1.5 Hz), 9.76 (d, 1, H_1, $J_{1,2}$ = 8.2 Hz); MS, *m/e* (relative intensity) 298 (M^+, 100), 270 (14.3); HRMS, calcd for $C_{20}H_{10}O_3$ 298.0629, found 298.0622.

Reduction of Lactone 9 with $LiAlH_4$. The lactone **9** (10 mg) in 20 mL of THF was added at room temperature for 5 min to a stirred suspension of 10 mg of $LiAlH_4$ in 20 mL of THF. After stirring 1 h at room temperature, conventional workup gave 10 mg of crude product, which was purified by chromatography on Florisil. Elution by CH_2Cl_2/hexane (80:20) and CH_2Cl_2/EtOAc (95:5) gave **10** (6 mg) as a thick oil. Spectral properties: NMR δ 2.75 (br s, 1, OH), 4.45 (s, 2, CH_2OH), 5.1 (s, 1, CHOH), 5.6 (s, 1, OH), 7.0 (d, 1, H ortho to OH, *J* = 10.5 Hz), 7.15-7.8 (m, 9 H); MS, *m/e* (relative intensity) 304 (M^+, 24.8), 286 (100).

Oxidation of Benzo[*a*]pyrene (14) with CAS. Benzo[*a*]pyrene (**14**) (0.12 g, 0.5 mmol) was allowed to react with CAS (0.54 g, 1.0 mmol) under the conditions used for oxidation of **1**. The crude product was purified by chromatography on silica gel. Elution by hexane afforded the unreacted hydrocarbon. Further elution with CH_2Cl_2/hexane (80:20) afforded a mixture of the 1,6- and 3,6-quinones **17** and **18** (60 mg, 43%): MS, *m/e* (relative intensity) 282 (M^+, 100), 258 (37.7). These two diones were separated by HPLC, using a linear gradient from 40-100% CH_3OH in H_2O at 2 mL/min. Their retention volumes (71 mL, **18**, and 68.8 mL, **17**) and UV were identical with those of reference samples.

Oxidation of Benzo[*a*]anthracene (15) by CAS. Benz[*a*]anthracene (**15**) (0.11 g, 0.5 mmol) on oxidation with CAS (0.54 g, 1 mmol) as described for **1** gave a crude product, which was purified by chromatography on silica gel. Elution by hexane afforded the unreacted hydrocarbon. Elution with CH_2Cl_2/hexane (30:70) gave 7-oxo-12-hydroxy-7,12-dihydrobenz[*a*]anthracene (**19**, 10 mg, 8%), mp 181-183 °C (lit.[18] mp 186 °C). Spectral properties: IR 1652 cm^{-1}; NMR δ 7.4-8.0 (m, 7), 8.1-8.4 (m, 2), 8.5-8.7 (m, 1, H_1); MS, *m/e* (relative intensity) 260 (M^+, 100), 231 (63.6). Further elution by CH_2Cl_2 gave benz[*a*]anthracene-7,12-dione (**20**, 30 mg, 23%), mp 166-167 °C (lit.[19] mp 170-171 °C). Spectral properties: NMR δ 7.6-8.0 (m, 5, H_2, H_3, H_4, H_9, and H_{10}), 8.1-8.5 (m, 4, H_5, H_6, H_8, and H_{11}), 9.65 (dd, 1, H_1); MS, *m/e* (relative intensity) 258 (M^+, 100), 230 (41.3).

Oxidation of Chrysene (16) by CAS. Chrysene (**16**) (0.11 g, 0.5 mmol) on oxidation with CAS (0.54 g, 1 mmol) as described for **1** gave a crude product, which was purified by chromatography on silica gel. Elution by hexane afforded unreacted chrysene. Further elution with CH_2Cl_2/hexane (30:70) gave the lactone **21** (10 mg, 8%), mp 179-180 °C (lit.[19] mp 188-189 °C). Spectral properties: IR, 1730, 1735 cm^{-1}; NMR δ 7.58-7.68 (m, 3, H_2, H_3, and H_8), 7.78 (d, 1, H_{12}, $J_{11,12}$ = 9.1 Hz), 7.55-7.92 (m, 2, H_1, H_9), 8.08 (d, 1, H_{11}, $J_{11,12}$ = 9.0 Hz), 8.2 (d, 1, H_{10}, $J_{9,10}$ = 9.0 Hz), 8.48 (d, 1, H_7, $J_{7,8}$ = 9.1 Hz), 8.6 (d, 1, H_4, $J_{3,4}$ = 9.0 Hz); MS, *m/e* (relative intensity) 246 (M^+, 100), 218 (25.2); HRMS calcd for $C_{16}H_{10}O_2$ (M - H) 245.060, found, 245.062. Further elution by CH_2Cl_2 gave chrysene-5,6-dione (**22**, 30 mg, 23%), mp 239-240 °C (lit.[19] mp 240-241 °C). Spectral properties: NMR δ 7.4-7.95 (m, 6, H_1, H_2, H_3, H_8, H_9, and H_{12}), 8.0-8.3 (m, 3, H_7, H_{10}, and H_{11}), 9.4 (dd, 1, H_4); MS, *m/e* (relative intensity) 258 (M^+, 12.1), 230 (100).

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Stereochemistry of Addition of Allyl Grignard Reagents to (*R*)-(+)-Pulegone and Other α,β-Ethylenic Ketones

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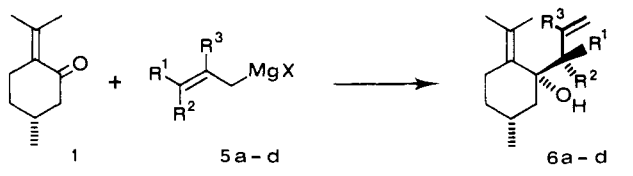
The 1,2-addition of allyl, crotyl, and 2-methyl-2-butenyl Grignard reagents to (*R*)-(+)-pulegone is regio- and stereoselective. In contrast, 3-penten-2-yl and 3-methyl-2-butenyl Grignard reagents undergo 1,2- and 1,4-additions. A "compact approach" stabilized by orbital interaction is the proposed mechanism. A further confirmation was obtained with acyclic enones.

Carbonyl alkylation has long been studied and constitutes one of the largest collections of fundamental bond construction reactions in organic synthesis. A great deal of work has been devoted to the stereochemistry of addition of Grignard reagents to cycloalkanones.[1] These reactions proceed via attack predominantly at the less hindered side of the carbonyl, i.e., generally equatorial attack.[1a,b]

The addition reactions of allyl Grignard compounds to cycloalkanones exhibit low selectivity and are, therefore, of little preparative interest.[2,3] Stereochemical and relative-rates studies suggest that carbonyl compounds react with allyl Grignard reagents via a noncyclic, bimolecular, electrophilic substitution mechanism (S_E2')[4] (substitution anti).[5] On the other hand, allylmagnesium derivatives

Scheme I[a]



[a] **a**, $R^1 = R^2 = R^3 = H$, X = Cl; **b**, $R^1 = CH_3$, $R^2 = R^3 = H$, X = Cl; **c**, $R^1 = R^2 = H$, $R^3 = CH_3$, X = Cl; **d**, $R^1 = R^3 = CH_3$, $R^2 = H$, X = Br.

(1) (a) Ashby, E. C.; Laemme, J. T. *Chem. Rev.* **1975**, *75*, 521. (b) Ashby, E. C.; Chao, C. L.; Laemme, J. T. *J. Org. Chem.* **1974**, *39*, 3258. (c) Reetz, M. T.; Steinbach, J.; Westermann, J.; Peter, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 1011. (d) Perry, M.; Maroni-Barnaud, Y. *Bull. Soc. Chim. Fr.* **1969**, 3574.
(2) (a) Cherest, M.; Felkin, H. *Tetrahedron Lett.* **1968**, 2205. (b) Abenhaim, D.; Henry-Basch, E.; Feron, P. *Bull. Soc. Chim. Fr.* **1969**, 4038.
(3) In contrast, the relative insensitivity of the allyl Grignard toward steric crowding about the carbonyl has obvious synthetic utility.
(4) (a) Felkin, H.; Gault, Y.; Roussi, G. *Tetrahedron* **1970**, *26*, 3761. (b) Cherest, M.; Felkin, H.; Frajerman, C. *Tetrahedron Lett.* **1971**, 379. (c) Cherest, M.; Felkin, H. *Tetrahedron Lett.* **1971**, 383. (d) Felkin, H.; Frajerman, C.; Roussi, G. *Ann. Chim. (Paris)* **1971**, *6*, 17.

