(phenylcarbonyl)piperidine, 37586-22-4; 4-((4-fluorophenyl)-carbonyl)piperidine, 56346-57-7; *N*-(2-(3,4-dimethoxyphenyl))-piperazine, 86136-56-3; *N*-methyl-3,4-dimethoxyphenethylamine, 3490-06-0; *N*-methyl-2,3,4-trimethoxyphenethylamine, 32042-11-8; *N*-methyl-3,4,5-trimethoxyphenethylamine, 4838-96-4; methylamine, 74-89-5; 4-((4-chlorophenyl)carbonyl)piperidine, 53220-41-0; 2-(3,4,5-trimethoxyphenyl)ethylamine, 54-04-6; *N*-ethyl-3,4,5-trimethoxyphenylethylamine, 112947-24-7; *N*-(methylethyl)-3,4,5-trimethoxyphenylethylamine, 58418-70-5; *N*-cyclopropyl-3,4,5-trimethoxyphenylethylamine, 112947-25-8; *N*-methyl-2,3,4-trimethoxyphenylpropylamine, 112947-26-9; *N*-methyl-2-(3,4-dimethoxyphenyl)propylamine, 112947-27-0.

Synthesis and Pharmacological Evaluation of 5,6-*exo*-Epoxy-7-oxabicyclo[2.2.1]heptane Derivatives[1]

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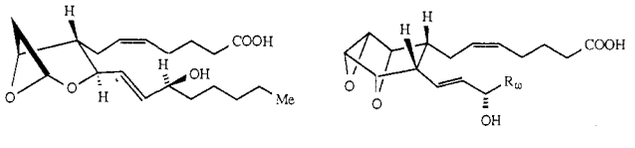
[1α,2β(5*Z*),3β(1*E*,3*S*),4α,5α,6α]-7-[5,6-Epoxy-3-(3-cyclohexyl-3-hydroxy-3-methyl-1-propenyl)-7-oxabicyclo[2.2.1]-hept-2-yl]-5-heptenoic acid (**31**) and [1α,2β(5*Z*),3β(1*E*,3*S*),4α,5α,6α]-7-[5,6-epoxy-3-[3-hydroxy-5-(*p*-hydroxyphenyl)-1-pentenyl]-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic acid (**37**) were found to be selective TxA_2 antagonists at the platelet and pulmonary thromboxane receptors. An efficient stereospecific synthesis of these compounds and a series of structural analogues is described. Compounds **31** and **37** both inhibited the bronchoconstriction induced by arachidonic acid in the anesthetized guinea pig.

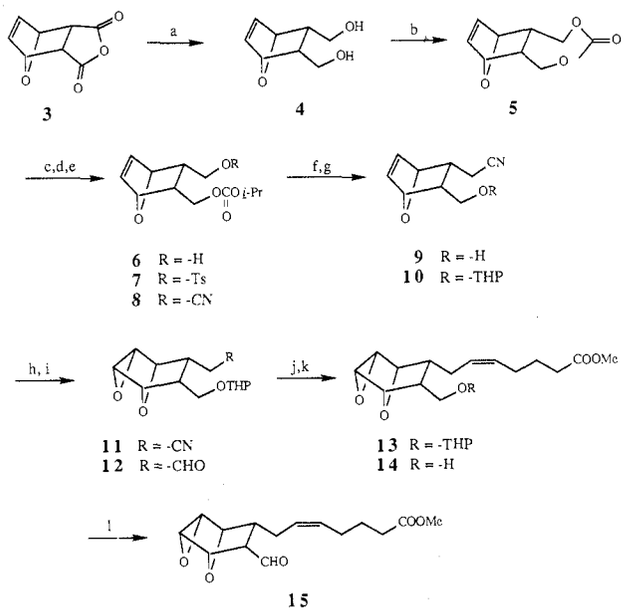
Arachidonic acid (AA) is metabolized by platelets into thromboxane A_2 (TxA_2),[2] which is a powerful inducer of platelet aggregation[3] and of vascular[4] and pulmonary[5] smooth muscle contraction. Overproduction of TxA_2 has been implicated in several pathophysiological conditions including thrombosis, asthma, ischemia, and myocardial infarction.[6] In recent years considerable efforts have been directed toward identification of agents that would either inhibit TxA_2 biosynthesis[7] or block its action at the thromboxane receptor.[8] Over the past few years several 7-oxabicyclo[2.2.1]heptane derivatives have been reported to be potent TxA_2 antagonists.[9-15] Inspection of Dreiding models indicated a striking resemblance between the proposed structure of TxA_2 and that of the 7-oxabicyclo-

Chart I



1 2

Scheme I[a]



3 4 5

6 R = -H
7 R = -Ts
8 R = -CN

9 R = -H
10 R = -THP

11 R = -CN
12 R = -CHO

13 R = -THP
14 R = -H

15

[a] (a) LAH/THF; (b) $COCl_2$ (1 equiv)/THF, 0 °C; Py/CH_2Cl_2, −50 °C; (c) *i*-PrOH/TsOH (cat.), Δ; (d) Py/TsCl, room temperature; (e) NaCN (2 equiv)/DMSO, 90–95 °C; (f) 1% K_2CO_3/MeOH–H_2O, room temperature; (g) CH_2Cl_2/DHP/TsOH (cat.); (h) MCPBA/CH_2Cl_2, room temperature; (i) DIBAH/toluene, −78 °C; (j) K-*tert*-amylate/$Ph_3P{\cdot}Br(CH_2)_4COOH$/THF–toluene, −20 °C; CH_2N_2/ether; (k) MeOH/amberlyst, room temperature; (l) PCC/CH_2Cl_2, room temperature.

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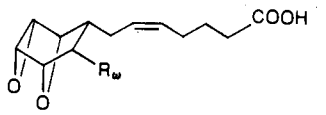
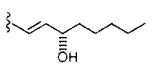
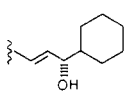
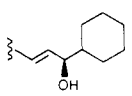
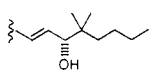
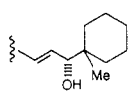
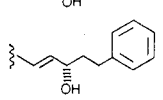
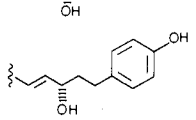
(15) Phillips, M. B.; Harris, D. N.; Michel, I. M.; Goldenberg, H. J.; Haslanger, M. F. *Pharmacologist* **1983**, *25*, 204.

