20 mL, 15 mL, and 10 mL of CH_2Cl_2 and the combined extracts filtered, concentrated, and transferred to a dry box. The solid concentrate consisted mostly of 1, but contained significant amounts of 2, 4, and catecholborate impurities. A single reprecipitation from CH_2Cl_2–ether gave 250 mg of 1 as a yellow solid contaminated with 15% and 10% of 2 and 4, respectively. This sample was used for the NMR titration experiments. A second reprecipitation yielded an analytical sample. Calcd for $C_{30}H_{16}B_2O_4$: C, 77.98; H, 3.49; B, 4.68. Found: C, 74.76; H, 3.72; B, 5.01. The low value for C is probably due to retained CH_2Cl_2 (observable by NMR), which could not be removed because of the thermal instability of 1. As little as 0.25 equiv of retained CH_2Cl_2 would depress the C value to 75.17% while marginally affecting the data for H and B. The exact amount of the retained solvent could not be determined by NMR because of contamination of the only suitable NMR solvent, CD_2Cl_2, with protio solvent. ^1H NMR (CD_2Cl_2): δ 7.04 and 7.08 (AA'BB', 8, catechol H), 7.55 (B of ABC, 2, H3 and H6), 7.98 (C of ABC, 2, J = 7 Hz, 1 Hz, H4 and H5), 8.17 (A of ABC, 2, H2 and H7), 8.58 (s, 1, H10), 9.59 (s, 1, H9). ^{13}C NMR (CD_2Cl_2): δ 112.4 (catechol C2), 119.1 (C1 and C8), 123.0 (catechol C3), 123.2 (C9), 125.1 (C3 and C6), 130.8 (C4 and C5), 131.4 (C10), 133.0 (C2 and C7), 147.8 (catechol C1). ^{11}B NMR (CD_2Cl_2): δ 26 (phenylethynyl catechol boronate, prepared analogously to 1 from (phenylethynyl)lithium, had $\delta(^{11}B)$ = 24 ppm). Mass spectrum: 462 (M^+). Since phenylethynyl catechol boronate was only prepared while determining the feasibility of reaction, it was not further characterized.

Acknowledgment. I am grateful to A. M. Mujsce for obtaining the mass spectra. I also thank W. R. Reents, L. H. Dubois, C. W. Dirk, and M. F. Katz for help in plotting and fitting the equilibrium constant data and B. Askew for useful discussions.

Registry No. 1, 119818-99-4; 2, 119796-30-4; 3, 119796-31-5; 4, 78053-58-4; T, 288-47-1; M4P, 3438-46-8; M5P, 2036-41-1; $Ni(acac)_2$, 3264-82-2; Me_3SiC_2MgBr, 61210-52-4; 1,8-dichloroanthracene, 14381-66-9; catecholboron chloride, 55718-76-8.

Synthesis of Exogonic Acid and Related Compounds

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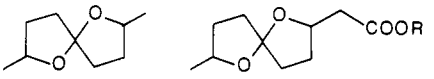
Hydroxymercuration, cyclization, and reduction of appropriate hydroxy ketones or enones carrying a suitably located α,β-unsaturated ester function is an efficient route to exogonic acid (2-(carboxymethyl)-7-methyl-1,6-dioxaspiro[4.4]nonane), a resin constituent of the Brazilian tree *Ipomoea operculata* (Martin), and related [4.5] and [5.5] spiroketal systems. Procedures incorporating stereocontrol at C-2 and C-7 of exogonic acid are also reported and involve sequential alkylation with epoxypropane and 1,2-epoxy-4-(tetrahydropyranyloxy)butane of anions (or dianions) derived from methyl acetoacetate or acetone dimethylhydrazone.

Introduction

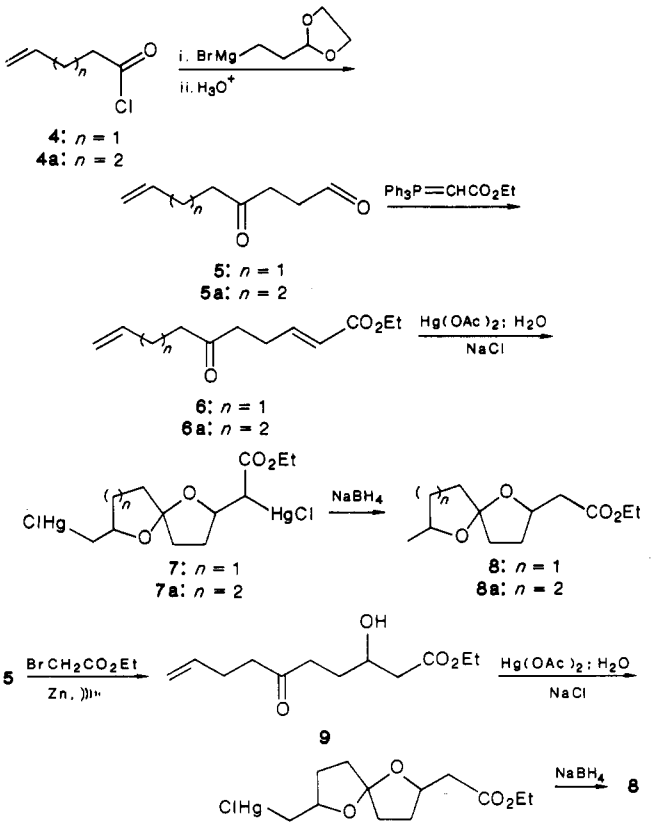
Spiroketals of relatively low molecular weight have been identified as grandular components in a variety of insect species,[1,2] and determinations of chirality, largely by capillary gas chromatography using chiral stationary phases, have been undertaken on some of these in the context of their anticipated pheromonal behavior.[3,4] Although the simple spiroketal, 2,7-dimethyl-1,6-dioxaspiro[4.4]nonane (1), is unknown as a natural product, its structural isomer,



1 2, R = H 3, R = CH_3

2-methyl-1,6-dioxaspiro[4.5]decane, has been identified in species of wasp[1a] and fruit fly.[5] 1 is structurally related to 2-(carboxymethyl)-7-methyl-1,6-dioxaspiro[4.4]nonane (exogonic acid) (2), a constituent of the resin of the Brazilian tree *Ipomoea operculata* (Martin).[6] Graf and

Scheme I



Dahlke[6] reported that methyl exogonate (3) was an optically active diastereomeric mixture, and we became interested in establishing some stereochemical detail for both

(1) See for example, (a) Francke, W.; Hindorf, G.; Reith, W. *Naturwissenschaften* **1979**, *66*, 618. (b) Bergström, G.; Tengö, J.; Reith, W.; Francke, W. *Z. Naturforsch.* **1982**, *37C*, 1124. (c) Baker, R.; Herbert, R.; Howse, P. E.; Jones, O. T.; Francke, W.; Reith, W. *J. Chem. Soc., Chem. Commun.* **1980**, 52. (d) Francke, W. *Les Médiateurs chimiques, INRA* Versailles, 1982, 81.

(2) Kitching, W.; Lewis, J. A.; Fletcher, M. T.; Drew, R. A. I.; Moore, C. J.; Francke, W. *J. Chem. Soc., Chem. Commun.* **1986**, 853.

(3) Haniotakis, G.; Francke, W.; Mor, K.; Redlich, H.; Schurig, V. *J. Chem. Ecol.* **1986**, *12*, 1559.

(4) Kitching, W.; Lewis, J. A.; Perkins, M. V.; Drew, R. A. I.; Moore, C. J.; Schurig, V.; König, W. A.; Francke, W. submitted to *J. Org. Chem.*

(5) Perkins, M. V.; Drew, R. A. I.; Kitching, W. unpublished results.

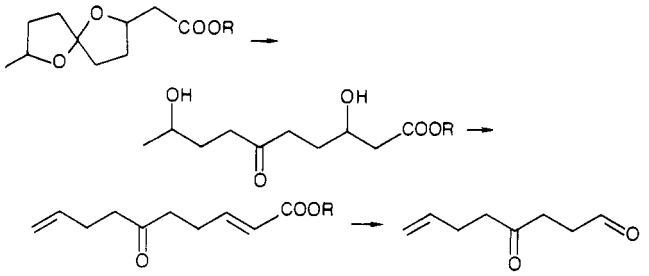
(6) Graf, E.; Dahlke, E. *Chem. Ber.* **1964**, *97*, 2785. Considerable additional information is contained in Dahlke, E., Dissertation, Univ. Tübingen, 1964.

0022-3263/89/1954-2183$01.50/0

2 and 3. As a prelude to this, and to acquire spectroscopic familiarity with the diastereomers of systems such as 2, straightforward syntheses based on organomercury chemistry have been developed. In addition, separate procedures incorporating stereocontrol at C2 and C7 of exogonic acid are also reported and are based on (epoxide) alkylation of anions or dianions derived from methyl acetoacetate or acetone dimethylhydrazone.

