Stereoselective Synthesis of "Multifidenes" and Related Structures. Contribution to the Synthetic Chemistry of Cis-Disubstituted Alken-1-ylcyclopentenes

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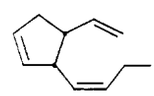
Received May 21, 1979

Multifidene **8b**, a major constituent of the essential oil of *Cutleria multifida*, was recognized as a chemical signal for gamete union. In order to test the specificity of the plant receptor system, we developed a new synthesis for structures like **8b**, which combines broad variability with a high degree of stereoselectivity. Starting from a suitably functionalized derivative of dicyclopentadiene **1a**, which allows selective transformation or introduction of side chains, a retro-dien-cleavage of the dimeric system gives easy access to homologues and structurally related compounds of the naturally occurring chemical messenger.

In recent years many remarkable olefinic hydrocarbons—lacking additional functional groups—have been isolated from marine organisms, particularly from several brown algae.[1] In some of the more carefully examined species, these hydrocarbons are chemical signals, released from unfertilized mature females, which exert important control during the early stages of gamete union.[2] A more detailed study of the Mediterranean seaweed *Cutleria multifida* (Smith) revealed that its eggs produce three $C_{11}H_{16}$ hydrocarbons of different ring size. Among them multifidene **8b**, *cis*-3-(*cis*-1-butenyl)-4-vinylcyclopentene, is the major constituent and the true biologically active substance.[3,4]



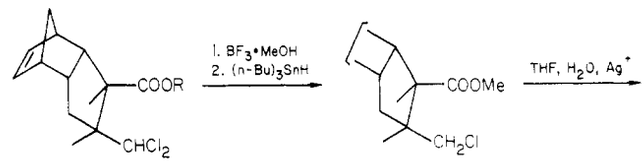
8b

Preliminary biogenetic hypotheses[5,6] were envisioned taking account of the close similarity of these substances with catabolites of polyunsaturated fatty acids. No attempt has been made as yet to obtain information about the primary chemoreceptor process. Current concepts propose binding of the messenger to an appropriately constructed receptor pit. To gauge the dimensions and shape of receptors in other systems, homologues of the ligand have proven to be useful in numerous instances.[7] For the same purpose we wished to synthesize various compounds—closely related to **8b**—with different chain length, increasing steric hindrance, or additional functional groups with altered electronic properties. Subsequent application of these substances in comparative receptor studies with *Cutleria* androgametes should then allow one to draw a more detailed picture of the primary events of chemoreception in brown algae.

It is a clear consequence of the above hypotheses that all of the synthesized compounds must have a well-defined and unambiguous stereochemistry.

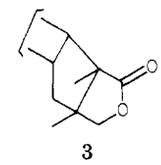
Although our previously reported synthesis[8] made **8b** and its isomers readily accessible, the last step in this synthetic sequence was accompanied by a Cope rearrangement, thus leading to a mixture of isomers which is not easily separated. We report here a new and carefully revised synthesis which combines earlier advantages with broad variability and a very high degree of stereoselectivity.

As the starting material the isomerically pure acid **1a**[8] was chosen, which is available from dicyclopentadiene and dichloroacetyl chloride in two steps and an overall yield of about 30%. Compound **1a** was converted to the methyl ester **1b** by using $BF_3 \cdot Et_2O$ in absolute methanol.[9] Dichloride **1b** was then treated with tri-*n*-butyltin hydride for 7 h at 105 °C. When the resulting monochloro ester **2** was heated in THF/H_2O containing 1 equiv of silver salt, **2** underwent neighboring-group-assisted ring closure to the lactone **3**.



1a, R = H
b, R = CH_3

2



3

Partial reduction of **3** proceeded smoothly with diisobutylaluminum hydride at −70 °C and led to the tetracyclic aluminum salt **4**, which was immediately subjected to a Wittig reaction without preceding hydrolysis of the metal–organic bond. In accordance with a mechanism postulated by Zakharkin and co-workers[10] for the partial reduction of esters, we assume that **4** rearranges at temperatures above −40 °C to the free aldehyde **5**. The latter is easily converted to an alkene, if an appropriate phos-

(1) L. Jaenicke, *Naturwiss. Rundsch.*, **31**, 236–41 (1978); R. E. Moore, *Acc. Chem. Res.*, **10**, 40–7 (1977); D. G. Müller, *Ber. Dtsch. Bot. Ges.*, **85**, 363–9 (1972).

(2) L. Jaenicke and D. G. Müller, *Fortscher. Chem. Org. Naturst.*, **30**, 61–100 (1973); L. Jaenicke, *Chiuz*, **9**, 50–8 (1975); D. G. Müller in "Marine Natural Products Chemistry", D. J. Faulkner and D. J. Fenical, Eds., Plenum Press, New York, 1977.

(3) L. Jaenicke, D. G. Müller, and R. E. Moore, *J. Am. Chem. Soc.*, **96**, 3324–25 (1974).

(4) L. Jaenicke and W. Boland, *Justus Liebigs Ann. Chem.*, 1135–42 (1976).

(5) L. Jaenicke in "Biochemistry of Sensory Functions", L. Jaenicke, Ed., Springer Verlag, Heidelberg, New York, 1974, pp 307–9.

(6) R. E. Moore, Abstracts, 116th National Meeting of the American Chemical Society Chicago, 1973; No. AGFD 056.

(7) W. A. Kafka, *Umschau*, 464–8 (1971); O. L. Chapman, J. A. Klun, K. C. Mattes, R. S. Sheridan, and St. Maini, *Science*, **201**, 926–8 (1978).