0022-2623/88/1831-0930$01.50/0

Table I. 5,6-exo-Epoxy-7-oxabicyclo[2.2.1]heptane Analogues[a]



no.	R_ω	yield,[b] %	formula[c]	I_{50}[d] for inhibn of platelet aggregation[e,f] induced by AA, μM	n
19		36.5	$C_{21}H_{32}O_5$	15.3 ± 3.0	3
24		32.5	$C_{22}H_{32}O_5$	5.2 ± 0.5	3
25		8.0	$C_{22}H_{32}O_5 \cdot 0.27H_2O$	17.0 ± 3.7	3
28		24.1	$C_{23}H_{36}O_5$	2.2 ± 0.5	3
31		18.5	$C_{23}H_{34}O_5 \cdot 0.5H_2O$	0.53 ± 0.1	5
34		13.5	$C_{24}H_{30}O_5$	1.6 ± 0.3	3
37		13.2	$C_{24}H_{30}O_6 \cdot 0.6H_2O$	0.27 ± 0.1	2
BM 13177[g]				38.5 ± 3.5	2
indomethacin				6.0 ± 3.3	5
SQ 29548[h]				0.02 ± 0.01	2

[a] All compounds were viscous oil and were prepared as racemates. [b] Overall yield of chromatographically purified compound from aldehyde 15. [c] All compounds were analyzed for C and H, and the analytical values were within ±0.4% of calculated values. [d] For details of the methods used, see ref 24b; I_{50} values reported are either the mean ± SEM or the mean ± range (n = 2) of experimental values. [e] None of these compounds except 24 and 25 were effective in inhibiting platelet aggregation induced by ADP. I_{50} values for inhibition of ADP-induced platelet aggregation for 24 and 25 are 173.0 ± 11.6 μM (n = 3) and 134.0 ± 23.7 μM (n = 3), respectively. [f] Compound 20 is an inducer of platelet aggregation and has an A_{50} value of 12.4 ± 1.9 μM (n = 3). A_{50} is the concentration of an agonist required to elicit 50% of the maximal response. [g] For its structure, see ref 34. [h] For its structure, see ref 10.

[2.2.1]heptane nucleus. We reasoned that introduction of a 5,6-*exo*-epoxy linkage in the 7-oxabicyclo[2.2.1]heptane nucleus might increase its structural resemblance to TxA_2 (Chart I) and as such would lead to potent TxA_2 antagonists. In an attempt to design such antagonists, we retained the α-heptenoic acid side chain and varied the nature and stereochemistry of the ω-octenol side chain. Such variations led to the synthesis of the 16-cyclohexyl-16-methyl and 16-*p*-hydroxyphenethyl derivatives **31** and **37**, which were found to be selective TxA_2 antagonists at the platelet and pulmonary thromboxane receptors. The synthesis and pharmacological properties of these compounds and their structural analogues are reported here.

Chemistry. Compounds **31**, **37**, and their structural analogues **19**, **20**, **24**, **25**, **28**, and **34** were synthesized as outlined in Scheme I and Table I. Key steps in the synthesis required conversion of anhydride **3**[16] to a monoprotected diol **6**, which, through one-carbon extension, followed by stereospecific epoxidation, functional group manipulations, and Wittig condensation, led to aldehyde **15**. This aldehyde served as the common intermediate for the synthesis of all ω side chain modified analogues.

Accordingly, anhydride **3** was reduced with $LiAlH_4$ in THF at 0 °C–room temperature to afford diol **4** (91% yield), which on treatment with 1 equiv of phosgene in THF at 0 °C formed a monochloroformate. Dropwise addition of a solution of pyridine in CH_2Cl_2 to a solution of crude chloroformate in CH_2Cl_2 at −50 °C furnished crystalline cyclic carbonate **5** in 78% overall yield from **4**. Reaction of **5** with 2-propanol under reflux in presence of catalytic *p*-toluenesulfonic acid formed alcohol carbonate **6** in quantitative yield. Tosylation of **6** followed by displacement of tosylate with sodium cyanide in DMSO at 90–95 °C cleanly formed nitrile **8** in 75% yield. Removal of the carbonate protecting group under mild basic conditions (1% K_2CO_3, MeOH–H_2O, room temperature) followed by reprotection of alcohol as a tetrahydropyranyl ether afforded **10** in 64% overall yield from **8**. Stereospecific introduction of the 5,6-epoxide was achieved by treatment of **10** with *m*-chloroperoxybenzoic acid in CH_2Cl_2 at room temperature, which afforded a single epoxide **11** (as a mixture of epimers at the anomeric tetrahydropyranyl

Table II. Effects of 31 and 37 (1 mg/kg iv) on Arachidonic Acid Induced Bronchoconstriction in the Anesthetized Guinea Pig[a,b]

compd	% inhibn of increases in pulmonary resistance 3′	10′	30′	n
31	85 ± 5	67 ± 13	22 ± 22	3
37	90 ± 1	83 ± 2	46 ± 9	5
BM 13177	89 ± 3	82 ± 6	40 ± 11	5
SQ 29548	97 ± 1	98 ± 1	96 ± 1	5

[a] For details of the methods used, see ref 31c. [b] Experimental values are reported as mean ± SEM.

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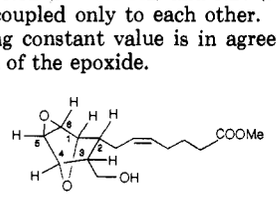
carbon) in 93% yield. Since the presence of epimers due to the tetrahydropyran group in 11 made unambiguous interpretation of its ^1H and ^{13}C NMR spectra difficult, the exo orientation of the 5,6-epoxide was established by analysis of ^1H and ^{13}C NMR spectra of the later intermediate 14.[17] Moreover, an exclusive approach of the peracid to the 5,6-olefin from the less hindered exo face of the molecule was anticipated from the Dreiding model and literature precedence on related compounds.[18] Epoxy nitrile 11 was now reduced with diisobutylaluminum hydride in toluene at −78 °C to obtain aldehyde 12 in 73% yield.

Elaboration of aldehyde 12 to the α-heptenoic acid side chain via a Wittig condensation required careful manipulations of the normal Wittig conditions due to the base sensitivity of 12. Dropwise addition of 1 equiv of a preformed ylide solution of (4-carboxybutyl)triphenylphosphorane[19] to a precooled solution of aldehyde 12 in THF at −20 °C and brief warming to 0 °C, followed by esterification with ethereal diazomethane, provided 13 in 40–45% yield. Subsequent deprotection of the THP protecting group with amberlyst acid exchange resin in methanol formed alcohol 14 (91% yield), which was oxidized with pyridinium chlorochromate[20] to afford aldehyde 15. Aldehyde 15 was condensed with the appropriate phosphonates under the modified Roush–Masamune conditions[21] to form enones, which were reduced with sodium borohydride[22] to provide a mixture of epimeric alcohols. Separation of alcohol epimers[23] followed by saponification with lithium hydroxide in aqueous THF furnished the carboxylic acids (Table I).