Results and Discussion

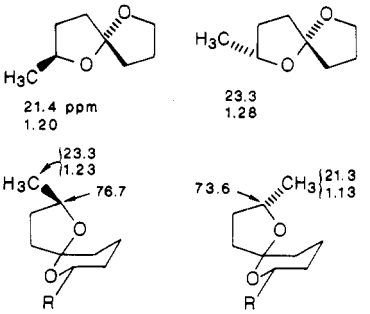
Retrosynthesis of 3 indicates that, provided oxymercuration of the α,β-unsaturated ester moiety is regiospecific,[7] the target is the keto aldehyde 4-oxo-7-octenal, as shown below (compound 5 in Scheme I).



Slow addition of the Grignard reagent[8] from 2-(2-bromoethyl)-1,3-dioxolane to 4-pentenoyl chloride (4) (at dry ice–2-propanol bath temperature) provided the keto acetal, which was hydrolyzed to the keto aldehyde 5. The stabilized Wittig reagent, (carbethoxymethylene)triphenylphosphorane[9] was added to 5 (CH_2Cl_2 solution) with the expectation that addition would occur at the aldehyde group only. Chromatographic purification of the product (silica gel) led to ethyl 6-oxo-2,9-nonadienoate (6) as a pale yellow oil in excellent yield (95%). Hydroxymercuration of 6 using an acidified aqueous tetrahydrofuran (1:1) solution and mercuric acetate,[10] followed by NaCl treatment and extraction with CH_2Cl_2, etc., provided a white crystalline product (93%; mp 168–169 °C), analyzing for the dimercury compound 7. That spiroketalization had occurred in the desired manner was confirmed by the ^{13}C NMR shifts of the spiro carbon at ca. 115 ppm for the diastereomers formed, appropriate for a 1,6-dioxaspiro[4.4]nonane moiety. (Spirocarbon shifts for 1,6-dioxaspiro[4.5]decanes are ~105 ppm and ~95 ppm for 1,7-dioxaspiro[5.5]undecanes.) The major diastereomer of this mercurial system exhibited in the ^1H NMR spectrum diagnostic resonances at δ 3.92 (d, J = 6.5 Hz, $J_{^{199}Hg}$ = 320 Hz, ClHgC*H*CO_2Et), δ 4.4 and δ 4.9 (m, -CHO), and a "tight" AB part of an ABX pattern at δ 2.3–2.4 (-C*H*$_2$-HgCl). The ^{13}C and ^1H NMR spectra are consistent with those of diastereomers of system 7 only.

Exogonic acid ethyl ester (2-[(ethoxycarbonyl)-methyl]-7-methyl-1,6-dioxaspiro[4.4]nonane) (8) was acquired by reductive removal of mercury from 7 with $NaBH_4$ under phase-transfer conditions.[10,11] However, 8 (~63%) was accompanied by ca. 20% of 6, the product of deoxymercuration.[7] Compound 8 was a diastereomeric mixture with spiro carbon shifts of 114.76, 114.93, 114.97, and 115.29 ppm, along with other appropriate signals. The ^1H NMR spectrum (400 MHz) confirmed the presence of four diastereomers of 8 in comparable amounts. The energy differences between *E,E*, *E,Z*, and *Z,Z* diastereomers in [4.4] spiroketal systems generally are not large so that all possible diastereomers may appear under equilibrating conditions. In [5.5] and even [4.5] spiroketals the anomeric effect is operative and renders the *E,E* isomer of lower free energy.[12] Compound 8 was obtained by an alternative procedure, utilizing (formal) intramolecular hydroxymercuration of ethyl 3-hydroxy-6-oxo-9-decenoate (9) obtained by Reformatsky (ethoxycarbonyl)methylation of 5 (Zn dust; ethyl bromoacetate; sonication). The above chemistry is summarized in Scheme I. Exogonic acid methyl ester (methyl exogonate (3)) was also made (by employing (carbomethoxymethylene)triphenylphosphorane) and three diastereomers (ca. 4:1:1.8) were resolved on capillary VPC. The ^1H and ^{13}C NMR spectra were very similar to those of the ethyl ester and the ^1H NMR spectrum corresponded satisfactorily with the published spectrum[6] (56 MHz) of natural methyl exogonate (two diastereomers). Previously, Smith et al.[13] had reported a synthesis of methyl exogonate starting with the lithium salt of γ-(carboxymethyl)-γ-butyrolactone and 3-lithio-3-butyn-2-yl tetrahydropyranyl ether, but a significant amount of dimethyl adipate also formed. The stereoisomeric distribution in the product was not determined.

The four diastereomers (one enantiomer of each) are shown below, and from the ^{13}C NMR spectra of different mixtures of the isomers, four sets of resonances were identified. Allocation of the signal sets to the four diastereomers are made primarily on the basis of the C*C*H_3, C*C*H_2, and CH_3C*O* chemical shifts and some ^1H NMR data, following the information available,[14] which is summarized below.



In essence, C*H*$_3$ (and CH_3C*O*) when cis to the oxygen of the second ring resonates at lower field than when trans to the oxygen (or cis to CH_2) of the second ring. On this basis the following ^{13}C and ^1H NMR (400 MHz) assignments could be made to the *E,E*, *E,Z*, *Z,E*, and *Z,Z* diastereomers (R = C_2H_5). The -C*H*$_2$C*O*$_2$Et groups appear as AB parts of ABX patterns and have the following chemical shifts: (*E,E*) 2.62, 2.43; (*E,Z*) 2.73, 2.51; (*Z,E*) 2.59, 2.42; (*Z,Z*) 2.76, 2.53. These ^1H NMR shift trends mirror those for C*C*H_3 as indicated on the structures below.

On comparison with the data for the model spiroketals, a reassuring correspondence is evident. Our initial studies[15] of natural methyl exogonate (^1H, ^{13}C NMR) suggest

(7) Thaisrivongs, S.; Seebach, D. *J. Am. Chem. Soc.* **1983**, *105*, 7407 and references therein.

(8) (a) Bal, S. A.; Marfat, A.; Helquist, P. *J. Org. Chem.* **1982**, *47*, 5046. (b) Stowell, J. C. *J. Org. Chem.* **1976**, *41*, 560.

(9) Isler, O.; Gutmann, H.; Montavon, M.; Rüegg, R.; Ryser, G.; Zeller, P. *Helv. Chim. Acta* **1957**, *40*, 1242.

(10) Kitching, W.; Lewis, J. A.; Fletcher, M. T.; De Voss, J. J.; Drew, R. A. I.; Moore, C. J. *J. Chem. Soc., Chem. Commun.* **1986**, 855.

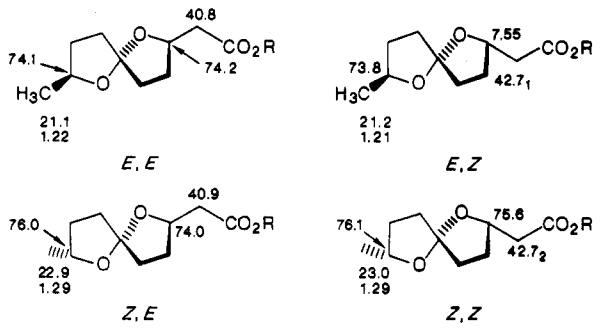
(11) See, for example: Paquet, F.; Sinay, P. *Tetrahedron Lett.* **1984**, *25*, 3071. Benhamon, M. C.; Etemad-Moghadam, G.; Speziale, V.; Lattes, A. *Synthesis* **1979**, 891.

(12) Deslongchamps, P.; Rowan, D. D.; Pothier, N.; Sauve, T.; Saunders, J. K. *Can. J. Chem.* **1981**, *59*, 1106.

(13) Jacobsen, R.; Taylor, R. J.; Williams, H. J.; Smith, L. R. *J. Org. Chem.* **1982**, *47*, 3140.

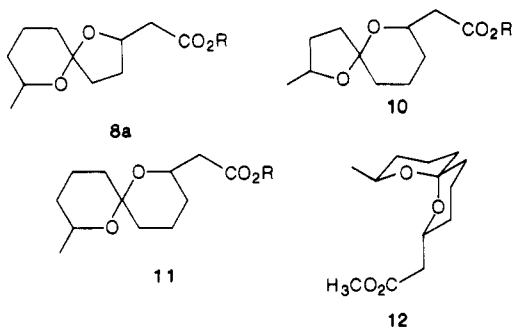
(14) (a) Francke, W.; Reith, W.; Sinnwell, V. *Chem. Ber.* **1980**, *113*, 2686. (b) Dederichs, E. Dissertation, Techischen Hochschule, Aachen, 1986, p 70. We are grateful to D. Enders for a copy of this dissertation. (c) Mori, K.; Ikunaka, M. *Tetrahedron* **1984**, *40*, 3471.

(15) Jamie, J.; Kitching, W. unpublished results.



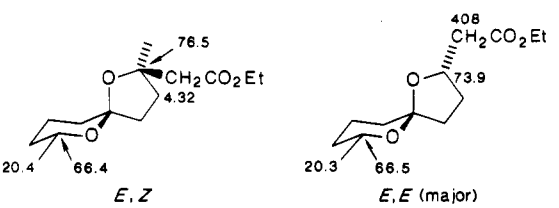
that the *E,E* and *Z,Z* diastereomers greatly predominate, and these differ in configuration at the spiro center only. Confirmation of this and other stereochemical details should result from stereocontrolled syntheses currently in progress[15] and chiral gas chromatographic comparisons, etc.

