during the decomposition of quaternary ammonium perchlorates. This suggests that decomposition may be initiated by transfer of a proton from the cation to the anion. If a similar mechanism were to pertain for the permanganates, the observed ignitions would be in agreement with the violent oxidative nature of permanganic acid. It has been observed that $HMnO_4$ reacts explosively when brought into contact with any type of organic material.[66]

One of the objectives of this work was to prepare an inexpensive quaternary ammonium or phosphonium permanganate that had good solubility properties and was at the same time stable enough to be safely handled. Our studies have led us to the conclusion that, by use of the procedures described herein, several such compounds can be easily prepared. When using any of these compounds, however, precautions are in order. The solids should be held in cold storage at all times and care should be exercised whenever they are being handled.

For long term shelf stability, benzyltriethylammonium permanganate seems to be the best choice despite the fact that it has been reported to be an explosive compound.[13,14] We have stored this compound in our laboratory in solid form for over two years without any problems. Methyltriphenylphosphonium permanganate may be considered as a second choice, but it is expensive to prepare when compared with the benzyltriethylammonium salts. In the interest of maximum laboratory safety it is recommended that no attempt be made to store large amounts of these potentially explosive compounds.[12-14]

For very slow reactions, which take several days to complete, (*p*-fluorobenzyl)tributylammonium permanganate may be suggested because it has very good stability in solution. However, the corresponding quaternary ammonium halide is not available commercially thus making its preparation more time consuming and expensive.

In dichloromethane, which appears to be the best solvent for these compounds,[5] the solubility of benzyltriethylammonium permanganate seems to be sufficient. However, in highly nonpolar solvents (such as carbon tetrachloride) methyltri-*n*-octylammonium permanganate should be used because of its greater solubility. When all of the various factors such as solubility, stability, cost, and reactivity are taken into consideration, the use of benzyltriethylammonium permanganate in methylene chloride would be recommended for most preparative purposes.

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Registry No. $QMnO_4$ (Q = tetraethylammonium), 76710-78-6; $QMnO_4$ (Q = tetra-*n*-propylammonium), 35638-40-5; $QMnO_4$ (Q = tetra-*n*-butylammonium), 35638-41-6; $QMnO_4$ (Q = tetra-*n*-pentylammonium), 35638-41-6; $QMnO_4$ (Q = tetra-*n*-hexylammonium), 35638-43-8; $QMnO_4$ (Q = tetra-*n*-heptylammonium), 34293-34-0; $QMnO_4$ (Q = tetra-*n*-octylammonium), 82444-41-5; $QMnO_4$ (Q = methyltri-*n*-butylammonium), 82444-42-6; $QMnO_4$ (Q = methyltri-*n*-octylammonium), 82444-43-7; $QMnO_4$ (Q = *n*-butyltri-*n*-propylammonium), 92282-95-6; $QMnO_4$ (Q = benzyltriethylammonium), 68844-25-7; $QMnO_4$ (Q = benzyltri-*n*-butylammonium), 60754-79-2; $QMnO_4$ (Q = *n*-hexadecyltrimethylammonium), 73257-07-5; $QMnO_4$ (Q = (*p*-nitrobenzyl)-tri-*n*-butylammonium), 92282-96-7; $QMnO_4$ (Q = (*p*-fluorobenzyl)tri-*n*-butylammonium), 92282-97-8; $QMnO_4$ (Q = (*p*-fluorobenzyl)triethylammonium), 92282-98-9; $QMnO_4$ (Q = methyltriphenylphosphonium), 73335-41-8; $QMnO_4$ (Q = ethyltriphenylphosphonium), 92282-99-0; $QMnO_4$ (Q = *n*-propyltriphenylphosphonium), 92283-00-6; $QMnO_4$ (Q = *n*-butyltriphenylphosphonium), 92283-01-7; $QMnO_4$ (Q = *n*-pentyltriphenylphosphonium), 92283-02-8; $QMnO_4$ (Q = *n*-hexyltriphenylphosphonium), 92283-03-9; $QMnO_4$ (Q = *n*-heptyltriphenylphosphonium), 92283-04-0; $QMnO_4$ (Q = benzyltriphenylphosphonium), 92283-05-1; $QMnO_4$ (Q = (trichloromethyl)triphenylphosphonium), 92283-06-2; $QMnO_4$ (Q = (2,6-dichlorobenzyl)tris(*p*-chlorophenyl)phosphonium), 92283-07-3; $QMnO_4$ (Q = (*p*-fluorobenzyl)tris(*p*-fluorophenyl)phosphonium, 92283-08-4; $QMnO_4$ (Q = (*p*-fluorobenzyl)triphenylphosphonium, 92283-09-5; $Q(MnO_4)_2$ (Q = 1,2-ethylenebis(triphenylphosphonium), 76710-76-4; $QMnO_4$ (Q = potassium 18-crown-6 complex), 74218-78-3; $KMnO_4$, 7722-64-7.

