isomeric alkenes, which upon protonation, would afford carbocations that are predicted to meet these criteria. These isomeric pairs are the benzobicyclo[3.2.1]alkenes **8** and **9**, benzobicyclo[2.2.1]alkenes **10** and **11**, and benzobicyclo[4.2.1]alkenes **12** and **13**. Important precedents for the use of benzobicyclo frameworks in such studies are found in much earlier work of Lawton et al.[9] and Tanida and Muneyuki[10], who found modest rate accelerations due to aromatic π electron participation in the ionization of primary aryl sulfonates at the site of the tertiary carbocations that would be formed by protonation of the double bond in **8** or **10**, respectively.

In the present work, computations were performed using the M06 hybrid functional of Zhao and Truhlar[11] together with the cc-pVTZ basis set proposed by Dunning[12] for the carbocations derived from alkenes **8**, **10**, and **12**. The results encouragingly showed optimized equilibrium geometries for these three carbocation–π complexes **8H**$^+$, **10H**$^+$, and **12H**$^+$, as depicted in Figure 1. These have their positive centers 2.68 Å, 2.56 Å, and 2.66 Å, respectively, from the midpoint of the closest carbon–carbon bond of the benzene ring. These distances are slightly shorter but similar to our calculated

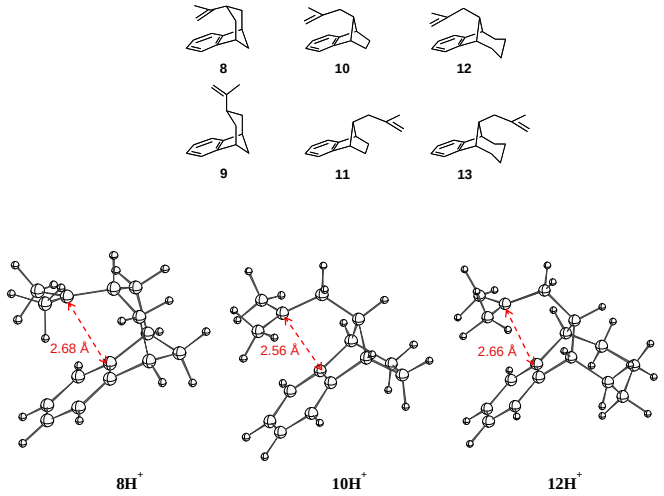
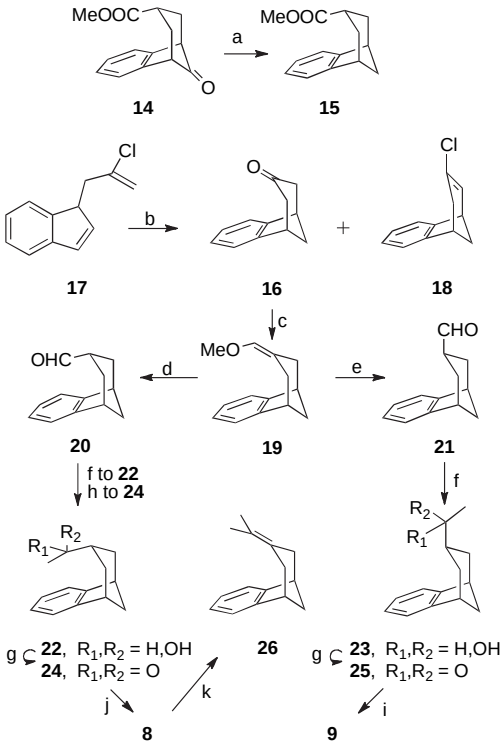


Figure 1. Structures of carbocations **8H**$^+$, **10H**$^+$, and **12H**$^+$ showing the distances from the carbocationic center to the midpoint of the closest C–C bond of the benzene ring calculated at the M06/cc-pVTZ level.

value of 3.06 Å for the analogous distance in the π complex of the *tert*-butyl cation with benzene,[7] which agrees closely with the value of 3.02 Å reported by Heidrich[6] using the MP2/6-31+G** method.

2. Benzobicyclo[3.2.1]octenes 8 and 9

Among the several reported methods[9,13–16] for constructing the benzobicyclo[3.2.1]octene ring system of alkenes **8** and **9**



Scheme 1. [a]Reagents: (a) (i) $ArSO_2NHNH_2$ (ii) $ZnCl_2$, $NaBH_3CN$; (b) 300 equiv 97% HCOOH, △, 18 h; (c) $MeOCH_2PPh_3Cl$, KO^{t}Bu, THF; (d) 10% HCl, THF, 25 min, rt; (e) *p*-TsOH, H_2O, dioxane, 20 h, △; (f) MeMgI, Et_2O; (g) PCC, CH_2Cl_2; (h) (i) $TMSCHN_2$, $MgBr_2$, hexanes, (ii) TBAF, THF; (i) $MePPh_3I$, KO^{t}Bu; (j) CH_2Br_2, Zn, $TiCl_4$, THF; (k) SiO_2.

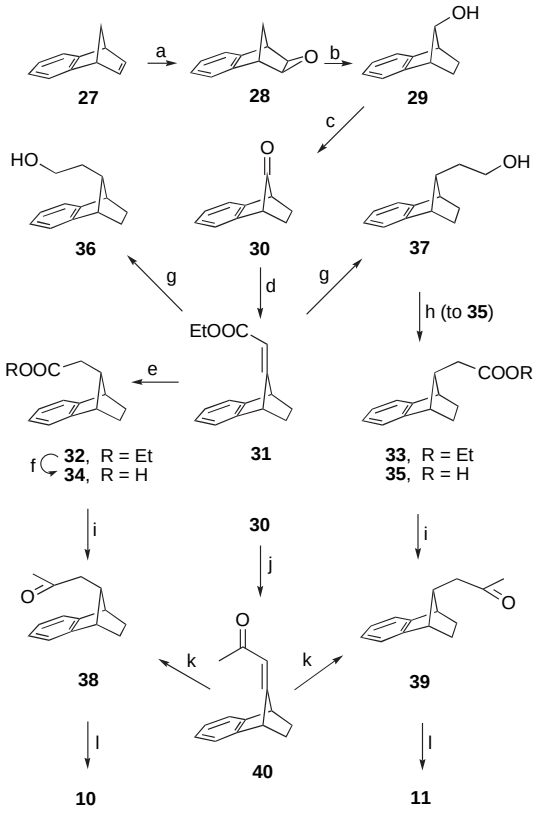
containing functionality suitable for introduction of the bridgehead propenyl group, two[9,15] were pursued experimentally (Scheme 1). Initially, Lawton's concise approach[9] to ketoester **14** by reaction of the pyrrolidine enamine of 2-indanone[17] with methyl β, β′-dibromoisobutyrate[18] was explored. This reaction afforded 33% of **14**, a slight improvement over the reported 28%,[9] but it proved difficult to remove the ketone carbonyl group without concomitantly epimerizing the carbomethoxyl group from the axial to the equatorial position. The best result in this reduction was obtained by the procedure of Kim et al.,[19] which afforded 29% of **14**, but the overall yield of **15** thus obtained led us to explore an alternate approach.

Lansbury's approach to ketone **16**,[14] modified slightly to incorporate Mazzochi's procedure[20] for the alkylation of indene to produce 70% of **17**, afforded the key intermediate **16** in 64% yield accompanied by 30% of **18**,[21] as shown in Scheme 1. Reaction of **16** with methoxymethylenetriphenylphosphorane afforded enol ether **19** in 85% yield, and **19** could be converted essentially quantitatively by mild acid hydrolysis (kinetic equatorial protonation) to axial aldehyde **20** or by vigorous acid hydrolysis to equatorial aldehyde **21**. The stereochemical assignments were supported by the shielding of the aldehyde proton in **20** (δ 8.68) versus that in **21** (δ 9.41), and confirmed by computations of chemical shifts at HFGIAO/6-31g* for B3LYP/cc-pVTZ optimized geometries of **20** (δ 8.65) and **21** (δ 9.35). These aldehydes were each converted with methyl Grignard reagent to secondary alcohols **22** and **23**, which were then oxidized to methyl ketones **24** and **25**, respectively. Because the yields of **22** and **23** were modest, direct conversion of aldehydes **20** and **21** to methyl ketones **24** and **25** was explored. In the case of **20**–**24** this was achieved in 55% yield by use of trimethylsilyldiazomethane,[22] followed by treatment with TBAF. To try to complete the syntheses of desired alkenes **8** and **9**, **24** and **25** were subjected to standard Wittig methylenation, but only equatorial alkene **9** was obtained from either ketone.

Methylenation of **24** without epimerization could be achieved, however, by use of Lombardo's reagent,[23] which gave 70% of **8** plus ca. 3% of rearranged alkene **26**, which could be obtained quantitatively from **8** upon silica gel chromatography.

3. Benzobicyclo[2.2.1]heptenes 10 and 11

The bicyclic framework of alkenes **10** and **11** was forged by the familiar Diels–Alder reaction of benzyne with cyclopentadiene to form benzonorbornadiene **27**.[24] Installation of functionality at the bridgehead was accomplished by the sequence of Bartlett and Giddings,[25] via epoxidation to **28**, reductive rearrangement to **29**, and oxidation to **30**, as shown in Scheme 2. Modifications to the



Scheme 2. [a]Reagents: (a) $MeReO_3$, H_2O_2, py, CH_2Cl_2; (b) $LiAlH_4$; (c) DMSO, ClCOCOCl, Et_3N, CH_2Cl_2; (d) NaH, THF, $EtOOCCH_2PO(OEt)_2$; (e) H_2, PtO_2 or Pd/C; (f) NaOH, H_2O; EtOH, △; (g) NH_3, Na, ^tBuOH, THF, −78 °C;(h) CrO_3, H_5IO_6, MeCN; (i) (i) 3 equiv CH_3Li, THF, (ii) TMSCl; (j) THF, NaH, $CH_3COCH_2PO(OMe)_2$; (k) H_2, Pd/C; (l) KO^tBu, $MePPh_3I$, PhMe.

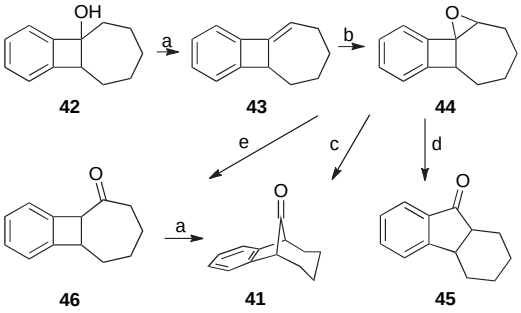
original sequence included the use of methyltrioxorhenium catalyzed epoxidation[26] of **27** in 97% yield, because the use of peracids appeared to induce some rearrangement of the type involved in the conversion of **28** to **29**, and the use of Swern oxidation[27] to convert **29** to **30** in 86% yield.

Ketone **30** has been converted by Tanida and Muneyuki[10] via Horner–Wadsworth–Emmons adduct **31** and catalytic hydrogenation to varying ratios of esters **32** and **33** depending on the reduction conditions. Separation of **32** and **33** by gas phase chromatography and hydrolysis afforded Tanida and Muneyuki[10] the individual carboxylic acids **34** and **35**. In our hands, catalytic hydrogenation of **31** invariably gave a preponderance of *syn* ester isomer **32**, so that this route led usefully only to acid **34**. On the other hand, dissolving metal reduction of **31** led to a 1:3 mixture of diols **36** and **37**, from which the isomeric carboxylic acid **35** could be obtained by crystallization, after oxidation of the mixture of **36** and **37** to **34** plus **35** with CrO_3 and H_5IO_6.[28] Treatment of each of **34** and **35** with excess methyl lithium according to Rubottom and Kim's procedure[29] produced isomeric methyl ketones **38** and **39**, respectively, in modest yields.