(8) W. Boland and L. Jaenicke, *Chem. Ber.*, 111, 3262–75 (1978).

(9) J. L. Marshall, K. C. Erickson, and T. K. Folsom, *Tetrahedron Lett.*, 4011–12 (1970).

(10) L. I. Zakharkin and J. P. Sorokina, *Zh. Obshch. Khim.*, **37**, 651–7; *Chem. Abstr.*, **67**, 43362 (1967).

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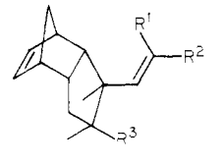
Table I. Preparation of the Olefinic Alcohols 6a-i

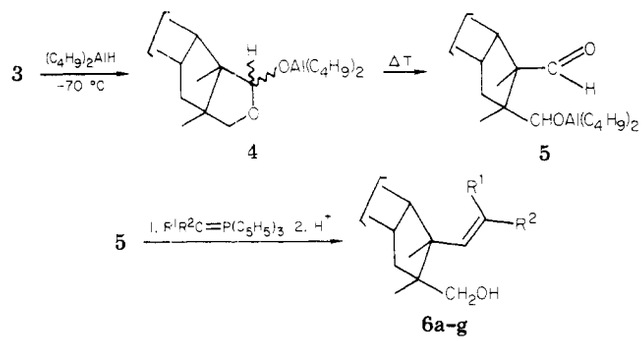


6a-i

	R^1	R^2	R^3	% yield[a]	n_D	IR (KBr, film) ν_{max}, cm^{-1}	^1H NMR (CCl_4) δ
6a	H	H	CH_2OH	52	n^{22}_D 1.5222	3320, 3060, 3040, 2950, 2920, 2850, 1630, 1000, 910, 800, 740	0.80-1.86 (m, 5 H), 1.90-3.08 (m, 6 H), 3.10-3.65 (ABX, 2 H), 4.83-6.08 (m, 3 H), 6.15 (s, 2 H)
6b	CH_3	H	CH_2OH	57	n^{22}_D 1.5250	3320, 3040, 3000, 2950, 2920, 2850, 1650, 1030, 730	0.80-2.95 (m, 8 H), 1.60 (d, 3 H), 2.70 (s, br, 2 H), 3.00 (s, 1 H), 3.12-3.64 (ABX, 2 H), 5.38 (m, 2 H), 6.18 (s, 2 H)
6c	C_2H_5	H	CH_2OH	74	n^{22}_D 1.5194	3320, 3040, 3000, 2950, 2860, 1060, 1040, 1020, 740	0.80-3.00 (m, 11 H), 0.97 (t, 3 H), 2.75 (s, br, 2 H), 3.14-3.68 (ABX, 2 H), 5.34 (m, 2 H), 6.17 (s, 2 H)
6d	C_3H_7	H	CH_2OH	67	n^{22}_D 1.5122	3330, 3030, 3000, 2950, 2910, 2850, 1640, 1050, 1030, 1010, 735	0.80-3.05 (m, 12 H), 0.96 (t, 3 H), 2.72 (s, br, 3 H), 3.13-3.76 (ABX, 2 H), 5.32 (m, 2 H), 6.17 (s, 2 H)
6e	C_4H_9	H	CH_2OH	65	n^{24}_D 1.5127	3320, 3050, 3000, 2950, 2920, 2860, 1050, 1030, 1010, 735	0.70-2.98 (m, 15 H), 0.95 (t, 3 H), 2.73 (s, br, 2 H), 3.08-3.67 (ABX, 2 H), 5.34 (m 2 H), 6.17 (s, 2 H)
6f	C_5H_{11}	H	CH_2OH	78	n^{21}_D 1.5105	3320, 3050, 3000, 2950, 2920, 1050, 1030, 1010, 735	0.80-3.00 (m, 17 H), 0.96 (t, 3 H), 2.73 (s, br, 2 H), 3.10-3.70 (ABX, 2 H), 5.35 (m, 2 H), 6.20 (s, 2 H)
6g	CH_3	CH_3	CH_2OH	54	n^{21}_D 1.5207	3320, 3040, 2950, 2920, 2860, 1035, 1010, 735	0.83-2.95 (m, 9 H), 1.59 and 1.71 (2 s, 6 H), 2.72 (s, br, 2 H), 3.15-3.65 (ABX, 2 H), 5.02 (d, 1 H), 6.08 (s, 2 H)
6h	C_2H_5	H	$COOCH_3$	74	n^{23}_D 1.5003	3040, 3000, 2970, 2920, 2860, 1740, 1460, 1440, 1200, 1165, 740	0.80-3.25 (m, 10 H), 0.96 (t, 3 H), 2.72 (s, br, 2 H), 3.55 (s, 3 H), 5.02-5.60 (m, 2 H), 6.20 (s, 2 H)
6i	C_2H_5	H	$CH(OH)CH_3$	77	n^{22}_D 1.5165	3370, 3050, 3000, 2980, 2950, 2880, 1075, 740	0.80-2.95 (m, 10 H), 0.96 (t, 3 H), 1.03 (d, 3 H), 1.65 (s, 1 H), 2.73 (s, br, 2 H), 3.65 (q, 1 H), 5.10-5.60 (m, 2 H), 6.21 (s, 2 H)

[a] Overall yield of isolated products.

