

ent¹⁰ to 1 and successive cleavage of a vinyl carbon-oxygen bond could occur to generate an alkenyl radical intermediate 3. This transient intermediate might then abstract a hydrogen atom from the butyl group of the resulting organocopper species, giving the product 2 along with 1-butene.¹¹

In summary, diethyl (Z)-1-[(diethoxyphosphinyl)oxy]-F-1-alkene-1-phosphonates 1, easily prepared from F-alkanoic acid chlorides and diethyl phosphite, undergo reduction efficiently with lithium dibutylcuprate⁶ to give good yields of the corresponding (Z)-1-hydryl-F-1-alkene-1-phosphonates 2, which have been shown to be good precursors for synthesizing a variety of organofluorine compounds.^{4d-g}

Experimental Section

Infrared spectra (IR) were taken on a Shimadzu IR-400 infrared spectrometer using a polystyrene film for calibration. ¹H NMR spectra were recorded with a Varian EM-390 or a JEOL PMX-60si spectrometer for solutions in carbon tetrachloride (CCl₄) with tetramethylsilane (Me₄Si) as an internal standard. A Varian EM-390 spectrometer or a JEOL FX-90Q computer-controlled spectrometer was used to measure ¹⁹F NMR spectra in CCl₄ or chloroform-*d* (CDCl₃) with internal trichlorofluoromethane (CFCl₃). ³¹P NMR spectra were obtained on a JEOL FX-90Q computer-controlled spectrometer in CDCl₃ with 85% phosphoric acid as an external reference. Mass spectra were determined with a Hitachi RMS-4 mass spectrometer operating at an ionization potential of 70 eV.

Materials. All chemicals were of reagent grade and used without further purification. Solvents were distilled (or vacuum-distilled) through a 25-cm Vigreux column and, if necessary, were purified in the conventional manner prior to use. F-Alkanoic acid chlorides were prepared by the literature method.¹² The starting fluoroalkenephosphonates 1 were obtained in 65-80% yields according to our recently reported method.⁵

General Procedure for the Reaction of (Z)-1-[(Diethoxyphosphinyl)oxy]-F-1-alkene-1-phosphonate 1 with Lithium Dibutylcuprate⁶ Reagent. In a four-necked flask fitted with a thermometer, a mechanical stirrer, an inlet tube for nitrogen, and a rubber septum were placed cuprous iodide (23.8 g, 125.0 mmol), anhydrous TMEDA (14.5 g, 125.0 mmol), and 250 mL of dry THF. This suspension was cooled to -78 °C by immersing in a dry ice-methanol bath, and butyllithium (147 mL, 220.0 mmol) in hexane (1.5 M) was gradually added to it by use of a syringe. After the reaction mixture was stirred for 30 min at -78 °C, a solution of 1 (50.0 mmol) in 25 mL of dry THF was added to the resulting dark-brown solution at such a rate that the reaction temperature did not rise above -60 °C. The whole mixture was stirred for 15 min at -78 °C. To this reaction mixture, which had been brought to -50 to -40 °C, was added successively 10 mL of water and 200 mL of a saturated aqueous solution of ammonium chloride. After being stirred for a while at room temperature, the mixture was subjected to extraction with ether (4 × 100 mL). The ethereal extracts were washed three times with water, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residual oil was distilled in vacuo or chromatographed on silica gel (Wako gel C-200) by using ether as an eluent to give analytically pure product 2.

Diethyl (Z)-1-hydryl-F-1-propene-1-phosphonate (2a): 65% yield; bp 60 °C (17 mmHg); IR (film) 2950 (m), 1700 (m), 1485 (w), 1450 (m), 1400 (m), 1365 (s), 1250 (s), 1215 (s), 1165 (s), 1105 (m), 1060 (s), 1030 (vs), 975 (s), 830 (m) cm⁻¹; ¹H NMR (CCl₄) δ 1.37 (t, *J* = 7.2 Hz, 6 H), 4.10 (dq, *J* = 7.2 and 7.2 Hz, 4 H), 5.83 (dd, *J* = 40.0 and 2.9 Hz, 1 H); ¹⁹F NMR (CCl₄) δ -73.9 (d, *J* = 9.9 Hz, 3 F), -108.8 (ddq, *J* = 40.0, 9.9 and 2.8 Hz, 1 F); ³¹P NMR (CDCl₃) δ 7.54; mass spectrum, *m/e* (relative intensity) 249 (M⁺ - 1, 1.9), 195 (100). Anal. Calcd for C₇H₁₁F₃O₃P: C, 33.61; H, 4.43; F, 30.38. Found: C, 33.83; H, 4.59; F, 30.04.