Pharmacology. In Vitro. The 5,6-epoxy derivatives were tested for their ability to inhibit platelet aggregation induced by arachidonic acid (AA) and adenosine diphosphate (ADP) in human platelet-rich plasma (PRP). The test methods have been described earlier,[24] and the results are summarized in Table I. Based on these platelet data, a few general conclusions can be reached. Analogous to the 7-oxabicyclo[2.2.1]heptanes,[8d,9,11,14] these 5,6-*exo*-epoxy derivatives are, as a class, potent inhibitors of platelet aggregation with the exception of an epimer (**20**) of the hydroxyl group on the natural side chain, which is a platelet aggregation stimulator (A_{50} = 12.4 μM). This finding is similar to the one observed in the 7-oxabicyclo[2.2.1]heptane series.[9] Unlike in the 7-oxabicyclo[2.2.1]heptane series, both 16-cyclohexyl alcohol epimers **24** and **25** are inhibitors of platelet aggregation induced by AA (I_{50} = 5.2 and 17.0 μM, respectively) and by ADP (I_{50} = 173 and 134 μM, respectively). We have previously shown that compounds with this platelet inhibitory profile are partial PGD_2/PGI_2 agonists and adenylate cyclase stimulators.[25] The 16,16-dimethyl analogue **28** is 7 times more potent (I_{50} = 2.2 μM) than the natural side chain analogue **19** (I_{50} = 15.3 μM). Similarly, the 16-cyclohexyl-16-methyl derivative **31** is about 1 order of magnitude more potent (I_{50} = 0.53 μM) than the 16-cyclohexyl analogue **24** (I_{50} = 5.2 μM). In addition, unlike **24**, **31** is devoid of any residual PGD_2/PGI_2-like activity. Replacement of the natural side chain with an arylalkyl moiety (compound **34**) caused 1 order of magnitude increase in potency (I_{50} = 1.6 μM), while introduction of a *p*-hydroxyl function in the aromatic ring (compound **37**) resulted in an additional sixfold enhancement (I_{50} = 0.27 μM). The 16-cyclohexyl-16-methyl analogue **31** (I_{50} = 0.53 μM) and the *p*-hydroxyphenethyl analogue **37** (I_{50} = 0.27 μM) are thus the two most active inhibitors of AA-induced platelet aggregation in this series. Identification of these analogues as potent inhibitors prompted further investigations regarding their mechanism of action. Compounds **31** and **37** were therefore tested for their ability to inhibit platelet aggregation induced by the stable PGH_2 analogue U46619,[26] which is a thromboxane mimetic on the PGH_2/TXA_2 receptor.[27–29] Both **31** and **37** inhibited platelet aggregation induced by U46619 (10 μM) in a dose-dependent manner with I_{50} values of 2.0 and 2.2 μM, respectively. Measurement of TxA_2 synthesis in lysed human platelet preparations[24b,30] in the absence and presence of either **31** or **37** at concentrations up to 1000 μM indicated that neither of these analogues influenced conversion of AA to TxA_2 to any significant extent. Thus, **31** and **37** are not inhibitors of either cyclooxygenase or thromboxane synthetase.

In Vivo. Compounds **31** and **37** were also tested for their efficacy in inhibiting AA-induced changes in lung mechanics in anesthetized guinea pigs.[31] At a dose of 1 mg/kg, iv, both **31** and **37** inhibited bronchoconstriction and systemic hypertension in response to injections of AA (0.5 mg/kg, iv) (Table II). This inhibition lasted for 10 min after treatment with **31** and for 30 min with **37**. The

(17) The stereochemistry of the 5,6-epoxide is clearly cis-exo as evidenced by the resonance multiplicities observed for H-1, H-4, H-5, and H-6 protons. H-1 and H-4 appeared as singlets at δ 4.44 and 4.15. The lack of coupling between H-1 and H-6, H-4 and H-5 is consistent with exo orientation of the epoxide, since the dihedral angles are ~90°. H-5 and H-6 appeared as doublets at δ 3.32 (J = 3.2 Hz) and 3.26 (J = 3.2 Hz). These protons are coupled only to each other. Furthermore, this small coupling constant value is in agreement with the cis configuration of the epoxide.



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(19) The corresponding phosphonium bromide is commercially available from several sources (Aldrich, Fluka).

(20) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

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(23) The fast-moving and the slow-moving alcohol epimers were tentatively assigned the 15*S* and 15*R* configurations based on TLC mobilities compared to natural prostaglandins.

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systemic hypertensive response after arachidonate challenge was reversed to a systemic hypotensive response after treatment with both these compounds. This is consistent with the mode of action of both **31** and **37** as TxA_2 receptor antagonists.[32] Before treatment, AA caused an 85% increase in blood pressure. At 3 min after treatment with **31** and **37**, AA decreased blood pressure by 13 ± 8% and 62 ± 4%, respectively.

Conclusions

In the course of these studies we have demonstrated that the 5,6-*exo*-epoxy-7-oxabicyclo[2.2.1]heptanes are inhibitors of platelet aggregation with the exception of **20**, which is a platelet aggregation stimulator. In this respect, these derivatives are very similar to the 7-oxabicyclo[2.2.1]heptanes. Modification of the ω-octenol side chain in this series led to a number of potent inhibitors (Table I). The pharmacological profiles of the two most potent analogues **31** and **37** have been studied in detail. The results of this study indicate that both these analogues are selective TxA_2 receptor antagonists at the platelet, vascular, and airway TxA_2 receptors. In studies with PRP in vitro, **31** and **37** inhibited platelet aggregation induced by AA and a stable TxA_2 agonist without inhibiting ADP-induced aggregation and without inhibiting platelet TxA_2 synthesis. These compounds thus meet sufficient criteria to be considered TxA_2 antagonists.[10,24b] Similarly, in anesthetized guinea pigs both **31** and **37** significantly inhibited AA-induced bronchoconstriction and reversed the systemic hypertensive response after AA challenge to a hypotensive effect. These results are consistent with their mechanism of action as TxA_2 antagonists.[11,32] It is believed that agents like **31** and **37** might prove therapeutically useful in treatment of diseases involving increased levels of TxA_2.