A much more direct and efficient preparation of **38** and **39** was achieved by reaction of **30** with dimethyl acetylmethylphosphonate,[30] which gave **40** in 86% yield. Hydrogenation of **40** over 10% Pd/C gave a 1.1:1 mixture of **38** and **39**, which proved readily separable by chromatography. Wittig reactions of **38** and **39** then provided the desired alkenes **10** and **11** in 74% and 73% yield, respectively.

4. Benzobicyclo[4.2.1]nonenes 12 and 13

Key intermediate ketone **41** in the benzobicyclo[4.2.1]nonene series was prepared by the method of Lombardo et al.[31] via the adduct **42** of benzyne with cycloheptanone enolate anion, which was obtained according to the procedure of Adam et al.[32] Conversion of **42** to **41** required acid-catalyzed dehydration to **43**, epoxidation to **44**, and carefully controlled rearrangement of **44** to **41**, as depicted in Scheme 3. Elution of **44** through an acidic alumina column as described[31] led in our hands to **41** contaminated with



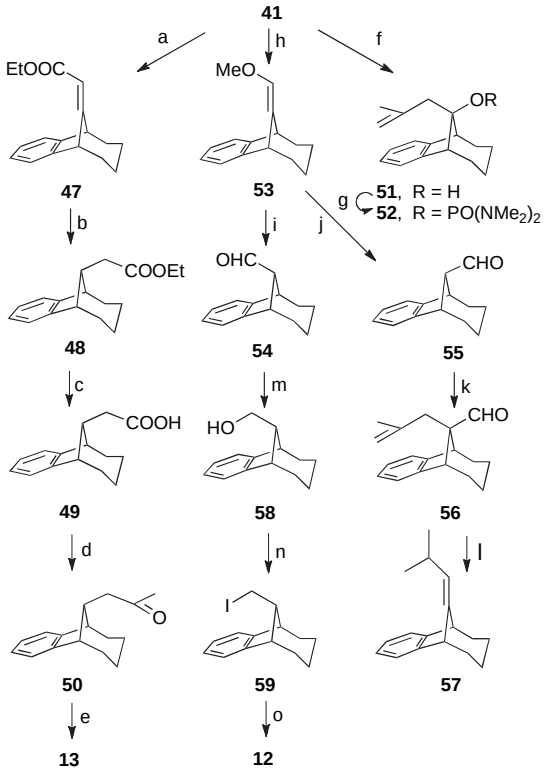
Scheme 3. [a]Reagents: (a) pTsOH, PhH, △; (b) *m*CPBA, CH_2Cl_2; (c) acidic Al_2O_3, CH_2Cl_2, 0 °C, 20 min; (d) acidic Al_2O_3 chromatography; (e) as in (c) with old Al_2O_3.

a considerable amount of alternate rearrangement product **45**. Stirring **44** in CH_2Cl_2 with fresh acidic alumina at 0 °C for 40 min afforded our best results, yielding 68% of **41** unaccompanied by **45**. Use of older alumina gave a mixture of **41** and **46**, although the latter could be converted to **41** upon further treatment with acid.

The first approach attempted for conversion of **41** to the desired alkenes **12** and **13** proceeded via Horner–Wadsworth–Emmons reaction to produce unsaturated ester **47** in 75% yield, as shown in Scheme 4, analogously to the Tanida approach[10] to bridgehead substitution in the benzobicyclo[2.2.1]heptene series. In that series, addition of hydrogen occurred from both sides of the alkene in useful amounts, but hydrogenation of **47** gave almost exclusively **48**, containing only 3% of its stereoisomer, in which the methylene quartet of the ester is slightly shielded relative to that in **48**. It was thus easy to complete synthesis of the *anti* alkene isomer **13**, via hydrolysis of **48** to **49**, reaction with excess CH_3Li[29] to give **50**, and Wittig methylenation to afford 78% of **13**.

Since our results with hydrogenation of **47** indicated a strong preference for addition *syn* to the benzene ring, our first approach to synthesis of isomeric *syn* alkene **12** consisted in addition of methallyl Grignard reagent to **41** to form **51**, followed by attempts to remove the tertiary hydroxyl group. When Ireland's method was used,[33] **51** was converted to tetramethylphosphoramidate **52**, but treatment of **52** with Li/NH_3 afforded only *anti* alkene **13** in 69% yield.[34]

The next approach to **12** commenced with Wittig methoxymethylenation of **41** to give 68% of enol ether **53**. As with enol ether **19** in the bicyclo[3.2.1]octene series, acidic hydrolysis of **53** could be conducted to afford either a kinetic or thermodynamic aldehyde product. In the case of **53**, the product of mild acid hydrolysis was *anti* aldehyde **54**, and the more stable product was **55** with the functional group in the *syn* position, the opposite order of stability



Scheme 4. [a]Reagents: (a) $EtOOCCH_2PO(OEt)_2$, NaH, THF; (b) H_2, PtO_2; (c) NaOH, H_2O, EtOH; (d) (i) 3 equiv MeLi, THF, (ii) TMSCl; (e) KO^{t}Bu, $MePPh_3I$, PhMe; (f) $H_2C{=}C(CH_3)CH_2Cl$, Mg, Et_2O; (g) ^{n}BuLi, THF, TMEDA, Cl_2PONMe_2; (h) $MeOCH_2PPh_3Cl$, KO^{t}Bu, THF; (i) 10% HCl, THF, △, 1.5 h; (j) 10% HCl, THF, rt, 45 min; (k) THF, KH, $H_2C{=}C(CH_3)CH_2Br$; (l) $(Ph_3P)_3RhCl$, PhCN, 180°C,8 h; (m) $NaBH_4$, EtOH; (n) Ph_3P, Im, I_2, MeCN. Et_2O; (o) Et_2O, Li, $H_2C{=}C(Br)CH_3$, −10 °C, 45 min, then CuI. (p) **52**→**13**: Li, NH_3, −78 °C; ^{t}BuOH, THF.

from aldehydes **20** and **21**. The key stereochemical assignments to **54** and **55** were made on the basis of their NMR spectra in comparison to literature data[35] and on the results of computation.[7] The bridgehead protons appear at δ 3.27 in **54** and at δ 2.82 in **55**. Tanida and Irie[35] report that the corresponding *anti* and *syn* isomers with a bridgehead hydroxyl group instead of a formyl group have their bridgehead protons at δ 4.72 and δ 4.27. (The formyl group proton of **54**, on the other hand appears at δ 9.62, shielded relative to the δ 10.25 signal for that proton in **55**.) The bridgehead proton of **54** is coupled with J=6.9 Hz to the benzylic protons, consistent with their computationally determined[7] 40° angular relationship, whereas the bridgehead proton of **55** displays negligible coupling to its benzylic protons, consistent with their 87° angular relationship. Optimized geometries and relative Gibbs free energies (G^{298}) calculated at the M06/cc-pVTZ level[7] predicted **55** to be 1.9 kcal/mol more stable than **54**, further confirming the stereochemical assignments.

The first attempt to convert **55** to target alkene **12** involved alkylation with methallyl bromide[36] to afford 59% of **56**, whose stereochemistry was clear from the correspondence between the ^{1}H NMR chemical shift of its aldehyde proton (δ 10.24 ppm) with that of *anti* aldehyde **55** (δ 10.25 ppm). Decarbonylation of **56** with Wilkinson's catalyst,[37,38] however, afforded no **12** and the ^{1}H NMR spectrum of the product suggested that rearranged alkene **57** had been formed, perhaps via elimination to a diene and selective reduction of the terminal double bond.[39]

Success in preparing *syn* alkene **12** was finally realized by reduction of aldehyde **54** to alcohol **58**,[40] conversion to iodide **59**,[41] and reaction of **59** with a 2-propenylcuprate.[42,43] The ^{1}H NMR spectra of **12** and **13** confirmed their stereochemistries. The bridgehead allylic methylene group of **12** appears at 2.49 ppm, but that in **13** is more shielded at 2.03. The bridgehead proton in **12** has δ 2.38, whereas that in **13** has δ 2.74 and shows larger coupling to the benzylic protons, as in **54**.

With all three isomeric pairs of alkenes, **8** and **9**, **10** and **11**, and **12** and **13**, in hand, studies of formation of tertiary carbocation by protonation of each of these compounds has become possible, and such experiments will be undertaken with the hope of gaining experimental evidence to compare with computational analyses of carbocation−π interactions in these systems.

5. Experimental section

5.1. Synthesis. General

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ unless otherwise indicated and are reported in units of δ, referenced to the solvent: ^{1}H, 7.27 ppm; ^{13}C 77.23 ppm. IR spectra of oils were recorded on a thin film between salt plates; IR spectra of solids were obtained from KBr pellets or from films deposited by evaporation of a CH_2Cl_2 solution on a polyethylene IR card. Melting points are uncorrected. Thin layer chromatography (TLC) was performed on EM or Whatman polyester sheets pre-coated with silica gel 60 F-254, Selecto Scientific polyester sheets pre-coated with Alumnia B F-254 200 m, or Whatman $MKC_{18}F$ reverse phase plates. All plates were visualized by a UV_{254} light source, exposure to iodine vapors, or staining with 5% phosphomolybdic acid in isopropyl alcohol. Flash column chromatography was carried out on EM Reagent or TSI Scientific silica gel 60 (230–400 mesh), aluminum oxide (activated basic, Brockmann I, 150 mesh), or Bakerbond™ Octadecyl (C_{18}) reverse phase 40 mM prep LC packing. Silica gel was used unless otherwise specified. HPLC was conducted using a Waters model 510 pump, model U-6 K injector, and model 481 tunable absorbance detector at 254 nm on a 5 μm Ultrasphere ODS semi-preparative HPLC column (10×300 mm, beckmann) with MeOH/H_2O (85:15, v/v) as eluent at a flow rate of 3 mL/min. $MgSO_4$ was used as a drying agent, unless otherwise noted. All reactions were magnetically stirred and performed under N_2. THF and ether were distilled from sodium and benzophenone. Methylene chloride, pyridine, diisopropylamine, and triethylamine were distilled from CaH_2. Chlorotrimethylsilane (TMSCl) was distilled from quinoline. Acetone was stirred over 3 Å sieves for 24 h and then distilled. Toluene was dried over 4 Å sieves overnight and then distilled onto 4 Å sieves. Dimethyl sulfoxide (DMSO) was distilled under reduced pressure onto 4 Å sieves, discarding the first 20% distilled. *tert*-Butyl alcohol was distilled from CaH_2 onto 3 Å sieves. Bromobenzene was dried over $CaCl_2$, refluxed with, and fractionally distilled from sodium (1% w/v). *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine (TMEDA) was refluxed with and distilled from KOH. Acetonitrile was refluxed with and fractionally distilled from CaH_2 onto 4 Å sieves. Benzonitrile was dried over $CaCl_2$, and distilled from P_4O_{10} under reduced pressure (69C/10 Torr). Powdered potassium hydride was obtained by washing KH (35% dispersion in mineral oil) three times with hexane under nitrogen, followed by drying the resulting white-light gray powder under vacuum at rt for 1 h prior to use. Copper(I) cyanide was dried overnight over KOH under vacuum at rt prior to use. Copper(I) iodide was dried overnight under vacuum at rt prior to use. Solvents were obtained from Fisher Scientific or Pharmco. All other reagents, unless otherwise noted, were obtained from Aldrich Chemical Co., Fisher Scientific, Acros Organics, Lancaster, or Janssen Chemica and were used without further purification unless otherwise indicated.