Diethyl (Z)-1-hydryl-F-1-butene-1-phosphonate (2b): 81% yield; bp 65 °C (17 mmHg); IR (film) 2980 (m), 2930 (m), 1685 (s), 1475 (vs), 1440 (m), 1390 (m), 1365 (m), 1340 (s), 1325 (s), 1260 (s), 1205 (vs), 1165 (s), 1090 (s), 1040 (vs), 970 (s), 825 (m), 715 (m) cm⁻¹; ¹H NMR (CCl₄) δ 1.37 (t, *J* = 7.4 Hz, 6 H), 4.10 (dq, *J* = 7.4 and 7.4 Hz, 4 H), 5.89 (dd, *J* = 38.9 and 2.7 Hz, 1 H); ¹⁹F NMR (CCl₄) δ -84.3 (dt, *J* = 7.0 and 2.1 Hz, 3 F), -104.9 (ddtq, *J* = 38.9, 7.0, 12.4, and 2.8 Hz, 1 F), -121.8 (dm, *J* = 12.4 Hz, 2 F); ³¹P NMR (CDCl₃) δ 7.07; mass spectrum, *m/e* (relative intensity) 299 (M⁺ - 1, 1.6), 245 (100). Anal. Calcd for C₉H₁₁F₃O₃P: C, 32.01; H, 3.69; F, 37.98. Found: C, 32.22; H, 3.86; F, 37.77.

Diethyl (Z)-1-hydryl-F-1-octene-1-phosphonate (2c): 62% yield; IR (film) 3000 (m), 2950 (m), 1690 (m), 1485 (w), 1450 (m), 1400 (m), 1375 (m), 1345 (m), 1250 (vs), 1205 (vs), 1150 (s), 1100 (s), 1030 (s), 980 (s), 835 (m), 815 (m), 740 (m), 720 (s) cm⁻¹; ¹H NMR (CCl₄) δ 1.38 (t, *J* = 7.5 Hz, 6 H), 4.13 (dq, *J* = 7.5 and 7.5 Hz, 4 H), 5.91 (dd, *J* = 37.9 and 3.0 Hz, 1 H); ¹⁹F NMR (CCl₄) δ -81.6 (br s, 3 F), -103.5 (dm, *J* = 37.9 Hz, 1 F), -118.3 (dt, *J* = 12.7 and 12.7 Hz, 2 F), -121.2 to -124.2 (m, 6 F), -125.0 (m, 2 F); ³¹P NMR (CDCl₃) δ 7.11. Anal. Calcd for C₁₂H₁₁F₃O₃P: C, 28.82; H, 2.22; F, 53.18. Found: C, 28.63; H, 2.36; F, 52.92.

Diethyl (Z)-1-hydryl-F-1-decene-1-phosphonate (2d): 80% yield; IR (film) 3000 (m), 2950 (m), 1695 (m), 1485 (w), 1450 (w), 1400 (m), 1380 (m), 1350 (m), 1240 (s), 1205 (vs), 1155 (s), 1120 (s), 1045 (s), 1030 (s), 980 (s), 830 (m), 810 (m), 715 (m), 705 (m) cm⁻¹; ¹H NMR (CCl₄) δ 1.37 (t, *J* = 7.2 Hz, 6 H), 4.13 (dq, *J* = 7.2 and 7.2 Hz, 4 H), 5.92 (dd, *J* = 39.3 and 2.8 Hz, 1 H); ¹⁹F NMR (CCl₄) δ -81.8 (t, *J* = 9.0 Hz, 3 F), -103.6 (dm, *J* = 39.3 Hz, 1 F), -118.3 (br s, 2 F), -121.0 to -124.3 (m, 10 F), -126.7 (br s, 2 F); ³¹P NMR (CDCl₃) δ 7.08. Anal. Calcd for C₁₄H₁₁F₃O₃P: C, 28.02; H, 1.85; F, 56.98. Found: C, 27.91; H, 1.95; F, 56.79.