phorane is present in the reaction mixture. This simple and direct conversion of a lactone into an olefin proved to be very straightforward and resulted in better yields and purer products than the same reaction performed with the isolated free hemiacetal.[11]



6a-g

The resulting alcohols **6b-f** (Table I) were stereochemically homogeneous in spite of the newly formed double bond which was introduced with almost better than 94% cis geometry, as deduced from their infrared spectra (no to very weak absorption at 965 cm^{-1}). Furthermore, analysis of the olefinic region in the ^1H NMR spectra of the corresponding end products **8b-f** allowed a more accurate determination of the isomer distribution.[12] The additional two derivatives **6h** and **6i** were obtained from **6c** by oxidation (pyridinium chlorochromate[13]) to the aldehyde followed either by Grignard reaction (methylmagnesium bromide) to give the secondary alcohol **6i** or subsequent oxidation (Ag_2O) to yield after treatment with diazomethane the corresponding methyl ester **6h**.

In contrast to our earlier synthesis,[8] the protected bisallylic arrangement of ring and side chain double bonds—as in the natural product **8b**—is now constructed at an earlier stage of synthesis, thus allowing regeneration of the cyclopentene system by flash pyrolysis without concomitant Cope rearrangement.

Surprisingly, it was found that neither the free alcohols **6a-g** (very low volatility) nor their aldehydes or esters gave satisfactory results, since the pyrolyzed compounds contained appreciable amounts of trans-disubstituted cyclopentenes.[14] Intermediate formation of biradicals[15] or enolization of the carbonyl moiety may be regarded as the reason for this isomerization. This difficulty could be easily circumvented, if the silyl ethers of **6a-g** were sub-

(11) Whether this new reaction is of general applicability or remains restricted to γ-lactones of type **3** was not investigated.

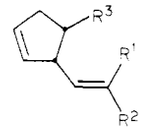
(12) This analysis was mainly performed with **8b**. Its ^1H NMR and complete GLC analysis is fully described in ref 8. However, since all other compounds were prepared by analogy, a very similar stereochemical course has to be expected.

(13) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647-9 (1975).

(14) Since the tertiary protons of **8a-f** are located at δ 2.9 and 3.6, whereas the corresponding trans-disubstituted multifidenes[8] show resonances at δ 2.6 and 3.3, respectively, a good method is at hand to determine stereochemical purity. A similar shift of resonances for cis- and trans-disubstituted multifidenes of type **9b-i** was observed.

(15) W. v. E. Doering, M. Franck-Neumann, and R. L. Kaye, *J. Am. Chem. Soc.*, 3833-44 (1972).

Table II. Preparation of the Olefinic Alcohols 7a-h

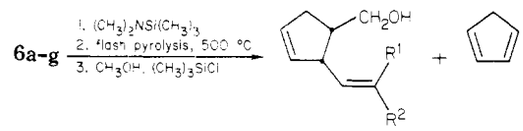


7a-h

	R^1	R^2	R^3	% yield[a]	bp,[b] °C (torr)	n_D	IR (KBr, film) ν_{max}, cm^{-1}	^1H NMR δ
7a	H	H	CH_2OH	84	79 (13)	$n^{21}{}_D$ 1.4900	3320, 3060, 3040, 2980, 2920, 2830, 1650, 1035, 1000, 915, 740, 720, 700	1.85-3.00 (m, 4 H), 3.20-3.75 (m, 3 H), 4.90-5.25 (m, 2 H), 5.50-6.08 (m, 3 H)
7b	CH_3	H	CH_2OH	87	40 (0.1)	$n^{22}{}_D$ 1.4950	3320, 3050, 3005, 2930, 2850, 1650, 1620, 1080, 1020, 750, 710	1.69 (d, 3 H), 1.90-2.80 (m, 4 H), 3.20-3.84 (m, 3 H), 5.02-5.85 (m, 4 H)
7c	C_2H_5	H	CH_2OH	87	42 (0.01)	$n^{23}{}_D$ 1.4896	3320, 3040, 3000, 2950, 2920, 2860, 2840, 1650, 1025, 750, 710	1.00 (t, 3 H), 1.80-2.75 (m, 6 H), 3.15-3.85 (m, 3 H), 5.03-5.92 (m, 4 H)
7d	C_3H_7	H	CH_2OH	83	55 (0.05)	$n^{21}{}_D$ 1.4894	3330, 3040, 3000, 2950, 2920, 2860, 1650, 1610, 1020, 750, 710	0.91 (t, 3 H), 1.40 (sextet, 2 H), 1.80-2.72 (m, 6 H), 3.15-3.82 (m, 3 H), 5.05-5.92 (m, 4 H)
7e	C_4H_9	H	CH_2OH	84	70 (0.18)	$n^{21}{}_D$ 1.4861	3320, 3040, 3000, 2950, 2920, 2860, 2850, 1650, 1610, 1020, 750, 710	0.95 (t, 3 H), 1.38 (m, 4 H), 1.75-2.74 (m, 6 H), 3.15-3.83 (m, 3 H), 5.03-5.93 (m, 4 H)
7f	C_5H_{11}	H	CH_2OH	78	89 (0.15)	$n^{21}{}_D$ 1.4863	3320, 3040, 3000, 2950, 2920, 2860, 2830, 1640, 1610, 1025, 710	0.89 (t, 3 H), 1.32 (m, 6 H), 1.75-2.75 (m, 6 H), 3.17-3.83 (m, 3 H), 5.02-5.90 (m, 4 H)
7g	CH_3	CH_3	CH_2OH	81	40 (0.08)	$n^{24}{}_D$ 1.4919	3330, 3045, 2950, 2920, 2860, 2835, 1660, 1610, 1040, 1020, 885, 720	1.72 (s, br, 6 H), 1.95-2.65 (m, 4 H), 3.27-3.75, (m, 3 H), 5.00 (d, 1 H), 5.42-5.85 (m, 2 H)
7h	C_2H_5	H	$CHOHCH_3$	82	48 (0.10)	$n^{21}{}_D$ 1.4875	3020, 3040, 3000, 2950, 2920, 2860, 2830, 1600, 1050, 980, 960, 750, 715	0.98 (t, 3 H), 1.10 (d, 3 H), 1.22 (s, 1 H), 1.90-2.50 (m, 5 H), 3.50 (t, 1 H), 3.77 (q, 1 H), 5.02-5.90 (m, 4 H)