Appropriate extensions of the chemistry described above provided access to homologues of exogonic acid (ester), as described below for **8a**, **10**, and **11**.



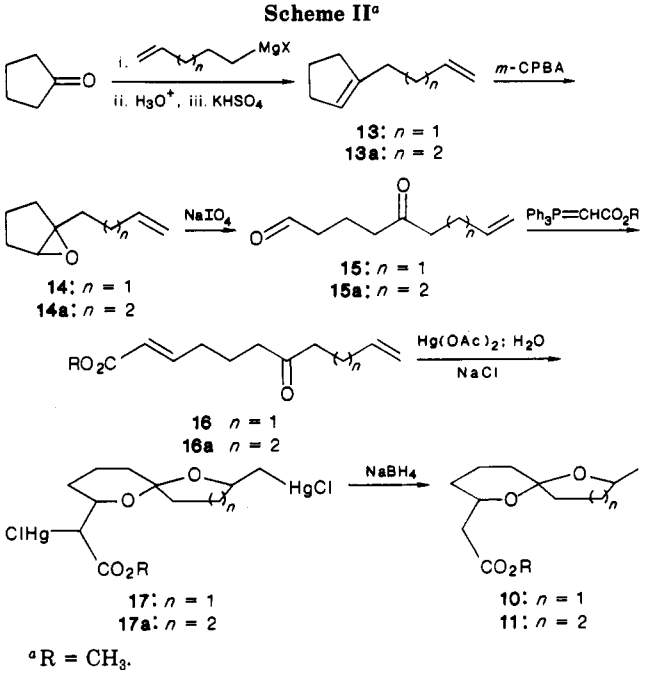
Thus, reaction of 5-hexenoyl chloride (**4a**) with the Grignard reagent from 2-(2-bromoethyl)-1,3-dioxolane[8] provided 4-oxo-8-nonenal (**5a**), which was transformed to ethyl 6-oxo-2,10-undecadienoate (**6a**) in the normal way with (carbethoxymethylene)triphenylphosphorane (refluxing in CH_2Cl_2) (see Scheme I).

Subsequent treatment with $HgOAc_2$, etc., and cyclization led to a dimercury compound (**7a**) (mp ~156–160 °C) in good yield. This white solid consisted of four diastereomers with spiro carbon shifts of 106.26 (major), 106.61, 106.93, and 107.12 ppm and diagnostic ^1H NMR shifts at δ 3.34 (d, J = ~7 Hz and $J_{^{199}Hg}$ = ~328 Hz), 3.52, 3.57, and 3.58 for C*H*HgCl. Reductive demercuration provided **8a** together with some deoxymercuration product, and separation was achieved by preparative gas chromatography to furnish **8a** as a 1.3:1 diastereomeric mixture (M^+ = 242 (5%)) with spiro carbon shifts of 106.43 and 106.22 ppm, appropriate for the [4.5] spiro system. In the ^1H NMR spectrum, characteristic resonances appeared at δ 1.107 and 1.112 (d, J = ~6.3 Hz; CH_3), δ 2.46–2.69 (AB parts of ABX patterns, $CH_2C(=O)$-), and δ 4.43, 4.53, 3.84–3.95 (>C*H*O). The two diastereomers formed most probably correspond to the arrangements below, with the *E,E* marginally favored. (Chemical shifts of CH_2CO_2Et are (*E,E*) 2.46, 2.62; (*E,Z*) 2.49, 2.69.)



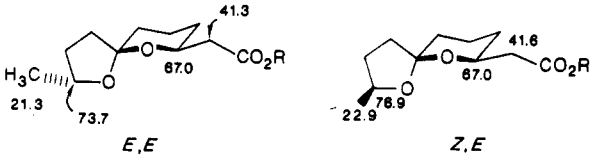
For the synthesis of **10** and **11**, the starting point was the addition of 3-butenylmagnesium bromide (or 4-pentenylmagnesium bromide) to cyclopentanone, followed by dehydration of the resulting tertiary alcohol to yield predominantly the 1-alkenylcyclopentene (**13**, **13a**). These dienes were regioselectively epoxidized with *m*-chloroperbenzoic acid to give epoxides **14** and **14a** and cleaved (periodate) to provide the unsaturated keto aldehyde, (**15**, **15a**), which on treatment with [carbomethoxy (or -ethoxy)methylene]triphenylphosphorane in the normal way furnished the α,β-unsaturated ester (**16**, **16a**). Oxymercuration of the ester **16** led to a diastereomeric mixture (~5 isomers) of mercurials but with two compounds greatly predominating. (^1H NMR: >C*H*HgCl at δ 3.35 and δ 3.47, d, J = ~6 Hz with $J_{^{199}Hg}$ = ~290 Hz: ^{13}C spiro carbon shifts at 106.88 and 107.35 ppm appropriate for the dioxaspiro[4.5] system.) The ethyl ester was also made and showed very similar properties. Demercuration was conducted to provide, for example, 2-methyl-7-[(ethoxycarbonyl)methyl]dioxaspiro[4.5]decane (**10**, R = C_2H_5) as a 3.5:1 diastereomeric (mixture (M^+ = 242, 3%) (see Scheme II).

Scheme II[a]



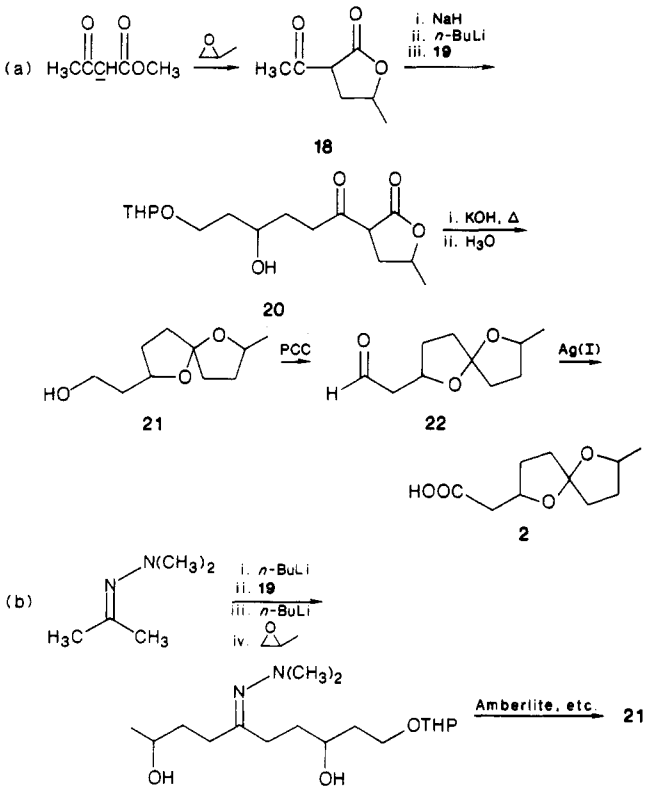
[a] R = CH_3.

The corresponding methyl ester was obtained as a 1.6:1 *E,E*:*Z,E* mixture as shown below. These relative configurations are based on trends in the ^{13}C NMR shifts as outlined above for similar systems.



Addition of 4-pentenylmagnesium bromide to cyclopentanone, followed by the sequence outlined above provided methyl 7-oxo-2,11-dodecadienoate (**16a**, R = CH_3) (Scheme II). Oxymercuration, etc., was most efficient and led to the dimercury compound (**17a**; R = CH_3) (mp 70–74 °C) in high yield (98%). As anticipated for the 1,7-dioxaspiro[5.5]undecane system,[13] this mercurial was very predominantly one diastereomer, expected to be the anomerically stabilized (*E,E*). In the ^1H NMR spectrum, key resonances were located at δ 2.07 and 2.31 (J = ~200 Hz to ^{199}Hg) (AB pattern for CH_2HgCl), δ 3.25 (d, J = ~8 Hz with $J_{^{199}Hg}$ = ~280 Hz; >C*H*HgCl), and >C*H*O at δ 4.05 and 4.03. The ^{13}C NMR spectrum confirmed the presence

Scheme III



of one predominant diastereomer (13 signals) with the signal at δ 97.70 confirming the 1,7-dioxaspiro[5.5]undecane skeleton. Reductive demercuration yielded 2-[(methoxycarbonyl)methyl]-8-methyl-1,7-dioxaspiro[5.5]-undecane (**11**, R = CH_3) as a pale yellow oil easily purified by preparative gas chromatography (>98%) (M^+ = 242, 11%). That this stereoisomer was the *E,E* diastereomer **12** was confirmed by the ^{13}C NMR resonances and detailed examination of the 400-MHz ^1H NMR spectrum, which was essentially fully assigned. Key absorptions were located at δ 1.15 (d, J = ~6.2 Hz, CH_3), δ 2.41 and 2.47 (AB of ABX, J_{AB} = ~14.8 Hz, J_{BX} = 5.10 Hz, J_{AX} = 8.9 Hz, $CH_2C{=}O$), δ 3.69 (OCH_3) and 4.06, 3.76 (CHO).