*5.1.1. 10-Oxo-6,7,8,9-tetrahydro-5H-5,9-methano-benzocycloheptene-7-endo-carboxylic acid methyl ester (**14**).* According to the procedure of Haslanger et al.,[9] 2-(*N*-pyrrolidyl)indene, prepared by the method of Blomquist and Moriconi,[17] and a 17:1 mixture of methyl ß,ß′-dibromoisobutyrate and methyl 2-(bromomethyl)

acrylate, prepared by the method of Cassady et al.,[44] were converted to a black solid that was sublimed at 85–95 °C (0.1 mm Hg) to yield 33% of colorless **14**, which was recrystallized from 1:1 hexanes/ether: mp 112–113 °C (lit.[9] yield 28%, mp 106–108 °C); ^{1}H NMR 7.20 (m, 4H), 3.37 (m, 2H), 3.17 (s, 3H), 3.02 (d, 2H), 2.47 (t, 1H), 2.33 (quartet of d, 2H); (lit.[9] ^{1}H NMR 7.25 (s, 4H), 3.6 (s, 3H)); ^{13}C NMR 216.6, 173.5, 139.0, 127.9, 124.5, 51.7, 51.2, 35.7, 35.1.

*5.1.2. 6,7,8,9-Tetrahydro-5H-5,9-methano-benzocycloheptene-7-endo-carboxylic acid methyl ester (**15**).* According to a procedure by Kim et al.[19] 1.00 g (4.35 mmol, 1.00 equiv) of **14** and 0.866 g (4.66 mmol, 1.07 equiv) of *p*-toluenesulfonylhydrazine were dissolved in 12 mL of methanol and stirred at rt under N_2 for 10 min. To the yellow solution was slowly added a mixture of 0.487 g (2.17 mmol, 0.50 equiv) of $ZnCl_2$ (precipitated from ether with dioxane)[45] and 0.279 g (4.43 mmol, 1.02 equiv) of sodium cyanoborohydride. The resulting solution was stirred at rt under N_2 for 20 min and then heated at reflux under N_2 for 7 h. After cooling, the solution was diluted with 16 mL of 0.1 N NaOH and extracted with 4×75 mL of ether. The ether extracts were washed with 2×50 mL of water, 2×50 mL of brine, dried, filtered, and evaporated to afford 1.03 g of an oily, yellow solid, which was chromatographed with 9:1 hexanes/EtOAc to afford 0.282 g (30%) of **15** as a clear oil, which crystallized in the refrigerator from 1:1 hexanes/ether to afford 0.275 g (29%) of **15**: mp 38.5–39.5 °C; ^{1}H NMR 7.15–7.18 (m, 4H), 3.11 (s, 3H), 3.09 (m, 2H), 2.53 (m, 2H), 2.45 (t, *J*=7.5 Hz, 1H), 2.22–2.30 (m, 1H), 1.95 (dd, *J*=13.8, 7.2 Hz, 2H), 1.71 (d, *J*=10.5 Hz, 1H); ^{13}C NMR 175.0, 145.9, 126.5, 123.9, 51.1, 45.4, 40.1, 35.9, 30.8. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.66; H, 7.49.

*5.1.3. 1-(2-Chloro-allyl)-1H-indene (**17**).* According to the procedure of Mazzocchi et al.,[20] indene was alkylated with 2,3-dichloropropene to give, after distillation, 70% of **17**: bp 79–80 °C, 2.0 mm Hg; ^{1}H NMR 7.61–7.29 (m, 4H), 6.95 (dd, 1H), 6.65 (dd, 1H, *J*=1.8, 5.7 Hz), 5.42 (s, 1H), 5.37 (m, 1H), 3.95 (m, 1H), 2.83 (dd, 1H, *J*=7.0, 7.2 Hz), 2.56 (dd, 1H, *J*=7.2, 8.8 Hz); (lit.[20] yield 71%, lit.[13b] ^{1}H NMR (CCl_4): 7.16 (m, 4H), 6.5 (q, 2H), 5.19 (s, 1H), 5.04 (s, 1H), 3.70 (m, 1H), 2.48 (dd, 2H)); ^{13}C NMR 146.4, 144.3, 141.5, 138.3, 131.7, 131.6, 127.1, 123.4, 121.4, 114.1, 47.7, 41.5.

*5.1.4. 7-Chloro-6,9-dihydro-5H-5,9-methano-benzocycloheptene (**18**) and 5,6,8,9-tetrahydro-5,9-methano-benzocyclohepten-7-one (**16**).* According to the procedure of Lansbury et al.,[14b] **17** was treated with 97% formic acid to afford, after chromatography on neutral alumina, 30% of brown, oily **18**: (lit.[14b] yield 29%); ^{1}H NMR 7.30 (m, 4H), 6.34 (d, *J*=7.8 Hz, 1H), 3.47–3.51 (m, 2H), 2.93 (m, 1H), 2.36 (dd, *J*=6.3, 11.1 Hz, 2H), 2.09 (d, 1H); (lit.[14b] ^{1}H NMR (90 MHz) 7.35 (m, 4H), 6.34 (d, 1H, *J*=9.0 Hz), 3.30–3.55 (m, 2H), 2.89 (m, 1H), 2.12–2.43 (m, 2H), 2.01 (d, 1H)); ^{13}C NMR 150.5, 145.4, 131.0, 129.5, 127.5, 126.6, 123.7, 120.9, 41.4, 41.3, 41.0, 39.8. Further elution gave material, which was triturated with *n*-pentane to afford 64% of **16**: mp 63.5–65 °C (lit.[14b] yield 59%, mp 64–66 °C); ^{1}H NMR δ 7.12–7.25 (m, 4H), 3.47 (m, 2H), 2.61 (q, 4H), 2.32–2.41 (m, 1H), 1.99 (d, *J*=11.1 Hz, 1H); ^{13}C NMR 209.8, 145.9, 127.4, 123.3, 49.0, 42.3, 40.2.

*5.1.5. 7-Methoxymethylene-6,7,8,9-tetrahydro-5H-5,9-methano-benzocycloheptene (**19**).* According to a modification of a procedure by Castedo et al.,[21] to a solution of 6.64 g (59.2 mmol) of potassium *tert*-butoxide in 175 mL of dry THF was added 12.2 g (35.5 mmol) of methoxymethyltriphenylphosphonium chloride. The resulting red mixture was stirred at rt under N_2 for 1.5 h and then 2.04 g (11.8 mmol) of **16** dissolved in 10 mL of dry THF was added in one portion. The mixture was stirred at rt under N_2 for 1 h, heated at reflux for 3 h, and quenched with saturated NH_4Cl solution. Most of the THF was evaporated and the resulting mixture was extracted with 4×30 mL of CH_2Cl_2, dried, filtered, and evaporated to ~5 mL. To this was added 20 mL of iodomethane and the resulting mixture was stirred at rt under N_2 for 1 h and flushed through a plug of silica gel with 4:1 hexanes/EtOAc. The filtrate was evaporated and dried in vacuo to afford 2.04 g (86%) of deep orange oily **19**, which was chromatographed with 9:1 hexanes/EtOAc to afford 1.89 g (80%) of **19** as a yellow oil: ^{1}H NMR 7.12–7.22 (m, 4H), 5.55 (s, 1H), 3.31 (s, 3H), 3.24 (m, 2H), 2.80 (m, 1H), 2.51 (m, 1H), 2.38 (m, 1H), 2.25 (m, 1H), 2.12 (m, 1H), 1.88 (d, *J*=10.8 Hz, 1H); ^{13}C NMR 147.1, 146.7, 143.6, 126.5, 126.3, 122.6, 122.4, 112.3, 59.1, 44.5, 41.6, 40.9, 35.6, 31.5. Anal. Calcd for $C_{14}H_{16}O$: C, 83.95; H, 8.05. Found: C, 83.77; H, 7.99.

*5.1.6. 6,7,8,9-Tetrahydro-5H-5,9-methano-benzocycloheptene-7-endo-carbaldehyde (**20**).* To 1.13 g (5.65 mmol) of **19** dissolved in 50 mL of THF was added 50 mL of 10% HCl. The resulting mixture was stirred at rt under N_2 for 25 min and extracted with 3×50 mL of CH_2Cl_2. The extracts were washed with 2×50 mL of water, dried, filtered, and evaporated to afford 1.04 g (99%) of orange, oily **20**, which was used without purification for further reactions: ^{1}H NMR 8.68 (s, 1H), 7.16 (m, 4H), 3.19 (m, 2H), 2.35 (m, 2H), 2.24 (m, 1H), 2.07 (m, 3H), 1.71 (d, *J*=10.8 Hz, 1H); ^{13}C NMR 202.5, 145.5, 127.6, 123.9, 44.4, 43.1, 39.9, 31.1. HRMS: calcd for $C_{13}H_{14}O$ (M^+): 186.1045. Found: 186.1046.

*5.1.7. 6,7,8,9-Tetrahydro-5H-5,9-methano-benzocycloheptene-7-exo-carbaldehyde (**21**).* A mixture of 0.471 g (2.74 mmol) of *p*-toluenesulfonic acid monohydrate, 31.5 mL of water, 132 mL of dioxane, and 2.25 g (11.2 mmol) of **19** was heated at reflux for 20 h, cooled to rt, diluted with 100 mL of water, and extracted with 5×50 mL of ether. The ether extracts were washed with 2×50 mL of water, dried, filtered, and evaporated to afford 1.54 g (75%) of orange, oily **21**, which was used without purification for further reactions: ^{1}H NMR 9.41 (s, 1H), 7.09 (m, 4H), 3.17 (m, 2H), 2.15 (m, 1H), 1.55–1.82 (m, 5H), 1.52 (d, *J*=10.8 Hz, 1H); ^{13}C NMR 204.3, 145.5, 127.0, 122.5, 44.2, 44.1, 40.1, 29.6. HRMS: calcd for $C_{13}H_{14}O$ (M^+): 186.1045. Found: 186.1041.