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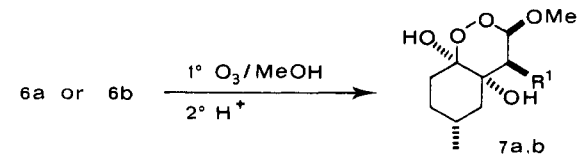
Scheme II[a]



[a] **7a**, R^1 = H; **7b**, R^1 = CH_3.

undergo rapid metallotrophic shifts even at low temperatures,[6] resulting in poor stereo- and regioselectivity.[7]

In contrast to the addition of Grignard reagents to cycloalkanones, very little is known about the stereochemistry of Grignard addition to cycloalkenones or alkenylcycloalkanones.[8]

We report herein the results of the addition reactions of allyl Grignard reagents, methylmagnesium iodide, and Reformatsky reagent with (*R*)-(+)-pulegone (**1**), and allyl Grignard reagents with mesityl oxide (**2**), 3-penten-2-one (**3**), and crotonaldehyde (**4**). Pulegone derivatives are of interest since they have been shown to exhibit useful properties as chiral auxiliaries[9] and chiral precursors for asymmetric synthesis.[14]

Results

The addition of allyl Grignard compounds **5a–d** to **1** gives rise to allylpulegols **6a–d** (Scheme I). The yield is much improved if the Barbier process is used.[22,23] The ^{13}C NMR spectrum of each product after a purification by chromatography on silica gel was consistent with the presence of only one diastereoisomer per Grignard reagent. The infrared spectra of alcohols **6b** and **6d** (CCl_4) contained a relatively narrow band due to the free hydroxyl group. A broader band at a lower frequency was assigned to the intramolecular OH–π interaction. We would expect the conformational population of the hydrogen-bonded species to be higher in the threo than in the erythro isomer.[24]

Ozonolysis of **6a** and **6b** leads respectively to **7a** and **7b** (methanol, and acidic workup) (Scheme II).

The structure of crystalline endoperoxide **7b** was assigned on the basis of spectroscopic measurements and was confirmed by X-ray crystallography, which clearly indicated the relative positions, of the two methyl, two hydroxyl, and methoxy groups.[25] In addition, the infrared absorption for the two hydroxyl groups at 3568 and 3482 cm^{-1} (concentration-independent bands) was in agreement with a cis ring junction.[26] The ^1H NMR spectrum showed the coupling constant of the anomeric proton (J = 4.8 Hz) to be consistent with a cis arrangement of vicinal protons.[27]

The stereochemistry of alcohols **6c** and **6d** was assigned by CD studies of ketols **8a** and **8b**, respectively, after ozonolysis followed by dimethyl sulfide addition. The infrared spectra of **8a** and **8b** in carbon tetrachloride each showed only a concentration-independent band at 3495 cm^{-1}. The CD curve of **8a** showed a very weak positive Cotton effect (see Table I) consistent with an equilibrium

Table I. CD Data of Cyclohexanones

compd	solv	temp, °C	λ_{max}, nm	$[\theta]_{max}$
8a	MI[a]	25	285	75
8a	methanol	25	288	55
			315	60
8b	MI	25	285	4200
			313	−1100
8b	MI	−136	285	3840
			292	2750
			302	2100
			319	−460
8b	ethanol	25	287	3000
8b	ethanol	−104	285	3200 (sh)
			293	4130
			302	4130
			313	2160 (sh)
17	MI	25	287	2900
17	MI	−97	295	3400
17	MI	−140	295	3870
17	dioxane	25	290	3225
17	methanol	25	290	2700
20	MI	25	290	1900
20	MI	−140	303	750
21	MI	25	292	4000
21	MI	−125	287	7250
			296	6000 (sh)

[a] MI solvent is composed of methylcyclohexane–isopentane in the ratio 1:3 by volume.

(5) (a) Anh, N. T. *J. Chem. Soc., Chem. Commun.* **1968**, 1089. (b) Anh, N. T. *Les règles de Woodward-Hoffmann*; Ediscience Ed.: Paris, 1970; p 163.

(6) Benkeser, R. A. *Synthesis* **1971**, 347.

(7) (a) Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69*, 1. (b) Abenhaim, D.; Henry-Basch, E.; Feron, P. *Bull. Soc. Chim. Fr.* **1969**, 4043. (c) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. (d) For examples of allylation of chiral ketones, see: Soai, K.; Ishizaki, M. *J. Org. Chem.* **1986**, *51*, 3290 and references therein.

(8) (a) Kharach, M. S.; Reinmuth, O. *Grignard Reactions of Nonmetallic Substances*; Constable: London, 1954. (b) Tomioka, K.; Koga, K. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1983; Vol. 2, Part A, pp 201–223.

(9) A number of methods for obtention of chiral auxiliaries from pulegone have been proposed: 1,3-oxathiane;[10] 8-phenylmenthols;[11] 8-*p*-anisylmenthol;[12] iron tricarbonyl–pulegone.[13]

(10) (a) Eliel, E. L.; Lynch, J. E. *Tetrahedron Lett.* **1981**, *22*, 2855. (b) Eliel, E. L.; Soai, K. *Tetrahedron Lett.* **1981**, *22*, 2859. (c) Eliel, E. L. *Phosphorus Sulfur* **1985**, *24*, 453.

(11) (a) Whitesell, J. K.; Liu, C. L.; Buchanan, C. M.; Chen, H. H.; Minton, M. A. *J. Org. Chem.* **1986**, *51*, 551 and references cited therein. (b) Herzog, H.; Scharf, H. D. *Synthesis* **1986**, 420.

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(14) For examples of synthetic efforts in this area, see the obtention of vitamin E,[15] dihydrosphingonine,[16] phytol,[17] (*R*)-muscone,[18] lactones,[19] and various pheromones[20] or sesquiterpenes.[21]

(15) Koreeda, M.; Brown, L. *J. Org. Chem.* **1983**, *48*, 2122.

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(22) Blomberg, C.; Hartog, F. A. *Synthesis* **1977**, 18.

(23) Essentially the same ratio of the products was formed in the in situ reaction or conventional condensation between crotylmagnesium chloride and trimethylchlorosilane; see: Sakurai, H.; Kudo, Y.; Miyoshi, H. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1433.

(24) Sicher, J.; Cherest, M.; Gault, Y.; Felkin, H. *Collect. Czech. Chem. Commun.* **1963**, *28*, 72.

(25) Details of the crystallographic measurements on this compound will be published elsewhere (Baldy, A.; Pierrot, M.; El Idrissi, M.; Santelli, M.).

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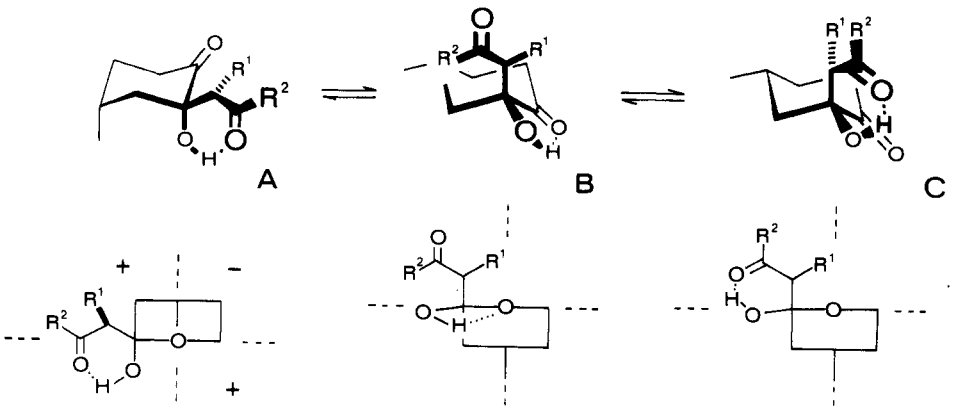
(27) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry* 2nd ed.; Pergamon: New York, 1969; p 288.

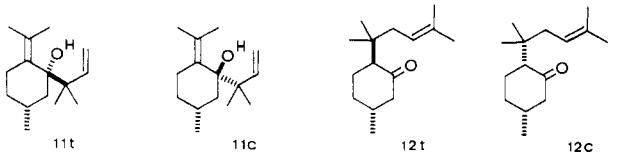
Scheme III[a]



[a] **8a**, R^1 = H, R^2 = CH_3; **8b**, R^1 = R^2 = CH_3; **20**, R^1 = H, R^2 = OEt.

