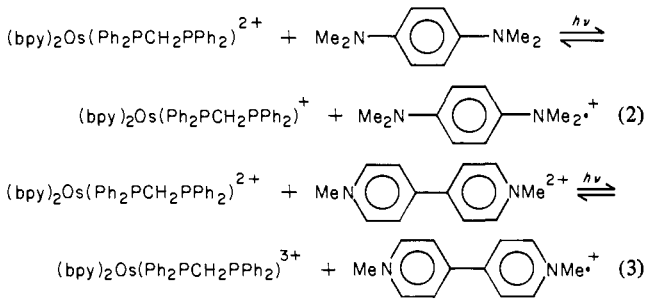


variations in excited-state energies, lifetimes, and redox potentials. Comparison with related MLCT excited states of other metals should give general insight into the photochemical and photophysical properties of MLCT excited states and, therefore, into the factors at the molecular level needed to synthesize long-lived excited states.

Acknowledgements are made to the Department of Energy under Grant No. ER-78-S-05-6034 for support of this research, the National Science Foundation for a fellowship for W.J.D., and the Morehead Foundation for a fellowship for E.M.K.

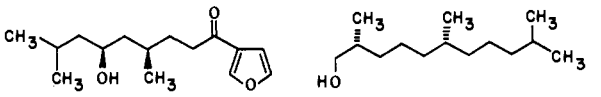
(12) Sullivan, B. P.; Kober, E. M., work in progress.

Edward M. Kober, B. Patrick Sullivan, Walter J. Dressick
Jonathan V. Caspar, Thomas J. Meyer*
Department of Chemistry
The University of North Carolina
Chapel Hill, North Carolina 27514
Received June 2, 1980

Remote Asymmetric Induction. A Stereoselective Approach to Acyclic Diols via Cyclic Hydroboration[1]

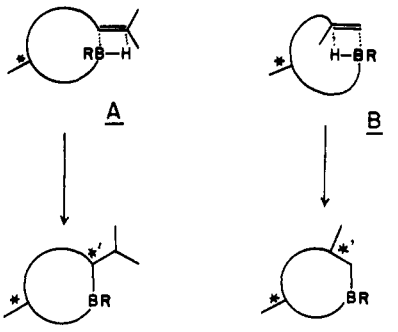
Sir:

When the synthesis of stereochemically complex acyclic molecules is considered, two synthetically significant types of diastereomeric relationships may be distinguished. Pairs of asymmetric centers may be either directly connected (adjacent) or separated by one or more atoms (remote). The efficient addition of new asymmetric centers relative to preexisting ones (relative asymmetric induction) is one of the most important problems facing would-be architects of complex acyclic structures,[2] and although several useful methods for building up adjacent stereocenters with high 1,2-asymmetric induction have been devised,[3] general approaches to the construction of remote asymmetric relationships by efficient 1,>2-asymmetric induction are rare.[4] Previous solutions to the remote stereochemistry problem have largely avoided remote asymmetric induction and have relied on the coupling of optically active fragments[5] or on increasing the separation of proximate asymmetric centers by some form of chirality transfer.[6] Recently, however, Bartlett's phosphate chain extended epoxidation[7] (1,3-asymmetric induction) and Kishi's bis(homoallylic) alcohol epoxidation[8] (1,4-asymmetric induction) demonstrated that general methods for acyclic remote asymmetric induction were within grasp and could be synthetically useful processes. In this paper we wish to describe interesting preparations of nonvicinal, acyclic diols which proceed stereoselectively with 1,3-, 1,4-, and 1,5-asymmetric induction. The methodology involves the cyclic hydroboration[9] of nonconjugated dienes, and its utility is illustrated by stereoselective synthesis of racemic forms of a naturally occurring dihydromyoporone (**1**)[10] and the vitamin E side chain (**2**).[5b,6b]