Supplementary Material Available: Packing diagrams and tables containing infrared data, final least-squares, positional and thermal parameters, details of the molecular geometry, and the equation of least-squares planes for α and β forms of methyltriphenylphosphonium and *n*-heptyltriphenylphosphonium permanganates (25 pages). Ordering information is given in any current masthead page.

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Absolute Configuration of Multifidene as Deduced by Total Synthesis of the Unnatural Levorotatory Enantiomer

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The powerful sperm attractant of the brown alga *Cutleria multifida*, (+)-multifidene (**1**), is shown to possess the 3*S*,4*S* configuration. The protocol, which parallels our earlier synthesis of the racemic polyolefinic hydrocarbon, begins with (−)-*cis*-(5-vinyl-2-cyclopentenyl)acetic acid (**2**) of known absolute configuration. Thus, the stereogenic nature of (+)-**1** is identical with that of the naturally occurring prostaglandins.

Sexual reproduction by the brown alga *Cutleria multifida* is recognized to originate by release of a pheromone bouquet by mature female gynogametes.[1] The active component of this luring substance has been identified as

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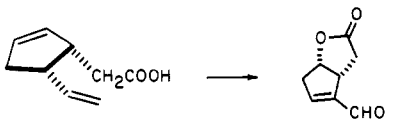
multifidene (1).[1b,2] Its specific function is to attract large

(+)-1 (−)-1

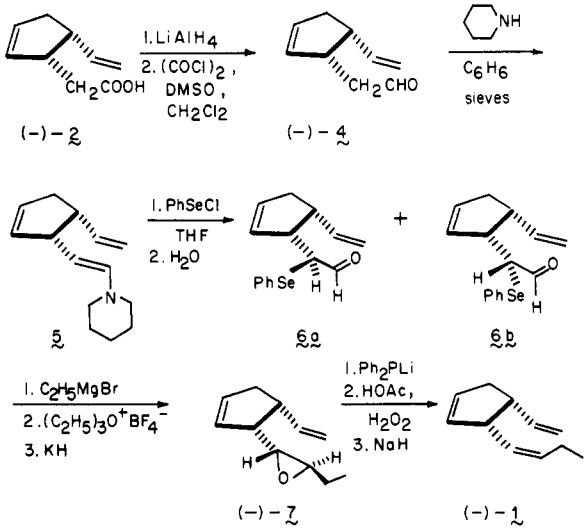
numbers of male androgametes. Once mating has occurred, the supernumerary cells lose interest and depart.[3] Stereoselective total synthesis of this powerful sperm attractant has been reported by the Jaenicke–Boland team[4] and by this group.[5] Additionally, the naturally occurring dextrorotatory enantiomer of 1 has been determined to be 100 times more active than the (−)-antipode.[6] However, the absolute configuration of these volatile polyolefinic hydrocarbons remained to be unraveled. Only in this fashion can an accurate imprint of the receptor–pheromone interaction ultimately become fully appreciated. For these reasons, we have adapted the key elements of our earlier synthetic pathway to the enantiospecific preparation of (−)-1. The present investigation establishes that natural (+)-multifidene possesses the 3*S*,4*S* configuration as shown in the formulas.[7]