Diethyl (Z)-1,11-dihydryl-F-1-undecene-1-phosphonate (2e): 70% yield; IR (film) 2990 (m), 2945 (m), 1686 (m), 1482 (w), 1445 (w), 1394 (m), 1340 (m), 1250 (s), 1207 (vs), 1150 (vs), 1050 (s), 1020 (s), 970 (m), 827 (m), 800 (m), 729 (m) cm⁻¹; ¹H NMR (CCl₄) δ 1.37 (t, *J* = 7.5 Hz, 6 H), 4.13 (dq, *J* = 7.5 and 7.5 Hz, 4 H), 5.87 (dd, *J* = 40.5 and 3.0 Hz, 1 H), 6.05 (tt, *J* = 54.5 and 5.3 Hz, 1 H); ¹⁹F NMR (CDCl₃) δ -102.3 (br d, *J* = 40.5 Hz, 1 F), -118.3 (br s, 2 F), -122.1 to -122.9 (br m, 10 F), -123.7 (br s, 2 F), -129.7 (br s, 2 F), -137.5 (br d, *J* = 54.5 Hz, 2 F); ³¹P NMR (CDCl₃) δ 6.97. Anal. Calcd for C₁₅H₁₂F₃O₃P: C, 28.50; H, 1.91; F, 57.10. Found: C, 28.71; H, 2.13; F, 56.78.

The Bridgehead Decalin Radicals: An MM2 and MNDO Study

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Introduction

ESR evidence has recently been presented¹ which indicates the existence of distinguishable bridgehead radicals derived from *cis*- and *trans*-decalin. They are thought to be nonplanar at the radical sites, but considerably flattened from normal tetrahedral geometry. Chemical evidence of this was presented earlier by Bartlett et al.² and by Greene and Lowry.³ Greene³ studied the free radical decomposition of the *cis*- and *trans*-9-decalylcarbonyl hypochlorites to give the 9-chlorodecalins and deduced that two different 9-decalyl radical intermediates were required. They concluded that radicals which were either pyramidal or planar at the radical sites could account for the observed results.

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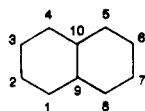
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Table I. Calculated Geometries and Heats of Formation for *cis*- and *trans*-Decalins^a

| molecule | method | bond lengths | | | | | angle | | ΔH | diff ^b |
|----------|--------|--------------------------------|--------------------------------|---------------------------------|--------------------|-------------------|--|--------|------------|-------------------|
| | | C ₉ -C ₁ | C ₉ -C ₈ | C ₉ -C ₁₀ | C ₁₀ -H | C ₉ -H | C ₈ -C ₉ -C ₁ | | | |
| trans | MM2 | 1.538 | 1.538 | 1.541 | 1.117 | 1.117 | 111.3 | -43.76 | | |
| cis | MM2 | 1.536 | 1.539 | 1.546 | 1.118 | 1.118 | 114.1 | -35.84 | 7.9 | |
| trans | MNDO | 1.550 | 1.550 | 1.562 | 1.121 | 1.121 | 112.4 | -41.70 | | |
| cis | MNDO | 1.548 | 1.553 | 1.563 | 1.121 | 1.122 | 113.4 | -37.59 | 4.1 | |

^a Bond lengths are in angstroms, angles in degrees, and heats of formation in kcal/mol. ^b The calculated *cis* and *trans* energy difference.

Table II. Calculated Geometries and Heats of Formation for *cis*- and *trans*-Decalyl Radicals^a

| radical | method | bond lengths | | | | angles | | ΔH | diff |
|--------------|--------|--------------------------------|--------------------------------|---------------------------------|--------------------|--|------------|------------|------|
| | | C ₉ -C ₁ | C ₉ -C ₈ | C ₉ -C ₁₀ | C ₁₀ -H | C ₈ -C ₉ -C ₁ | α^b | | |
| trans | MM2 | 1.513 | 1.513 | 1.516 | 1.117 | 115.8 | 34.4 | -6.75 | |
| trans-planar | MM2 | 1.511 | 1.511 | 1.514 | 1.117 | 118.4 | 0.0 | -2.04 | 4.71 |
| cis | MM2 | 1.512 | 1.512 | 1.514 | 1.117 | 117.1 | 34.8 | -5.94 | 1.81 |
| cis-planar | MM2 | 1.505 | 1.507 | 1.510 | 1.117 | 119.9 | 0.0 | -0.91 | 5.84 |
| trans | MNDO | 1.506 | 1.504 | 1.511 | 1.124 | 117.6 | 8.2 | -21.90 | |
| trans-planar | MNDO | 1.496 | 1.496 | 1.501 | 1.128 | 116.6 | 0.0 | -21.16 | 0.74 |
| cis | MNDO | 1.499 | 1.507 | 1.512 | 1.123 | 119.0 | 0.6 | -20.93 | 0.97 |
| cis-planar | MNDO | 1.495 | 1.487 | 1.509 | 1.125 | 120.6 | 0.0 | -20.44 | 1.46 |

^a See footnotes for Table I. ^b α is defined as the angle between the C₉-C₁₀ bond and the plane formed by C₈-C₉-C₁.