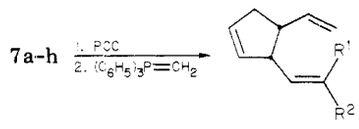
[a] Overall yield of isolated products. [b] Boiling points were determined in a microdistillation apparatus.

jected to flash pyrolysis. Under these conditions the amount of the trans impurities was limited to less than 3–4 %.



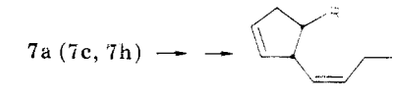
7a-h

Silylation of **6a–g** was best accomplished by using (trimethylsilyl)dimethylamine,[16] since only volatile by-products are formed. After pyrolysis and removal of the silyl protective group (MeOH, catalytic amount of $(CH_3)_3SiCl$) the monomeric alcohols **7a–h** were purified by distillation and oxidized (pyridinium chlorochromate[13]) to the corresponding aldehydes. A final treatment of these carbonyl compounds with methylenetriphenylphosphorane gave the modified multifidenes **8a–f** (Table III) in modest yield but exceptional stereochemical purity: cis disubstitution,[14] ≥96%; side chains,[12] ≥94% cis geometry.



8a-f

A second series of modified multifidens **9a–i** (Table IV) was obtained by alteration of the C_2 side chain, for which the alcohols **7a**, **7c**, and **7h** served as starting materials. Since the synthesis of these compounds followed no general scheme, the reagents and conditions are listed in Table V.



9a-i

All of the synthesized compounds were finally purified by preparative GLC to almost complete stereochemical purity (except **6h** and **7c**, which still contained some trans-disubstituted impurities after GLC separation) and applied in comparative receptor studies with *Cutleria* and *Ectocarpus* androgametes.[17]

Experimental Section

All melting and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 337 spectrophotometer. ^1H NMR spectra were obtained on a Varian EM-390 90-MHz

(16) E. W. Yankee and G. L. Bundy, *J. Am. Chem. Soc.*, **94**, 3651–2 (1972).

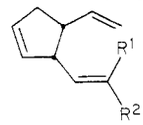
(17) Preliminary, but not representative, results have been published by D. G. Müller, *Z. Pflanzenphysiol.*, **80**, 120–30 (1976).

(18) R. Greenwald, M. Chaikovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128–9 (1963).

(19) R. Appel, R. Kleinstück, and K. D. Ziehn, *Chem. Ber.*, **104**, 2025–6 (1971).

(20) L. Horner, H. Oediger, and H. Hoffmann, *Justus Liebigs Ann. Chem.*, **626**, 26–34 (1959).

Table III. Modified "Multifidenes" 8a-f



8a-f

	R¹	R²	% yield[a]	n_D	molecular formula[b]	IR (KBr) ν_{max}, cm^{-1}	^{1}H NMR δ
8a	CH_3	H	47	n^{22}_D 1.4775	$C_{10}H_{14}$ (134.22)	3060, 3040, 3005, 2970, 2920, 2830, 1640, 1610, 990, 910, 750, 705	1.63 (d, 3 H), 2.00-2.65 (m, 2 H), 2.94 (q, 1 H), 3.61 (t, 1 H), 4.80-6.05 (m, 7 H)
8b[c]	C_2H_5	H	52	n^{22}_D 1.4779	$C_{11}H_{16}$ (148.25)		
8c	C_3H_7	H	53	n^{23}_D 1.4754	$C_{12}H_{18}$ (162.28)	3060, 3040, 3000, 2950 2920, 2860, 2830, 1640, 1610, 990, 910, 755, 710	0.9 (t, 3 H), 1.37 (sextet, 2 H), 1.80-2.65 (m, 4 H), 2.92 (q, 1 H), 3.60 (t, 1 H), 4.80-6.10 (m, 7 H)
8d	C_4H_9	H	48	n^{20}_D 1.4762	$C_{13}H_{20}$ (176.30)	3060, 3040, 3000, 2950, 2920, 2870, 2850, 1650, 1610, 990, 910, 755, 710	0.91 (t, 3 H), 1.30 (m, 4 H), 1.70-2.68 (m, 4 H), 2.92 (q, 1 H), 3.58 (t, 1 H), 4.80-6.05 (m, 7 H)
8e	C_5H_{11}	H	50	n^{20}_D 1.4779	$C_{14}H_{22}$ (190.33)	3060, 3040, 3000, 2950, 2920, 2860, 2850, 1640, 1610, 990, 910, 750, 710	0.90 (t, 3 H), 1.35 (m, 6 H), 1.70-2.62 (m, 4 H), 2.92 (q, 1 H), 3.58 (t, 1 H), 4.80-6.25 (m, 7 H)
8f	CH_3	CH_3	46	n^{23}_D 1.4795	$C_{11}H_{16}$ (148.25)	3060, 3040, 3000, 2970, 2920, 2830, 1670, 1640, 1610, 990, 910, 730	1.63 and 1.71 (2 s, 6 H), 2.05-2.70 (m, 2 H), 2.92 (q, 1 H), 3.51 (t, 1 H), 4.82-5.10 (m, 3 H), 5.45-6.06 (m, 3 H)