During our previous development of a protocol for the stereocontrolled preparation of precursors to all the primary prostaglandins from butadiene,[8] the readily available[9] *cis*-(5-vinyl-2-cyclopentenyl)acetic acid was resolved with *endo*-bornylamine. The enantiomerically pure dextrorotatory enantiomer, $[\alpha]^{23}_{D}$ +157°, was demonstrated to be (3*S*,4*S*)-**2** by conversion via several steps to (+)-**3** of known absolute configuration.



(+)-2 (+)-3

For the synthesis of **1**, selected fractions obtained from the mother liquors of the preceding resolution were acidified. This processing gave (−)-**2** possessing a rotation of −47.1°, indicative of a 30% enantiomeric excess of the 3*R*,4*R* antipode. With a secure supply of (−)-**2** in hand, we proceeded to effect its conversion to aldehyde **4** via tandem hydride reduction and Swern oxidation.[10] When



(−)-2 (−)-4 5 6a 6b (−)-7 (−)-1

4 was allowed to react with dry piperidine in benzene solution containing molecular sieves, enamine **5** was produced in 99% unpurified yield. Direct exposure of **5** to a slight excess of phenylselenenyl chloride in cold (−115 °C) tetrahydrofuran[11] followed by aqueous hydrolysis at 25 °C provided the desired α-seleno aldehyde **6** in 47% yield as a 9:1 mixture of diastereomers. This product distribution is the same as that obtained from electrophilic phenylselenation of the (*E*)-(trimethylsilyl)oxy analogue.[5]

With a suitable control element in place, proper installation of the *cis*-butenyl side chain was undertaken. The course of ethylmagnesium bromide addition to the carbonyl group in **6** is suitably controlled by the α-phenylselenyl substituent.[12] When the alcohol mixture was exposed to triethyloxonium tetrafluoroborate and cyclization subsequently effected with potassium hydride,[5] essentially pure (−)-**7** was obtained. Some partitioning of the diastereomers undoubtedly occurs during these two steps, perhaps as the result of different ring closure rates. Addition of lithium diphenylphosphide[13] to (−)-**7**, followed in turn by acidification, oxidation with hydrogen peroxide, and elimination with sodium hydride according to Bridges and Whitham,[14] produced (−)-**1**. The $[\alpha]^{25}_{D}$ of a sample purified by vapor-phase chromatography was −80°. On the basis of the reported rotation of optically pure (−)-**1** (−271°),[6] it is clear that no loss of stereochemical integrity was incurred during our synthetic scheme.

Precise knowledge of the spatial arrangement of the double bonds within (+)-**1** now shifts attention to the details of chiral recognition by the algal receptor system. The significantly lessened pheromone activity of more highly saturated congeners of (+)-**1**[7] instructively demonstrates that all three double bonds of multifidene are necessary to achieve the proper biological response. Perhaps chemoreception by this brown alga is especially dependent on mutual dipolar interaction between the unsaturated centers in (+)-**1** and the receptor matrix.[2c,3c] In any case, signal recognition evidently requires proper superimposition of the double bonds of the side chains and cyclopentene ring.

Finally, it is interesting and perhaps significant that the absolute configuration of (+)-multifidene is analogous to that of the prostaglandins, several of which are well-known

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to be produced in substantial amounts under comparable aquatic conditions.

Experimental Section

(-)-*cis*-(5-Vinyl-2-cyclopentenyl)acetic Acid (2). Various mother liquor fractions obtained from resolution of the racemic acid with *endo*-bornylamine[8] were acidified with 10% hydrochloric acid and extracted with ether (3 × 50 mL). The combined organic layers were washed with brine, dried, and evaporated to provide 4.56 g of **2**, $[\alpha]^{25}_D$ -47.1° (*c* 0.035, C_2H_5OH), which was directly reduced without further purification.