*5.1.8. 1-(6,7,8,9-Tetrahydro-5H-5,9-methano-benzocyclohepten-7-endo-yl)-ethanol (**22**).* According to a procedure by Leonard et al.,[45] in a flame-dried 250-mL 3-necked round-bottomed flask was placed 1.02 g (42.0 mmol, 5.0 equiv) of magnesium turnings, which had been washed in ether and dried under N_2 overnight, and a small crystal of iodine. Then a solution of 2.51 mL (40.3 mmol, 4.8 equiv) of iodomethane in 20 mL of ether was added slowly via syringe. The resulting mixture was stirred under N_2 as it turned cloudy and came to reflux on its own. After the magnesium was consumed and the reaction was no longer exothermic, a solution of 1.56 g (8.40 mmol, 1.0 equiv) of **20** in 40 mL of ether was added via syringe and the reaction was heated at reflux under N_2 for 4 h, allowed to cool to rt, poured over a mixture of 300 g of ice and 100 mL of sulfuric acid, and extracted with 4×50 mL of ether. The extracts were washed with 2×50 mL of brine, dried, filtered, and evaporated to afford 1.76 g (104%) of dark brown solid **22**, which was chromatographed with 15:83:1:1 EtOAc/hexanes/triethylamine/methanol to afford 0.88 g (53%) of pale yellow **22**, mp 83–86 °C, which was decolorized with carbon black and recrystallized from hexanes to afford 0.87 g (52%) of **22**: mp 85–86 °C; ^{1}H NMR 7.19 (m, 4H), 3.10 (m, 2H), 2.28 (m, 1H), 2.01 (m, 4H), 1.81 (d, 1H), 1.61 (m, 2H), 0.85 (d, 3H, and m, 1H); ^{13}C NMR 148.4, 148.2, 127.2, 127.0, 122.9, 122.8, 70.2, 43.7, 40.1, 39.5, 31.7, 29.6, 22.7. Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.98. Found: C, 82.98; H, 9.04.

*5.1.9. 1-(6,7,8,9-Tetrahydro-5H-5,9-methano-benzocyclohepten-7-exo-yl)-ethanol (**23**).* As in the preparation of **22**, 1.56 g (8.40 mmol, 1.0 equiv) of **21** was treated with methyl magnesium iodide and worked up to afford 1.76 g (104%) of dark brown solid **23**, which

was chromatographed with 15:83:1:1 EtOAc/hexanes/triethylamine/methanol to afford 0.85 g (50%) of pale yellow solid **23**, which was recrystallized from hexanes to afford 0.82 g (48%) of **23**: mp 60–61 °C; ^{1}H NMR δ 7.21 (m, 4H), 3.67 (m, 1H), 3.24 (m, 2H), 2.28 (m, 2H), 1.85 (m, 1H), 1.67 (d, 2H), 1.51 (m, 2H), 1.04 (d, 3H), 0.96 (m, 1H); ^{13}C NMR ($CDCl_3$) 146.5, 146.4, 126.5, 126.4, 122.3, 122.2, 71.9, 44.6, 40.8, 40.7, 37.7, 32.7, 31.7, 20.7. Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.98. Found: C, 83.26; H, 9.14.

*5.1.10. 1-(6,7,8,9-Tetrahydro-5H-5,9-methano-benzocyclohepten-7-endo-yl)-ethanone (**24**). Method* A. According to a procedure by Corey and Suggs,[46] to a suspension of 2.15 g (9.99 mmol, 2.0 equiv) of pyridinium chlorochromate (PCC) in 10 mL of CH_2Cl_2 was added a solution of 0.94 g (4.65 mmol, 1.0 equiv) of **22** in 12 mL of CH_2Cl_2. The mixture was stirred under N_2 at rt for 2.5 h and 20 mL of anhyd ether was added. The supernatant liquid was decanted and the insoluble black gum was washed several times with ether. The supernatant liquid and combined ether washings were passed through a short pad of Florisil, evaporated, and dried to afford 0.88 g (93%) of pale yellow **24**, mp 48–51 °C, which was decolorized with carbon black and recrystallized from hexanes to afford 0.86 g (92%) of **33**: mp 64–65 °C; ^{1}H NMR 7.13 (m, 4H), 3.11 (m, 2H), 2.58 (m, 2H), 2.25 (m, 2H), 2.03 (dd, 2H), 1.74 (d, 1H), 1.69 (s, 3H); ^{13}C NMR 208.2, 145.9, 126.9, 123.8, 45.4, 44.7, 39.9, 30.4, 26.7. Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 84.05; H, 8.12.

Method B. According to a modification of a procedure by Aoyama and Shioiri,[22] to solution at 0 °C of 530 mg (2.8 mmol, 1.0 equiv) of **20** in 28 mL of ether and 4.3 mL of a 1 M solution of $MgBr_2$ (4.3 mmol, 1.5 equiv) was added 1.7 mL of a 2.0 M solution of trimethylsilyldiazomethane in hexanes (3.4 mmol, 1.2 equiv), dropwise. The mixture was stirred under N_2 at 0 °C for 30 min and at rt for 4 h, and then was treated with a cold solution of 945 mg (3.6 mmol, 1.27 equiv) of tetrabutylammonium fluoride in THF, stirred for 3 min, diluted with 50 mL of water, and extracted with 4×50 mL of ether. The ether extracts were washed with 2×75 mL of water and 2×75 mL of brine, dried, filtered, and evaporated to afford 626 mg of yellow oily **24**, which was chromatographed with 9:1 heptane/EtOAc to afford 322 mg (57%) of **24**.

*5.1.11. 1-(6,7,8,9-Tetrahydro-5H-5,9-methano-benzocyclohepten-7-exo-yl)ethanone (**25**).* As in the preparation of **24** by method A, 0.973 g (4.81 mmol) of **23** was oxidized with PCC and worked up to afford 0.860 g (89%) of oily **25**: ^{1}H NMR 7.19 (m, 4H), 3.26 (m, 2H), 2.21 (m, 1H), 1.99 (s, 3H), 1.81 (m, 5H), 1.61 (d, 1H); ^{13}C NMR 211.8, 145.8, 127.0, 122.6, 44.9, 44.2, 40.6, 31.8, 28.2. Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.70; H, 8.18.

*5.1.12. 7-endo-Isopropenyl-6,7,8,9-tetrahydro-5H-5,9-methano-benzocycloheptene (**8**).* According to a procedure by Lombardo,[23] to a suspension of 4.19 g (64.1 mmol, 4.3 equiv) of zinc dust, which had been activated by washing with 10% HCl for 10 min, followed by filtration, rinsing with water and acetone, and drying in a vacuum oven overnight, and 1.46 mL (21.0 mmol, 1.4 equiv) of CH_2Br_2 in 38 mL of THF under N_2 at −40 °C was added 1.65 mL (15.0 mmol, 1.0 equiv) of titanium tetrachloride, dropwise over 15 min. The mixture was stirred under N_2 for 80 h at −5 °C, during, which time it became a gray slurry, and was then added in portions to a solution of 294 mg (1.46 mmol) of **24** in 30 mL of CH_2Cl_2 until TLC indicated complete consumption of starting material. The reaction mixture was poured into saturated aqueous $NaHCO_3$/water (2:1) and ether and shaken until a clear organic layer was obtained. The organic layer was washed with 2×15 mL of water, dried, filtered, and evaporated to afford 271 mg (93%) of a 3:1 mixture of oily **8** and **26**. HPLC with 85:15 MeOH/H_2O afforded separation of **8**: ^{1}H NMR of **8**: 7.14 (m, 4H), 4.40 (s, 1H), 4.25 (s, 1H), 3.13 (m, 2H), 2.58 (m, 1H), 2.39–2.22 (m, 2H), 1.91–2.14 (m, 4H), 1.44 (s, 3H); ^{13}C NMR 149.6, 147.7, 126.4, 126.3, 122.7, 122.4, 108.6, 69.6, 40.5, 39.5, 36.7, 31.8, 25.6, 21.2. HRMS: calcd for $C_{15}H_{18}$ (M^+): 198.1409. Found: 198.1407.

*5.1.13. 7-Isopropylidene-6,7,8,9-tetrahydro-5H-5,9-methano-benzocycloheptene (**26**).* Flash chromatographic purification of 271 mg of crude **8** on silica gel (Lagand Chemical Company, pH 6–7) with 4:1 hexanes/EtOAc yielded 146 mg (50%) of pale yellow solid **26**, which was recrystallized from *n*-pentane to afford 140 mg (48%) of **26**: mp 59.5–61 °C; ^{1}H NMR 7.16 (m, 4H), 3.20 (m, 2H), 2.44 (q, 4H), 2.25 (m, 1H), 1.79 (d, 1H), 1.44 (s, 6H); ^{13}C NMR 147.7, 126.4, 125.1, 122.4, 43.1, 41.0, 35.7, 20.2. Anal. Calcd for $C_{15}H_{18}$: C, 90.85; H, 9.15. Found: C, 90.83; H, 9.13.

*5.1.14. 7-exo-Isopropenyl-6,7,8,9-tetrahydro-5H-5,9-methano-benzocycloheptene (**9**).* According to a modification of a procedure by Deb et al.,[47] to a slurry of 1.05 g (3.36 mmol) of methyltriphenylphosphonium iodide in 4 mL of toluene was added 3.36 mL of a 1 M solution of potassium *tert*-butoxide (3.36 mmol) in toluene. The mixture was stirred under N_2 at rt for 20 min. To the resulting yellow solution was added 224 mg (1.12 mmol, 1.0 equiv) of **25** in 3.5 mL of toluene dropwise. The resulting mixture was heated at reflux for 2 h while being stirred under N_2, allowed to cool to rt, quenched with 20 mL of saturated NH_4Cl solution, and extracted with 5×20 mL of ether. The extracts were washed with 2×30 mL of 5% aqueous NH_4Cl and 2×50 mL of water, dried, and filtered. Most of the solvent was evaporated and the residue was dissolved in petroleum ether, treated with 10 mL of iodomethane, stirred under N_2 at rt for 1 h, and passed through a plug of silica gel with 4:1 hexanes/EtOAc. The filtrate was evaporated and dried in vacuo to afford 168 mg of material that was chromatographed with hexanes to afford 111 mg (50%) of colorless, oily **9**. ^{1}H NMR 7.19 (m, 4H), 4.66 (s, 1H), 4.63 (s, 1H), 3.24 (br s, 2H), 2.27 (m, 1H), 1.65–1.77 (m, 6H), 1.65 (s, 3H); ^{13}C NMR 149.9, 146.6, 126.7, 122.4, 108.8, 45.1, 41.4, 37.9, 35.0, 21.2. HRMS: calcd for $C_{15}H_{18}$ (M^+): 198.1409. Found: 198.1412.

*5.1.15. (1α,4α)-Dihydro-1,4-methano-naphth[2,3-β]oxirene (**28**).* According to a procedure by Rudolph et al.,[26] in a 100-mL round-bottomed flask was placed 7.9 g (0.056 mol) of **27**, prepared by the method of Mich et al.,[24] 0.073 g (0.5 mol %) of methyltrioxorhenium, 0.55 mL (12 mol %) of pyridine and 40 mL of CH_2Cl_2. The flask was placed in an ice–water bath and 10 mL (0.11 mol, 2 equiv) of 30% H_2O_2 was added via syringe and the reaction was allowed to warm to rt and stirred overnight. The aqueous layer was separated, a few milligrams of MnO_2 was added to the organic layer, and the CH_2Cl_2 layer was dried over Na_2SO_4 filtered, and evaporated to give 8.57 g (97%) of **28**: ^{1}H NMR: 7.35–7.34 (m, 2H), 7.18–7.15 (m, 2H), 3.51–3.49 (m, 4H), 2.08–2.05 (d, J=9.0 Hz, 1H), 1.67–1.62 (t, J=8.7 Hz, 1H) (lit.[48] ^{1}H NMR): 7.25–7.00 (m, 4H), 3.36 (m, 4H), 1.97 (dt, J=1.5, 8.8 Hz, 1H), (1.49 (m, 1H)). If necessary, the crude **28** could be chromatographed on silica gel that had been washed with 19:1 hexanes/Et_3N, eluting with 99:1 hexanes/Et_2N to afford a 93% recovery.