[a] Overall yield from alcohols 7b-g. [b] All products gave satisfactory mass spectra and microanalyses: C, ±0.08; H, ±0.09; the microanalyses were performed by I. Beetz, D-3251 Kronach. [c] For a detailed spectroscopic description see ref 8.

spectrometer in CCl_4 solution with tetramethylsilane as an internal standard. The mass spectra were obtained with a Finnigan 3200 GC/MS spectrometer. Analytical GLC was performed on a Hewelett-Packard research gas chromatograph 5750 (glass columns, 2 m × 3 mm) and preparative GLC on a Wilkens Aerograph 1520 (stainless steel colums, 2 m × 5 mm). Stationary phases and supports were (a) 15% SE 30 on Chromosorb W (80–100 mesh), (b) 20% PEG 4000 on Chromosorb P (60–80 mesh), AW, DMCS treated, (c) 20% Fractionitrile III on Chromosorb P (60–80 mesh), Aw, DMCS treated, and (d) 10% DEGS on Chromosorb W (80–100 mesh). All solvents and reagents were purified prior to use. Reactions were carried out under an argon atmosphere, unless otherwise stated.

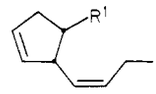
Methyl 4*c*-(Dichloromethyl)tricyclo[5.2.1.0^{2,6}]dec-8-ene-3*r*-carboxylate (1b). In a solution of 35 g (0.27 mol) of BF_3·Et_2O in 400 mL of absolute methanol was suspended 40.0 g (0.15 mol) of the pure and recrystallized acid **1a**.[8] The whole mixture was brought to reflux for 24 h and, after cooling to room temperature, treated with 150 mL of water. Most of the solvent was evaporated in vacuo and the residue was dissolved in 300 mL of ether. The two layers were separated and the organic phase was extracted carefully with a saturated $NaHCO_3$ solution and finally water to remove acidic byproducts. After drying ($MgSO_4$) the solvent was evaporated and the remaining highly viscous oil distilled under reduced pressure to yield 38.5 g (92%) of the pure ester **1b**, bp 112–114 °C (0.5 mm).

4*c*-(Hydroxymethyl)tricyclo[5.2.1.0^{2,6}]dec-8-ene-3*r*-carboxylic acid lactone (3). Dichloride **2** (25.0 g, 0.1 mol) and 30.0 g (0.11 mol) of tri-*n*-butyltin hydride were mixed without solvent and the reactants were stirred at 105 °C for 7 h. After cooling to room temperature, the mixture was placed on a silica gel column (350 g of silica gel), which was eluted first with pure hexane to remove the organotin compound. Then the solvent was changed (50% ether in hexane) and the elution was continued (GLC control, SE 30) until all of the ester **2** was removed from the column. Evaporation of the solvent gave 19.5 g (90%) of a crude product which was usually contaminated with about 4–5% completely dehalogenated ester and 2% starting material. This crude ester was dissolved in 200 mL of THF and treated with 20.0 g (0.12 mol) of $AgNO_3$ and 25 mL of water. The heterogeneous mixture was stirred for 5 h under reflux and another 3 h at ambient temperature. Then 100 mL of a saturated NaCl solution was added and the precipitated silver salts were filtered by suction. The filtrate was poured into 300 mL of ether and the two layers were separated. The aqueous phase was extracted with ether (2 × 100 mL) and the combined organic extracts were washed carefully with saturated $NaHCO_3$ solution and water (2 × 100 mL) to remove acidic byproducts. After drying ($MgSO_4$) and evaporation of the solvent, the crude lactone **3** was purified by column chromatography on silica gel (25% ether in hexane to remove the above-mentioned byproducts followed by 50% ether in hexane for elution of the lactone, GLC control, SE 30). Removal of the solvent yielded 16.5 g (96%) of the pure lactone **4** as a colorless viscous oil (n^{20}_D 1.5283), which solidified on standing: mp 41.5 °C; MS (70 eV) *m/e* 190 (0.15%, M^+), 141 (0.1%), 125 (23%), 97 (2%), 91 (2%), 79 (11%), 77 (5%), 66 (100%); ^{1}H NMR (CCl_4) δ 0.75–2.10 (m, 4 H), 2.20–3.20 (m, 6 H), 3.75–4.40 (ABX, 2 H), 6.20 (s, 2 H); IR (KBr, film) 3050, 2980, 2930, 2900, 2880, 1770, 1380, 1360, 1140/1190, 980, 740 cm^{-1}.

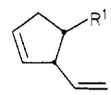
Anal. Calcd for $C_{12}H_{14}O_2$ (190.24): C, 75.76; H, 7.42. Found: C, 75.63; H, 7.53.