Although the oxymercuration of α,β-unsaturated esters provides methyl exogonate and related compounds in an efficient way, our aim of determining the absolute stereochemistry of the natural material required enantiocontrolled syntheses. In this regard, two approaches have been developed, each of which involves sequential anion alkylation with appropriate epoxides. In the first, alkylation of the monoanion of methyl acetoacetate with epoxypropane provides the known[14c] 2-acetyl-4-pentanolide (**18**), the dianion of which on alkylation with 1,2-epoxy-4-(tetrahydropyranyloxy)butane (**19**) yields **20**, which was not purified, but treated with potassium hydroxide and then acid to effect hydrolysis, decarbonylation, deprotection, and cyclization to the previously reported[6] exogonol (**21**), which was fully characterized spectroscopically. Oxidation of **21** with pyridinium chlorochromate led to exogonal (**22**), which was further oxidized (Ag_2O) to exogonic acid (**2**) (Scheme III, a). Alternatively, exogonol (**21**) was acquired by (i) alkylation of the anion of acetone dimethylhydrazone with epoxide **19** and (ii) in situ anion reformation at the second methyl group and alkylation with epoxypropane.[14b,16] Careful quenching with acetic acid, etc., was followed by treatment with Amberlite IR-120 (plus) ion exchange resin to effect hydrolysis and cyclization to exogonol (**21**) (Scheme III, b).

Use of the readily available enantiomers of epoxypropane[17] and of 1,2-epoxy-4-(tetrahydropyranyloxy)butane[14c] (**19**) in the alkylation steps of Scheme III would thus provide enantio control at C_2 and C_7 of exogonol (**21**) and finally in methyl exogonate. This aspect of the work will be reported at a later date together with stereochemical aspects of (natural) exogonic acid.

Experimental Section

Spectra. ^1H and ^{13}C NMR spectra were obtained on either JEOL JNM-FX-100 or JEOL-GX-400 spectrometers. Chemical shifts for ^{13}C NMR spectra are referenced to the central peak of the $CDCl_3$ (solvent): triplet at 77.00 ppm. ^1H NMR spectra (for $CDCl_3$ solvent) are referenced to internal $(CH_3)_4Si$. Combined gas chromatography–mass spectrometry was performed on a Hewlett-Packard 5992B instrument fitted with an OV101 capillary column. Low resolution mass spectral data quoted refer to GC–MS measurements, and high-resolution mass spectra were obtained with a Kratos MS25 instrument. Reagent gas NH_3 was employed for the chemical ionization measurements. Preparative gas chromatography was performed on a Shimadzu preparative gas chromatograph.

Compounds and Reactions. 4-Oxo-7-octenal (5). The Grignard reagent from 2-(2-bromoethyl)-1,3-dioxolane[9] (10.0 g, 55.2 mmol) and magnesium (1.5 g, 61.7 g·atom) was prepared in THF (70 mL) over a period of 30 min at 30–35 °C. The cooled (0 °C) solution was added via syringe to 4-pentenoyl chloride (6.6 g, 55.2 mmol) in dry THF (20 mL) cooled by a dry ice–2-propanol bath. This addition required about 25 min. After warming the solution to room temperature (over 1 h), the THF was removed (rotary evaporator) and the residual oil was poured into water (100 mL) and then extracted with ether (200 mL). After a standard workup (washed with NH_4Cl solution and then H_2O; separated, dried ($MgSO_4$) and evaporated) the oil (9.7 g, 96%) was added to 167 mL of 0.5 N HCl and vigorously stirred at 50 °C for 25 min. The solution was cooled, extracted with ether, washed with aqueous $NaHCO_3$, dried ($MgSO_4$), and evaporated. This provided 6.0 g (81%) of a colorless oil (bp 46–47 °C; 0.05 mm). Mass spectrum: (m/z, %): (140, 0, M^+), (96, 10), (85, 55), (83, 14), (57, 18), (56, 10), (55, 100), (53, 12), (43, 10), (41, 17), and (39, 32). ^1H NMR: 2.03–2.68 (m, 4 H), 2.70 (s, 4 H), 4.80–5.28 (m, 2 H), 5.50–6.18 (m, 1 H), 9.79 (br s, 1 H).

Ethyl 6-Oxo-2,9-decadienoate (6). 4-Oxo-7-octenal (**5**; 0.5 g, 3.57 mmol) and (carbethoxymethylene)triphenylphosphorane (1.22 g, 3.50 mmol) were dissolved in dichloromethane (20 mL) and refluxed for 3 h. After solvent removal, a white oily solid remained, which was chromatographed (silica gel) and eluted with *n*-hexane–ether (1:1) to provide 0.71 g (95%) of **6** as a pale yellow oil. Mass spectrum: (210, 0, M^+) (165.8, 8, M^+ – OEt), (164, 21), (155, 11), (137, 15), (136, 23), (127, 39), (119, 117), (109, 25), (100, 12), (99, 46), (85, 11), (83, 40), (82, 11), (81, 27), (68, 15), (55, 100), (54, 16), (53, 24). ^1H NMR: 1.27 (t, 3 H), 2.32 (q, 1 H), 2.47 (q, 1 H), 2.53 (t, 1 H), 2.59 (t, 1 H), 4.16 (q, 2 H), 5.50–4.96 (m, 2 H), 5.84–5.76 (m, 1 H), 6.94–6.88 (m, 1 H). ^{13}C NMR: 14.26, 25.92, 27.72, 40.65, 41.85, 60.23, 115.39, 122.07, 136.87, 147.10, 166.37, 208.09.

Mercurial 7. **6** (100 mg, 0.48 mmol) was added to $Hg(OAc)_2$ (303 mg, 0.95 mmol) dissolved in THF–H_2O (1:1) (1% in $HClO_4$) (~20 mL) and stirred at room temperature for 2 h. A saturated NaCl solution was added and the whole mixture extracted with dichloromethane, which was separated and washed with 5% $NaHCO_3$ and then H_2O. The organic layer was dried ($MgSO_4$) and evaporated to leave a white oily solid. This was washed with *n*-hexane–chloroform (1:1) and filtered to give 310 mg (93%) of the dimercury compound **7** (diastereomeric mixture) as white crystals, mp 168–169 °C dec. Anal. Calcd for $C_{12}H_{18}O_4Hg_2Cl_2$: C, 20.64; H, 2.59. Found: C, 20.17; H, 2.50. ^1H NMR: 1.0 (3 H, t, CH_3), 1.4–2.55 (10 H, ring CH_2 and CH_2Hg), 3.8–4.05 (3 H,

(16) For this sequence, see: Enders, D. In *Current Trends in Organic Synthesis*; Nozaki, H., Ed.; Pegamon Press: Oxford, U.K. 1983; p 151.

(17) Koppenhoefer, B.; Weber, R.; Schurig, V. *Synthesis* **1982**, 316 and references therein.

OCH_2, >CHHgCl), 4.35–4.6 and 4.85–4.92 (2 H, >CHO). ^{13}C NMR (major diastereomer): 14.14 (CH_3), 34.90, 35.29, 36.43, 36.45, 38.51 (CH_2), 56.28 (CHHgCl), 59.78 (OCH_2), 79.79, 80.01 (>CHO), 115.53 (spiro C), 173.52 (C=O); (Second diastereomer) 14.14, 34.37, 34.49, 34.69, 34.69, 36.03, 36.93, 56.67, 59.80, 77.63, 79.18, 115.53, 173.21.

2-[(Ethoxycarbonyl)methyl]-7-methyl-1,6-dioxaspiro-[4.4]nonane (8). Method A. Reductive removal of mercury from mercurial **7** using $NaBH_4$ in a biphasic system yielded **8** (63%) and deoxymercuration product **6** (22%). VPC examination of **8** revealed four diastereomers in the ratio of 2.1:1.3:1.4:1.0. Mass spectrum: (228, 3, M^+), (213, 11), (184, 36), (183, 47), (173, 42), (155, 11), (142, 10), (141, 100), (129, 38), (127, 36), (123, 16), (112, 34), (101, 20), (100, 12), (99, 24), (98, 67), (97, 25), (96, 14), (95, 17), (85, 85), (83, 23), (82, 10), (81, 19), (71, 11), (70, 1k). Accurate mass: 228.1346 (calcd for $C_{12}H_{20}O_4$ 228.1361), 229.1452 (calcd for M + 1 229.1439). Reduction of an essentially two-component diastereomeric mixture of **7** provided **8** as a mixture of diastereomers, being 45.1% (**8a**), 29.7% (**8b**), 6.3% (**8c**), and 3.6% (**8d**) by VPC examination. ^1H NMR: (**8a**) 1.25 (t, J = 7.1 Hz, CH_2CH_3), 1.21 (d, J = 6.10 Hz, CH_3), 1.6–~2.3 (m, 3,4,8,9-CH_2), 2.53 (dd, J = 16, 6.7 Hz, CH_2COOEt), 2.73 (dd, J = 16, 7.5 Hz), 4.14 (q, J = ~7.1 Hz, CH_2CH_3), 4.43 (q, H-2), 4.15–4.25 (m, H-7); (**8b**) 1.25 (t, J = ~7.1 Hz, CH_2CH_3), 1.285 (d, J = 6.10 Hz, CH_3), 1.6–2.3 (m, 3,4,8,9-CH_2), 2.42 (dd, J = 16, 7.5 Hz, CH_2COOEt), 2.59 (d of d, J = 16, 6.7 Hz, CH_2COOEt), 4.14 (q, J = 7.1 Hz, CH_2CH_3), 4.15–4.25 (m, H-7), 4.50 (q, H-2). ^{13}C NMR: (**8a**) 14.22, 21.19, 30.68, 31.87, 34.74, 35.96, 42.71, 60.27, 73.83, 75.52, 114.93, 171.57; (**8b**) 14.22, 22.86, 29.92, 32.55, 34.66, 36.60, 40.87, 60.37, 73.98, 76.03, 114.78, 171.09; (**8c**) 14.22, 21.09, 30.12, 32.10, 35.11, 35.42, 40.81, 60.36, 74.13, 74.22, 114.97, 171.06; (**8d**) 14.22, 23.02, 30.66, 36.56, 35.73, 36.10, 42.72, 60.25, 75.57, 76.14, 114.76, 171.61. The above assignments are based on spectra of different diastereomeric mixtures (resulting from different cyclization and reduction conditions) and assignments of the signal groups to the E,E, E,Z, and Z,Z diastereomers are discussed in the text. The general features of our ^1H NMR spectra were in satisfactory agreement with the published[6] spectrum of natural methyl exogonate, and a full correspondence in properties with methyl exogonate formed from exogonic acid recently isolated by us.[15]