Experimental Section

^1H NMR spectra were measured at 270 MHz on a JEOL FX-270 spectrometer with Me_4Si as an internal standard. ^{13}C NMR spectra were taken at 67.5 MHz on JEOL FX-270 and at 15 MHz on JEOL FX-60 instruments. Chemical shifts are reported in δ units relative to Me_4Si, $CHCl_3$ assigned at δ 7.26 or $CDCl_3$ at δ 77.00. All ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solution unless otherwise noted. Mass spectra were recorded with an Extranuclear Simulscan or a Finnigan TSQ mass spectrometer in either CI or EI mode. Melting points were recorded on a Thomas-Hoover capillary melting point apparatus and are uncorrected. All reactions were carried out in oven-dried glassware under an argon atmosphere. All solvents were purified before use unless otherwise indicated; THF and ether were distilled from sodium benzophenone ketyl, CH_2Cl_2 was distilled from P_2O_5, and toluene was distilled from sodium and stored over activated 4A molecular sieves. Flash chromatography was performed as described by Still et al.[33] with use of J. T. Baker "Flash" grade silica gel.

***exo-cis*-7-Oxabicyclo[2.2.1]hept-5-ene-2,3-dimethanol (4).** A solution of *exo-cis*-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid anhydride (**3**) (20 g, 120 mmol) in anhydrous THF (150 mL) was added dropwise at 0 °C to a suspension of lithium aluminum hydride (6.84 g, 180 mmol) in THF (200 mL) over a period of 1 h. The reaction mixture was stirred at 25 °C for 24 h. Excess hydride was now quenched by dropwise addition of saturated sodium sulfate solution at 0–5 °C. Addition was continued until all inorganic salts were precipitated as white granular solids. Anhydrous magnesium sulfate was added to the reaction mixture and was filtered. The residue was thoroughly washed with methylene chloride, followed by 10% acetonitrile in ethyl acetate (500 mL). The combined filtrate was concentrated in vacuo and was then purified by flash chromatography with 1:1 EtOAc/hexane, followed by EtOAc and 9:1 EtOAc/MeOH as eluents to afford diol **4** (17.25 g, 92%) as a colorless viscous oil: ^1H NMR δ 6.37 (s, 2 H), 4.67 (s, 2 H), 3.90 (br s, 2 H), 3.77 (m, 4 H), 1.92 (m, 2 H); ^{13}C NMR δ 135.67, 81.16, 62.60, 42.40; MS, *m/z* 157(M^+), 139 ($M^+ - H_2O$), 121 ($M^+ - 2H_2O$). Anal. ($C_8H_{12}O_3 \cdot 0.15H_2O$) C, H.

***exo-cis*-7-Oxabicyclo[2.2.1]hept-5-ene-2,3-dimethanol Carbonate (5).** A solution of diol **4** (16.73 g, 107.4 mmol) in anhydrous THF (200 mL) was treated dropwise with a 12.5% by weight solution of phosgene in toluene (90 mL, 112.5 mmol) at 0–5 °C. After 15 min, argon was bubbled through the reaction mixture to remove excess phosgene and hydrogen chloride. The reaction mixture was concentrated in vacuo to obtain crude monochloroformate, which was dissolved in CH_2Cl_2 (50 mL) and cooled to −50 °C, and a solution of pyridine (25 mL) in CH_2Cl_2 (50 mL) was added dropwise. The reaction mixture was stirred at −50 °C for 30 min. The reaction mixture was diluted with water, and the CH_2Cl_2 layer was separated. The CH_2Cl_2 layer was washed with water (three times), dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was triturated with ether to afford carbonate **5** (15.25 g, 78%): mp 149–150.5 °C; ^1H NMR δ 6.45 (s, 2 H), 4.73 (s, 2 H), 4.58 (d, 1 H), 4.50 (d, 1 H), 4.43 (d, 1 H, *J* = 3.7 Hz), 4.35 (d, 1 H, *J* = 3.7 Hz), 2.36–2.32 (m, 2 H); ^{13}C NMR δ 135.73, 80.26, 69.27, 40.00. Anal. ($C_9H_{10}O_3$) C, H.

***exo-cis*-2-[[(*p*-Tolylsulfonyl)oxy]methyl]-3-[[[(isopropyloxy)carbonyl]oxy]methyl]-7-oxabicyclo[2.2.1]hept-5-ene (7).** A suspension of carbonate **5** (15.25 g, 83.8 mmol) and *p*-TsOH (1 g) in 2-propanol (200 mL) was heated under reflux for 8 h. The cooled reaction mixture was concentrated under reduced pressure. Residual oil was partitioned between CH_2Cl_2 and aqueous $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (three times). Combined CH_2Cl_2 extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give **6** (22.53 g, 100%) as a highly viscous oil.

To a solution of **6** (22.53 g, 83.8 mmol) in pyridine (100 mL) was added *p*-TsCl (19.2 g, 101 mmol). The reaction mixture was stirred at 25 °C for 24 h and was then diluted with CH_2Cl_2. The reaction mixture was washed with saturated $CuSO_4$ solution (three times) and water (three times). The aqueous layer was extracted with CH_2Cl_2 (2 × 200 mL). The combined CH_2Cl_2 extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. It was triturated with ether at 0 °C and filtered to obtain tosylate **7** (28.3 g, 80%), mp 92–95 °C. The mother liquor was concentrated under reduced pressure and chromatographed on a silica gel column with 15–30% EtOAc/hexane as eluents to obtain additional 5.2 g of tosylate **7** (14.7%): ^1H NMR δ 7.8 (d, 2 H, *J* = 8 Hz), 7.35 (d, 2 H, *J* = 8 Hz), 6.33 (m, 2 H), 4.87 (m, 1 H), 4.79 (s, 1 H), 4.76 (s, 1 H), 4.15 (m, 2 H), 3.95 (m, 2 H), 2.45 (s, 3 H), 2.06 (m, 2 H), 1.29 (d, 6 H, *J* = 6.3 Hz); ^{13}C NMR δ 154.09, 144.91, 135.53, 135.17, 132.58, 127.75, 127.47, 80.18, 79.96, 72.09, 69.58, 66.31, 39.59, 39.31, 21.59, 21.48. Anal. ($C_{19}H_{24}SO_7$) C, H, S.