Preparation of the Olefinic Alcohols 6a-g (General Procedure). To a well-stirred solution of 5.0 g (25 mmol) of **3** in 70 mL of absolute toluene was added dropwise at −78 °C as a solution of 5.0 g (35 mmol) of diisobutylaluminum hydride in 10 mL of the same solvent. The reactants were stirred for 1 h at −78 °C and then poured at once into an earlier prepared solution of an appropriate phosphorane (40 mmol). The Wittig reagents were prepared as THF solutions from alkyltriphenylphosphonium bromides, using *n*-butyllithium as base. After 1 h of stirring at ambient temperature the excess of the phosphorane was hydrolyzed by addition of 100 mL of diluted hydrochloric acid and the two layers were separated. The aqueous phase was extracted with two portions of ether (100 mL) and the combined organic extracts were washed with two 100-mL portions of water. Removal of the solvent in vacuo gave a crude product, which was redissolved in 300 mL of ether and again thoroughly washed with water. After drying ($MgSO_4$) and evaporation of the solvent, the residue was treated with 300 mL of hexane and set aside overnight at −20 °C to precipitate most of the triphenylphosphine oxide formed. The clear filtrate was concentrated in vacuo and further purified by column chromatography on silica gel (10% ether in hexane, GLC control, SE 30). The physical properties of the alcohols **6a–g** are summarized in Table I.

Table IV. Modified "Multifidenes" 9a-i[a]



9b-i



9a

	R¹	entry	% yield[b]	n_D	molecular formula[c]	IR (KBr, film) ν_{max}, cm⁻¹	¹H NMR (CCl_4) δ
9a	= / \ C_2H_5	7a	67	$n^{24}D$ 1.4775	$C_{11}H_{16}$ (148.25)	3060, 3040, 3005, 2970, 2920, 2860, 2830, 1640, 1610, 995, 915, 750, 705	0.94 (t, 3 H), 1.85-2.80 (m, 4 H), 3.25 (m, 2 H), 4.79-6.00 (m, 7 H)
9b	/=\ CH_3	7c	55	$n^{24}D$ 1.4798	$C_{12}H_{18}$ (162.28)	3050, 3000, 2950, 2920, 2860, 2830, 1650, 1610, 760, 710	0.94 (t, 3 H), 1.60 (d, 3 H), 1.82-2.69 (m, 4 H), 3.22 (q, 1 H), 3.57 (t, 1 H), 4.95-5.86 (m, 6 H)
9c	/=\ C_2H_5	7c	68	$n^{20}D$ 1.4798	$C_{13}H_{20}$ (176.30)	3045, 3000, 2950, 2920, 2860, 2830, 1650, 1610, 760, 710	0.96 (t, 6 H), 2.03 (q, 4 H), 2.20-2.75 (m, 2 H), 3.20 (q, 1 H), 3.53 (t, 1 H), 4.95-5.82 (m, 6 H)
9d	CH_3 /=(CH_3	7c	52	$n^{20}D$ 1.4825	$C_{13}H_{20}$ (176.30)	3050, 3005, 2960, 2930, 2870, 1610, 750, 710	0.91 (t, 3 H), 1.55 and 1.65 (2 s, 6 H), 1.82-2.60 (m, 4 H), 3.07 (q, 1 H), 3.52 (t, 1 H), 4.93-5.85 (m, 5 H)
9e	/=\ $CH(CH_3)_2$	7c	48	$n^{24}D$ 1.4730	$C_{14}H_{22}$ (190.33)	3040, 2995, 2950, 2920, 2860, 2830, 1610, 770, 745, 715	0.96 (t, 3 H), 0.92 (d, 6 H), 1.83-2.80 (m, 5 H), 3.20 (q, 1 H), 3.52 (t, 1 H), 4.94-5.78 (m, 6 H)
9f	/C≡N	7c	46	$n^{21}D$ 1.4808	$C_{10}H_{13}N$ (147.21)	3040, 3000, 2950, 2920, 2860, 2230, 1610, 745, 715	1.01 (t, 3 H), 2.12 (q, 2 H), 2.55-2.85 (m, 2 H), 3.18 (quartet, 1 H), 3.78 (t, 1 H), 5.12-5.90 (m, 4 H)
9g	$COOCH_3$ /	6h	87	$n^{20}D$ 1.4705	$C_{11}H_{16}O_2$ (180.25)	3040, 2995, 2950, 2860, 1740, 1220, 1190, 1165, 740, 710	0.96 (t, 3 H), 2.10 (q, 2 H), 2.25-3.15 (m, 2 H), 3.22 (quartet, 1 H), 3.55 (s, 3 H), 3.88 (t, 1 H), 4.87-5.85 (m, 4 H)
9h	$COCH_3$ /	7h	84	$n^{22}D$ 1.4791	$C_{11}H_{16}O$	3040, 3000, 2960, 2920, 2860, 1720, 1610, 1350, 1215, 1170, 750, 715	1.01 (t, 3 H), 2.00 (s, 3 H), 2.15 (q, 2 H), 2.60-3.13 (m, 2 H), 3.37 (quartet, 1 H), 3.97 (t, 1 H), 4.85-5.87 (m, 4 H)
9i	$=\sim CH_3$	7h	37	$n^{20}D$ 1.4818	$C_{11}H_{16}$ (148.25)	3050, 3000, 2960, 2930, 2860, 2810, 1610, 945, 800, 775, 740, 705	0.99 (t, 3 H), 1.61 (2 d, 3 H), 2.12 (q, 2 H), 2.96 (m, 2 H), 3.90-4.21 (m, 1 H), 4.89-5.89 (m, 5 H)

[a] For reagents and conditions see Table V. [b] Yields of isolated products. [c] All products gave satisfactory mass spectra and microanalyses: C, ±0.15; H, ±0.12.