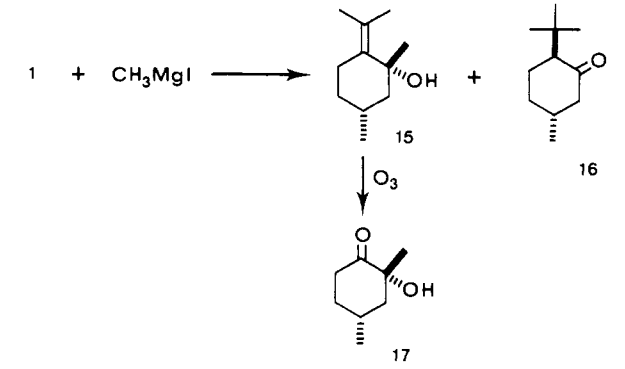
of three chair conformations **8aA**, **8aB**, and **8aC** as expected from the octant rule[28] (Scheme III). The negative effect of **8aA** would be neutralized by the strong positive contributions of **8aB** and **8aC**. The CD curve of **8b** in isopentane–methylcyclohexane (3:1) showed a decrease in the positive rotational strength associated with a red shift, with subsequent lowering of temperature[29] (see Table I and Scheme III). The relatively negative effect anticipated for the hydroxyl group of **8aA** would be outweighed by the strong positive contribution of the 1-methyl-2-oxoprop-1-yl group of **8bB** and **8bC**. The more stable conformer, **8aA**, would make an increasing contribution to the apparent rotational strength as the temperature was lowered. Therefore, the result would be a net decrease in the Cotton effect amplitude. However, in ethanol solution, the amplitude increased with lower temperature. It is presumed that the intramolecular hydrogen bond would be broken in the polar solvent so that the free 1-methyl-2-oxoprop-1-yl group of the preferred **8bA** conformation is completely in the positive octant. These assignments are in agreement with the findings that report that axial hydroxyl groups cause a red shift of the CD curve peak by about 13 nm whereas an equatorial hydroxyl group results in a blue shift of about 2–10 nm.[29b,30]

Addition of (3,3-dimethylallyl)magnesium bromide (**9**) to **1** gave four main products, which were identified as alcohols **11t** and **11c** and ketones **12t** and **12c** (relative proportions, respectively, 4:2:2:1; overall yield 80%). The

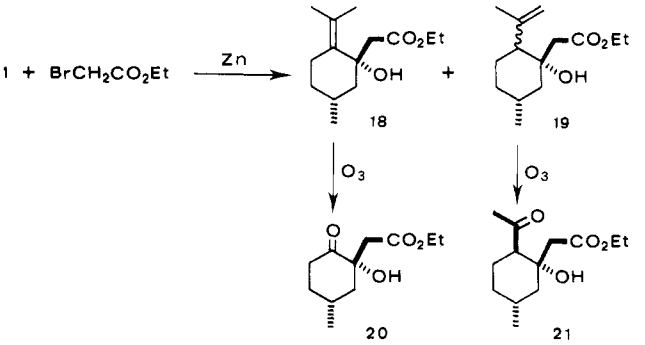


condensation was conducted at 0 °C, and reversibility of the addition is evidenced by the fact that the allylic Grignard reagent afforded a dimethyl substitution on the

Scheme IV

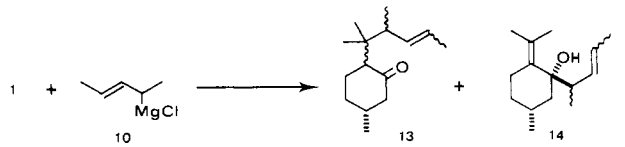


Scheme V



reactive center.[31] Nevertheless, addition of the 1,1-dimethylallyl moiety led to a 2:1 excess of alcohols **11** vs ketones **12** (in contrast, in refluxing ether, **12** are major products).

Interestingly, we observed that addition of 3-penten-2-yl magnesium chloride (**10**) to **1** leads mainly to ketone **13** (**13**:**14** = 1.2:1). Ketone **13** was a mixture of six isomers (relative proportions of isomers 3.8:1.2:9:2:4.2:1, *E*:*Z* isomers, 5:1).[32] The alcohol **14** consisted of only two isomers.



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(29) For conformational studies of 2-hydroxycyclohexanones by temperature-dependent circular dichroism, see: (a) Wellman, K. M.; Briggs, W. S.; Djerassi, C. *J. Am. Chem. Soc.* **1965**, *87*, 73. (b) Suga, T.; Shishibori, T.; Matsuura, T. *J. Org. Chem.* **1967**, *32*, 965. (c) Shishibori, T.; Suga, T.; Watanabe, S.; Matsuura, T. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 3284. For configurational studies in the field of steroids, see: (d) Bull, J. R.; Enslin, P. R. *Tetrahedron* **1970**, *26*, 1525.

(30) (a) Cookson, R. C.; Dandegaonker, S. H. *J. Chem. Soc.* **1955**, 352. (b) Crabbe, P. *Applications de la Dispersion Optique et du Dichroisme Circulaire optique en Chimie Organique*; GauthierVillars: Paris, 1968; p 324.

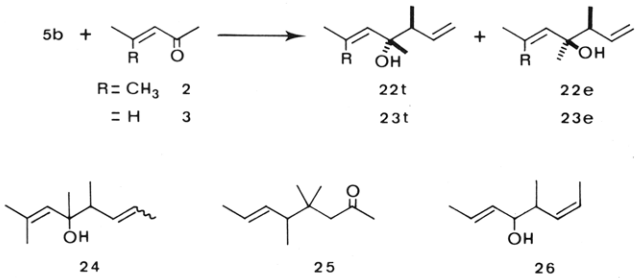
(31) (a) Benkeser, R. A.; Broxterman, W. E. *J. Am. Chem. Soc.* **1969**, *91*, 5162. (b) Benkeser, R. A.; Siklosi, M. P. *J. Org. Chem.* **1976**, *41*, 3212. (c) Barbot, F.; Miginiac, P. *Bull. Soc. Chim. Fr.* **1977**, 113. (d) Holm, T. *Acta Chem. Scand., Ser. B* **1976**, *B30*, 985. (e) Benkeser, R. A.; Siklosi, M. P.; Mozdzen, E. C. *J. Am. Chem. Soc.* **1978**, *100*, 2134.

We also compared the addition of methylmagnesium iodide and Reformatsky reagent on **1**. Addition of methylmagnesium iodide gives rise to **15**[33] and **16**[34] in the approximative ratio 4:1 (Scheme IV). The *R* configuration of the new chiral center of **15** was determined by circular dichroism studies of ketol **17** resulting from oznolysis (intramolecular hydrogen bond, concentration-independent band at 3512 cm^{-1}). Again, a strong positive Cotton effect was observed increasing at low temperature (see Table I), as expected from the octant rule[28] with equatorial hydroxyl group.[29]

Reformatsky reagent[35] (ethyl bromoacetate, zinc, dimethoxymethane) addition to **1** provided a separable mixture of hydroxy esters **18** (45% yield) and **19** (6.4% yield).[36] To determine their stereochemistry, we ozonized each hydroxy ester and obtained keto esters **20** and **21** (Scheme V).

The analysis of CD and IR data of **20** was consistent with an equilibrium of the three chair conformers **20A**, **20B**, and **20C** resulting from axial addition of the Reformatsky reagent (Scheme III). The infrared spectrum of **20** showed only a concentration-independent band at 3495 cm^{-1} resulting from an intramolecular hydrogen-bond between the hydroxyl and the lone-pair electrons on the carboxy oxygen atoms. The CD curves of **20** in isopentane–methylcyclohexane (3:1) show a decrease in the positive rotational strength associated with a bathochromic shift with lowering of temperature (see Table I). For reasons similar to those described previously for **8b**, an *S* configuration was predicted for the new chiral center of **18**.