***exo-cis*-2-(Cyanomethyl)-3-[[[(isopropyloxy)carbonyl]oxy]methyl]-7-oxabicyclo[2.2.1]hept-5-ene (8).** A solution of tosylate **7** (5.3 g, 12.99 mmol) and powdered anhydrous sodium cyanide (1.28 g, 26 mmol) in dry DMSO (50 mL) was heated (bath temperature 90–95 °C) for 2 h. The cooled reaction mixture was poured into ether (200 mL) and washed with water (three times). The aqueous layer was extracted with ether (2 × 150 mL). The combined ether extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. It was chromatographed on a silica gel column with 25–50% EtOAc/hexane as eluents to afford **8** (2.58 g, 75%): mp 34–36 °C; ^1H NMR δ 6.41 (s, 2 H), 4.87 (m, 1 H), 4.83 (d, 2 H, *J* = 14.2 Hz), 4.15 (d, 1 H, *J* = 2.6 Hz), 4.12 (d, 1 H, *J* = 2.6 Hz), 2.62 (dd, 1 H, *J* = 16.4, 2.1 Hz), 2.37 (dd, *J* = 16.4, 10.5 Hz), 2.06 (m, 2 H), 1.3 (d, 6 H, *J* = 6.3 Hz); ^{13}C NMR δ 154.23, 136.12, 135.12, 118.74, 82.30, 80.74, 72.43, 66.62, 39.48, 37.30, 21.68, 17.88. Anal. ($C_{13}H_{17}NO_4$) C, H, N.

***exo-cis*-2-(Cyanomethyl)-3-[[(tetrahydropyranyl)oxy]methyl]-7-oxabicyclo[2.2.1]hept-5-ene (10).** A solution of **8** (2.58 g, 9.8 mmol) in methanol (10 mL) was added to a solution of potassium carbonate (1 g) in methanol (75 mL) and water (25 mL) at 0–5 °C. The reaction mixture was stirred at 0–5 °C for 15 min and at 25 °C for 6 h. It was acidified with 1 N aqueous HCl solution and concentrated under reduced pressure. The reaction mixture was now exhaustively extracted with CH_2Cl_2 (12 times).

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(33) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(34) Patscheke, H.; Stegmeier, K. *Thrombosis Res.* **1984**, *33*, 277.

The combined extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification was effected by chromatography on a silica gel column with 25–50% EtOAc/hexane as eluents to obtain alcohol **9** (1.23 g, 75%).

A solution of cyano alcohol **9** (1.23 g, 7.36 mmol) in CH_2Cl_2 (20 mL) was treated with dihydropyran (800 μL, 8.29 mmol) and catalytic *p*-TsOH at 0–5 °C. The reaction mixture was stirred at 0–5 °C for 4 h. It was then diluted with ether and washed with aqueous $NaHCO_3$ solution. The aqueous layer was extracted with ether (two times). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was chromatographed on a silica gel column with 10–25% EtOAc/hexane as eluents to obtain **10** (1.61 g, 86%): mp 52–59 °C; ^1H NMR δ 6.38–6.45 (m, 2 H), 4.85 (s, 1 H), 4.78, 4.76 (s, each 1 H), 4.58 (m, 1 H), 3.75–3.85 (m, 2 H), 3.50 (m, 1 H), 3.40 (q, 1 H), 2.75 (dt, 1 H), 2.40 (m, 1 H), 2.00–2.12 (m, 2 H), 1.8 (m, 2 H), 1.55 (m, 4 H). Anal. ($C_{14}H_{19}NO_3$) C, H, N.

***exo*-*cis*-5,6-*exo*-Epoxy-2-(cyanomethyl)-3-[[(tetrahydropyranyl)oxy]methyl]-7-oxabicyclo[2.2.1]heptane (11).** A solution of **10** (1.61 g, 6.4 mmol) in CH_2Cl_2 (20 mL) was treated with 85% *m*-chloroperoxybenzoic acid (1.66 g, 9.6 mmol) at 0–5 °C. The reaction mixture was stirred at 0–5 °C for a few minutes and then at 25 °C for 6 h. The reaction mixture was diluted with ether and then stirred for 30 min with aqueous sodium metabisulfite solution. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (two times). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification was done by chromatography on a silica gel column with 25–67% EtOAc/hexane as eluents to obtain epoxide **11** (1.57 g, 93%) as a colorless oil: ^1H NMR δ 4.51 (m, 1 H), 4.41, 4.40 (s, each 1 H), 4.34, 4.32 (s, each 1 H), 3.76 (m, 2 H), 3.55 (m, 1 H), 3.38 (m, 3 H), 2.68 (m, 1 H), 2.43 (m, 1 H), 2.2–2.4 (m, 2 H), 1.8 (m, 2 H), 1.54 (m, 4 H); ^{13}C NMR δ 118.88, 99.29, 98.79, 78.17, 76.69, 64.92, 64.86, 62.71, 62.21, 49.24, 48.85, 43.38, 43.21, 40.03, 30.33, 30.27, 24.94, 19.50, 19.16, 16.37. Anal. ($C_{14}H_{19}NO_4$) C, H, N.

***exo*-*cis*-5,6-*exo*-Epoxy-2-(formylmethyl)-3-[[(tetrahydropyranyl)oxy]methyl]-7-oxabicyclo[2.2.1]heptane (12).** A solution of nitrile **11** (1.57 g, 5.88 mmol) in toluene (25 mL) was treated dropwise with a 25% by weight solution of DIBAH (6.8 mL, ~12 mmol) at −78 °C. The reaction mixture was stirred for 4 h at −78 °C and was then quenched by dropwise addition of glacial acetic acid (1 mL). The cooling bath was removed, and silica gel (20 g) was added with stirring; water (1.5 mL) was then added dropwise. The resulting mixture was stirred for 30 min and filtered. Residual silica gel was washed successively with THF, 19:1 EtOAc/CH_3CN, and acetone. The combined filtrate was concentrated under reduced pressure. Purification was done by chromatography on a silica gel column with 1:1 EtOAc/hexane and EtOAc as eluents to obtain aldehyde **12** (1.16 g, 73%): mp 67–73 °C; ^1H NMR δ 9.79, 9.78 (s, each 1 H), 4.55 (m, 1 H), 4.36, 4.33 (s, each 1 H), 4.12 (s, 1 H), 3.85 (m, 1 H), 3.70 (m, 1 H), 3.50 (m, 1 H), 3.41 (d, 1 H, J = 3.2 Hz), 3.33–3.35 (m, 1 H), 3.28 (m, 1 H), 2.85–2.10 (m, 4 H), 1.9–1.45 (m, 6 H); ^{13}C NMR δ 200.67, 99.60, 98.79, 79.18, 76.64, 66.01, 65.73, 62.89, 62.27, 49.63, 43.22, 43.05, 42.52, 36.35, 36.16, 30.58, 25.28, 19.75, 19.33. Anal. ($C_{14}H_{20}O_5$) C, H.