Table V

entry	alkyltriphenylphosphonium bromide	product
7a	*n*-propyltriphenylphosphonium bromide	9a
7c	ethyltriphenylphosphonium bromide	9b
7c	*n*-propyltriphenylphosphonium bromide	9c
7c	isopropyltriphenylphosphonium bromide	9d
7c	isobutyltriphenylphosphonium bromide	9e

Preparation of the Alcohols 7a-g (General Procedure). (a) Silylation of the Alcohols 6a-g. The alcohols **6a-g** (15 mmol) were dissolved in 40 mL of absolute dichloromethane and treated with 30 mmol of (trimethylsilyl)dimethylamine.[16] Stirring was continued for 2 h at ambient temperature after which the solvent and byproducts were evaporated in vacuo. The pure silyl ethers were obtained in essentially quantitative yield.

(b) Flash Pyrolysis of the Silyl Ethers. The previously obtained (see above) 15 mmol of the silyl ethers was pyrolyzed at 500 °C with argon as carrier gas. The technique of this pyrolytic cleavage corresponded in all respects to our earlier procedure, which is fully described in ref 8.

(c) Cleavage of the Silyl Ethers. For removal of the protecting group, the products of pyrolysis were dissolved in 10 mL of absolute methanol and treated with 50 mg of trimethylchlorosilane. After 15 min of stirring at room temperature, the solvent was removed in vacuo and the residue distilled under reduced pressure to give the pure alcohols **7a-g** (Table II) in about 80% overall yield from **6a-g**.

General Procedure for Pyridinium Chlorochromate[13] Oxidations. To a solution of 5 mmol of alcohol in 30 mL of absolute dichloromethane was added with stirring 15 mmol of pyridinium chlorochromate (3.2 g). After a short period the orange-red suspension turned black; the progress of the reaction was monitored by GLC using SE 30 or DEGS as stationary phases. When all of the starting material had been consumed, 60 mL of pentane was added and the precipitated chromium salts were filtered off. The solution was concentrated in vacuo and the residue redissolved in 50 mL of pentane, which precipitated the last traces of inorganic salts. After drying ($MgSO_4$) and evaporation of the solvent, the aldehydes were obtained in excellent yield (about 90%). An inert atmosphere proved to be unnecessary.

Preparation of Alcohol 6i. Alcohol **6c** (2.18 g, 10 mmol) was oxidized as described above, and the aldehyde thus obtained was added dropwise to a solution of 20 mmol of methylmagnesium bromide in 20 mL of THF. Stirring was continued for 30 min at 0 °C followed by hydrolysis with 2 N hydrochloric acid. The two layers were separated and the aqueous phase was extracted with two 50-mL portions of ether. The combined organic extracts were washed neutral ($NaHCO_3$ solution and water) and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave the crude alcohol **6i**, which could be further purified by column chromatography on silica gel (10% ether in hexane).

Methyl 3*c*-(*cis*-1-Butenyl)tricyclo[5.2.1.0^{2,6}]dec-8-ene-4*r*-carboxylate (6h) (Table I). Alcohol **6c** (1.1 g, 5 mmol) was oxidized as described above, and the aldehyde thus obtained was oxidized further to the corresponding acid as follows: To a solution containing 1.0 g (4.6 mmol) of aldehyde and 1.8 g (10.5 mmol)

of $AgNO_3$ in 18 mL of aqueous ethanol (4:1 (v/v)) was added slowly a solution of 3.6 g (64 mmol) of KOH in 30 mL of water. Stirring was continued for 1 h at ambient temperature, after which the whole contents of the flask was poured into 100 mL of water. The dark precipitate was filtered off and the aqueous phase was carefully extracted with three 50-mL portions of ether. Then the alkaline solution was acidified with concentrated hydrochloric acid and the pale yellow oil which precipitated was extracted into ether (2 × 100 mL). Drying ($MgSO_4$) and evaporation of the solvent gave the crude acid, which was immediately esterified with diazomethane. The ester **6h** was purified by column chromatography on silica gel (10% ether in hexane).

As determined by ^1H NMR this ester contained up to 15% of a trans-disubstituted isomer, which may have originated from exposure of the aldehyde to the strongly basic reaction conditions. This could be further confirmed by base ($NaOCH_3$/MeOH) induced cis–trans isomerization of the above obtained ester. After 5 h of reflux, the mixture consisted predominantly (about 80%) of the epimerized isomer.

Modified "Multifidenes" 8a–f (General Procedure). (a) Preparation of "Salt-Free" Wittig Reagents. To a suspension of 7 mmol of an appropriate alkyltriphenylphosphonium bromide in 30 mL of absolute THF was added slowly with stirring a solution of 7 mmol of sodium dimethylsulfinate (prepared from 7 mmol of sodium hydride an 10 mL of dimethyl sulfoxide according to a procedure of Greenwald et al.)[18] After 30 min of further stirring, Wittig reagents were ready for use.

(b) Wittig Reactions. Alcohols **7a-f** (5 mmol) were oxidized with pyridinium chlorochromate[13] as described above. The thus obtained aldehydes were dissolved in 5 mL of absolute THF and added slowly to a solution of 7 mmol of methylenetriphenylphosphorane. The reactants were stirred for 30 min at ambient temperature after which the contents of the flask was poured into 50 mL of water. The two layers were separated and the aqueous phase was extracted with two 50-mL portions of pentane. The combined organic extracts were thoroughly washed with water, dried ($MgSO_4$), and evaporated in vacuo. The residue was redissolved in 50 mL of pentane and set aside overnight to precipitate the triphenylphosphine oxide formed. The clear filtrate was concentrated in vacuo and further purified by column chromatography on silica gel (pure pentane for elution, which was monitored by GLC, SE 30). A final purification by preparative GLC (PEG 4000 or Fractonitril III) yielded the modified "multifidenes" **8a–f** in about 98% stereochemical purity. Their physical properties and yields, respectively, are compiled in Table III.