*5.1.16. 1,2,3,4-Tetrahydro-1,4-methano-naphthalen-9-one (**30**).* Reduction of **28** with $LiAlH_4$, according to the procedure of Bartlett and Giddings,[25] afforded 86% of **29**, mp 99.5–100.5 °C (lit.[21] mp 103.0–104.6 °C). According to a procedure by Mancuso et al.,[27] in an oven-dried 250-mL, 3-necked round-bottomed flask, fitted with a $CaSO_4$ drying tube, an addition funnel, and a septum, was placed 50 mL of CH_2Cl_2 and 12.0 mL of a 2.0 M solution of oxalyl chloride in CH_2Cl_2, and the flask was placed in a dry ice–acetone bath. A solution of 3.40 mL (0.0479 mol, 2.2 equiv) of anhyd DMSO in 10 mL of CH_2Cl_2 was added via addition funnel. The mixture was stirred for 2 min, and a solution of 3.41 g (0.0214 mol) of **29** in 20 mL of CH_2Cl_2 was added over 5 min. The reaction was stirred for 15 min, 15.0 mL (0.108 mol, 5 equiv) of Et_3N was added, and the cooling bath was removed. The

mixture was stirred overnight, diluted with 100 mL of distilled H_2O, and the layers were separated. The aqueous layer was extracted with 6×25 mL of CH_2Cl_2. The combined organic layers were washed with 50-mL portions of 1% HCl, H_2O, 5% Na_2CO_3, H_2O, and 25 mL of brine. The organic layer was dried, filtered, and evaporated to give 3.57 g of brown oil, which was chromatographed with CH_2Cl_2 to give 2.89 g (86%) of oily **30**: ^{1}H NMR 7.34–7.24 (m, 4H), 3.37–3.35 (t, *J*=2.1 Hz, 2H), 2.24–2.20 (m, 2H), 1.42–1.36 (m, 2H); (lit.[49] ^{1}H NMR (CCl_4)): 7.18 (6 m, 4H), 3.22 (m, 2H), 2.08 (m, 2H), 1.24 (m, 2H).

*5.1.17. (1,2,3,4-Tetrahydro-1,4-methano-naphthalen-9-ylidene)-acetic acid ethyl ester (**31**).* According to a modification of a procedure by Schmidt et al.,[50] to a stirred suspension of 2.42 g (60.4 mmol) of NaH (60% dispersion in mineral oil) in 70 mL of THF cooled to −78 °C was added 10.6 mL (53.4 mmol) of triethylphosphonoacetate via syringe. The dry ice–acetone bath was removed and the resulting homogeneous solution was stirred at rt for 1 h. The mixture was cooled to −78 °C, and a solution of 4.16 g (26.3 mmol) of **30** in 10 mL of THF was added dropwise. The dry ice–acetone bath was removed and the resulting solution was stirred overnight. The mixture was poured over ice, extracted with 3×125 mL of ether, and the combined ether extracts were washed with water and brine, dried, filtered, and evaporated to give 11.9 g of a yellow oil, which was chromatographed on basic alumina with 19:1 hexanes/EtOAc to give 5.55 g (92%) of oily **31**: ^{1}H NMR 7.31–7.19 (m, 4H), 5.47 (s, 1H), 4.80–4.79 (d, *J*=3.6 Hz, 1H), 4.27–4.20 (q, *J*=7.2 Hz, 2H), 3.66–3.65 (d, *J*=3.6 Hz, 1H), 2,13–2.09 (m, 2H), 1.45–1.43 (d, *J*=6.6 Hz, 2H), 1.38–1.33 (t, *J*=7.2 Hz, 3H).

*5.1.18. 2-(1,2,3,4-Tetrahydro-1,4-methano-naphthalen-9-endo-yl)-ethanol (**36**) and 2-(1,2,3,4-Tetrahydro-1,4-methano-naphthalen-9-exo-yl)-ethanol (**37**).* In a flame-dried 50-mL 3-necked round-bottomed flask was placed 5 mL of THF, 0.51 g (22.4 mmol, 9.6 equiv) of freshly cut Na, 0.53 g (2.3 mmol) of **31**, and 0.65 g (8.8 mmol, 3.8 equiv) of *tert*-butyl alcohol in 5 mL of anhyd THF. The flask was placed in a dry ice–acetone bath and 20 mL of NH_3 was introduced by distillation. The cooling bath was removed and the mixture was stirred for 45 min and diluted with 50 mL of ice water. The aqueous layer was extracted with 4×25 mL of CH_2Cl_2. The combined CH_2Cl_2 layers were dried, filtered, and evaporated to give 0.40 g (92%) of a 1:3 mixture of **36** and **37**, as indicated by ^{1}H NMR integration of the benzylic proton signals. Chromatography using either silica gel with 7:3 hexanes/EtOAc or C_{18} reverse phase packing with 19:1 MeOH/H_2O afforded no separation of **36** and **37**: ^{1}H NMR 7.20–7.07 (m, 8H), 3.71–3.66 (t, *J*=6.9 Hz, 3H), 3.59–3.11 (t, *J*=6.8 Hz, 1H), 3.15 (s, 1H), 3.11 (s, 3H), 2.19 (s, 0.17H), 2.12 (t, 0.53H), 2.01–1.94 (m, 6H), 1.75 (br s, 2H), 1.59–1.52 (m, 3H), 1.32–1.25 (m, 1H), 1.22–1.15 (m, 1H).

*5.1.19. (1,2,3,4-Tetrahydro-1,4-methano-naphthalen-9-endo-yl)-acetic acid (**34**).* According to a procedure by Adams et al.,[51] in a 100-mL 3-necked round-bottomed flask was placed 50 mL of EtOAc, 2.70 g (0.18 mmol) of **31**, and 0.057 g (2 mol %) of PtO_2. The flask was flushed several times with H_2, and the mixture was stirred under balloon pressure of H_2 for 22 h and filtered through a bed of Celite with EtOAc. The solvent was evaporated to give 2.45 g (90%) of a 4:1 mixture of **32** and **33**, as determined by integration of the benzylic proton signals in the ^{1}H NMR spectrum: 3.21 (s, 1.5H), 3.18 (s, 0.4H). According to a modification of a procedure by Muneyuki and Tanida,[10] a mixture of 7.83 g (0.0340 mol) of a 4:1 mixture of **32** and **33**, 2.76 g (0.0689 mol, 2 equiv) of NaOH, 90 mL of H_2O, and 30 mL of EtOH was heated at reflux and stirred for 3 h, cooled to rt and stirred overnight, then brought to pH ~0 by addition of 6 M HCl, and extracted with 4×100 mL of ether. The combined ether layers were dried over Na_2SO_4, filtered, and evaporated to give 5.28 g (77%) of a 4:1 mixture of acids **34** and **35**, as indicated by ^{1}H NMR. Recrystallization twice from hexane provided 2.45 g (45%) of **34**: mp 103–104.5 °C (lit.[10] mp 104.5–105.5 °C); ^{1}H NMR 7.20–7.10 (m, 4H), 3.22 (s, 2H), 2.39–2.34 (t, *J*=6.6 Hz, 1H), 2.10–2.00 (m, 4H), 1.27–1.20 (m, 2H); ^{13}C NMR 180.2, 145.5, 126.3, 122.4, 56.3, 47.8, 33.2, 27.5.

*5.1.20. (1,2,3,4-Tetrahydro-1,4-methano-naphthalen-9-exo-yl)-acetic acid (**35**).* According to a procedure by Zhao et al.,[28] to a solution of 0.1307 g (0.695 mmol) of a 1:3 mixture of **36** and **37** in 10 mL of CH_3CN at 0 °C was added 11.5 mL of a solution of 0.0020 M CrO_3 and 0.44 M H_5IO_6 in CH_3CN over 20 min. The mixture was stirred at 0 °C for 40 min, and a solution of 0.75 g of K_2HPO_4 in 10 mL of water was added, followed by 15 mL of toluene. The organic layer was extracted with 2×10 mL of a 1:1 brine/water, a solution of 0.22 g of $NaHCO_3$ in 5 mL of water, and 5 mL of brine, dried, filtered, and evaporated to give 0.13 g (95%) of a 3:1 mixture of **35** and **34**, as indicated by ^{1}H NMR. Recrystallization from hexanes afforded 0.027 g (29%) of **35**: mp 93.5–95 °C (lit.[10] 99–99.5 °C): ^{1}H NMR 7.18–7.08 (m, 4H), 3.20 (s, 2H), 2.38–2.32 (m, 3H), 1.96–1.93 (m, 2H), 1.24–1.18 (m, 2H); ^{13}C NMR 179.2, 148.4, 125.8, 120.7, 54.7, 46.4, 34.1, 24.2.

*5.1.21. 1-(1,2,3,4-Tetrahydro-1,4-methano-naphthalen-9-ylidene)-propan-2-one (**40**).* According to a procedure by Thangaraj et al.,[30] in an oven-dried 50-mL round-bottomed flask, under N_2, were placed 10.0 mL of THF, 0.077 g of NaH (60% dispersion in mineral oil, 1.93 mmol, 1.4 equiv), and 0.26 mL (1.88 mmol, 1.4 equiv) of dimethyl acetylmethylphosphonate. The resulting mixture was stirred at rt for 1 h and a solution of 0.21 g (1.33 mmol) of **30** in 5.0 mL of THF was added. The mixture, which turned thick and opaque, was stirred at rt overnight and then poured over 50 mL of distilled H_2O. The aqueous layer was extracted with 3×50 mL of $CHCl_3$. The combined $CHCl_3$ layers were dried, filtered, and evaporated to give 0.47 g of pale yellow oil, which was chromatographed with 9:1 hexanes/ether to give 0.23 g (86%) of **40**: ^{1}H NMR 7.35–7.24 (m, 4H), 5.89 (s, 1H), 4.83–4.82 (d, *J*=3.6 Hz, 1H), 3.66–3.64 (d, *J*=3.6 Hz, 1H), 2.31 (s, 3H), 2.18–2.13 (m, 2H), 1.51–1.48 (m, 2H); ^{13}C NMR 198.6, 171.0, 145.4, 145.0, 126.7, 126.6, 121.0, 120.5, 110.6, 48.6, 43.8, 31.3, 26.1, 25.9. Anal. Calcd for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 84.57; H, 7.18.

*5.1.22. 1-(1,2,3,4-Tetrahydro-1,4-methano-naphthalen-9-endo-yl)-propan-2-one (**38**). Method* A. According to a procedure by Rubottom and Kim,[29] to an ice-cold solution of 1.01 g (4.99 mmol) of **34** in 40 mL of THF was added 10.8 mL (14.8 mmol, 3 equiv) of MeLi (1.37 M in ether) all at once via syringe. The mixture was stirred at 0 °C for 2.5 h, then 13.0 mL (0.102 mol, 21 equiv) of TMSCl, freshly distilled from quinoline, was added quickly with vigorous stirring. The ice bath was removed and the reaction mixture was stirred overnight. Then 40 mL of 1 N HCl was added and the mixture was stirred for 0.5 h and extracted with 3×60 mL of ether. The combined ether layers were washed with 50 mL of water, dried, filtered, and evaporated to give 1.05 g of pale yellow oil, which was chromatographed with CH_2Cl_2 to afford 0.50 g (50%) of oily **38**: ^{1}H NMR 7.19–7.09 (m, 4H), 3.16 (s, 2H), 2.41–2.35 (t, *J*=7.1 Hz, 1H), 2.18–2.15 (d, *J*=6.9 Hz, 2H), 2.04–2.00 (overlapping 3H and 2H m), 1.22–1.16 (m, 2H); ^{13}C NMR 208.8, 146.0, 126.2, 122.2, 55.6, 47.8, 42.5, 30.7, 27.6. Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.80; H, 8.13.