[1α,2β(5*Z*),3β,4α]-7-[5,6-*exo*-Epoxy-3-[(tetrahydropyranyloxy)methyl]-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid Methyl Ester (13). A suspension of freshly dried (carboxybutyl)triphenylphosphonium bromide (5.77 g, 13.03 mmol) in freshly distilled THF (50 mL) was treated dropwise with a 1.5 M solution of potassium *tert*-amylate (12 mL, 19.2 mmol) in toluene at 0–5 °C. The yellow-orange suspension was stirred at 0 °C for 30 min and at 25 °C for 1 h. The reaction mixture was then cooled to −20 °C, and a solution of aldehyde **12** (2.33 g, 8.69 mmol) in THF (10 mL) was added dropwise. The resulting mixture was stirred at −20 °C for 2 h and at 0 °C for 15 min and then quenched with glacial acetic acid. The mixture was poured into water and extracted with ether (three times). The combined ether extracts were washed with saturated $NaHCO_3$ solution. The combined aqueous extracts were dried ($MgSO_4$), filtered, and concentrated. The residue was esterified with excess diazomethane in ether and purified by chromatography on a silica gel column with 15–40% EtOAc/hexane as eluents to afford **13** (1.27 g, 40%) as a colorless oil: ^1H NMR δ 5.41 (m, 2 H), 4.57 (m, 1 H), 4.43, 4.40 (s, each 1 H), 4.15 (s, 1 H), 3.83 (m, 2 H), 3.66 (s, 3 H), 3.5 (m, 1 H), 3.35 (m, 1 H), 3.33 (d, 1 H, J = 3.2 Hz), 3.25 (d, 1 H, J = 3.2 Hz), 2.3 (t, 2 H), 2.05 (m, 5 H), 1.9–1.5 (m, 9 H). Anal. ($C_{20}H_{30}O_6$) C, H.

[1α,2β(5*Z*),3β,4α]-7-[5,6-*exo*-Epoxy-3-(hydroxymethyl)-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid Methyl Ester (14). A solution of **13** (1.27 g, 3.46 mmol) in methanol (30 mL) was stirred with powdered and dried amberlyst-15 acid exchange resin at 25 °C for 6 h. The reaction mixture was diluted with ether, filtered (through a pad of $MgSO_4$), and concentrated under reduced pressure. The crude residue was chromatographed on a silica gel column with 50–75% EtOAc/hexane as eluents to obtain alcohol **14** (892 mg, 91%) as a colorless oil: ^1H NMR δ 5.39 (m, 2 H), 4.44 (s, 1 H), 4.15 (s, 1 H), 3.72 (dd, 1 H), 3.65 (s, 3 H), 3.62 (dd, 1 H), 3.32 (d, 1 H, J = 3.7 Hz), 3.26 (d, 1 H, J = 3.2 Hz), 2.30 (t, 2 H, J = 7.3 Hz), 1.85–2.1 (m, 7 H), 1.68 (q, 2 H); ^{13}C NMR δ 173.95, 130.99, 129.31, 78.26, 77.22, 61.18, 51.95, 50.47, 50.38, 46.45, 43.80, 33.84, 27.17, 25.69, 25.11. Anal. ($C_{15}H_{22}O_5 \cdot 0.29H_2O$) C, H.

[1α,2β(5*Z*),3β,4α]-7-[5,6-*exo*-Epoxy-3-formyl-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid Methyl Ester (15). A solution of alcohol **14** (211 mg, 0.75 mmol) in CH_2Cl_2 (2 mL) was added to a stirred suspension of pyridinium chlorochromate (325 mg, 1.51 mmol) and Celite (325 mg) in CH_2Cl_2 (20 mL). The reaction mixture was stirred at 25 °C for 4 h, diluted with ether (100 mL), and filtered (through Florisil). The filtrate was washed with water. The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure to obtain aldehyde **15** (174 mg, 83%). The crude aldehyde was used immediately without any further purifications: ^1H NMR δ 9.56 (d, 1 H, J = 3.2 Hz), 5.55–5.30 (m, 2 H), 4.75 (s, 1 H), 4.31 (s, 1 H), 3.67 (s, 3 H), 3.35 (s, 2 H), 2.55 (dd, 1 H), 2.30 (t, 2 H, J = 7.4 Hz), 2.25–2.00 (m, 5 H), 1.69 (m, 4 H); MS, m/z 281 (M^+), 279 (M^-).

General Procedure for the Synthesis of Enones. The synthesis of enones followed the procedure described below for **16**.

[1α,2β(5*Z*),3β(1*E*),4α,5α,6α]-7-[5,6-Epoxy-3-(3-oxo-1-octenyl)-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid Methyl Ester (16). A suspension of dry lithium bromide (90 mg, 1 mmol) in CH_2Cl_2 (5 mL) was treated with triethylamine (140 μL, 1 mmol), followed by a solution of dimethyl (2-oxoheptyl)phosphonate (222 mg, 1 mmol) in CH_2Cl_2 (1 mL). The reaction mixture was stirred at 25 °C for 15 min and then a solution of aldehyde **15** (174 mg, 0.62 mmol) in CH_2Cl_2 (3 mL) was added dropwise. The reaction mixture was stirred at 25 °C overnight. It was then diluted with ether and washed with water. The aqueous layer was extracted with ether (two times). The combined ether extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude residue was purified by chromatography with 15–30% EtOAc/hexane as eluents to obtain enone **16** (175 mg, 75%) as a colorless oil: ^1H NMR δ 6.67 (dd, 1 H, J = 15.83 Hz, 10.28 Hz), 6.08 (d, 1 H, J = 15.83 Hz), 4.26 (s, 1 H), 4.21 (s, 1 H), 3.63 (s, 3 H), 3.33 (d, 1 H, J = 3.2 Hz), 3.29 (d, 1 H, J = 3.7 Hz), 2.62 (t, 1 H), 2.52 (t, 2 H, J = 7.4 Hz), 2.28 (t, 2 H, J = 7.4 Hz), 2.1–1.8 (m, 5 H), 1.7–1.5 (m, 4 H), 1.29–1.27 (m, 4 H), 0.86 (t, 3 H), 5.5–5.25 (m, 2 H).