(-)-*cis*-(5-Vinyl-2-cyclopentenyl)acetaldehyde (4). A slurry of (-)-**2** (4.56 g, 30.0 mmol) and lithium aluminum hydride (2.0 g, 52.6 mmol) in anhydrous ether (100 mL) was stirred at the reflux temperature for 1 h. The reaction mixture was cooled in an ice bath while treated dropwise sequentially with water (2 mL), 15% sodium hydroxide solution (2 mL), and again with water (6 mL). The solids were separated by filtration and rinsed well with ether. The combined filtrates were evaporated to give 3.24 g (78%) of alcohol: $[\alpha]^{25}_D$ -40.1° (*c* 0.041, C_2H_5OH); ^1H NMR (300 MHz, $CDCl_3$) δ 5.85-5.76 (m, 1 H), 5.70 (s, 2 H), 5.03-4.93 (m, 2 H), 3.60 (t, J = 6.1 Hz, 2 H), 2.88-2.72 (m, 2 H), 2.41-2.13 (AB of ABMX, J_{AB} = 14 Hz, 2 H), 1.66-1.39 (m, 2 H); ^{13}C NMR ($CDCl_3$) ppm 139.8, 134.4, 129.8, 114.7, 61.9, 46.1, 44.9, 37.5, 33.8; *m/z* calcd (M^+) 138.1044, obsd 138.1034.

A cold (-78 °C) solution of oxalyl chloride (0.40 mL, 4.58 mmol) in dichloromethane (5 mL) was treated dropwise with a solution of dimethyl sulfoxide (0.71 mL, 10.0 mmol) in the same medium (2 mL). After 10 min, the above alcohol (248 mg, 1.79 mmol) in dichloromethane (5 mL) was introduced and the reaction mixture was stirred at -78 °C for 30 min. Following the addition of triethylamine (3 mL, 21.5 mmol), the solution was allowed to warm to room temperature during 1 h and treated with water (10 mL). The aqueous phase was extracted with dichloromethane and the combined organic phases were washed with brine, dried, and evaporated. MPLC purification of the residue (silica gel, elution with 5% ethyl acetate in petroleum ether) afforded 130 mg (50%) of **4**, $[\alpha]^{25}_D$ -34.4° (*c* 0.036, C_2H_5OH), identical in all respects with the known racemic material.

Enamine 5. A mixture of (-)-**4** (500 mg, 3.68 mmol), freshly distilled piperidine (2.0 mL, 20.2 mmol), and activated 3-Å molecular sieves (2.0 g) in dry benzene was stirred at 25 °C for 14 h. The reaction mixture was filtered, and the filtrate was evaporated to provide 733 mg (99%) of **5** which was used directly without further purification: ^1H NMR (300 MHz, $CDCl_3$) δ 6.20-5.80 (m, 1 H), 5.76 (s, 2 H), 5.10 (m, 2 H), 4.85 (m, 2 H), 4.20 (m, 2 H), 2.80 (m, 4 H), 2.2-2.0 (m, 2 H), 1.60 (br s, 6 H).

Phenylselenation of 5. A solution of **5** (733 mg, 3.64 mmol) in dry tetrahydrofuran (15 mL) was cooled to -115 °C under an argon atmosphere prior to dropwise addition of phenylselenenyl chloride (740 mg, 3.86 mmol) in 5 mL of the same solvent. The reaction mixture was stirred at -110 °C for 5 min, warmed to -78 °C during 15 min, treated with water (20 mL) and ether (80 mL), and stirred vigorously at room temperature for 4 h. The separated organic layer was dried and evaporated to leave a residue which was purified by MPLC on silical gel. Elution with 3% ethyl acetate in petroleum ether provided 500 mg (47%) of **6a** and **6b** as a 9:1 mixture (^1H NMR analysis); $[\alpha]^{25}_D$ -56.3° (*c* 0.010, C_2H_5OH). The spectral properties of this mixture were identical with those reported earlier.[5]

Epoxide 7. Reaction of (-)-**6** (500 mg, 1.72 mmol) with ethylmagnesium bromide [prepared from freshly distilled ethyl bromide (0.30 mL, 4.02 mmol) and magnesium turnings (100 mg, 4.17 mmol)] in ether (25 mL) at -116 °C to -78 °C as outlined previsouly[5] returned 70 mg of unreacted **6** and gave 353 mg (74% based on recovered **6**) of selenyl alcohol, $[\alpha]^{25}_D$ -39.1° (*c* 0.011, C_2H_5OH).