Method B. According to a procedure by Horning et al.,[52] in a 500-mL round-bottomed flask was placed 6.71 g (0.0338 mol) of **40**, 250 mL of EtOAc, and 2.160 g (2.03 mmol, 6 mol %) of 10% Pd/C. The flask was flushed with N_2, then several times with H_2. The reaction mixture was stirred overnight under balloon pressure of H_2 and then filtered through a bed of Celite with EtOAc. The solvent was evaporated to give 6.48 g (96%) of a 1.1:1 mixture of **38** and **39**. The mixture was chromatographed with 9:1 hexanes/EtOAc to give 2.79 g (41%) of **38**, 1.40 g of a 1:4.4 mixture of **38** and **39**, and 2.29 g (34%) of **39**.

*5.1.23. 1-(1,2,3,4-Tetrahydro-1,4-methano-naphthalen-9-exo-yl)-propan-2-one (**39**).* Prepared as described above: ^{1}H NMR 7.17–7.06 (m, 4H), 3.13–3.12 (m, 2H), 2.42–2.40 (d, *J*=7.2 Hz, 2H), 2.32–2.27 (t, *J*=7.8 Hz, 1H), 2.17 (s, 3H), 1.92–1.88 (m, 2H), 1.27–1.15 (m, 2H); ^{13}C NMR 208.1, 148.6, 125.7, 120.7, 54.4, 46.4, 43.5, 30.4, 24.3. Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.82; H, 7.97.

*5.1.24. 9-endo-(2-Methyl-allyl)-1,2,3,4-tetrahydro-1,4-methano-naphthalene (**10**).* As in the preparation of **9**, 3.55 g (32.2 mmol) of potassium *tert*-butoxide, 12.77 g (32.0 mmol) of methyltriphenylphosphonium iodide, and 2.30 g (0.010 mol) of **38** gave 7.35 g of orange oil, which after treatment with 3.0 mL of iodomethane, gave 2.20 g of yellow oil, which was chromatographed with hexanes to give 1.47 g (74%) of colorless oily **10**: ^{1}H NMR 7.32–7.22 (m, 4H), 4.82 (m, 1H), 4.64 (m, 1H), 3.25 (s, 2H), 2.35–2.30 (t, *J*=7.5 Hz, 1H), 2.14–2.10 (m, 2H), 1.86–1.82 (overlapping 3H s and 2H m), 1.35–1.33 (m, 2H); ^{13}C NMR 146.3, 145.5, 125.8, 122.0, 110.5, 59.1, 47.6, 36.1, 27.7, 23.2. Anal. Calcd for $C_{15}H_{18}$: C, 90.85; H, 9.15. Found: C, 90.64; H, 9.01.

*5.1.25. 9-exo-(2-Methyl-allyl)-1,2,3,4-tetrahydro-1,4-methano-naphthalene (**11**).* As in the preparation of **10**, 0.96 g (4.82 mmol) of **39** afforded 1.79 g of yellow oil, which was chromatographed with hexane to give 0.70 g (73%) of **11** as a colorless oil: ^{1}H NMR 7.21–7.10 (m, 4H), 4.81–4.78 (m, 2H), 3.13–3.11 (m, 2H), 2.16–2.11 (t, *J*=7.5 Hz, 1H), 2.05–1.99 (m, 2H), 1.80 (s, 3H), 1.23–1.17 (m, 2H); ^{13}C NMR 149.4, 144.7, 125.5, 120.6, 111.0, 57.7, 46.2, 37.3, 24.4, 22.8. Anal. Calcd for $C_{15}H_{18}$: C, 90.85; H, 9.15. Found: C, 90.57; H, 9.26.

*5.1.26. 5,6,7,8,9,9a-Hexahydro-benzo[3,4]cyclobuta[1,2]cyclohepten-4b-ol (**42**).* According to the procedure of Adam et al.,[32] cycloheptanone and bromobenzene were converted in 90% yield to **42** as a yellow solid, which was recrystallized from hexanes to give colorless **42**: mp 95.5–97.5 °C (lit.[32] mp 95 °C); ^{1}H NMR 7.31–7.14 (m, 4H), 3.51–3.46 (d of d, 1H), 2.35 (s, 1H), 2.21–2.14 (m, 2H), 1.93 (t, 1H), 1.85–1.62 (m, 4H), 1.54–1.38 (m, 3H); (lit.[32] ^{1}H NMR 7.50–7.10 (4H), 3.35 (m, 1H), 2.30 (s, 1H), 2.20–1.10 (m, 10H)); ^{13}C NMR 149.4, 145.9, 129.4, 127.7, 123.2, 120.9, 83.9, 60.6, 36.4, 32.2, 31.0, 27.8, 24.4.

*5.1.27. 5,6,7,8-Tetrahydro-4bH-benzo[3,4]cyclobuta[1,2]cycloheptene (**43**).* According to a procedure by Caubere et al.,[53] a mixture of 7.60 g (40.4 mmol) of **42**, 0.437 g (2.29 mmol) of *p*-toluenesulfonic acid monohydrate, and 280 mL of benzene was heated at reflux for 20 h. The mixture was cooled to rt, washed with 5% NaHCO solution, water, and brine, dried, filtered, and evaporated to give 6.56 g (95%) (lit.[52] 80%) of **43** as a brown oil, which solidified in the freezer at −15 °C: ^{1}H NMR 7.26–7.12 (m, 4H), 6.07–6.02 (t of d, 1H), 3.82–3.76 (d of d, 1H), 2.33–2.24 (m, 3H), 2.12–2.04 (m, 1H), 1.96–1.88 (m, 1H), 1.59–1.20 (m, 3H); (lit.[53] ^{1}H NMR δ (CCl_4) 7.35–6.77 (m, 4H), 6.07–5.78 (t of d, 1H), 3.95–3.50 (m, 1H), 2.50–0.85 (m, 8H)); ^{13}C NMR 148.7, 145.9, 143.4, 127.9, 127.7, 122.2, 119.4, 118.5, 52.5, 32.8, 30.7, 29.3, 28.9.

*5.1.28. 5,6,7,8,9,9a-Hexahydro-benzo[3,4]cyclobuta[1,2]-cyclohepten-4,5β-oxirene (**44**).* According to the procedure of Lombardo et al.,[31] **43** was epoxidized to afford 92% of oily **44**: ^{1}H NMR 7.39–7.12 (m, 4H), 3.83–3.78 (d of d, 1H), 3.54–3.52 (m, 1H), 2.29–2.21 (m, 1H), 2.17–2.11 (m, 1H), 2.00–1.91 (m, 1H), 1.87–1.47 (m, 5H); (lit.[31] ^{1}H NMR δ (CCl_4) 7.40–6.86 (m, 4H), 3.90–3.48 (m, 1H), 3.43–3.23 (m, 1H), 2.48–1.18 (m, 8H)); ^{13}C NMR 147.7, 143.9, 129.8, 128.2, 121.8, 121.5, 70.4, 59.4, 51.5, 28.9, 26.8, 25.2, 17.3.

*5.1.29. Tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-trien-13-one (**41**).* According to a modification of a procedure by Lombardo et al.,[31] to a stirred suspension of 61.2 g of Brockmann I activated, acidic alumina in 250 mL of CH_2Cl_2 at 0 °C was added a solution of 1.24 g (6.66 mmol) of **44** in 5 mL of CH_2Cl_2. The resulting slurry was stirred for 20 min at 0 °C and filtered through a fritted funnel. The alumina pad was washed several times with CH_2Cl_2. The total contact time of the organic material with alumina was 40 min. Evaporation of the filtrates gave 0.720 g (58%) of **41** as a pale yellow oil: ^{1}H NMR 7.30–7.22 (m, 4H), 3.61–3.58 (d of d, 2H), 2.04–1.95 (m, 2H), 1.73–1.66 (m, 2H), 1.44–1.32 (m, 4H); (lit.[54] ^{1}H NMR (CCl_4) 7.2 (s, 4H), 3.47 (m, 2H), 2.5–0.7 (m, 8H)); ^{13}C NMR: 217.7, 142.8, 127.9, 123.7, 52.9, 32.1, 24.7.

*5.1.30. Conversion of **44** to **41** plus 1,2,3,4,4a,9a-hexahydro-fluoren-9-one (**45**).* According to a modification of a procedure by Lombardo et al.,[31] 2.51 g (13.5 mmol) of **44** was left adsorbed on a Brockmann I activated, acidic alumina column (175 g) in hexane for 12 min. The column was then eluted with 19:1 hexanes/EtOAc to give 0.051 g (2%) of **41** containing a small amount of impurities by NMR. During the collection of fractions warming of the bottom of the column was observed. Further elution gave 1.11 g (44%) of a 2:1 mixture of **41** and **45** as a pale yellow oil: ^{1}H NMR 7.76 (d, 1H, **45**), 7.58 (5, 1H, **45**), 7.46 (d, 1H, **45**), 7.37 (t, 1H, **45**), 7.30–7.22 (m, 4H, **41**), 3.61–3.58 (d of d, 2H, **41**), 3.43–3.36 (m, 1H, **45**), 2.80–2.74 (m, 1H, **45**), 2.17–2.06 (m, 2H, **45**), 2.04–1.95 (m, 2H, **41**), 1.83–1.15 (m, 6H, **45**+m, 6H, **41**) (lit.[55] ^{1}H NMR for **45** 7.80–7.27 (m, 4H), 3.42–3.34 (m, 1H), 2.79–2.73 (m, 1H), 2.17–2.04 (m, 2H), 1.81–1.16 (m, 6H)).

*5.1.31. Conversion of **44** to 4b,6,7,8,9,9a-hexahydro-benzo[3,4]cyclobuta[1,2]cyclohepten-5-one (**46**) and **41**.* According to a modification of a procedure by Lombardo et al.,[31] to a stirred suspension of 36 g of Brockmann I activated, acidic alumina (old reagent) in 150 mL of CH_2Cl_2 at 0 °C was added a solution of 0.72 g (3.91 mmol) of **44** in 5 mL of CH_2Cl_2. The slurry was stirred for 20 min at 0 °C and filtered through a fritted funnel. The alumina pad was washed several times with CH_2Cl_2. The total contact time of the organic material with alumina was 35 min. Evaporation of the filtrates gave 0.51 g (71%) of a 1.5:1 mixture of **46** and **41** as a colorless viscous oil: ^{1}H NMR 7.32–7.08 (m, 4H, **46** and m, 4H, **41**), 4.55 (d, 1H, **46**), 3.91–3.83 (m, 1H, **46**), 3.62–3.59 (d of d, 2H, **41**), 2.62–1.27 (m, 8H, **46** and m, 8H, **41**); (lit.[31] ^{1}H NMR ($CDCl_4$) for **46**: 7.23–6.84 (m, 4H), 4.35 (d, 1H), 3.75 (m, 1H), 2.63–1.16 (m, 8H)). Then, according to a procedure by Lombardo et al.,[31] 0.16 g (0.84 mmol) of *p*-toluenesulfonic acid monohydrate was added to a solution of 0.373 g (2.00 mmol) of the 1.5:1 mixture of **46**:**41** in 45 mL of benzene, and the resulting solution was heated at reflux for 5 min, and then allowed to cool to rt. The benzene was evaporated and the resulting residue was dissolved in 100 mL of ether, washed with 5% $NaHCO_3$ solution to neutral pH and brine, dried, and passed through a neutral alumina plug. Evaporation of the filtrate gave 0.313 g of **41** (73% conversion of **46** to **41**) as a yellow oil containing traces of impurities by NMR.