Method B. To a suspension of zinc dust (210 mg, 3.23 mmol) (previously washed with 5% NaOH solution, 5% aqueous acetic acid, water, ethanol, acetone, ether and dried) in dry THF (30 mL) was added a mixture of **5** (300 mg, 2.14 mmol), ethyl bromoacetate (540 mg, 3.23 mmol), and a trace of iodine. The resulting suspension was sonicated at 20–25 °C (sonicating bath) under a static N_2 pressure for 1.5 h after which the mixture was poured into a saturated NH_4Cl solution and ether. The layers were separated, and the aqueous layer was further extracted with ether. The combined organic layer was dried, and solvent and excess ethyl bromoacetate were removed under reduced pressure to provide crude ethyl 3-hydroxy-6-oxo-9-decenoate (**9**) (390 mg, 80%). This compound was employed in the next step without further purification. Mass spectrum: (228, 0, M^+), (210, 24, $M^+ - H_2O$), (123, 46), (122, 16), (96, 12), (95, 21), (94, 12), (88, 29), (83, 15), (82, 25), 81, 100), (79, 14), (77, 14), (70, 14), (67, 13), (61, 18), (60, 25), (55, 63), (54, 31), (53, 38).

Treatment of **9** with $Hg(OAc)_2$ (1.1 equiv) and then H_2O–NaCl as described above, followed by reductive removal of mercury, provided **8** as a diastereomeric mixture (1.1:1.6:1.3:1). The NMR spectra were identical with those described above for **8**.

4-Oxo-8-nonenal (5a) (6.6 g, 78%) was obtained from 5-hexenoyl chloride (7.3 g, 55 mmol) and the Grignard reagent from 2-(2-bromoethyl)-1,3-dioxolane in the manner described for the preparation of **5**. Mass spectrum: (154, 0, M^+), (110, 11), (100, 34), (97, 14), (85, 45), (84, 11), (72, 12), (69, 51), (67, 11), (58, 19), (57, 31), (55, 51), (54, 12), (53, 14), (43, 38), (42, 16), (41, 100). ^1H NMR: 1.70 (q, 2 H), 2.06 (q, 2 H), 2.49 (t, 2 H), 2.70–2.77 (m, 4 H), 4.97–5.04 (m, 2 H), 5.73–5.78 (m, 1 H), 9.80 (br, s, 1 H). ^{13}C NMR: 22.81, 33.03, 34.71, 37.46, 41.79, 115.27, 137.90, 200.53, 208.59.

Ethyl 6-Oxo-2,10-undecadienoate (6a). Treatment of the above keto aldehyde with (carbethoxymethylene)triphenylphosphorane (1.20 g, 3.49 mmol) in the manner described previously afforded the title compound (718 mg, 99%) after column chromatography, as a yellow oil. Mass spectrum: (224, 0, M^+) (133, 12), (127, 22), (124, 13), (109, 14), (99, 33), (97, 28), (96, 45), (81, 22), (69, 49), (68, 20), (55, 53), (54, 21), (53, 26), (43, 29), (41, 100). ^1H NMR: 1.28 (t, 3 H), 1.69 (m, 2 H), 2.06 (q, 2 H), 2.43 (t, 2 H), 2.47 (q, 2 H), 2.57 (t, 2 H), 4.18 (q, 2 H), 4.97–5.04 (m, 2 H), 5.72–5.85 (m, 1 H), 5.82 (d, 1 H), 6.89–6.96 (m, 1 H). ^{13}C NMR: 14.26, 22.74, 25.99, 33.07, 40.66, 41.96, 60.26, 115.35, 122.08, 137.88, 147.24, 166.34, 208.90.

Treatment of this keto ester (718 mg, 3.21 mmol) with $HgOAc_2$ in THF–H_2O followed by NaCl solution in the normal way provided a white solid (2.41 g, 92%, mp 156–160 °C) analyzing for the dimercury compound **7a**. Anal. Calcd for $C_{13}H_{20}O_4Hg_2Cl_2$: C, 21.92; H, 2.83. Found: C, 22.14; H, 2.82. The key ^{13}C and ^1H NMR data are discussed in the text.

2-[(Ethoxycarbonyl)methyl]-7-methyl-1,6-dioxaspiro-[4.5]decane (8a). Reductive removal of mercury in the normal way with $NaBH_4$ led to a mixture of **8a** and deoxymercuration product **6a** (~19%). Pure **8a** as a diastereomeric mixture (1.3:1) was obtained by preparative gas chromatography. This compound was characterized by its mass spectrum and ^1H and ^{13}C NMR spectra. Mass spectrum: (242, 5, M^+), (198, 16), (197, 30), (173, 100), (172, 30), (170, 36), (155, 57), (128, 21), (127, 55), (124, 19), (112, 25), (97, 24), (88, 34), (85, 70), (83, 73), (82, 27), (69, 28), (57, 22), (55, 93). ^1H NMR: 1.10 and 1.11 (d, J = 6.3 Hz, CH_3C), 1,26 (t, J = ~7.1 Hz, CH_3CH_2), 1.5–2.3 (m, CH_2(ring), 10 H), 2.4–2.75 (AB parts of ABX, 2 H, CH_2CO), 3.84–3.95, 4.01, ~4.23, 4.43–4.53 (m, 2 H, >CHO), 4.15 (2 H, q, CH_2CH_3). ^{13}C NMR: 14.24, 14.25, 20.32, 20.38, 21.91, 22.02, 29.51, 29.85, 32.61, 32.64, 33.00, 33.24, 37.69, 38.77, 40.79, 43.22, 60.29, 60.34, 66.40, 66.50, 73.90, 76.48, 106.22, 106.43, 171.27, 171.58. Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 59.80; H, 9.05. (Preparative VPC sample). Accurate mass: 242.1527 (calcd for $C_{13}H_{22}O_4$ 242.1517), 243.1813 (calcd for M + NH_4OH 243.1834).

1-(3′-Butenyl)cyclopentene (13). Cyclopentanone (12.4 g, 0.148 mol) was added dropwise to the cooled (−30 °C) Grignard reagent prepared from 4-bromo-1-butene (20.0 g, 0.148 mol) and magnesium (4.0 g, 0.165 g-atom) in dry ether under N_2. After being stirred at room temperature for 2 h, the mixture was poured into a system consisting of 5% HCl and ether. The ether solution was worked up in the usual way to provide a pale yellow oil, which was distilled (77–78 °C/23 mm) to provide the tertiary alcohol, 1-(but-3′-enyl)cyclopentan-1-ol (14.6 g, 70%). Mass spectrum: (140, 0, M^+), (122, 22, M − 18), (111, 20), (85, 84), (83, 30), (81, 41), (80, 22), (79, 42), (67, 54), (57, 37), (55, 100), (53, 26). Accurate mass: (M − 18 peak) 122.1101 (calcd for $C_9H_{16}O{\cdot}H_2O$ 122.1095), 158.1547 (calcd for M + 18 158.1544). IR: 905 (s), 995 (m), 1460 (m), 2970 (s), 3380 (br, s). ^1H NMR (δ, $CDCl_3$): 1.52–1.70 (9 H, m), 1.75–1.84 (2 H, m), 2.17–2.24 (2 H, m), 4.93–5.07 (2 H, m), 5.83–5.93 (1 H, m). ^{13}C NMR: 23.73 (2 C), 29.25, 39.71 (2 C), 40.49, 82.46, 114.28. 139.23. This alcohol (9.8 g, 0.07 mol) and potassium hydrogen sulfate (10.9 g, 0.08 mol) were heated (120 °C) and stirred for 2 h. Solids were removed by decantation and after washing with CH_2Cl_2, and the combined organic fractions were washed with saturated K_2CO_3, dried over $MgSO_4$, filtered, and evaporated to provide the crude dienes. Purification by distillation afforded 7.7 g (91%) of a mixture (5:1) of dienes with the desired one (**13**) predominating. (bp 155–156 °C/760 mm). Mass spectrum: (122, 28, M^+), (94, 17), (93, 26), (81, 99), (80, 44), (79, 100), (77, 25), (67, 24), (53, 28). ^{13}C NMR: 23.45, 30.64, 32.11, 32.45, 35.15, 114.30, 123.53, 138.82, 144.22.