Modified "Multifidenes" 9a–e (Table IV). Oxidation and subsequent Wittig reactions were carried out as described for **8a–f**. The reagents and starting materials are listed in Table V.

***cis*-2-(*cis*-1-Butenyl)cyclopent-3-enenitrile (9f).** Alcohol **7c** (1.1 g, 7.2 mmol) was oxidized with pyridinium chlorochromate and the aldehyde thus obtained was dissolved in 50 mL of aqueous ethanol (45/5 (v/v)) and treated with 1.5 g (22 mmol) of hydroxylamine hydrochloride. Then a solution of 2.0 g (14.5 mmol) of K_2CO_3 in 10 mL of water was added slowly with stirring. After 1 h at ambient temperature, most of the ethanol was evaporated in vacuo and the residue taken up in 100 mL of ether. Two washings with water (50 mL) removed the inorganic salts and after drying ($MgSO_4$) and evaporation of the solvent, the crude aldoxime was obtained. For conversion of this oxime to the nitrile the following dehydration step was used:[19] 1.0 g (6.1 mmol) of the crude oxime and 4.0 g (40 mmol) of triethylamine were dissolved in 20 mL of tetrachloroethane and brought to reflux. Then 2.6 g (10 mmol) of triphenylphosphine in 10 mL of absolute tetrachloromethane was gradually added with stirring. Stirring was continued for an additional 2 h, while the process of the reaction was monitored by GLC (DEGS). The solvent was evaporated in vacuo and the crude residue redissolved in 100 mL of pentane to remove the phosphine oxide formed. The clear filtrate was concentrated in vacuo and the crude nitrile further purified by column chromatography on silica gel (10% ether in hexane). The final purification could be easily achieved by preparative GLC with DEGS as the liquid phase. However, it must be noted that the compound contained about 5% of the trans-disubstituted material, which may originate from the strongly basic conditions used in both steps.

Methyl *cis*-2-(*cis*-1-Butenyl)cyclopent-3-enecarboxylate (9g). This product was obtained via flash pyrolysis of the ester **6h**. Since the starting material **6h** contained appreciable amounts of trans-disubstituted ester, **9g** was obtained in only 92% stereochemical purity.

***cis*-2-(*cis*-1-Butenyl)cyclopent-3-enyl Methyl Ketone (9h).** Alcohol **7h** (5 mmol) was oxidized with pyridinium chlorochromate as described above.

3-(*cis*-1-Butenyl)-4-ethylidene-1-cyclopentene (9i). Alcohol **7h** (5 mmol) was added slowly to a solution of 10 mmol of triphenylphosphonium dibromide[20] in 20 mL of absolute benzene. Stirring was continued for 30 min, after which 100 mL of ether was added. The insoluble material was filtered off and the solution was washed neutral with a saturated $NaHCO_3$ solution and water. After drying ($MgSO_4$), the solvent was distilled off and the residue prepurified by column chromatography on silica gel (pure pentane for elution). Final purification was achieved by preparative GLC using PEG 4000 as the liquid phase.

Acknowledgment. The authors thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support. We also thank D. Rossius for her skilled technical assistance.

Registry No. 1a, 71975-07-0; **1b**, 71975-08-1; **2**, 71975-09-2; **3**, 71975-10-5; **6a**, 71975-11-6; **6a** silyl ether, 71975-12-7; **6b**, 71975-13-8; **6b** silyl ether, 71975-14-9; **6c**, 71975-15-0; **6c** aldehyde, 71975-16-1; **6c** silyl ether, 71975-17-2; **6d**, 71975-18-3; **6d** silyl ether, 71975-19-4; **6e**, 71975-20-7; **6e** silyl ether, 71975-21-8; **6f**, 71975-22-9; **6f** silyl ether, 71975-23-0; **6g**, 71975-24-1; **6g** silyl ether, 71975-25-2; *cis*-**6h**, 71975-26-3; *trans*-**6h**, 71975-27-4; **6i**, 71975-28-5; **7a**, 71975-29-6; **7a** aldehyde, 71975-30-9; **7b**, 71975-31-0; **7b** aldehyde, 71975-32-1; **7c**, 71975-33-2; **7c** aldehyde, 71975-34-3; **7d**, 71975-35-4; **7d** aldehyde, 71975-36-5; **7e**, 71975-37-6; **7e** aldehyde, 71975-38-7; **7f**, 71975-39-8; **7f** aldehyde, 71975-40-1; **7g**, 71975-41-2; **7h**, 71975-42-3; **8a**, 71975-43-4; **8b**, 68366-04-1; **8c**, 71975-44-5; **8d**, 71975-45-6; **8e**, 71975-46-7; **8f**, 71975-47-8; **9a**, 72028-57-0; **9b**, 71975-48-9; **9c**, 71975-49-0; **9d**, 71975-50-3; **9e**, 71975-51-4; **9f**, 71975-52-5; **9g**, 71975-53-6; **9h**, 71975-54-7; **9i**, 71975-55-8.