It was pointed out that the radicals are after all derived from *cis* and *trans* precursors and that radical site planarity might not preclude conformational differences elsewhere. The chemical and spectroscopic evidence agrees on the principal of distinguishable radicals, but the nature of the geometry at the radical sites is far from settled. Therefore, a theoretical study was initiated to predict structures for these radicals. Two approaches were chosen for this study: the empirical force-field MM2⁴ and the semiempirical MNDO⁵ methods.

The molecular mechanics program developed by Allinger (MM2) has recently been applied to alkyl radicals by Imam and Allinger.⁶ The parameterization they proposed was based primarily on the results of *ab initio* calculations on simple alkyl radicals. Calculations were reported on the cyclohexyl radical, but no structural details were given beyond the fact that the chair conformation is the lowest in energy. The only tertiary radical studied was the *tert*-butyl radical. For this system the degree of nonplanarity α^7 was calculated to be 23.9°. This reproduces satisfactorily the 21.7° value of α based on the data given in ref 6 for *ab initio* calculations and is in accord with experimental observations.⁸

The semiempirical MNDO method has also been applied to a large number of free radical systems with satisfactory results. Bischoff and Friedrich⁹ concluded that the UHF-MNDO treatment gave good thermodynamic and structural results for a wide range of organic radicals. MNDO has also been shown to give better results than MINDO/3 for radicals¹⁰ and in some cases to be superior to minimum basis set *ab initio* calculations¹¹ and, therefore,

was chosen for this study along with the MM2 method.

Results and Discussion

The MM2 and MNDO results for the structural parameters (bond distances and angles) at the radical site and the computed heats of formation are given in Tables I and II for the completely optimized molecules and radicals, as well as for the radicals constrained to planarity. The pyramidalization of the radical site is measured by the out-of-plane angle α defined as the angle between the bridging bond (C₉-C₁₀) and the plane formed by atoms C₈-C₉-C₁.

The parent *cis*- and *trans*-decalin molecules have been studied by a combination of molecular mechanics and electron diffraction,^{12,13} and the molecular parameters from the present calculations are in general agreement with these previous results. The calculated heats of formation should be compared with the measured values¹⁴ of -40.43 and -43.52 kcal/mol for *cis*- and *trans*-decalin, respectively. The experimental *cis*-*trans* energy difference is 3.09 kcal/mol. The MNDO value for the energy difference is considerably better than the MM2 value, although both methods give the correct ordering.

A comparison of Tables I and II reveals that the radicals are predicted to have considerably shortened carbon-carbon bonds to the radical site and that the C₈-C₉-C₁ bond angles are increased relative to the parent hydrocarbons. These effects are more pronounced with MNDO than with MM2. Both methods predict that the optimized *trans* radical is of lowest energy, but the *cis*-*trans* energy gap is larger with MM2 than with MNDO. The heats of formation from the MNDO calculations are much more negative than the MM2 results. This is consistent with earlier comparisons between MNDO calculations and experimental heats of formation for simple radicals.⁹ Imam and Allinger⁶ used 12 different organic radicals to param-

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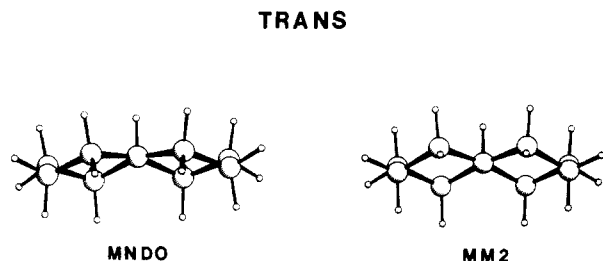


Figure 1. Optimized structures for the *trans*-decalyl radical. The view is along the bridging bond from the radical site.

eterize their heat of formation calculations and were able to reproduce the experimental results by about 0.8 kcal/mol. The reported error from the MNDO study of Bischoff and Friedrich⁹ was about 12 kcal/mol, suggesting that the MM2 heats are closer to the actual values.

Previous ESR results¹ led to the conclusions that the *trans* radical was of lower energy and the higher energy *cis* radical interconverted to *trans*-decalin through a common planar radical transition structure. An attempt was made to locate such a planar species by constraining the radical sites to planarity while allowing full relaxation of all other parameters. Depending upon the choice of starting geometry (*cis* or *trans*) two different "planarized" radicals resulted. Both of these planarized radicals were of higher energy than the fully relaxed radicals, and they are geometrically quite different (Table II). The present calculations do not preclude direct equilibration between the *cis* and *trans* radicals, but as only *cis* to *trans* isomerization is observed¹⁻³ this hypothesis seems unlikely. Furthermore, radical species derived from *trans*-decalin must quench with hydrogen atoms to give only *trans*-decalin. This suggests that the *cis* to *trans* isomerization results from the quenching of a *cis*-derived radical species by hydrogen atom abstraction to give *trans*-decalin, the lowest energy species on the manifold.