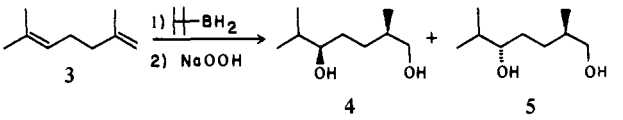
1 2

The effect upon which we wish to focus is the asymmetric induction which occurs during an intramolecular hydroboration where the cycle being closed contains one or more asymmetric centers (*). As illustrated, this operation can create new asymmetry (*′) and may proceed via either fused or bridged intermediates (A or B, respectively). Since the object of this study



was exploration of methodology for the remote control of stereochemistry, we hoped that the diastereomeric relationship of asymmetric centers thus produced could be made to rely less on a direct and necessarily weak interaction between widely separated substituents and more on the overall conformation(s) of the transition state(s) leading to the boracycles. Factors which determine the detailed geometry of such transition states are not well understood; however, first approximation considerations may include the energetically accessible conformations of the ring being closed and any stereoelectronic constraints inherent to hydroboration itself.

The cyclic hydroboration of diene **3** was particularly instructive.



3 4 5

Although **3** reacted rapidly with borane (THF, −78 °C) almost

(1) This work was presented at the Bürgenstock Stereochemical Conference at Bürgenstock, Switzerland, on April 28, 1980, and at the Third IUPAC Symposium on Synthesis at Madison, WI on June 16, 1980.

(2) Relative and internal asymmetric induction is discussed in a recent review on acyclic stereochemical control: P. A. Bartlett, *Tetrahedron*, **36**, 2 (1980).

(3) For example: B. E. Rossiter, T. R. Verhoeven, and K. B. Sharpless, *Tetrahedron Lett.*, 4733 (1979); E. D. Mihelich, *ibid.*, 4729 (1979); P. A. Bartlett and J. Myerson, *J. Am. Chem. Soc.*, **100**, 3950 (1978); W. C. Still and J. H. McDonald, *Tetrahedron Lett.*, 1031 (1980); W. C. Still and J. Schneider, *ibid.*, 1035 (1980), and references cited therein.

(4) A few specific transformations by remote asymmetric induction are known and include such operations as stereoselective reduction of 15-keto-prostaglandins: E. J. Corey, K. B. Becker, and R. K. Varma, *J. Am. Chem. Soc.*, **94**, 8616 (1972); E. J. Corey and J. Moinet, *ibid.*, **95**, 6831 (1973).

(5) For example: (a) E. J. Corey, H. Shirahama, H. Yamamoto, S. Terashima, A. Venkateswarlu, and T. K. Schaaf, *J. Am. Chem. Soc.*, **93**, 1490 (1971); (b) N. Cohen, W. F. Eichel, R. J. Lopresti, C. Neukom, and G. Saucy, *J. Org. Chem.*, **41**, 3505 (1976); (c) G. Stork, Y. Nakahara, Y. Nakahara, and W. J. Greenlee, *J. Am. Chem. Soc.*, **100**, 7775 (1978); (d) D. B. Collum, J. H. McDonald, and W. C. Still, *ibid.*, **102**, 2117, 2118, 2120 (1980).

(6) For example: (a) G. Stork and S. Raucher, *J. Am. Chem. Soc.*, **98**, 1583 (1976); (b) K.-K. Chan and G. Saucy, *J. Org. Chem.*, **42**, 3828 (1977); (c) B. M. Trost and T. P. Klun, *J. Am. Chem. Soc.*, **101**, 6756 (1979).

(7) P. A. Bartlett and K. K. Jernstedt, *J. Am. Chem. Soc.*, **99**, 4829 (1977).

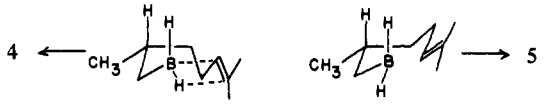
(8) T. Fukuyama, B. Vranesic, D. P. Negri, and Y. Kishi, *Tetrahedron Lett.*, 2741 (1978).

(9) For a review of the nonstereochemical aspects of cyclic hydroboration, see H. C. Brown and E.-I. Negishi, *Tetrahedron*, **33**, 2331 (1977). See also T. A. Bryson and W. E. Pye, *J. Org. Chem.*, **42**, 3214 (1977).

(10) L. T. Burka and J. Iles, *Phytochemistry*, **18**, 873 (1979).