[1α,2β(5*Z*),3β(1*E*),4α,5α,6α]-7-[5,6-Epoxy-3-(3-oxo-3-cyclohexyl-3-methyl-1-propenyl)-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid Methyl Ester (29): mp 43–45 °C; ^1H NMR δ 6.83 (dd, 1 H, J = 15.3 Hz, 10.3 Hz), 6.53 (d, 1 H, J = 15.3 Hz), 5.4 (m, 2 H), 4.29 (s, 1 H), 4.21 (s, 1 H), 3.66 (s, 3 H), 3.33 (d, 1 H, J = 3.2 Hz), 3.30 (d, 1 H, J = 3.2 Hz), 2.65 (t, 1 H), 2.29 (t, 2 H), 2.02 (m, 6 H), 1.75–1.2 (m, 11 H), 1.08 (s, 3 H). Anal. ($C_{24}H_{34}O_5$) C, H.

[1α,2β(5*Z*),3β(1*E*),4α,5α,6α]-7-[5,6-Epoxy-3-[3-oxo-5-[*p*-[(*tert*-butyldimethylsilyl)oxy]phenyl]-1-pentenyl]-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid Methyl Ester (35): ^1H NMR δ 7.00 (d, 2 H), 6.72 (d, 2 H), 6.66 (dd, 1 H, J = 15.8 Hz and 10.3 Hz), 6.10 (d, 1 H, J = 15.8 Hz), 5.4 (m, 1 H), 5.3 (m, 1 H), 4.25 (s, 1 H), 4.2 (s, 1 H), 3.63 (s, 3 H), 3.32 (d, 1 H, J = 3.7 Hz), 3.28 (d, 1 H, J = 3.7 Hz), 2.85 (br s, 4 H), 2.6 (t, 1 H), 2.26 (t, 2 H), 2.1–1.8 (m, 5 H), 1.65 (q, 2 H), 0.97 (s, 9 H), 0.16 (s, 6 H).

General Procedure for the Synthesis of Allylic Alcohols. The synthesis of allylic alcohols followed the procedure described below for **17** and **18**.

[1α,2β(5Z),3β(1E,3S),4α,5α,6α]-7-[5,6-Epoxy-3-(3-hydroxy-1-octenyl)-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid Methyl Ester (17) and [1α,2β(5Z),3β(1E,3R),4α,5α,6α]-7-[5,6-Epoxy-3-(3-hydroxy-1-octenyl)-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid Methyl Ester (18). Cerium(III) chloride (170 mg) was added to a stirring solution of enone **16** (170 mg, 0.45 mmol) in 1:1 THF/CH_3OH (10 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 10 min and was then cooled to −50 °C. Sodium borohydride (20 mg, 0.5 mmol) was added. The mixture was stirred at −50 °C for 1 h and then quenched by addition of aqueous NH_4Cl solution. The reaction mixture was diluted with ether. The organic layer was separated, and the aqueous layer was extracted with ether and CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude residue was purified by chromatography with 30–50% EtOAc/hexane to give fast-moving alcohol epimer **17** (130 mg, 76%) (^{13}C NMR δ 174.24, 136.01, 130.23, 129.14, 128.84, 79.65, 77.14, 72.45, 51.47, 50.02, 49.57, 47.23, 45.67, 37.13, 33.23, 31.66, 27.09, 26.61, 25.05, 24.60, 22.51, 13.92) and slow-moving alcohol epimer **18** (40 mg, 23%).

General Procedure for the Synthesis of Acids. The synthesis of acids followed the procedure described below for **19**.

[1α,2β(5Z),3β(1E,3S),4α,5α,6α]-7-[5,6-Epoxy-3-(3-hydroxy-1-octenyl)-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid (19). A solution of alcohol **17** (130 mg, 0.34 mmol) in THF (5 mL) was treated with 1 N aqueous LiOH solution (2 mL). The reaction mixture was stirred at 25 °C for 8 h, diluted with ether, and acidified to pH 1 with 1 N aqueous HCl solution. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (two times). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude residue was purified on a silica gel column with 2–3% MeOH in CH_2Cl_2 as eluents to give acid **19** (80 mg, 64%) as a colorless oil: ^1H NMR δ 6.55 (br s, 2 H), 5.65–5.30 (m, 4 H), 4.20 (s, 1 H), 4.14 (s, 1 H), 4.09 (q, 1 H), 3.3 (d, 1 H, J = 3.2 Hz), 3.26 (d, 1 H, J = 3.2 Hz), 2.48 (t, 1 H, J = 8.4 Hz), 2.28 (t, 2 H, J = 6.8 Hz), 2.1–1.2 (m, 15 H), 0.87 (t, 3 H, J = 6.3 Hz); ^{13}C NMR δ 177.05, 135.09, 130.12, 129.81, 129.42, 79.51, 77.00, 72.98, 50.13, 49.63, 47.34, 45.89, 36.96, 32.53, 31.61, 26.84, 26.28, 25.00, 24.24, 22.54, 13.95. Anal. ($C_{21}H_{32}O_5$) C, H.

[1α,2β(5Z),3β(1E,3R),4α,5α,6α]-7-[5,6-Epoxy-3-(3-hydroxy-1-octenyl)-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid (20): ^1H NMR δ 5.75 (br s, 2 H), 5.6–5.3 (m, 4 H), 4.22 (s, 1 H), 4.18 (s, 1 H), 4.1 (m, 1 H), 3.3 (d, 1 H, J = 3.7 Hz), 3.27 (d, 1 H, J = 3.7 Hz), 2.5 (t, 1 H), 2.31 (t, 2 H, J = 6.9 Hz), 2.2–1.2 (m, 15 H), 0.87 (t, 3 H); ^{13}C NMR δ 178.02, 135.31, 130.23, 129.37, 128.84, 79.43, 72.45, 77.00, 50.16, 49.66, 47.12, 45.67, 37.02, 32.72, 31.66, 27.20, 26.36, 25.08, 24.30, 22.57, 13.97; MS, m/z 347 ($M^+ - H_2O$), 329 ($M^+ - 2\ H_2O$). Anal. ($C_{21}H_{32}O_5 \cdot 1.0H_2O$) C, H.