*5.1.32. Tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-trien-13-ylidene-acetic acid ethyl ester (**47**).* As in the preparation of **31**, 2.67 g (66.7 mmol) of NaH (60% dispersion in mineral oil) and 11.9 mL (59.9 mmol) of triethylphosphonoacetate, plus 5.47 g (29.4 mmol) of **41** gave 5.61 g (75%) of **47** as a pale yellow oil. A small amount of this oil was rechromatographed (19:1 hexanes/EtOAc) to give a colorless oil, which crystallized to afford colorless **47**: mp 41–41.5 °C; ^{1}H NMR 7.22–7.14 (m, 4H), 5.87–5.86 (m, 1H), 4.80–4.78 (d of d, 1H), 4.25–4.17 (q of d, 2H), 3.91–3.89 (d of d, 1H), 2.28–2.18 (m, 1H), 1.85–1.76 (m, 2H), 1.71–1.63 (m, 1H), 1.48–1.36 (m, 2H), 1.32 (t, 3H), 1.26–1.07 (m, 2H); ^{13}C NMR 170.4, 166.5, 147.1, 144.3, 127.6, 127.3, 123.3, 122.9, 112.9, 59.9, 51.9, 47.3, 36.3, 33.3, 25.0, 24.4, 14.6. Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86; Found: C, 79.56; H, 7.87.

*5.1.33. Tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-trien-13-exo-yl-acetic acid ethyl ester (**48**).* According to a modification of a procedure by Adams et al.,[51] a mixture of 2.01 g (7.85 mmol) of **47** and 0.041 g (0.180 mmol) of PtO_2 in 50 mL of EtOAc was stirred at rt under an

H_2 atmosphere for 22 h. The mixture was passed through a short pad of Celite and the solvent was evaporated to give 1.87 g (92%) of a colorless oil. A small amount of this oil was chromatographed with 19:1 hexanes/EtOAc to give oily **48** containing ca. 3% of the *syn* isomer as indicated by ^{1}H NMR: ^{1}H NMR 7.16 (s, 4H), 4.23–4.15 (q, 2H), 3.33–3.28 (m, 2H), 2.96 (quintet, 1H), 2.74 (d, 2H), 1.97–1.86 (m, 2H), 1.82–1.72 (m, 2H), 1.49–1.36 (m, 2H), 1.30 (t, 3H), 1.25–1.09 (m, 2H); ^{13}C NMR 173.6, 148.6, 126.7, 123.4, 60.5, 46.0, 44.4, 33.7, 31.5, 25.1, 14.5. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58; Found: C, 79.11; H, 8.57.

*5.1.34. Tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-trien-13-exo-yl-acetic acid (**49**).* Roughly as in the preparation of **34**, a mixture of 1.49 g (5.77 mmol) of **48**, 0.467 g (11.7 mmol) of crushed NaOH pellets, and 60 mL of 1:3 EtOH/H_2O was heated at reflux for 20 h, cooled to 0 °C, and acidified with 6 M HCl to pH=0, which precipitated 1.15 g (87%) of colorless **49**, mp 119.5–124.5 °C, which was recrystallized from hexane to give **49**: mp 136–136.5 °C; ^{1}H NMR 7.17 (s, 4H), 3.38–3.33 (m, 2H), 2.97 (quintet, 1H), 2.81 (d, 2H), 1.98–1.88 (m, 2H), 1.84–1.74 (m, 2H), 1.49–1.35 (m, 2H), 1.22–1.10 (m, 2H); ^{13}C NMR 179.5, 148.4, 126.8, 123.4, 45.9, 44.1, 33.3, 31.5, 25.1. Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88; Found: C, 78.09; H, 7.86.

*5.1.35. 1-Tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-trien-13-exo-yl-propan-2-one (**50**).* Roughly as in the preparation of **38**, to an ice-cold solution of 0.626 g (2.72 mmol) of **49** in 30 mL of THF was added 6.00 mL of a 1.4 M solution of MeLi in ether (8.40 mmol) and the resulting mixture was stirred at 0 °C for 2.5 h. Then 8.00 mL (63.0 mmol) of distilled TMSCl was added at once and the mixture was allowed to warm to rt, stirred for 20 h, diluted with 30 mL of 1 M HCl, stirred at rt for 0.5 h, and extracted with ether. The ether extracts were washed with water and brine, dried, filtered, and evaporated to give 0.708 g of a viscous oil, which was chromatographed with 9:1 hexanes/EtOAc to give 0.369 g (60%) of oily **50**: ^{1}H NMR 7.16 (s, 4H), 3.31–3.26 (m, 2H), 2.98 (quintet, 1H), 2.86 (d, 2H), 2.24 (s, 3H), 1.91–1.70 (m, 4H), 1.47–1.34 (m, 2H), 1.21–1.08 (m, 2H); ^{13}C NMR 208.6, 148.6, 126.7, 123.4, 45.9, 43.1, 42.8, 31.7, 30.4, 25.1; IR: 1715 cm^{-1}. Anal. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 83.89; H, 8.80.

*5.1.36. 13-exo-(2-Methyl-allyl)-tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-triene (**13**).* As in the preparation of **9**, 0.624 g (1.54 mmol) of methyltriphenylphosphonium iodide, 0.174 g (1.55 mmol) of potassium *tert*-butoxide, and 0.117 g (0.513 mmol) of **50** gave 0.404 g of material, which after treatment with 0.12 mL (1.93 mmol) of iodomethane, gave 0.139 g of a yellow oil, which was chromatographed with hexanes to give 0.090 g (78%) of **13** as a colorless oil: ^{1}H NMR 7.19 (s, 4H), 4.87–4.86 (m, 1H), 4.84–4.83 (m, 1H), 3.28–3.23 (m, 2H), 2.74 (quintet, 1H), 2.50 (d, 2H), 2.06–1.96 (m, 2H), 1.84 (s, 3H), 1.82–1.71 (m, 2H), 1.57–1.44 (m, 2H), 1.24–1.11 (m, 2H); ^{13}C NMR 149.3, 145.4, 126.5, 123.4, 110.9, 46.2, 46.1, 36.6, 31.6, 25.3, 22.7. Anal. Calcd for $C_{17}H_{22}$: C, 90.20; H, 9.80. Found: C, 90.12; H, 9.92.

*5.1.37. 13-endo-(2-Methyl-allyl)-tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-trien-13-ol (**51**).* According to a modification of a procedure by Paquette et al.,[56] to a flame-dried flask containing 0.714 g (29.4 mmol) of Mg powder were added a few crystals of iodine and 4 mL of ether. This mixture was heated at reflux and treated dropwise with a solution of 1.00 mL (10.1 mmol) of distilled methallyl chloride in 17 mL of ether. The mixture turned into a viscous gray slurry, which was stirred at reflux for 1 h. Then 0.977 g (5.25 mmol) of **41** in 10 mL of ether was added dropwise and the resulting mixture was heated at reflux for 18.5 h, cooled in an ice bath, quenched with 2 M HCl solution, and extracted with ether. The combined ether extracts were washed with saturated $NaHCO_3$ solution (to neutral pH) and brine, dried, filtered, and evaporated to give 1.45 g of a yellow oil, which was chromatographed with 3:1 hexanes/CH_2Cl_2 to give 0.652 g (51% or 69% based on reacted **41**) of **51** as a colorless oil: ^{1}H NMR 7.19–7.11 (m, 4H), 4.95–4.93 (m, 1H), 4.70–4.69 (m, 1H), 3.14–3.12 (d of d, 2H); 2.27 (s, 2H), 2.09–1.98 (m, 3H), 1.83 (s, 3H), 1.75–1.53 (m, 4H), 1.22–1.10 (m, 2H); ^{13}C NMR 146.6, 143.4, 126.9, 124.0, 115.0, 83.2, 51.9, 49.6, 31.4, 25.3, 25.0.

Further elution with CH_2Cl_2 gave 0.248 g (25%) of **41**.

5.2. Synthesis of 13 via 52

According to a procedure by Liu et al.,[57] to a solution of 0.407 g (1.68 mmol) of **51** in 10 mL of 4:1 THF/TMEDA was added 1.14 mL (2.52 mmol) of a 2.21 M solution of ^{n}BuLi in hexane. The resulting dark yellow slurry was stirred at rt for 20 min and upon addition of 1.00 mL (8.39 mmol) of Cl_2PONMe_2 again became a clear yellow solution which was stirred at rt for 20 h during which time it turned into a milky slurry. The mixture was then cooled to 0 °C and treated with approximately 6.5 mL of Me_2NH, obtained by dropwise addition of 20 mL of 40 wt % Me_2NH solution over NaOH pellets, passage of the gas formed through a NaOH drying tube, and condensation on a cold finger. The mixture was then stirred at 0 °C for 1 h, poured into water, and extracted with ether. The combined ether extracts were washed with water, saturated NH_4Cl solution (to neutral pH), dried, filtered, and evaporated to give 0.599 g of a viscous yellow oil, which was chromatographed with 3:1 CH_2Cl_2/EtOAc to give 0.338 g (53%) of **52** as a pale yellow oil: ^{1}H NMR 7.13–7.09 (m, 2H), 7.03–6.99 (m, 2H), 4.65 (s, 1H), 4.57–4.56 (m, 1H), 3.55–3.52 (d of d, 2H), 2.83 (s, 2H), 2.73 (s, 6H), 2.69 (s, 6H), 2.24–2.09 (m, 2H), 1.74–1.64 (m, 2H), 1.62–1.49 (m, 2H), 1.42 (s, 3H), 1.18–1.08 (m, 2H); ^{13}C NMR 145.7, 141.8, 126.9, 123.6, 114.5, 93.5, 52.3, 52.2, 48.2, 37.5, 37.4, 31.4, 24.5, 24.4.

According to a modification of procedures by Ireland et al.,[33] and Muchmore,[58] 0.016 g (2.31 mmol) of Li wire was added to 10 mL of NH_3 (condensed on a cold finger) at −78 °C. The resulting deep blue solution was stirred at −78 °C for 10 min, treated with a solution of 0.074 g (0.196 mmol) of **52** and 0.038 mL (0.40 mmol) of *tert*-butyl alcohol in 3 mL of THF, and stirred at −78 °C for 20 min. The dry ice–acetone bath was removed, the NH_3 was allowed to evaporate, and the mixture was cooled to 0 °C, quenched with water, and extracted with ether. The combined ether extracts were washed with saturated NH_4Cl solution (to neutral pH) and brine, dried, filtered, and evaporated to give 0.046 g of an oil, which was chromatographed (hexane) to give 0.031 g (69%) of **13** as a colorless oil containing small amounts of impurities as indicated by ^{1}H NMR.