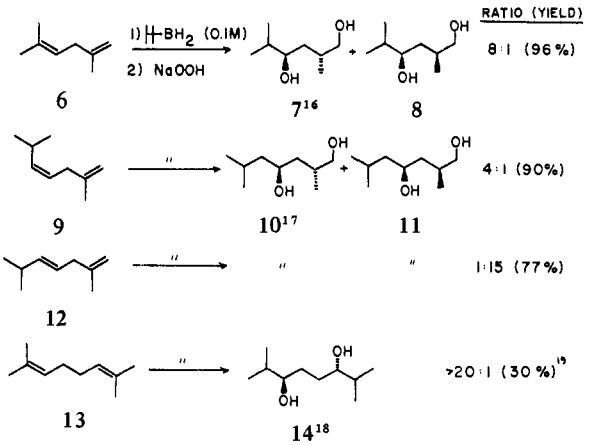
0002-7863/80/1502-7385$01.00/0

without stereochemical control, a similar reaction with thexylborane[11] produced substantial 1,4-asymmetric induction to give a 6:1 mixture of diastereomers (81% yield) in which **4** was the major product. This ratio as well as the others given here was determined by integration of the high-resolution (~3 data points/Hz) ^{13}C NMR at 20 MHz with calibration by an authentic mixture of diastereomers and a pure diastereomer prepared without stereochemical ambiguity by a different route. In this example, authentic samples of both **4**[12] and **5**[13] were prepared from isomenthone and menthone, respectively.[14] The identification of **4** as the major product provides evidence for the operation of a substantial stereoelectronic effect in the hydroboration reaction. Of the two most likely transition states, it will be seen that the major product **4** results from the boatlike geometry if it is assumed

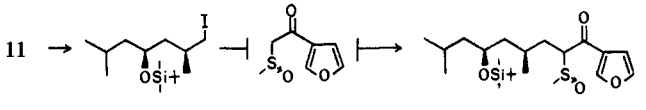


that nonhydrogen substitutents will predominantly select equatorial environments. The thexyl substituent in this reaction turns out to be lost as tetramethylethylene prior to cyclization,[15] and the preference for the boat over the chair may well reflect the situation that the boron–hydrogen bond eclipses the olefin π system in the former conformation but not in the latter.[16] The transition state for the second, intramolecular hydroboration would thus be a semiplanar, four-center one as suggested previously.[17]

Related diene hydroborations proceed by formation of a five-membered boracycle and do not appear to incorporate the unfavorable aspects of a boatlike transition state.[18] Although the scope of the reaction as presented here is somewhat limited by the requirement of a well-defined initial hydroboration, the examples demonstrate the crucial point that the second (intramolecular) hydroboration again occurs with substantial remote asymmetric induction. In the hydroboration of **9**, the relatively poor stereochemical control is in part due to competitive initial hydroboration of the cis-disubstituted olefin as indicated by isolation of ~5% of the isomeric 1,5-diol.[23] It is interesting to note that in each instance, the major product may be rationalized in terms of a transition state having eclipsed B—H and C=C bonds and what would appear to be the least strained conformation of the connecting chain. As in related cyclopentanoid systems, this preferred conformation would be expected to consist of trans adjacent substituents and pseudoequatorial nonadjacent ones. Only in the case of **12** is some ambiguity involved, and this is presumably due to a steric interaction between the isopropyl and thexyl substitutents.



A simple application of this methodology involves the synthesis of a potato stress metabolite, dihydromyoporone (**1**).[10] Diol **11** (from **12**) was monotosylated (*p*-TsCl, C_5H_5N), silylated (*t*-$BuMe_2SiCl$, imidazole, DMF), and iodo-exchanged (NaI, acetone) to give **15**. β-Keto sulfoxide alkylation (NaH, DMF; 25 °C; 5 h) then produced **16** which was desulfurized (Al[Hg], THF–H_2O) and deprotected (HOAc–H_2O; 50 °C) to give (±)-dihydromyoporone (**1**). An analogous sequence starting with **10** (from **9**) gave the epimer of **1** which showed obvious spectral differences with natural dihydromyoporone only by ^{13}C NMR.[24] Since the



(11) Cyclic hydroboration of **3** is typical of the hydroborations described in this paper and was accomplished by preparation of 1.25 equiv of thexylborane from BH_3–THF and tetramethylethylene (G. Zweifel and H. C. Brown, *J. Am. Chem. Soc.*, **85**, 2066 (1963)) in tetrahydrofuran to make a 0.1 M solution. The solution was then chilled to −78 °C, the diene was added in a single portion, and the mixture was allowed to warm to room temperature. Alkaline peroxide workup in the usual way gave the products indicated. In the case of **3** and presumably the other dienes examined, the product stereochemistry appears to be kinetic since the ratio of **4**:**5** was not changed by extended reaction times or the addition of BH_3 after the initial cyclization.