The most important difference between the MM2 and MNDO results is in the optimized geometries. The MNDO optimized *cis* and *trans* radicals are both highly planarized ($\alpha = 0.6^\circ$ and 8.2° , respectively). The MM2 method predicts more pyramidal radical sites ($\alpha = 34.8^\circ$ and 34.4° , respectively), somewhat intermediate between tetrahedral (55°) and planar (0°). In comparing the results of Bischoff and Friedrich⁹ and Imam and Allinger⁶ for smaller organic radicals, it seems that the MNDO method gives radical sites that are too planar. It is possible that the energy changes are very small in the direction of the ring puckering, and, therefore, the calculated MNDO heats of formation will not change appreciably.

Examination of Figure 1 reveals that the overall ring structures for the *trans* radical can be regarded as retaining essentially chair-chair conformations in both calculations, although the MNDO geometry is "flatter" than the MM2 geometry. This is in agreement with previous studies which have noted that MNDO leads to structures with reduced puckering for cyclic systems.¹⁰ In contrast to the *trans* case, the two methods predict a major difference in the structure of the *cis* radical (Figure 2). The MNDO geometry is considerably distorted to a chair-pseudoboat form, while the MM2 calculation predicts retention of a chair-chair structure. Because of the previously noted tendency of the MNDO method to produce radical sites that are too planar and rings that are too flat, the MM2 geometries are probably more realistic.

Conclusions

This study indicates that two different conformations for the decalyl radical are possible, the more stable being

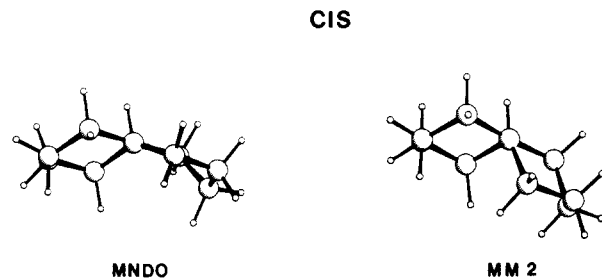


Figure 2. Optimized structures for the *cis*-decalyl radical. The view is along the bridging bond from the radical site.

the one derived from *trans*-decalin. The fully optimized radical structures were located by both MM2 and MNDO methods starting with the parent *cis*- and *trans*-decalin parameters. Both radicals are predicted to be nonplanar at the radical site, and no evidence is found for a planar transition structure. Elucidation of the nature of the interconversion process would be an interesting topic for future study. In addition, the structure of the *cis* radical is still uncertain, and more demanding theoretical work is under way.

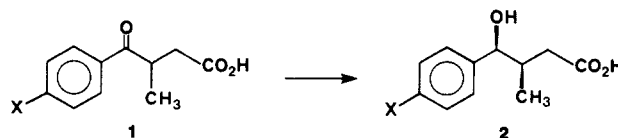
Stereoselective Reduction of γ -Oxo- γ -phenylbutanoic Acids

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In the course of research on selective receptor antagonists of leukotriene D₄, we were interested in devising an efficient and stereoselective synthesis of the (*RS,SR*)- γ -aryl- γ -hydroxy- β -methylbutanoic acid moiety **2** contained in the desired product,¹ that is, where the β -methyl and the γ -hydroxy groups are erythro.²



A logical method for the preparation of these γ -hydroxy- β -methyl acids was through a stereoselective reduction of the corresponding γ -oxobutanoic acids **1**. Although the erythro-selective reduction of α -substituted β -oxo acid derivatives is well documented,³ there are few examples of erythro-selective γ -keto ester or acid reduction.⁴ Initial attempts to obtain the desired (*RS,SR*)- γ -aryl- γ -hydroxy- β -methylbutanoic acids were discouraging. A ratio of 70:30 in favor of the desired isomers were obtained with sodium borohydride (as potentially a reagent which could deliver hydride from an internal complex) while $\text{Na}(\text{CH}_3\text{OCH}_2\text{CH}_2\text{O})_2\text{AlH}_2$ (Vitrider) showed a ratio of 50:50. Reduction of **1b** methyl ester using several reagents known to stereoselectively reduce α -substituted β -oxo acid derivatives was not more successful. For example, the hydrosilane-based reduction^{3e,5} and zinc boro-

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