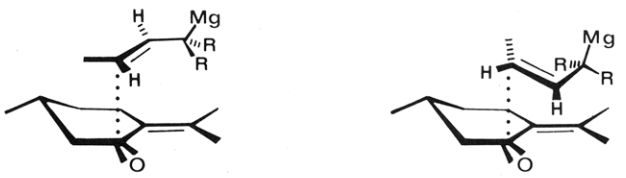
Condensation of crotylmagnesium chloride (**5b**) with open-chain enones such as **2** and **3** leads, in a quantitative yield (Barbier process), to a mixture of diastereoisomeric alcohols, respectively; the products of **2** being **22t** (threo isomer, 65%) and **22e** (erythro isomer, 35%)[37] and the products of **3** being **23t** (threo isomer, 60%) and **23e** (erythro isomer, 40%).[37] Curiously, addition of allylic



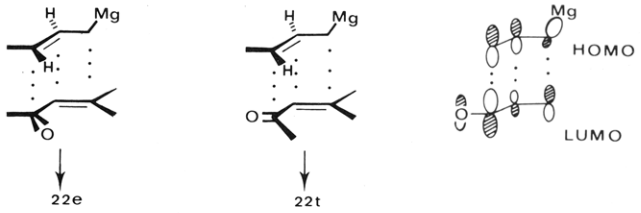
Grignard reagent **10** to **2** produces both 1,2- and 1,4-addition products, since we obtain alcohols **24** (complex mixture of isomers, 80%) and ketone **25** (20%, >95%, *E* isomer).[32]

The condensation of **10** with **4** gives inconsistent results, and alcohol **26** is obtained in low yield (20%). However, it should be noted that the double bond of the 3-pentenyl moiety is mainly *Z*.

Scheme VI



Scheme VII



Discussion

With the exception of the hindered allyl Grignard reagents, we have observed 1,2-addition on enones. In contrast to methylmagnesium iodide (and alkylmagnesium bromide)[38] addition, allylmagnesium bromide proved to be relatively insensitive to steric crowding about the carbonyl.[3]

For additions to **1**, the use of simple allyl Grignard reagents as nucleophiles is highly efficient and the stereoselectivity is virtually total.

The stereo- and regioselectivity data can be nicely accommodated by assuming an open transition state with respect to the Grignard reagent[39] and a boat- or chair-like conformation of the transition state corresponding to a compact approach.

The alkylation of **1** essentially takes place on the *si* face[40] in a quasi-axial fashion which corresponds to the least motion path.[41] Let us now consider the boat- or chair-like structure of the approach. The obtention of **6b** with an *R* configuration for the chiral center of the methylallyl substituent can result from a boat-like approach with the trans isomer for the Grignard species and a chair-like conformation with a cis isomer, respectively (Scheme VI, R = H).[42] Evidence has been reported that a slight preference for the cis form (*Z*:*E* = 54:46)[43] is found in the quenching experiments of butenyl Grignard reagents.[44,45]

(32) Stereoselectivity *E*:*Z* occurring during the condensation of 3-penten-2-ylmagnesium halides with electrophiles was variable. With bromide and acetone, *E*:*Z* = 2.4:1, ref 4d; cyclohexene oxide *E*:*Z* = 1:1, ref 4d; carbon dioxide *E*:*Z* = 0.18:1, ref 4d; chloride and trimethylchlorosilane *E*:*Z* = very large; see: Santelli-Rouvier, C. *Tetrahedron Lett.* **1984**, *25*, 4371.

(33) In previous works, methylmagnesium iodide addition led to methylisopulegene; see: (a) Grignard, V. Thesis, 1901; *Chem. Zentralbl.* **1901**, *72*, 624. (b) Wolinsky, J.; Chan, D. *J. Am. Chem. Soc.* **1963**, *85*, 937. (c) Lightner, D. A.; Vincent Crist, B. *Tetrahedron* **1981**, *37*, 385.

(34) Compound **16** has been obtained by copper-catalyzed addition of methylmagnesium iodide; see: Djerassi, C.; Hart, P. A.; Warawa, E. J. *J. Am. Chem. Soc.* **1964**, *86*, 78.

(35) For a review on the Reformatsky reaction, see: Rathke, M. W. *Org. React.* (*N.Y.*) **1975**, *22*, 423.

(36) For previous works, see: (a) Cure, J.; Gaudemar, M. *Bull. Soc. Chim. Fr.* **1968**, 3244. (b) Mousseron, M.; Mousseron-Canet, M.; Neyrolles, J. *C. R. Hebd. Seances Acad. Sci.* **1960**, *251*, 2447. (c) Perry, M.; Maroni-Barnaud, Y. *Bull. Soc. Chim. Fr.* **1969**, 3581.

(37) The threo isomer was attributed to the alcohol showing the higher apparent extinction coefficient; see ref 24.

(38) Dœuvre, J. *Bull. Soc. Chim. Fr.* **1939**, *6*, 1067.

(39) This mechanism is consistent with an association of magnesium (contained in any species of the Grignard solutions) with the enone oxygen atom. See: March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley: New York, 1985; p 820.

(40) For studies on the conformation of **1**, see: Singh, R. D.; Keiderling, T. A. *J. Am. Chem. Soc.* **1981**, *103*, 2387.

(41) For examples of axial selectivity, see: Trost, B. M.; Florez, J.; Jebaratnam, D. J. *J. Am. Chem. Soc.* 1987, *109*, 613.

(42) In order to find out the specific role of the exocyclic carbon–carbon double bond, one referee suggests to study the addition of crotylmagnesium chloride to (−)-*trans*-menthone. A 4:1 ratio of two isomers (2*S*,5*R*)-1-(1-methyl-2-propen-1-yl)-2-(1-methylethyl)-5-methylcyclohexanol was obtained.

(43) Hutchison, D. A.; Beck, K. R.; Benkeser, R. A.; Grutzner, J. R. *J. Am. Chem. Soc.* **1973**, *95*, 7075.

(44) The butenyl Grignard reagent is known to react with many electrophilic substrates and to give crotyl or α-methylallyl derivatives depending on the reaction conditions and the substrates used; see: ref 6, 7a, (a) Hill, E. A. *J. Organomet. Chem.* **1975**, *91*, 123.

(45) (a) Young, W. G.; Winstein, S.; Prater, A. N. *J. Am. Chem. Soc.* **1936**, *58*, 289. (b) Bank, S.; Schriesheim, A.; Rowe, C. A., Jr. *J. Am. Chem. Soc.* **1965**, *87*, 3244. (c) Bank, S. *J. Am. Chem. Soc.* **1965**, *87*, 3245.

The striking results observed during the addition of **10** to **1** or **2**, i.e., the formation of 1,4-addition products, are probably explained by the steric interaction between the methyl group nearer the magnesium of **10** and the isopropylidene group of **1** or **2**. This interaction is more severe with the boat-like approach which results in significant eclipsing of the methyl and isopropylidene groups (Scheme VI, R = H and CH_3).

With respect to the addition of **5b** to **2**, if we envision a boat-like (respectively chair-like) approach and a trans form (respectively cis form) for the Grignard species, the erythro isomer **22e** (35%) would predominate from the addition to *s-cis*-**2** and the threo isomer **22t** (65%) would be the preferred product from the addition to *s-trans*-**2** (Scheme VII). However, it is known that the enolate formed from addition of lithium dimethylcuprate to **2** is 64% *E* and 36% *Z*.[46] This is in striking agreement with our proposal.

Similarly, the mainly *Z* form of the alcohol **26** can be the result of a boat-like approach. The compact approach constitutes a HOMO/LUMO controlled situation. The allylic Grignard reagent system is closely related to the allylic anion[47] and can thus be regarded as a "soft" nucleophile in terms of the HSAB theory.[48,49] Its interaction with the "soft" electrophilic reagent that constitutes the enone moiety should be very likely to be dominated by frontier orbital interactions.[50] The molecular orbital diagram of the interactions shows that all interacting orbital pairs are matched (Scheme VII).

One may regard the carbonyl group as a type of allyl cation that is highly stabilized by an oxyanion substituent.[51] The most important interaction arises from the HOMO of the allyl anion and the LUMO of the allyl cation.[52]

Conclusion

The results described herein demonstrate that the reaction of butenyl and 2-methylbutenyl Grignard reagents with **1** is completely regio- and stereoselective. All the observations are in accordance with an open transition state mechanism for the allylic Grignard reagent and a chair- or, more probably, boat-like conformation for a compact approach.

To our knowledge, these results are the first example of very high selectivity in the reaction of allyl organometallic compounds with ketones. The allylic alcohols **6**, or their ozonolysis products are obtained with optical integrity. These products are potentially valuable precursors and versatile starting materials for the synthesis of naturally occurring complex molecules or as chiral templates in asymmetric induction reactions.

Experimental Section

General Methods. ^1H NMR spectra were determined with a Varian EM 360 (60 MHz) or a Varian XL 200 (200 MHz) spectrometer. ^{13}C NMR spectra of $CDCl_3$ solutions were recorded on a Varian XL 200 (50.309 MHz) with Me_4Si as the internal standard. Attributions were confirmed by *J*-modulated spin echo. Mass spectra were obtained on a Varian MAT 311 mass spectrometer. Circular dichroism values were measured on a Jouan-Roussel III instrument equipped with a Jobin-Yvon cell for low-temperature measurements. Optical rotations were measured on a Perkin-Elmer 241 in a thermostated 10-cm cell. Melting points are uncorrected. All reactions were done under an argon atmosphere.