(12) **4**: IR (neat) 3350, 2970, 2950, 2880, 1465, 1380, 1025, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.48 (d, 2 H, J = 6 Hz), 3.35 (m, 1 H), 1.8–1.2 (m), 0.90 (d, 9 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 76.5, 67.6, 35.0, 33.5, 30.3, 28.8, 18.6, 17.4, 16.2.

(13) **5**: IR (neat) 3350, 2970, 2950, 2880, 1465, 1380, 1025, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.49 (d, 2 H, J = 6 Hz), 3.35 (m, 1 H), 1.8–1.2 (m), 0.90 (d, 9 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 77.2, 67.4, 35.7, 31.2, 29.4, 18.6, 17.1, 16.8.

(14) Isomenthone and menthone were individually Baeyer–Villager lactonized (*meta*-chloroperbenzoic acid, CH_2Cl_2), converted into the silyl ketene acetal ((a) LDA, THF; (b) Me_3SiCl), and ozonized (Et_2O, −75 °C) with a reductive workup ($LiAlH_4$, 0 °C) to give **4** and **5**, respectively.

(15) Evidence for loss of thexyl in this reaction includes detection of no thexyl alcohol in the oxidized product and formation of an ethanol addition product prior to oxidation. Precedent for this type of reaction may be found in H. C. Brown, E.-I. Negishi, and J.-J. Katz, *J. Am. Chem. Soc.*, **97**, 2791 (1975). It is of further interest that the best yield and stereochemical control with **3** were obtained when the cyclic hydroboration was conducted in the presence of excess Et_3N. The fact that the other reactions reported appear to proceed without loss of the thexyl substituent may reflect the severe strain associated with cyclization of **3** having an axial thexyl group.

(16) We have no data which bears on the transition state leading to the minor diol **5**. It may derive either from the chair shown or from an axially substituted boat.

(17) For a discussion of the mechanism and the associated transition state geometry, see: G. M. L. Cragg, "Organoboranes in Organic Synthesis", Marcel Dekker, New York, 1973, pp 89–96. See also: S. Nagase, N. K. Ray, and K. Morokuma, *J. Am. Chem. Soc.*, **102**, 4536 (1980), and references cited therein.

(18) Formation of five-membered boracycles has been found previously to be quite facile and can even override the normal anti-Markovnikov preference of hydroboration. 1,4-Pentadiene, for example, gives a substantial quantity of 1,4-pentanediol on hydroboration: E.-I. Negishi, P. L. Burke, and H. C. Brown, *J. Am. Chem. Soc.*, **94**, 7431 (1972).

(19) Authentic **7** was prepared by catalytic reduction (H_2, Rh–Al_2O_3) of 2-methyl-4-isopropylbutenolide followed by hydride reduction ($LiAlH_4$). **7**: IR (neat) 3620, 2900, 1460, 1385, 1035, 990, 940, 915, 860, 840, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.40 (ABX, 2 H, δ_A = 3.54, δ_B = 3.28, J_{AB} = 8.5 Hz, J_{AX} = 3.5 Hz, J_{BX} = 6 Hz), 3.75 (1 H, –OH), 3.35 (m, 1 H), 1.8–1.0 (m), 0.85 (d, 9 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 75.5, 68.7, 39.3, 34.4, 34.3, 18.4, 17.8, 17.4.

(20) Authentic **10** was prepared as above[16] starting from 2-methyl-4-isobutylbutenolide. **10**: IR (neat) 3330, 2850, 1470, 1380, 1140, 1040, 970, 830, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.80–3.25 (m, 3 H), 2.35 (br s, 2 H, –OH), 1.9–1.2 (m), 0.92 (d, 9 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 68.7, 68.5, 47.7, 43.5, 34.2, 24.6, 23.2, 22.2, 17.8. **11**: IR (neat) 3330, 2850, 1470, 1380, 1215, 1140, 1040, 980, 755, 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.0–3.6 (m, 1 H), 3.53 (d, 2 H, J = 6 Hz), 1.8 (br s, 2 H, –OH), 1.9–1.15 (m), 0.93 (d, 3 H, J = 6 Hz), 0.91 (d, 6 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 67.6, 66.9, 46.5, 42.4, 31.9, 24.5, 23.1, 22.1, 17.6.