1-(3′-Butenyl)-1,2-epoxycyclopentane (14). To a stirred solution of the 5:1 diene mixture (**13** predominating) (5.7 g, 0.47 mol) in CH_2Cl_2 (140 mL) was added *m*-chloroperbenzoic acid (9.5 g, 0.047 mol), and the reaction was monitored by VPC. When epoxidation of the endocyclic double bond was complete (~2 h), the reaction mixture was washed thoroughly with saturated potassium carbonate solution, dried over $MgSO_4$ and evaporated to yield a 5:1 mixture of the monoepoxides (4.2 g, 65%). Mass spectrum: (138, 7, M^+), (120, 11), (97, 73), (91, 24), (84, 44), (83, 23), (79, 67), (77, 30), (69, 45), (67, 37), (55, 51), (53, 24), (41, 100). ^{13}C NMR (δ, $CDCl_3$): 19.52, 27.56, 29.49, 29.84, 31.11, 62.72, 67.50, 114.73, 138.23.

5-Oxo-8-nonenal (15). Periodic acid (4.9 g, 0.022 mol) was stirred in dry ether (260 mL) for 1 h, and the 5:1 mixture of monoepoxides (3.0 g, 0.22 mol) was added and stirred for an additional hour. The reaction solution was filtered through Celite and the filtrate washed well with 15% aqueous sodium carbonate and H_2O, dried ($MgSO_4$), and evaporated to yield a clear oil (69%).

The oil was distilled (100 °C/4 mm; Kugelrohr) to provide the unstable keto aldehyde. Mass spectrum: (154, 0, M^+), (99, 37), (83, 23), (79, 13), (71, 48), (55, 100), (43, 32), (42, 14), (41, 32), (39, 35). ^1H NMR (δ, $CDCl_3$): 1.87 (q, J = ~7 Hz), 2.27–2.32 (m), 2.44–2.49 (m) (methylene protons), 4.93–5.02 (2 H, m), 5.72–5.80 (1 H, m), 9.73 (1 H, t, J = ~1.4 Hz). ^{13}C NMR: 16.03, 27.75, 41.44, 41.81, 42.96, 115.32, 136.99, 201.87, 209.31.

Methyl 7-Oxo-2,10-undecadienoate (16). 5-Oxo-8-nonenal (2.05 g, 13.3 mmol) and (carbomethoxymethylene)triphenylphosphorane (5.40 g) were dissolved in CH_2Cl_2 (50 mL) and refluxed for 1 h, after which the solvent was removed to leave a white oily solid. Column chromatography (silica gel; *n*-hexane–ether 2:1) provided the keto ester **16** (2.35 g, 73%) as a pale yellow oil. Mass spectrum: (210, 0, M^+), (178, 16), (123, 20), (113, 34), (100, 14), (95, 42), (83, 34), (81, 32), (68, 42), (67, 23), (55, 100), (53, 20), (41, 29), (39, 34). ^1H NMR: (δ, $CDCl_3$): 1.76 (q, J = ~7.5 Hz), 2.19–2.25 (m), 2.30–2.35 (m), 2.44 (t, J = ~7.3 Hz), 2.50 (t, J = ~7.4 Hz) (CH_2 groups), 3.73. Accurate mass: 210.1238 (calcd for $C_{12}H_{18}O_3$ 210.1255), 211.1334 (calcd for M + 1 211.1334) ^1H NMR: (3 H, s), 4.96–5.0 (m), 5.75–5.86 (m), 6.89–6.96 (m). ^{13}C NMR (δ, $CDCl_3$): 21.81, 27.71, 31.37, 41.66, 41.86, 51.39, 115.26, 121.58, 136.99, 148.36, 166.89, 209.34. IR: 3075 (w), 2980 (m), 1720 (s), 1670 (m), 1440 (m), 1260 (s).

The corresponding ethyl ester (ethyl 7-oxo-2,10-undecadienoate) was also prepared. ^{13}C NMR (δ, $CDCl_3$): 14.27, 21.88, 27.76, 31.39, 41.73, 41.89, 60.23, 115.29, 122.05, 137.05, 148.07, 166.52, 209.43. (The mass spectrum and ^1H NMR spectrum were very similar to those for the methyl ester and are not detailed.)

Treatment of the above methyl ester (**16**) (1.87 g, 8.91 mmol) in THF/H_2O (ca. 1:1 with 1% $HClO_4$) with $HgOAc_2$ (5.68 g, 17.8 mmol) for 2 h, followed by addition of aqueous NaCl, led to the formation of the bis(chloromercury) derivative **17**. The solution was extracted with CH_2Cl_2 and washed with 5% $NaHCO_3$ and water. Drying, etc., of the organic phase and evaporation left a solid, which was washed with ether to yield 6.13 g (99%) of the mercurial **17**, mp 62–68 °C. Anal. Calcd for $C_{12}H_{18}O_4Hg_2Cl_2$: C, 20.64; H, 2.60. Found: C, 20.39; H, 2.65. This mercurial consisted of two predominant diastereomers. ^{13}C NMR: 19.98, 20.23, 33.04, 33.32, 33.38, 33.42, 33.45, 34.13, 38.16, 38.72, 39.63, 39.98, 51.93, 51.94, 57.29, 57.44, 69.53, 69.60, 77.26, 79.81, 106.88, 107.35, 172.16, 172.82. Characteristic ^1H NMR signals (>C*H*HgCl) are located at δ 3.35 and 3.47 (d, J = ~6 Hz with spin coupling to ^{199}Hg of ca. 290 Hz).

In a similar way, the mercurial from the ethyl ester was obtained as a white solid, mp 64–69 °C. Anal. Calcd for $C_{13}H_{20}O_4Hg_2Cl_2$: C, 21.92, H, 2.83. Found: C, 21.95; H, 2.74. ^{13}C NMR: 14.31, 19.60, 20.14, 20.20, 31.85, 33.08, 33.20, 33.30, 33.33, 33.44, 33.47, 34.14, 34.23, 38.15, 38.33, 38.54, 38.74, 39.62, 39.92, 57.45, 57.71, 57.94, 58.09, 60.91, 60.96, 61.08, 69.58, 69.66, 70.14, 70.58, 79.80, 80.77, 106.86, 107.00, 107.33, 171.66, 171.81, 171.89, 173.04. (Diastereomeric mixture).

2-Methyl-7-[(ethoxycarbonyl)methyl]-1,6-dioxaspiro-[4.5]decane (10) resulted from reductive demercuration of the mercurial **17** described above. A diastereomeric mixture (3.5:1) resulted. Mass spectrum: (242, 3, M^+), (197, 26), (155, 14), (143, 16), (142, 67), (123, 12), (114, 47), (111, 27), (101, 40), (99, 29), (98, 100), (97, 17), (96, 16), (95, 14), (85, 13), (81, 11), (71, 27), (70, 13), (69, 23), (68, 25), (67, 15). Similar demercuration of the methyl ester provided 2-methyl-7-[(methoxycarbonyl)methyl]-1,6-dioxaspiro[4.5]decane as a 1.6:1 *E,E*:*Z,E* diastereomeric mixture as outlined in the text. ^{13}C NMR: (*E,E*) 20.17, 21.25, 30.45, 31.19, 32.92, 37.72, 41.29, 51.43, 66.97, 73.71, 106.13, 171.90; (*Z,E*) 20.09, 22.91, 30.80, 31.76, 33.14, 39.24, 41.61, 52.36, 66.97, 76.90, 105.94, 171.85. ^1H NMR: (*E,E*) CH_3C (d, J = 7 Hz) δ 1.22; (*Z,E*) CH_3C (d, J = 7 Hz) δ 1.28.

1-(Pent-4′-enyl)cyclopentene (13a). 1-(Pent-4′-enyl)cyclopentan-1-ol was obtained in a fashion analogous to that for the but-3′-enyl derivative, except that pent-4-enyl Grignard reagent was added to cyclopentanone in the first step. Yield 72%; bp 98–99 °C/10 mm. Mass spectrum: (136, 12, M^+), (121, 10), (113, 29), (97, 12), (95, 29), (94, 16), (93, 17), (85, 88), (84, 25), (83, 16), (84, 14), (79, 43), (69, 94), (58, 36), (57, 29), (55, 79), (53, 24), (43, 34), (41, 100). ^1H NMR: 1.47–1.66 (m, 10 H), 1.76–1.82 (m, 2 H), 2.04–2.10 (m, 2 H), 4.9–5.04 (m, 2 H), 5.76–5.87 (m, 1 H). ^{13}C NMR: 23.83, 24.06, 34.26, 39.70, 40.98, 82.50, 114.53, 138.56. Dehydration of the above alcohol in the described manner provided, in 80% yield, a 4:1 mixture of dienes with the desired one (**13a**) predominating; bp 180–182 °C. Mass spectrum: (136, 18, M^+), (121, 17), (95, 17), (94, 25), (93, 29), (91, 13), (81, 20), (80, 21), (79, 68), (77, 21), (67, 100), (65, 14), (55, 14), (53, 19), (41, 42). ^1H NMR: 1.50–1.57 (m, 2 H), 1.81–1.88 (m, 2 H), 2.02–2.09 (m, 4 H), 2.19–2.24 (m, 2 H), 2.26–2.31 (m, 2 H), 4.91–5.03 (m, 2 H), 5.31–5.35 (m, 1 H), 5.75–5.88 (m, 1 H). ^{13}C NMR: 23.51, 27.14, 30.68, 32.48, 33.65, 35.11, 114.42, 123.39, 138.92, 144.63.