Materials. (+)-Pulegone was obtained by distillation and chromatography on silica gel from oil of *Mentha pulegium* (Morocco) ($[\alpha]^{20}_{578}$ +30.1° (*c* 2.24, hexane)).[53] Ethyl bromoacetate, allyl chloride, crotyl chloride, methallyl chloride, and 3,3-dimethylallyl bromide were all obtained from Fluka AG and distilled before use. 1-Bromo-2-methyl-2-butene was prepared by using the procedure previously reported.[4a] 2-Chloro-3-pentene was prepared as previously described.[54]

Obtention of Alcohols 6a–d. Method A. Condensation of Allyl Grignard Reagents on (*R*)-(+)-Pulegone. To a 150-mL ether solution of 0.1 mol of allyl Grignard reagent cooled at −15 °C was added pulegone (15.2 g, 0.1 mol) in 50 mL of ether. After 12 h at room temperature, the reaction mixture was hydrolyzed with ice–ammonium chloride. After extractive workup the crude product was chromatographed on silica gel with pentane–ether (9:1).

Method B. Condensation of Allyl Halides and (+)-Pulegone in the Presence of Magnesium. In a dry, two-necked reaction flask equipped with a magnetic stirrer, a reflux condenser, and a dropping funnel, magnesium (0.3 g-atom, 7.2 g) was placed in anhydrous ether (40 mL). The reaction was started by the addition of one crystal of iodine and 0.5 g of 1,2-dibromoethane. Upon cessation of gas evolution, the reaction flask was cooled with ice, and a solution of allyl halide (0.1 mol) and (+)-pulegone (15.2 g, 0.1 mol) in 200 mL of ether was added over 1.5 h. The reaction mixture was stirred at room temperature for 12 h, at which time 0.5 mL of allyl halide was added. After 3 h, the reaction mixture was poured onto ice–ammonium chloride. Excess magnesium was filtered with glass wool and ether washed. After usual workup, the pure alcohol **6** was obtained by chromatography on silica gel (pentane–ether, 9:1): GC yield, 95–98%.

(+)-(1*S*,5*R*)-1-(2-Propen-1-yl)-2-(1-methylethylidene)-5-methylcyclohexanol (6a). Method A. Addition of allylmagnesium chloride (**5a**) to **1** led to **6a** (75% yield). **Method B.** We used 7.6 g of allyl chloride. **6a**: ^1H NMR (60 MHz, $CDCl_3$) δ 6.20–5.43 (1, m), 5.22–4.73 (2, m), 1.98 (3, s), 1.69 (3, s), 0.87 (3, d, *J* = 6.0 Hz); ^{13}C NMR δ 134.33 (d), 133.60 (s), 125.06 (s), 118.01 (t), 77.17 (s), 50.40 (t), 43.49 (t), 34.93 (t), 30.00 (d), 28.69 (t), 23.53 (q), 22.34 (q), 22.18 (q); IR (neat) 3450, 1640, 1150, 1025, 1000, 910 cm^{-1}; IR (CCl_4, 10^{-3} M) 3622 (61%), 3592 (39%) cm^{-1}; $[\alpha]^{20}_{578}$ +52.3° (*c* 2.05, hexane).

(+)-(1*S*,5*R*)-1-((1*R*)-1-Methyl-2-propen-1-yl)-2-(1-methylethylidene)-5-methylcyclohexanol (6b). Method A. Addition of crotylmagnesium chloride (**5b**) to **1** led to **6b** (72–75% yield). **Method B.** We used 9.05 g of crotyl chloride. **6b**: bp 74 °C (0.5 mmHg); ^1H NMR (200 MHz, $CDCl_3$) δ 5.93 (1, d, *J* = 16.2 Hz, d, *J* = 11.2 Hz, d, *J* = 8.4 Hz), 5.08 (2, m), 2.04 (3, d, *J* = 1.4 Hz), 1.71 (6, s), 0.98 (3, d, *J* = 6.9 Hz), 0.85 (3, d, *J* = 6.1

(46) (a) Heathcock, C. H. *Stereodifferentiating Addition Reactions*; Morrison, J. D., Ed.; Academic: New York, 1984; Vol. 3, Part B, p 151. (b) Riviere, H.; Tang, P. W. *Bull. Soc. Chim. Fr.* **1973**, 2455.

(47) The results of addition of allyl Grignard reagents to saturated ketones lead one to think that the allylic moiety possesses substantial carbanion character in the transition state; see: Schlosser, M.; Hartmann, J. *J. Am. Chem. Soc.* **1976**, *98*, 4674.

(48) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: London, 1976.

(49) An ab initio approach to the mechanism of the Grignard reaction has shown that a critical factor influencing the mechanism is a favorable match between the Grignard reagent's HOMO and the substrate's LUMO energy level; see: Nagase, S.; Uchibori, Y. *Tetrahedron Lett.* **1982**, *23*, 2585.

(50) Allylic magnesium bromide can undergo $\pi^4 + \pi^2$ cycloadditions; see: (a) Duboudin, J. G.; Jousseaume, B.; Pinet-Vallier, M. *J. Organomet. Chem.* **1979**, *172*, 1. (b) Duboudin, J. G.; Jousseaume, B. *Synth. Commun.* **1979**, *9*, 53.

(51) Compare ref 48, p 115.

(52) The coefficients of the atomic orbitals in the HOMO of the allyl anion are roughly as those of the LUMO of the allyl cation; see ref 48, p 123.

(53) The highest rotation values recorded for (+)-pulegone are as follows: ref a, $[\alpha]_D$ 22.53°; ref b, $[\alpha]_D$ 22.58°; ref c, $[\alpha]^{26.5}_D$ 24.6° (*c* 2.88, $CHCl_3$); ref d, $[\alpha]^{22}_D$ 23.56°; ref e $[\alpha]^{25}_D$ 23.64°; ref e, $[\alpha]^{25}_D$ 23.64° (*c* 7.77, $CHCl_3$); ref f, $[\alpha]^{22}_D$ 23.56°; ref g, $[\alpha]^{23}_D$ 24° (*c* 2, ethanol). See: (a) Beckman, E.; Pleissner, M. *Justus Liebigs Ann. Chem.* **1891**, *262*, 1. (b) Dœuvre, J.; Perret, H. *Bull. Soc. Chim. Fr.* **1935**, *2*, 298. (c) Eisenbraun, E. J.; McElvain, S. M. *J. Am. Chem. Soc.* **1955**, *77*, 3383. (d) Houlihan, W. J. *J. Org. Chem.* **1962**, *27*, 4096. (e) Overberger, C. G.; Weise, J. K. *J. Am. Chem. Soc.* **1968**, *90*, 3525. (f) Ensley, H. E.; Parnell, C. A.; Corey, E. J. *J. Org. Chem.* **1978**, *43*, 1610. (g) Ensley, H. E.; Carr, R. v. C. *Tetrahedron Lett.* **1977**, 513. It would appear that pulegone from natural sources can be considered to be enantiomerically pure.[11a]

(54) Mayr, H.; Klein, H.; Kolberg, G. *Chem. Ber.* **1984**, *117*, 2555.

Hz); ^{13}C NMR δ 140.23 (d), 137.96 (s), 133.24 (s), 125.14 (t), 79.67 (s), 50.07 (t), 42.61 (d), 35.44 (t), 29.62 (d), 28.65 (t), 23.66 (q), 22.37 (q), 22.10 (q), 14.27 (q); IR (neat) 3500, 1640, 1005, 915 cm^{-1}; IR (CCl_4, 10^{-3} M) 3626 (72%), 3578 (28%) cm^{-1}; mass spectrum, *m/e* 208 (1), 193 ($M^+ - CH_3$, 3.4) (HRMS calcd for $C_{13}H_{21}O$ 193.1592, found 193.1588), 176 (8), 161 (17), 153 (100), 135 (10), 119 (13), 105 (61), 93 (44), 81 (15), 69 (25), 55 (24), 43 (28), 41 (43); $[\alpha]^{20}_{578}$ +56.4° (*c* 1.81, hexane).