*5.2.1. 13-Methoxymethylene-tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-triene (**53**).* According to a modification of a procedure by Novak and Salemink,[59] to 14.9 g (133 mmol) of potassium *tert*-butoxide in 250 mL of THF was added 32.0 g (93.3 mmol) of methoxymethyltriphenylphosphonium chloride, and the resulting brick red mixture was stirred at rt for 1.5 h. A solution of 4.96 g (26.6 mmol) of **41** in 23 mL of THF was added dropwise, the resulting mixture was stirred at rt for 1 h, heated at reflux for 15 h, cooled to rt, quenched with saturated NH_4Cl solution and extracted with ether. The ether extracts were washed with water and brine, dried, filtered, and evaporated to give 30.8 g of a burgundy oil, which was dissolved in 85 mL of CH_2Cl_2, treated with 30 mL of MeI, and stirred at rt for 2 h. Then the solution was diluted with 500 mL of 9:1 hexanes/EtOAc, and passed through a short pad of silica gel, which allowed separation of 16.7 of a brown granular solid. The resulting filtrate was evaporated to give 9.4 g of an orange solid, which was triturated with hexane to give 2.9 g of a white solid, and 5.1 g of a brown oil. This oil was chromatographed on basic alumina using gradient elution with hexanes, 32:1 and 19:1 hexanes/EtOAc to give 3.88 g

(68%) of oily **53**: ^{1}H NMR 7.17–7.14 (m, 4H), 5.99 (m, 1H), 4.60–4.13 (1H), 3.75–3.72 (1H), 3.60 (s, 3H), 2.00–1.90 (m, 1H), 1.82–1.58 (m, 3H), 1.54–1.41 (m, 2H), 1.24–1.04 (m, 2H); ^{13}C NMR 147.9, 147.2, 139.2, 126.9, 126.7, 125.1, 123.2, 122.9, 59.8, 46.1, 43.8, 37.7, 34.1, 25.3, 24.9. Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 83.93; H, 8.55.

*5.2.2. Tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-triene-13-endo-carbaldehyde (**54**).* According to a modification of a procedure by Novak and Salemink,[59] a mixture of 3.67 g (17.1 mmol) of **53**, 150 mL of 10% HCl solution, and 150 mL of THF was heated at reflux for 1.5 h, cooled to rt and extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed with water and brine, dried, filtered, and evaporated to give 3.60 g of yellow oil, which was chromatographed with 9:1 hexanes/EtOAc to give 2.79 g (81%) of oily **54**: ^{1}H NMR 9.62 (d, 1H, J=1.8 Hz), 7.19–7.16 (m, 4H), 3.73–3.70 (d of d, 2H), 2.82 (d, 1H, J=1.8 Hz), 2.00–1.90 (m, 2H), 1.85–1.75 (m, 2H), 1.53–1.42 (m, 2H), 1.28–1.16 (m, 2H); ^{13}C NMR 204.9, 146.2, 127.6, 123.5, 59.1, 44.3, 34.9, 24.9. HRMS: calcd for $C_{14}H_{16}O$ (M^+): 200.120115. Found: 200.119826.

*5.2.3. Tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-triene-13-exo-carbaldehyde (**55**).* According to a modification of a procedure by Novak and Salemink,[59] a mixture of 0.214 g (1.00 mmol) of **53**, 9 mL of 10% HCl solution, and 9 mL of THF was stirred at rt for 45 min and extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed with water and brine, dried, filtered, and evaporated to give 0.161 g (81%) of slightly impure yellow oily **55**: ^{1}H NMR 10.25 (s, 1H), 7.21 (s, 4H), 3.80–3.75 (m, 2H), 3.22 (t, 1H), 2.21–2.10 (m, 2H), 1.78–1.69 (m, 2H), 1.31–1.12 (m, 4H); ^{13}C NMR 203.8, 146.9, 127.3, 123.6, 58.1, 43.6, 32.3, 24.9.

*5.2.4. 13-endo(2-Methyl-allyl)-tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-triene-13-carbaldehyde (**56**).* According to a modification of a procedure by Groenewegen et al.[36] to a slurry of 0.043 g (1.07 mmol) of KH powder in 6 mL of THF was added 0.138 g (0.690 mmol) of **55** in 3 mL of THF to give, after bubbling ceased, a pale yellow solution, which was stirred at rt for 15 min. Then a solution of 0.100 mL (0.99 mmol) of methallyl bromide in 3 mL of THF was added dropwise, and the mixture was stirred at rt for 75 min, quenched with water, and extracted with ether. The ether extracts were washed with water and brine, dried, filtered, and evaporated to give 0.104 g (59%) of **56** as a pale yellow oil, which was chromatographed on basic alumina with 19:1 hexanes/EtOAc to give **56**: ^{1}H NMR 10.24 (s, 1H), 7.22–7.15 (m, 4H), 4.85–4.82 (m, 1H), 4.49–4.48 (m, 1H), 3.47–3.44 (d of d, 2H), 2.30 (s, 2H), 2.20–2.12 (m, 2H), 1.78–1.71 (m, 2H), 1.65 (s, 3H), 1.29–1.12 (m, 4H); ^{13}C NMR 206.7, 146.2, 141.6, 127.2, 124.1, 115.9, 61.5, 49.4, 47.6, 31.7, 24.7, 24.6. Anal. Calcd for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.70; H, 8.78.

5.3. Attempted decarbonylation of 56

According to a modification of a procedure by Ohno and Tsuji,[37] a mixture of 0.055 g (0.216 mmol) of **56**, 0.203 g (0.219 mmol) of Wilkinson's catalyst and 2 mL of benzonitrile was heated at 180 °C for 48 h, during which time the mixture turned from reddish-brown to dark brown-black. The mixture was cooled to rt, the benzonitrile was removed by distillation under vacuum, EtOH was added, and a black solid separated. This solid was removed by filtration, and evaporation of the brown filtrate gave 0.132 g of a brown solid residue. This residue was triturated with hexane to afford 0.066 g of a brown solid, and evaporation of the hexane solution gave 0.054 g of a residue, which was chromatographed with hexane to give 0.013 g of an oil, which contained **57** as indicated by the following characteristic signals in the ^{1}H NMR spectrum; ^{1}H NMR 7.17–7.14 (m, 4H), 5.19–5.15 (d, 1H), 4.00–3.99 (d, 1H), 3.70–3.67 (d of d, 1H), 1.04 (d, CH_3), 0.97 (d, CH_3).

*5.3.1. Tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-trien-13-endo-yl-methanol (**58**).* According to a modification of a procedure by Takahashi et al.,[40] to an ice-cold solution of 2.59 g (12.9 mmol) of **54** in 30 mL of absolute EtOH was added dropwise a solution of 0.340 g (8.99 mmol) of $NaBH_4$ in 100 mL of EtOH. The resulting solution was stirred at 0 °C for 1.5 h, quenched with 10% HCl solution and extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed with saturated $NaHCO_3$ solution, brine, dried, filtered, and evaporated to give 2.28 g (87%) of **58**, which crystallized after being kept under vacuum for 2 days. Recrystallization from hexane gave colorless **58**: mp 84.5–85 °C; ^{1}H NMR 7.18–7.12 (m, 4H), 3.46 (d, 2H), 3.20–3.17 (d of d, 2H), 2.34 (t, 1H), 1.96–1.85 (m, 2H), 1.78–1.68 (m, 2H), 1.55–1.43 (m, 3H), 1.23–1.11 (m, 2H); ^{13}C NMR 147.4, 127.0, 123.9, 66.1, 49.5, 45.9, 35.3, 25.1. Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.89; H, 8.93.

*5.3.2. 13-endo-Iodomethyl-tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-triene (**59**).* According to a modification of a procedure by Millar and Underhill,[60] to an ice-cold solution of 4.72 g (18.0 mmol) of triphenylphosphine and 1.23 g (18.0 mmol) of imidazole in 44 mL of 1:3 CH_3CN/ether was added 4.57 g (18.0 mmol) of iodine in three portions with vigorous stirring over 20 min to give a yellow-brown slurry, which was stirred at rt for 25 min, cooled to 0 °C, and a solution of 0.909 g (4.50 mmol) of **58** in 20 mL of 1:3 CH_3CN/ether was added dropwise. The resulting mixture was stirred at rt for 18 h, during which time it turned bright yellow. The mixture was cooled to 0 °C, 100 mL of pentane was added, and a bright yellow solid formed. The pentane was decanted and 100 mL of 5% $NaHCO_3$ solution was added gradually, producing a dark yellow granular sticky residue. After separation from the aqueous phase this residue was triturated with pentane, and the combined pentane extracts were dried, filtered, and evaporated to give 1.25 g of an oil, which was chromatographed with hexane to give 1.02 g (72%) of **59** as a colorless oil: ^{1}H NMR 7.21–7.14 (m, 4H), 3.26–3.23 (2H), 3.16 (d, 2H), 2.57 (t, 1H), 1.97–1.86 (m, 2H), 1.77–1.68 (m, 2H), 1.52–1.40 (m, 2H), 1.23–1.11 (m, 2H); ^{13}C NMR 146.5, 127.3, 124.3, 50.5, 50.4, 35.0, 24.8, 14.3. Anal. Calcd for $C_{14}H_{17}I$: C, 53.86; H, 5.49; I, 40.65. Found: C, 53.79; H, 5.51; I, 40.78.

*5.3.3. 13-endo-(2-Methyl-allyl)-tricyclo[6.4.1.0^{2,7}]trideca-2(7),3,5-triene (**12**).* According to modifications of procedures by Posner[42] and Vig et al.,[43] to a cooled (−10 °C) mixture of 0.241 g (34.7 mmol) of small pieces of Li wire in 8 mL of ether was added a solution of 1.54 mL (17.3 mmol) of 2-bromopropene in 5 mL of ether, and the mixture was stirred for 45 min, during which time all the Li dissolved. The resulting gray solution was transferred via syringe to a slurry of 1.65 g (8.68 mmol) of CuI in 12 mL of ether at −10 °C. The brown mixture was stirred for 30 min at −10 °C. A solution of 0.541 g (1.73 mmol) of **59** in 5 mL of ether was added dropwise, during which time the mixture turned black and was then stirred at −10 °C to −5 °C for 4 h, and at rt for 16 h. The mixture was quenched by addition of saturated NH_4Cl solution and extracted with ether. The combined ether extracts were washed with saturated NH_4Cl solution, water, and brine, dried, filtered, and evaporated to give 0.375 g of oil, which was chromatographed with hexane to give 0.244 g (62%) of **12** as a colorless oil: ^{1}H NMR 7.18–7.12 (m, 4H), 4.77–4.76 (m, 1H), 4.61–4.60 (m, 1H), 3.07–3.04 (2H), 2.32 (t, 1H), 1.98 (d, 2H), 1.92–1.81 (m, 2H), 1.74 (s, 3H), 1.72–1.65 (m, 2H), 1.52–1.42 (m, 2H), 1.22–1.09 (m, 2H); ^{13}C NMR 147.9, 145.2, 126.8, 124.0, 111.2, 49.0, 43.9, 43.3, 35.4, 25.2, 22.8. Anal. Calcd for $C_{17}H_{22}$: C, 90.20; H, 9.80. Found: C, 90.25; H, 9.83.

5.4. Computations

All structures and energies reported in this work were calculated using Gaussian 09.[61]

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