1-(4′-Pentenyl)-1,2-epoxycyclopentane (14a) resulted from epoxidation of the endocyclic double bond in **13a** as outlined above, in 81% yield; bp 96–97 °C/21 mm. Mass spectrum: (152, 3, M^+), (123, 10), (108, 15), (97, 21), (95, 27), (93, 52), (91, 36), (84, 32), (81, 48), (80, 26), (79, 48), (77, 28), (67, 56), (55, 58), (41, 100), (39, 91). Accurate mass: 152.1196 (calcd for $C_{10}H_{16}O$ 152.1201), 153.1273 (calcd for M + 1 153.1279). ^1H NMR: 1.48–2.12 (complex multiplets, 13 H), 4.93–5.4 (m, 2 H), 5.74–5.85 (m, 1 H). ^{13}C NMR: 19.56, 24.98, 27.63, 29.49, 31.25, 33.79, 62.68, 67.79, 114.76, 138.51.

5-Oxo-9-decenal (15a) resulted (73% yield) from periodate cleavage of the above epoxide in the manner described. Mass spectrum: (166, 0, M^+), (114, 15), (99, 66), (86, 20), (71, 45), (69, 47), (58, 45), (55, 54), (43, 39), (42, 23), (41, 100). ^1H NMR: 1.67 (q, J = ~7.4 Hz, 2 H), 1.89 (q, J = 7.1 Hz, 2 H), 2.02–2.08 (m, 2 H), 2.41 (t, J = 7.3 Hz, 2 H), 2.47 (t, J = ~7.1 Hz, 2 H), 2.48 (td, J = 7.1 Hz, 1.35 Hz, 2 H), 4.98–5.04 (m, 2 H), 5.72–5.79 (m, 1 H), 9.75 (t, J = 1.35 Hz, 1 H). ^{13}C NMR: 16.01, 22.69, 33.00, 41.35, 41.83, 42.90, 115.18, 137.86, 201.86, 209.99.

Methyl 7-Oxo-2,11-dodecadienoate (16a) was obtained in 85% yield by olefination of the above aldehyde with (carbomethoxymethylene)triphenylphosphorane. Mass spectrum: (224, 0, M^+), (123, 17), (113, 29), (110, 18), (97, 32), (95, 46), (81, 39), (69, 55), (68, 45), (67, 30), (59, 24), (55, 54), (53, 28), (41, 100). Accurate mass: 224.1421 (calcd for $C_{13}H_{20}O_3$ 224.1412) 225.1496 (calcd for M + 1 225.1490). IR: 3070 (w), 2960 (br, m), 1720 (s), 1660 (m), 1430 (m), 1310 (m), 1260 (m), 1196 (m), 1030 (m). ^1H NMR: 167 (q, J = ~7.4 Hz, 2 H), 1.75 (q, J = ~7.4 Hz, 2 H), 2.02–2.08 (m, 2 H), 2.19–2.24 (m, 2 H), 2.41 (t, J = ~7.4 Hz, 2 H), 2.43 (t, J = 7.4 Hz, 2 H), 3.72 (s, 3 H), 4.95–5.03 (m, 2 H), 5.72–5.79 (m, 2 H), 5.81–5.85 (m, 1 H), 6.89–6.96 (m, 1 H). ^{13}C NMR: 21.96, 22.81, 31.47, 33.13, 41.73, 42.03, 51.48, 115.30, 121.64, 138.00, 148.47, 167.00, 210.18. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.6; H, 9.0. Found: C, 68.8; H, 9.0.

Treatment of the above methyl ester with $Hg(OAc)_2$, etc., in the previously described fashion resulted in a bis(chloromercury) derivative (**17a**) in high yield (98%), mp 70–74 °C. Anal. Calcd for $C_{13}H_{20}O_4Cl_2Hg_2$: C, 20.64; H, 2.60. Found: C, 20.39; H, 2.65. This mercurial was essentially one diastereomer on the basis of its ^1H and ^{13}C NMR spectra. ^1H NMR: 1.08–2.02 (series of m, 12 H, ring CH_2), 2.07, 2.31 (AB pattern for C*H*$_2$HgCl), 3.25 (d, $J \simeq 8$ Hz, $J_{^{199}Hg}$ = 280 Hz, >C*H*HgCl), 3.68 (s, 3 H), 4.02–4.12 (m, 1 H), 4.22–4.34 (m, 1 H). ^{13}C NMR: 18.93, 18.99, 33.33, 34.39, 34.56, 34.64, 39.41, 51.87, 56.70, 68.58, 68.72, 97.70, 172.41.

(*E,E*)-2-[(Methoxycarbonyl)methyl]-8-methyl-1,7-dioxaspiro[5.5]undecane (11) was acquired in the normal way by reductive removal of mercury as described above. A sample of **11** was obtained by preparative VPC (separation from some deoxymercuration product) as a slightly pale yellow oil. Mass spectrum: (242, 11, M^+), (224, 11), (198, 13), (173, 31), (170, 24), (155, 28), (141, 19), (128, 35), (125, 19), (123, 28), (115, 100), (114, 20), (113, 26), (112, 69), (100, 25), (99, 21), (97, 75), (96, 64), (95, 28), (85, 19), (74, 15), (71, 49), (70, 17), (69, 53), (68, 24), (67, 28), (59, 33), (55, 83). The 400-MHz ^1H NMR spectrum confirmed the product as the *E,E* diastereomer on the basis of chemical shifts and coupling constants. ^1H NMR: 1.14 (H_{9a}), 1.22 (H_{3a}), 1.33, 1.36 (H_{11a}, H_{5a}), 1.45–1.65 (br m, equatorial H at positions 3, 4, 5, 9, 10, 11), 1.77 (H_{4a}), 1.93 (H_{10a}), 3.76 (H_8), 4.06 (H_2), 1.15 (d, J = ~6.2 Hz, C*H*$_3$), 2.41, 2.47 (AB part of ABX pattern, J = 14.8 Hz, 5.10 Hz, 8.9 Hz; C*H*$_2$CO), 3.69 (s, OCH_3). ^{13}C NMR: 18.59, 18.88, 21.85, 30.81, 32.76, 33.08, 35.07, 35.11, 41.37, 65.22, 66.09, 46.23, 172.09. Accurate mass: 242.1527 (calcd for $C_{13}H_{22}O_4$ 242.1518).

2-Acetyl-4-pentanolide (18) was synthesized from methyl acetoacetate and epoxypropane in the manner described by Mori.[14c] Bp 126 °C/8 mm (lit. 81–85 °C/3 mm).

2-(4′-Hydroxy-1′-oxo-6′-tetrahydropyranyloxy)-4-pentanolide (20). The dianion from **18** (6 g, 42 mmol) was generated

in THF–HMPA solution, using sequential addition of NaH and *n*-butyllithium in the reported way.[14c] To this reddish solution was added 1,2-epoxy-4-(tetrahydropyranyloxy)butane (in THF) (7.3 g, 42 mmol) with the temperature being maintained between −15 and 0 °C during the addition. After being stirred overnight at room temperature, the mixture was acidified with 5% aqueous HCl and saturated with solid NaCl. The mixture was extracted with ether and the ether extracts were dried ($MgSO_4$) and evaporated to yield crude **20** (8.1 g). (^1H and ^{13}C NMR analysis confirmed the formation of **20** but some loss of the THP group may have occurred.) Compound **20** was not purified but used directly in the next step.

2-(2′-Hydroxyethyl)-7-methyl-1,6-dioxaspiro[4.4]nonane (Exogonol) (21). A solution of KOH (4.8 g) in water (40 mL) was added to **20** (8 g) in methanol (140 mL) and the mixture was refluxed and stirred overnight. The solution was concentrated in vacuo and treated with 10% HCl solution until pH 2 was attained. The solution was saturated with NaCl and extracted with ether, such ether extracts being combined, dried ($MgSO_4$), and evaporated to produce **21** (exogonol), 2.1 g after distillation (105–107 °C/1 mm; 25% overall yield from the pentanolide **18**) (lit mp 81.5–82.5 °C/0.5 mm).