(+)-(1*S*,5*R*)-1-(2-Methyl-2-propen-1-yl)-2-(1-methylethylidene)-5-methylcyclohexanol (6c). Method A. Addition of methallylmagnesium chloride (**5c**) to **1** led to **6c** (65–70% yield). **Method B.** We used 9.05 g of methallyl chloride. **6c**: ^1H NMR (60 MHz, $CDCl_3$) δ 4.87 (1 H, br s), 4.73 (1, br s), 2.62 (1, 1/2 AB, *J* = 14.0 Hz), 2.10 (1/2 AB), 1.96 (3, s), 1.78 (3, s), 1.64 (3, s), 0.87 (3, d, *J* = 5.5 Hz); ^{13}C NMR δ 143.33 (s), 134.05 (s), 124.91 (s), 114.86 (t), 76.98 (s), 50.80 (t), 46.50 (t), 35.18 (t), 30.21 (d), 28.98 (t), 24.25 (q), 23.64 (q), 22.30 (q), 22.11 (q); IR (neat) 3490, 1640, 1260, 1145, 1100, 1075–1060, 890 cm^{-1}; IR (CCl_4, 10^{-3} M) 3618 (43%), 3572 (57%) cm^{-1}; mass spectrum, *m/e* 208 (1.3) (HRMS calcd for $C_{14}H_{24}O$ 208.1827, found 208.1830), 190 (5), 175 (23), 162 (14), 153 (100), 133 (11), 119 (46), 93 (36), 81 (35), 69 (45), 56 (61), 55 (63), 41 (45); $[\alpha]^{25}_{578}$ +18.7° (*c* 1.90, hexane).

(+)-(1*S*,5*R*)-1-((1*R*)-1,2-Dimethyl-2-propen-1-yl)-2-(1-methylethylidene)-5-methylcyclohexanol (6d). Method A. Addition of 2-methyl-2-buten-1-ylmagnesium bromide (**5d**) to **1** led to **6d** (65–70% yield). **Method B.** We used 14.9 g of 1-bromo-2-methyl-2-butene. **6d**: ^1H NMR (60 MHz, $CDCl_3$) δ 4.84 (2, br s), 2.70 (1, m), 2.04 (3, s), 1.82 (3, s), 1.68 (3, s), 0.98 (3, d, *J* = 7.0 Hz), 0.82 (3, d, *J* = 5.0 Hz); ^{13}C NMR δ 148.52 (s), 133.22 (s), 125.40 (s), 112.78 (t), 79.71 (s), 50.46 (t), 44.86 (d), 35.47 (t), 30.52 (d), 28.81 (t), 23.73 (q), 23.08 (q), 22.62 (q), 21.92 (q), 14.40 (q); IR (neat) 3540, 1635, 1255, 1155, 1105–1085, 975, 895 cm^{-1}; IR (CCl_4, 10^{-3} M) 3624 (55%), 3568 (45%) cm^{-1}; mass spectrum, *m/e* 222 (0.06), 204 ($M^+ - H_2O$, 0.36) (HRMS calcd for $C_{15}H_{24}$ 204.1878, found 204.1884), 153 (100), 109 (11), 107 (11), 93 (32), 81 (19), 69 (22), 55 (19), 43 (17), 41 (25); $[\alpha]^{25}_{578}$ +39.4° (*c* 2.09, hexane).

Ozonolysis of Compounds 6a,b. Obtention of 7a,b. Ozone in oxygen was bubbled through a solution of **6a** (10 mmol, 1.94 g) or **6b** (10 mmol, 2.08 g) in 60 mL of methanol which contained a few drops of an ethanolic solution of "Sudan III" (Eastman Kodak) (1/10000) (ozonizable red dye as internal standard)[55] at −60 °C until the solution turned yellow. While the solution was still at −60 °C, the system was flushed with nitrogen and then 10 mL of methanol containing one drop of concentrated sulfuric acid was added. The mixture was stirred at −15 °C overnight. Potassium carbonate (100 mg) was added. After filtration, the solvent was removed under vacuum and the crude product was chromatographed on silica gel with pentane–ether (2:3) to afford **7a** or **7b** (55–60% yield). **7a**: ^1H NMR (60 MHz, $CDCl_3$) δ 4.78 (1, d, d, *J* = 8.0 Hz, *J* = 3.5 Hz), 3.43 (3, s), 0.93 (3, d, *J* = 5.0 Hz); IR (neat) 3470, 1200, 1100, 890, 855 cm^{-1}; $[\alpha]^{25}_{578}$ +83° (*c* 1.6, hexane). **7b**: mp 133 °C (CCl_4); ^1H NMR (200 MHz, $CDCl_3$) δ 4.73 (1, d, *J* = 4.8 Hz), 3.45 (3, s), 1.14 (3, d, *J* = 7.2 Hz), 1.01 (3, d, *J* = 7.2 Hz); ^{13}C NMR δ 105.88 (d), 101.24 (s), 70.34 (s), 55.77 (q), 40.11 (q), 34.19 (t), 27.58 (t), 27.48 (t), 25.93 (d), 19.90 (q), 8.71 (q); IR (Nujol) 3550, 1200, 1075 cm^{-1}; IR (CCl_4, 10^{-3} M) 3568 (21%), 3482 (79%) cm^{-1}; $[\alpha]^{25}_{578}$ −16.6° (*c* 1.69, hexane); mass spectrum, *m/e* 200 ($M^+ - CH_3$ and OH, 8) (HRMS calcd for $C_{11}H_{20}O_3$ 200.1048, found 200.1020), 182 (8), 181 (9), 172 (5), 164 (8), 154 (21), 149 (6), 143 (28), 127 (28), 126 (48), 125 (84), 115 (21), 111 (41), 109 (16), 101 (12), 100 (25), 99 (20), 98 (19), 97 (75), 85 (100), 84 (25), 83 (44), 73 (79), 72 (53), 69 (93), 57 (94), 55 (82), 43 (56), 41 (49).

(−)-(2*S*,4*R*)-2-Hydroxy-2-(2-oxoprop-1-yl)-4-methylcyclohexanone (8a). Ozone in oxygen was bubbled through a solution of **6c** (10 mmol, 2.08 g) in 60 mL of methanol, which contained several drops of a solution of red dye (vide supra), at −60 °C until the solution turned yellow. While the solution was still at −60 °C, the system was flushed with nitrogen and then 2 mL of dimethyl sulfide was added. The mixture was stirred at room temperature overnight. The solvent was removed under vacuum, and the crude product was chromatographed on silica gel with pentane–ether (9:1) to afford **8a** (60%): mp 75 °C (pentane); ^1H NMR (60 MHz, $CDCl_3$) δ 1.93 (2, AB pattern, *J* = 2.0 Hz), 1.57 (3, s), 1.12 (3, d, *J* = 6.8 Hz); IR ($CDCl_3$) 3560, 1710, 1255, 1180–1190, 1160, 1055 cm^{-1}; mass spectrum, *m/e* 184 (0.7) (HRMS calcd for $C_{10}H_{16}O_3$ 184.1099, found 184.1092), 166 (3), 148 (6), 140 (6), 133 (7), 125 (4), 105 (9), 100 (12), 85 (13), 69 (16), 60 (25), 58 (19), 55 (14), 45 (34), 43 (100); $[\alpha]^{20}_{578}$ −21.75° (*c* 1.94, hexane); $[\alpha]^{20}_{578}$ −34.6 (*c* 2.4, ethanol).

(−)-(2*S*,4*R*)-2-Hydroxy-2-((1*S*)-1-methyl-2-oxoprop-1-yl)-4-methylcyclohexanone (8b). The experimental procedure was the same as that reported for the reaction of **8a**, with 1.98 g of **6d** (10 mmol). **8b** (55%): ^1H (60 MHz, $CDCl_3$) δ 3.03 (1, q, *J* = 7.0 Hz), 2.20 (3, s), 1.0 (3, d, *J* = 7.0 Hz), 0.97 (3, d, *J* = 6.0 (?) Hz); ^{13}C NMR δ 212.46 (s), 210.52 (s), 78.65 (s), 51.55 (d), 47.49 (t), 36.96 (t), 35.94 (t), 28.62 (d), 28.19 (q), 21.07 (q), 10.73 (q); IR (neat) 3470, 1700, 1235, 1165, 1115 cm^{-1}; $[\alpha]^{20}_{578}$ −10° (*c* 1.60, hexane).