A solution of this substance (350 mg, 1.09 mmol) in dry dimethoxyethane (10 mL) was stirred at 25 °C under nitrogen in a drybox as freshly prepared triethyloxonium tetrafluoroborate (277 mg, 1.44 mmol) was added in portions over a few minutes. After 2 h, the reaction mixture was transferred via syringe to a slurry of sodium hydride (3.54 mmol) in dry dimethoxyethane (5 mL), stirred for 30 min, and poured into brine. Following the predescribed workup[5] and MPLC on silica gel (elution with 5% ethyl acetate in petroleum ether), there was isolated 100 mg (56%) of (-)-**7**, $[\alpha]^{25}_D$ -47.5° (*c* 0.0305, C_2H_5OH). The spectral properties of this substance were identical with those reported earlier.[5]

(-)-Multifidene (1). A solution of diphenylphosphine (70 μL, 0.402 mmol) in anhydrous tetrahydrofuran (0.5 mL) was stirred at 0 °C as *n*-butyllithium in hexane (0.25 mL of 1.6 M) was added via syringe. A solution of (-)-**7** (32.3 mg, 0.196 mmol) in anhydrous tetrahydrofuran (1.5 mL) was then introduced and the reaction mixture was stirred at 25 °C for 14 h. Following recooling to 0 °C, acetic acid (0.25 mL) and 30% hydrogen peroxide (0.25 mL) were sequentially added. The solution was stirred at 0 °C for 4 h and diluted with dichloromethane (25 mL). The separated organic phase was washed with saturated sodium bicarbonate solution (10 mL) and brine (10 mL), dried, and evaporated to leave 92 mg of crude hydroxy phosphine oxide.

The above product was dissolved in dry dimethylformamide (1.5 mL) and slowly added to a stirred slurry of sodium hydride (2.5 mmol) in the same solvent (0.5 mL). After 16 h at 25 °C, the reaction mixture was quenched with water and extracted with petroleum ether (3 × 15 mL). The combined extracts were dried and carefully evaporated to provide 20 mg (69%) of (-)-**1**, $[\alpha]^{25}_D$ -80° (*c* 0.0005, CCl_4), whose spectra (MS, ^1H NMR) were identical with those of the natural product.

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Synthesis and Diels-Alder Reactions of 1,3-Dimethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole. A New Annulation Strategy for the Construction of Ellipticine and Isoellipticine

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The novel fused heterocycle 1,3-dimethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole (**4**) is synthesized from 3-ethylindole (**6**) in six steps (46% yield) or from indole-3-carboxaldehyde (**12**) in four steps (21% yield). Furoindole **4** undergoes Diels-Alder reactions with dimethyl acetylenedicarboxylate, *N*-phenylmaleimide, benzyne, and 3,4-pyridyne (**5**) to give the expected adducts **17**, **18a,b**, **19**, and **23a,b**, respectively. Deoxygenation and desulfonylation of **19** and **23a,b**, respectively, give benzocarbazole **22** and a readily separable mixture of the pyridocarbazole alkaloids ellipticine (**1a**) and isoellipticine (**2a**).

The 6*H*-pyrido[4,3-*b*]carbazole alkaloids ellipticine (**1a**) and 9-methoxyellipticine (**1b**) exhibit pronounced anticancer activity toward several experimental[1] and human[2] tumor systems, and 2-methyl-9-hydroxyellipticinium ace-

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