Alternative Synthesis of 2-(2′-Hydroxyethyl)-7-methyl-1,6-dioxaspiro[4.4]nonane (Exogonol) (21). *n*-Butyllithium (4.2 mL, 1.6 M in hexane, 6.8 mmol) was added dropwise to a stirred solution of acetone dimethylhydrazone (0.65 g, 6.5 mmol) in dry THF (10 mL) at −78 °C, under a N_2 atmosphere. After addition was complete, the reaction mixture was stirred for 1 h. During this time a white solid formed. 1,2-epoxy-4-(tetrahydropyranyloxy)butane (1.1 g, 6.5 mmol) was then added dropwise at −78 °C, and the reaction mixture was stirred for 12 h, during which time room temperature was attained. The solution was then cooled to −78 °C and treated with *n*-butyllithium (4.1 mL, 1.6 M in hexane, 6.6 mmol), followed by warming to room temperature and stirring (4 h). Recooling to −78 °C followed, at which temperature epoxypropane (0.38 g, 6.5 mmol) was added dropwise to the reaction mixture, which was allowed to attain room temperature and was stirred for 16 h. The mixture was acidified with glacial acetic acid (0.8 g, 13 mmol) and filtered (gravity) to remove the white solid, which was washed with a small quantity (1 mL) of acetic acid. The filtrates were placed in a round-bottomed flask (fitted with a reflux condenser) and Amberlite IR-120 (plus) ion exchange resin (sodium form) (9.75 g, 6.5 mmol) and $MgSO_4$ (6.5 g) were added. This mixture was refluxed and stirred for ca. 4 days, followed by filtering, with the solid being washed with THF (10 mL). The combined filtrates were evaporated and the residual oil was extracted into dichloromethane, which was washed with saturated sodium carbonate solution and water. The dried dichloromethane extract was evaporated to provide an oil (1.27 g, 92%), which GC–MS analysis indicated was a diastereomeric mixture (three components) of **21**·OTHP. Deprotection with a drop of concentrated HCl in methanol provided **21** (ca. 50%), which, after Kugelrohr distillation, was shown by GC–MS examination to be a diastereomeric mixture (9.7%; 34.5%; 55.8%).

21, obtained by these routes, exhibited IR and (low-field) ^1H NMR spectra consistent with the structure and in satisfactory agreement with reported data.[6] Full spectroscopic characterization of **21** (exogonol) is given below. Mass spectrum: (186, M^+, 1.0), (171, 3.4), (142, 14.5), (141, 100), (131, 20.5), (123, 14.5), (113, 23.1), (112, 24.0), (111, 15.7), (101, 59.8), (99, 10.3), (98, 14.6), (85, 76.0), (83, 24.0), (71, 24.7), (67, 15.2), (57, 29.2), (56, 43.0), (55, 66.5). (Mass spectra of other diastereomers were very similar.) ^1H NMR of four-component diastereomeric mixture: 1.15–1.30 (4 × d, J = 6 Hz, $4CH_3$), 1.40–2.15 (m, CH_2), 3.73 (br s, CH_2OH), 4.10–4.33 (m, *H*CO). ^{13}C NMR: 116.30, 115.09, 114.96, 114.92 (spiro C), 79.37, 79.32, 77.97, 77.92, 76.34, 76.04, 74.27, 74.16 (HCO), 61.53, 61.39, 61.10, 60.84 (CH_2O), 38.28, 37.49, 36.83, 36.51, 36.00, 35.98, 35.68, 35.10, 34.97, 34.61, 32.77, 32.55, 31.84, 30.75, 30.61, 30.45 (CH_2), 22.85, 22.40, 21.21, 21.02 (CH_3).

2-(Formylmethyl)-7-methyl-1,6-dioxaspiro[4.4]nonane (Exogonal) (22). To exogonol (**21**) in dry dichloromethane (0.4 g; 2 mmol in 20 mL) was added pyridinium chlorochromate (0.6 g, 3.2 mmol) with stirring. After 3 h (VPC monitoring) the reaction mixture was filtered through Florisil, which was then washed with ether (15 mL). The combined organic layer was evaporated to yield **22** (0.37 g; 87%), which was further purified (from chromium salts) by column chromatography (Florisil; hexane). GC–MS analysis showed the presence of three diastereomers of **22** (9:7:4), with another minor peak (5.5%) tentatively assigned as the fourth diastereomer of the system. Mass spectrum (one isomer only): (184, 2.6, M^+), (169, 6.2) (156, 8.4), (141, 38.6), (140, 9.8), (129, 28.0), (129, 28.0), (123, 12.7), (112, 23.0), (111, 49.0), (101, 72.6), (99, 15.0), (98, 38.6), (97, 14.7), (96, 17.0), (95, 13.5), (85, 86.3), (84, 11.5), (83, 51.9), (81, 21.3), (71, 11.9), (70, 15.4), (57, 37.3), (56, 68.1), (55, 100). Accurate mass: 184.1093 (calcd for $C_{10}H_{16}O_3$ 184.1099). ^{13}C NMR: 201.93, 201.85, 201.24, 201.16 (C=O), 115.06, 115.02, 114.87, (OCO), 77.20, 76.26, 76.13, 74.34, 74.17, 74.10, 73.96 (HCO), 51.25, 51.16, 49.44, 49.41 (CH_2CHO), 36.56, 36.21, 35.93, 35.73, 35.40, 35.16, 34.75, 34.70, (C-4, C-9), 32.57, 32.53, 32.07, 31.82, 30.90, 30.87, 30.43, 30.21 (C8, C3), 22.94, 22.85, 21.17, 21.05 (CH_3). ^1H NMR: (of four-component diastereomeric mixture) 0.95–~1.07 (4 × d, CH_3), 1.17–2.1 (m, CH_2), 2.3–2.65 (CH_2CHO), 3.85–4.45 (m, OC*H*), 9.45 (-HC(=O), 4 × dd). IR: 3435 (br, w), 2968 (s), 1726 (s), 1458 (m), 1379 (m), 1177 (s), 1072 (s), 918 (m), 867 (m). IR: 1060 (s), 1335 (m), 1370 (m), 1450 (m), 1730 (s), 2985 (s).

2-(Carboxymethyl)-7-methyl-1,6-dioxaspiro[4.4]nonane (2). To freshly prepared silver oxide (from 1.7 g of $AgNO_3$) in distilled water was added exogonol (**22**) and after reduction of Ag(I) to Ag(0) was complete, the solution was acidified (20% HNO_3) and extracted with ether to provide exogonic acid (**2**), identical in all aspects with the natural compound.[6,15] This was converted to the methyl ester **3** (diazomethane), which was identical by ^1H and ^{13}C NMR and GC–MS characteristics with the natural[6,15] and alternatively synthesized material.

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Registry No. **2**, 4316-49-8; **5**, 43160-79-8; **5a**, 119680-98-7; **6**, 119680-95-4; **6a**, 119680-99-8; **7**, 119694-43-8; **7a**, 119694-44-9; (*E*,*E*)-**8**, 119680-96-5; (*E*,*Z*)-**8**, 119719-86-7; (*Z*,*E*)-**8**, 119719-87-8; (*Z*,*Z*)-**8**, 119719-88-9; (*E*,*E*)-**8a**, 119681-00-4; (*E*,*Z*)-**8a**, 119719-89-0; **9**, 119680-97-6; (*E*,*E*)-**10**, R = Et, 119681-06-0; (*E*,*Z*)-**10**, R = Et, 119719-90-3; (*E*,*E*)-**10**, R = Me, 119681-07-1; (*E*,*Z*)-**10**, R = Me, 119719-91-4; (*E*,*E*)-**11**, R = Me, 119681-10-6; **13**, 53544-44-8; **13**, exo-alkene, 115678-80-3; **13**, exo-alkene, epoxide, 119681-02-6; **13a**, 16133-78-1; **13a**, exo-alkene, 53366-52-2; **14**, 119681-01-5; **14a**, 119681-08-2; **15**, 119681-03-7; **15a**, 106225-68-7; **16**, 119681-04-8; **16**, Et ester, 119681-05-9; **16a**, 119681-09-3; **17**, R = Et, 119694-46-1; **17**, R = Me, 119694-45-0; **17a**, R = Me, 119694-47-2; **18**, 3620-18-6; **19**, 88055-58-7; **20**, 119681-11-7; **21**, 91006-92-7; **21**, THP derivative, 119681-12-8; (*E*,*E*)-**22**, 119681-13-9; (*E*,*Z*)-**22**, 119719-92-5; (*Z*,*E*)-**22**, 119719-93-6; (*Z*,*Z*)-**22**, 119719-94-7; 2-(2-bromoethyl)-1,3-dioxolane, 18742-02-4; 4-pentenoyl chloride, 39716-58-0; (carbethoxymethylene)triphenylphosphorane, 1099-45-2; ethyl bromoacetate, 105-36-2; 5-hexenoyl chloride, 36394-07-7; cyclopentanone, 120-92-3; 4-bromo-1-butene, 5162-44-7; 1-(but-3′-enyl)cyclopentan-1-ol, 53544-43-7; (carbomethoxymethylene)triphenylphosphorane, 2605-67-6; pent-4-enyl Grignard, 34164-50-6; acetone *N*,*N*-dimethylhydrazone, 13483-31-3; epoxypropane, 75-56-9; 1-(pent-4′-enyl)cyclopentan-1-ol, 16133-77-0.