Addition of (3,3-Dimethylallyl)magnesium Bromide (9) to (*R*)-(+)-Pulegone (1). Method B. We used 14.9 g of 3,3-dimethylallyl bromide. Crude product (yield, 80%) (bp 60–120 °C (0.5 mmHg)) was analyzed by a combination of flash chromatography on silica gel, preparative GC, and GC/MS (order of elution on silicon phase: **11c**, **11t**, **12t**, **12c**).

(1*R*,5*R*)-1-(1,1-Dimethyl-2-propen-1-yl)-2-(1-methylethylidene)-5-methylcyclohexanol (11c): (18%); ^1H NMR (60 MHz, $CDCl_3$) δ 5.83–6.63 (1, m), 5.10 (1, m), 4.83 (1, m), 2.07 (3, br s), 1.73 (3, br s), 1.13 (6, s); ^{13}C NMR δ 147.47 (d), 133.45 (s), 128.12 (s), 111.71 (t), 80.80 (s), 49.05 (t), 46.71 (s), 34.64 (t), 30.17 (t), 30.00 (d), 24.48 (q), 24.26 (q), 23.98 (q) (2C), 23.07 (q); mass spectrum, *m/e* 207 (0.4), 189 (0.4), 169 (2), 153 (51), 152 (18), 137 (9), 110 (36), 109 (14), 95 (16), 93 (12), 82 (14), 81 (54), 70 (33), 69 (100), 67 (51), 55 (75), 53 (21), 43 (37), 41 (92); IR (neat) 3500, 3090, 1637, 1015, 915 cm^{-1}.

(−)-(1*S*,5*R*)-1-(1,1-Dimethyl-2-propen-1-yl)-2-(1-methylethylidene)-5-methylcyclohexanol (11t): (36%); ^1H NMR (60 MHz, $CDCl_3$) δ 5.97 (1, d, *J* = 17 Hz, d, *J* = 10 Hz), 5.08 (1, m), 4.85 (1, m), 1.97 (3, br s), 1.73 (3, br s), 1.10 (6, s); ^{13}C NMR δ 146.33 (d), 133.73 (s), 129.38 (s), 111.88 (t), 82.02 (s), 46.62 (s), 44.31 (t), 31.90 (t), 30.41 (?) (d), 27.45 (t), 24.31 (q), 24.26 (q), 23.91 (q), 22.34 (q), 22.28 (q); IR (neat) 3500, 1675, 1100–1090, 915 cm^{-1}; mass spectrum, *m/e* 189 (0.3), 161 (0.3), 154 (12), 153 (100), 109 (10), 107 (12), 95 (7), 93 (31), 91 (11), 81 (36), 79 (18), 77 (15), 70 (11), 69 (68), 67 (34), 55 (59), 53 (18), 43 (58), 41 (89); $[\alpha]^{20}_{578}$ −105° (*c* 1.05, hexane).

(2*S*,5*R*)-2-(2,5-Dimethyl-4-hexen-2-yl)-5-methylcyclohexanone (12t): (18%); ^1H NMR (60 MHz, $CDCl_3$) δ 5.1 (1, t, *J* = 6.0 Hz), 1.73 (3, br s), 1.60 (3, br s), 1.0 (6, s); ^{13}C NMR δ 212.06 (s), 133.10 (s), 120.90 (d), 56.94 (d), 52.49 (t), 38.60 (t), 36.49 (d), 35.35 (s), 34.89 (t), 28.36 (t), 26.15 (q), 25.19 (q), 24.26 (q), 22.39 (q), 17.92 (q); mass spectrum, *m/e* 222 (0.2), 189 (0.7), 179 (3), 153 (30), 139 (2), 111 (12), 110 (100), 109 (16), 95 (25), 81 (20), 69 (87), 55 (35), 43 (31), 41 (69); IR (neat) 1710 cm^{-1}.

(2*R*,5*R*)-2-(2,5-Dimethyl-4-hexen-2-yl)-5-methylcyclohexanone (12c): (9%); ^{13}C NMR δ 212.90 (s), 133.10 (s), 120.84 (d), 57.14 (d), 50.43 (t), 38.76 (t), 35.81 (s), 34.89 (t), 32.41 (d), 31.53 (t), 25.33 (q), 25.19 (q), 24.59 (q), 24.26 (q), 19.29 (q); mass spectrum, *m/e* 153 (10), 111 (12), 110 (100), 109 (17), 95 (27), 81 (19), 69 (97), 67 (16), 55 (35), 43 (25), 41 (74); IR (neat) 1710 cm^{-1}.

Addition of 3-Penten-2-ylmagnesium Chloride (10) to (+)-Pulegone (1). Method B. We used 10.45 g of 2-chloro-3-pentene. Crude product (bp 70–100 °C (0.1 mmHg)) was analyzed by preparative GC and flash chromatographed on silica gel. **13** (mixture of isomers) (44%): ^1H NMR (200 MHz, $CDCl_3$) δ 5.44 (0.83 dqd, *J* = 15.2, 5.6, 1.4 Hz), 5.36 (0.83, dd, *J* = 15.2, 7.3 Hz), 5.27 (0.17 tight m), 1.69–1.61 (3 m), 1.02–0.78 (12, m); ^{13}C NMR δ 212.92–212.20 (s), 134.38–133.66 (d), 124.82–123.28 (d), 56.75–56.30 (d), 52.67, 52.58, 50.60, 50.44 (t), 42.83–42.30 (d), 37.34, 37.11, 32.64, 32.47 (d), 35.04–34.95 (t or s), 31.74–31.63 (t), 28.59, 28.21, 24.31, 24.02 (t), 22.64–15.14 (q); IR (neat) 1715, 975 cm^{-1}. **14** (37%): ^1H NMR (60 MHz, $CDCl_3$) δ 5.4 (2, tight m), 1.7 (9, m), 0.97 (6, m); ^{13}C NMR (part) δ 133.19, 132.94, 124.92, 124.86 (d), 79.38, 78.83 (s); IR (neat) 3510, 1268, 1110–1100, 975 cm^{-1}.

(+)-(1*S*,5*R*)-1,5-Dimethyl-2-(1-methylethylidene)cyclohexanol (15). A solution of (+)-(*R*)-pulegone (10 mmol, 1.52 g) in ether (15 mL) was added dropwise to an ethereal solution of 10 mmol of methylmagnesium iodide at −15 °C with stirring. After

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hydrolysis with cold water containing ammonium chloride and usual workup, the ethereal solution was dried over magnesium sulfate. The crude product was chromatographed over silica gel with pentane–ether (20:1) (first eluted, **16**). Overall yield: 96% (**15**:**16** = 4:1). **15**: ^{1}H NMR (60 MHz, $CDCl_3$) δ 2.00 (3, s), 1.66 (3, s), 1.34 (3, s), 0.91 (3, d, J = 5.5 Hz); IR (neat) 3400, 1160, 1020, 740 cm^{-1}; $[\alpha]^{20}_{578}$ = +73° (c 2.10, hexane). **16**: see ref 34.

(+)-(2*R*,4*R*)-2-Hydroxy-2,4-dimethylcyclohexanone (17). Ozone in oxygen was bubbled through a solution of **15** (10 mmol, 1.42 g) in 30 mL of CH_2Cl_2 and 20 mL of ethanol, which contained several drops of a solution of red dye (vide supra), at −60 °C until the solution turned yellow. The same procedure previously used for the obtention of **8a** led to the crude product, which was chromatographed on silica gel with pentane–ether (3:2) to afford **17** (80% yield): ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.36 (3, s), 0.97 (3, d, J = 6.0 Hz); ^{13}C NMR δ 214.59 (s), 75.86 (s), 49.99 (t), 36.91 (t), 35.70 (t), 29.70 (d), 25.79 (q), 21.19 (q); IR (CCl_4, 10^{-3} M) 3512, 1720 cm^{-1}; $[\alpha]^{25}_{578}$ +79.5° (c 1.975, hexane).