[1α,2β(5Z),3β(1E,3S),4α,5α,6α]-7-[5,6-Epoxy-3-(3-cyclohexyl-3-hydroxy-1-propenyl)-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid (24): ^1H NMR δ 5.95 (br s, 2 H), 5.6–5.3 (m, 4 H), 4.20 (s, 1 H), 4.14 (s, 1 H), 3.83 (t, 1 H), 3.30 (d, ^1H, J = 3.2 Hz), 3.26 (d, 1 H, J = 3.7 Hz), 2.49 (t, 1 H), 2.28 (t, 2 H), 2.25 (m, 2 H), 2.0–1.5 (m, 10 H), 1.45–0.85 (m, 6 H); ^{13}C NMR δ 177.49, 133.47, 130.65, 130.10, 129.37, 79.54, 77.00, 50.10, 49.60, 47.40, 45.84, 43.44, 32.59, 28.65, 28.60, 26.84, 26.39, 26.28, 25.94, 24.24; MS, m/z 369 ($M^+ - H_2O$), 341 ($M^+ - 2\ H_2O$), 275. Anal. ($C_{22}H_{32}O_5$) C, H.

[1α,2β(5Z),3β(1E,3R),4α,5α,6α]-7-[5,6-Epoxy-3-(3-cyclohexyl-3-hydroxy-1-propenyl)-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid (25): ^1H NMR δ 5.8–5.3 (m, 6 H), 4.23 (s, 1 H), 4.18 (s, 1 H), 3.87 (t, 1 H), 3.32 (d, 1 H, J = 3.7 Hz), 3.27 (d, 1 H, J = 3.7 Hz), 2.52 (t, 1 H), 2.32 (t, 2 H), 2.09 (m, 2 H), 2.0–1.6 (m, 10 H), 1.5–0.90 (m, 6 H); ^{13}C NMR δ 177.52, 133.83, 130.26, 129.87, 129.42, 79.51, 77.00, 50.19, 49.71, 47.29, 45.70, 43.66, 28.87, 28.57, 27.31, 26.47, 26.39, 26.08, 24.33; MS: 399 (M^+ + Na), 375 (M^- − H). Anal. ($C_{22}H_{32}O_5 \cdot 0.27H_2O$) C, H.

[1α,2β(5Z),3β(1E,3R),4α,5α,6α]-7-[5,6-Epoxy-3-(3-hydroxy-4,4-dimethyl-1-octenyl)-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid (28): ^1H NMR δ 6.65 (br s, 2 H), 5.58 (m, 2 H), 5.43 (m, 2 H), 4.22 (s, 1 H), 4.15 (s, 1 H), 3.84 (m, 1 H), 3.3 (d, 1 H, J = 3.7 Hz), 3.28 (d, 1 H, J = 3.7 Hz), 2.53 (m, 1 H), 2.32 (t, 2 H), 2.15–1.8 (m, 5 H), 1.66 (q, 2 H), 1.25 (m, 6 H), 0.90 (t, 3 H, J = 6.3 Hz), 0.88 (s, 3 H), 0.84 (s, 3 H); ^{13}C NMR δ 177.24, 131.80, 131.38, 130.12, 129.40, 79.82, 79.59, 77.00, 50.13, 49.63, 47.57, 45.92, 38.55, 37.19, 32.64, 26.92, 26.31, 25.80, 24.30, 23.60, 22.82, 14.09; MS, m/z 375 ($M^+ - H_2O$). Anal. ($C_{23}H_{36}O_5$) C, H.

[1α,2β(5Z),3β(1E,3R),4α,5α,6α]-7-[5,6-Epoxy-3-(3-cyclohexyl-3-hydroxy-3-methyl-1-propenyl)-7-oxabicyclo[2.2.1]-hept-2-yl]-5-heptenoic Acid (31): ^1H NMR δ 6.80 (br s, 2 H), 5.60 (m, 2 H), 5.42 (m, 2 H), 4.22 (s, 1 H), 4.16 (s, 1 H), 3.84 (m, 1 H), 3.32 (d, 1 H, J = 3.7 Hz), 3.28 (d, 1 H, J = 3.7 Hz), 2.52 (m, 1 H), 2.32 (t, 2 H), 2.2–1.8 (m, 5 H), 1.66 (q, 2 H), 1.6–1.15 (m, 10 H), 0.88 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 177.22, 131.52, 131.43, 130.12, 129.42, 80.54, 79.59, 77.00, 50.13, 49.63, 47.57, 45.92, 37.22, 34.26, 33.78, 32.64, 26.92, 26.28, 24.27, 21.56, 18.72; MS, m/z 373 ($M^+ - H_2O$). Anal. ($C_{23}H_{34}O_5 \cdot 0.5H_2O$) C, H.

[1α,2β(5Z),3β(1E,3S),4α,5α,6α]-7-[5,6-Epoxy-3-(3-hydroxy-5-phenyl-1-pentenyl)-7-oxabicyclo[2.2.1]hept-2-yl]-5-heptenoic Acid (34): ^1H NMR δ 7.3–7.17 (m, 5 H), 6.86 (br s, 2 H), 5.65–5.41 (m, 4 H), 4.21, (s, 1 H), 4.15 (s, 1 H), 4.13 (m, 1 H), 3.3 (d, 1 H, J = 3.7 Hz), 3.27 (d, 1 H, J = 3.7 Hz), 2.7 (m, 2 H), 2.49 (t, 1 H), 2.30 (t, 2 H), 2.1–1.6 (m, 9 H); ^{13}C NMR δ 177.13, 141.59, 134.81, 130.18, 129.40, 128.36, 125.85, 79.48, 77.00, 72.28, 50.13, 49.60, 47.34, 45.89, 38.53, 32.53, 31.64, 26.89, 26.28, 24.21; MS, m/z 381 ($M^+ - H_2O$). Anal. ($C_{24}H_{30}O_5$) C, H.

[1α,2β(5Z),3β(1E,3S),4α,5α,6α]-7-[5,6-Epoxy-3-[3-hydroxy-5-(*p*-hydroxyphenyl)-1-pentenyl]-7-oxabicyclo-[2.2.1]hept-2-yl]-5-heptenoic Acid (37): ^1H NMR δ 7.00 (d, 2 H), 6.75 (d, 2 H), 5.6–5.3 (m, 4 H), 4.25 (s, 1 H), 4.15 (s, 1 H), 4.06 (q, 1 H), 3.32, (d, 1 H, J = 3.7 Hz), 3.27 (d, 1 H, J = 3.7 Hz), 2.6 (m, 2 H), 2.5 (t, 1 H), 2.25 (t, 2 H), 2.07 (m, 3 H), 2.00–1.50 (m, 7 H). Anal. ($C_{24}H_{30}O_6 \cdot 0.6H_2O$) C, H.

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