(+)-(1*S*,5*R*)-1-[(Ethoxycarbonyl)methyl]-2-(1-methylethylidene)-5-methylcyclohexanol (18). To a stirred suspension of powdered zinc (0.20 mol, 13.07 g) in 15 mL of dimethoxymethane at room temperature was added several drops of ethyl bromoacetate. The mixture was heated at reflux, at which time a solution of ethyl bromoacetate (0.1 mol, 16.8 g) and (+)-pulegone (0.1 mol, 15.2 g) in 60 mL of dimethoxymethane was added dropwise. The mixture was stirred under reflux during 1.5 h. After cooling, the mixture was hydrolyzed with ice and ammonium chloride. The ether layer was then washed with water and brine. The organic layer was dried ($MgSO_4$) and concentrated. The crude product was chromatographed with pentane–ether (9:1; about 7.5 g of (+)-pulegone are eluted, then about 11 g of **18** followed by about 1.6 g of **19** (mixture of isomers)). **18**: ^{1}H NMR (60 MHz, CCl_4) δ 4.07 (2, q, J = 7.2 Hz), 2.75 (1, 1/2 AB, J = 15.0 Hz), 2.37 (1, 1/2 AB), 1.95 (3, s), 1.65 (3, s), 1.21 (3, t, J = 7.2 Hz), 0.88 (3, d, J = 5.5 Hz); ^{13}C NMR δ 172.82 (s), 132.14 (s), 125.98 (s), 76.56 (s), 60.55 (t), 49.50 (t), 43.16 (t), 34.90 (t), 30.00 (d), 28.60 (t), 23.79 (q), 22.09 (q), (2C), 14.22 (q); IR (neat) 3510, 1715, 1200, 1170, 1025 cm^{-1}; mass spectrum, m/e 240 (2) (HRMS calcd for $C_{14}H_{24}O_3$ 240.1725, found 240.1719), 222 (15), 207 (14), 179 (30), 153 (41), 135 (47), 119 (42), 105 (30), 93 (39), 88 (44), 81 (45), 67 (35), 55 (36), 43 (100), 41 (51); $[\alpha]^{20}_{578}$ +27.5° (c 1.99, hexane).

(+)-(2*S*,4*R*)-2-[(Ethoxycarbonyl)methyl]-2-hydroxy-4-methylcyclohexanone (20). The experimental procedure was the same as that reported for the ozonolysis of **15**, with 2.40 g of **18** (10 mmol). The crude product was chromatographed on silica gel with pentane–ether (1:4) (60–65% yield). **20**: ^{1}H NMR (60 MHz, $CDCl_3$) δ 4.03 (2, q, J = 7.2 Hz), 3.09 (1, part A of AB pattern, J = 15.0 Hz), 2.64 (1, part B of AB pattern), 1.17 (3, t, J = 7.2 Hz), 1.00 (3, d, J = 5.5 Hz); ^{13}C NMR δ 212.02 (s), 169.90 (s), 76.72 (s), 60.78 (t), 50.16 (t), 43.45 (t), 37.12 (t), 36.44 (t), 29.63 (d), 20.95 (q), 14.05 (q); IR (neat) 3450, 1720, 1205, 1165, 1185, 1035 cm^{-1}; $[\alpha]^{25}_{578}$ +34.4° (c 1.86, hexane).

(+)-(1*S*,2*R*,5*R*)-2-Acetyl-1-[(ethoxycarbonyl)methyl]-5-methylcyclohexanol (21). The experimental procedure was the same as that reported for the ozonolysis of **15**, with 2.40 g of **19** (10 mmol). The crude product was chromatographed on silica gel with pentane–ether (1:4) (65% yield). **21**: ^{1}H NMR (60 MHz, $CDCl_3$) δ 4.03 (2, q, J = 7.2 Hz), 2.44 (2, s), 2.19 (3, s), 1.22 (3, t, J = 7.2 Hz), 0.84 (3, d, J = 6.0 Hz); ^{13}C NMR δ 216.26 (s), 171.18 (s), 71.77 (s), 60.48 (t), 54.38 (d), 46.78 (t), 44.93 (t), 33.95 (t), 30.40 (d), 27.02 (q), 25.62 (t), 21.96 (q), 14.22 (q); IR (neat) 3450, 1720–1690, 1200, 1175, 1020 cm^{-1}; IR (CCl_4, 10^{-3} M) 3495 cm^{-1}; $[\alpha]^{25}_{578}$ +32.0° (c 1.78, hexane).

3,4,6-Trimethyl-1,5-heptadien-4-ol (22). Method B. We used 9.05 g of crotyl chloride and 9.8 g of mesityl oxide. **22** (quantitative yield): bp 45 °C (0.5 mmHg); ^{1}H NMR (200 MHz, $CDCl_3$) **22t** δ 5.75 (1, d, J = 18.0 Hz, d, J = 9.6 Hz, d, J = 8.4 Hz), 5.18 (1, sept, J = 1.4 Hz), 5.03 (2, m), 1.80 (3, br s), 1.65 (3, br s), 1.22 (3, s), 0.98 (3, d, J = 6.9 Hz), **22e** δ 5.81 (1, d, J = 17.6 Hz, d, J = 9.8 Hz, d, J = 7.8 Hz), 5.18 (1, sept, J = 1.4 Hz), 5.03 (2, m), 1.80 (3, br s), 1.65 (3, br s), 1.20 (3, s), 0.96 (3, d, J = 6.9 Hz); ^{13}C NMR δ (respectively **22t**–**22e**) 140.70–140.65 (d), 134.02–134.31 (s), 129.74 (d), 115.72 (t), 74.42 (s), 49.86–49.34 (d), 27.53 (q), 26.62–26.53 (q), 18.98–19.07 (q), 14.92–14.49 (q); IR (neat) 3500, 3080, 1665–1640, 915 cm^{-1}; mass spectrum, m/e 154 (0.03), 136 (M^+ − H_2O, 0.75) (HRMS calcd for $C_{10}H_{16}$ 136.1252, found 136.1243), 121 (3), 99 (100), 83 (12), 81 (20), 55 (12), 53 (8), 43 (62).

3,4-Dimethyl-1,5-heptadien-4-ol (23). Method B. We used 9.05 g of crotyl chloride and 8.4 g of 3-penten-2-one. **23** (quantitative yield): bp 54–56 °C (7 mmHg); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.72 (3, m), 5.12 (1, tight m), 5.05 (1, tight m), 2.25 (1, sext, J = 7.2 Hz), 1.72 (**23t**) 1.69 (**23e**) (3, 2 s), 1.22 (1, d, J = 5.0 Hz), 1.01 (**23t**) 0.99 (**23e**) (3, 2 d, J = 7.2 Hz); ^{13}C NMR δ (respectively **23t**–**23e**) 140.49 (d), 136.38–136.57 (d), 123.29–123.62 (d), 115.89–115.67 (t), 73.96–74.02 (s), 48.96–48.52 (d), 25.86–25.13 (q), 17.73–17.77 (q), 15.06–14.51 (q); IR (CCl_4, 10^{-3} M) **23t** 3624 (61%), 3580 (39%), **23e** 3624 (69%), 3580 (31%).

Addition of 3-Penten-2-ylmagnesium Chloride (10) to Mesityl Oxide (2). Method B. We used 10.45 g of 2-chloro-3-pentene and 9.8 g of mesityl oxide. The crude product was chromatographed on silica gel with pentane–ether (20:1) (85% yield). **24**: complex mixture of alcohols; ^{1}H NMR (60 MHz, $CDCl_3$) δ 5.63–5.10 (3, m), 1.89 (3, m), 1.72 (6, br s), 1.5 (3, s), 0.97–0.90 (3, m); ^{13}C NMR (part) δ 135.18–134.75 (s), 125.74–123.13 (d), 113.90–113.83 (d), 111.90–110.77 (d), 77.99–77.21 (s); IR (neat) 3500, 1620, 975 cm^{-1}. **25**: ^{1}H (60 MHz, $CDCl_3$) δ 5.3 (2, tight m), 1.97 (2, s), 2.07 (3, s), 1.63 (3, d, J = 5.2 Hz), 0.95 (6, s), 0.89 (3, d, J = 7.0 Hz); ^{13}C NMR δ 209.32 (s), 133.77 (d), 125.35 (d), 52.73 (t), 45.62 (d), 36.02 (s), 32.54 (q), 24.78 (q), 24.09 (q), 18.04 (q), 15.29 (q); IR (neat) 1715, 1025, 975, 740 cm^{-1}.

5-Methyl-2,6-octadien-4-ol (26). Method B. We used 10.45 g of 2-chloro-3-pentene and 6 g of crotonaldehyde. The reaction was capricious, and sonochemical enhancement was necessary. **26** (20–30% yield): bp 40–50 °C (1 mmHg); ^{1}H NMR (60 MHz, $CDCl_3$) δ 5.53–5.13 (4, m), 3.68 (1, m), 1.63 (6, m), 0.88 (3, d, J = 6.8 Hz); ^{13}C NMR δ 135.38, 135.21, 134.99, 134.35, 132.17, 123.19 (d), 69.00 (d), 38.96, 33.79 (d), 23.46, 20.72, 20.30, 17.98 (q); IR (neat) 3400, 975, 740–725 cm^{-1}.

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