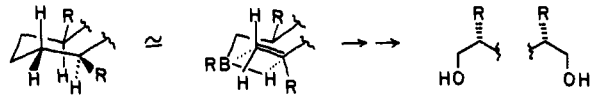
(21) Authentic **14** was prepared from (*E*,*E*)-2,7-dimethyl-3,5-octadiene by singlet oxygenation (MeOH, rose bengal) and reduction ((a) $NaBH_4$, MeOH; (b) H_2, Rh–Al_2O_3). **14**: IR (neat) 3250, 2960, 2850, 1460, 1360, 1125, 1050, 1025, 990 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.37 (m, 2 H), 1.90 (br s, 2 H, –OH), 1.8–1.4 (m), 0.90 (d, 12 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 75.2, 33.3, 30.6, 19.0, 17.5.

(22) The low yield in this example may be related to the fact that thexylborane hydroborates trisubstituted olefins only sluggishly. A careful examination of the reaction mixture showed that **14** was the only 1,4-diol formed with the limits of ^{13}C NMR detection.

(23) For relative rates of hydroboration of various olefins with thexylborane, see G. Zweifel and H. C. Brown, *J. Am. Chem. Soc.*, **85**, 2066 (1963).

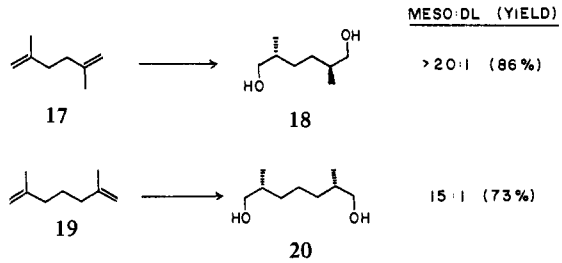
relative stereochemistry of the two asymmetric centers in dihydromyoporone has not been previously reported, this synthesis establishes the stereochemistry of the natural product as threo.

Although the extension of this method to the formation of more widely separated asymmetric centers seemed possible, we encountered substantial difficulties in accomplishing this goal. In particular, hydroboration of several homologues of **3** at various dilutions led to no obvious stereochemical control. The hydroborations thus far described are ones which proceed via a fused transition state (A). Some of the related bridged transition states (B, D) appear somewhat less flexible and have the interesting and useful property of resembling a low-energy conformational substructure found in a number of rings having more than six atoms (C). This geometrical similarity would suggest that transition



C D MESO

state D should not experience substantially more strain than that inherent to the ring being formed, and to the extent that the hydroboration is intramolecular, the product should be meso. Results with thexylborane (0.1 M, THF; -78-25 °C) seem to bear out this prediction. Thus hydroboration of dienes **17** and **19** proceeded by formation of seven- and eight-membered boracycles and gave the *meso*-diols with high 1,4- and 1,5-asymmetric induction. Here authentic mixtures of diastereomers were prepared from **17** and **19** with 9-borabicyclononane and samples of pure



17 18 19 20

18 and **20** were prepared by coupling enantiomerically pure fragments.[25] Product compositions could be determined only by high-resolution ^{13}C NMR.[26] Several attempts to extend the reaction to formation of a boracyclononane with 1,6-asymmetric induction have been unsuccessful.

A direct application of the last reaction is the preparation of the vitamin E side chain **2**. This synthesis is carried out by statistical monotosylation (*p*-TsCl, C_5H_5N; 0 °C) of **20** and bromide exchange (LiBr, DMF; 25 °C; 18 h), followed by coupling with excess isoamylmagnesium bromide (THF, Li_2CuCl_4; 0 °C; 1 h). The (±)-alcohol thus prouduced was identical by ^{13}C NMR with authentic (+)-**2**.[27]

Although numerous cyclic hydroborations are shown above to proceed with synthetically useful remote asymmetric induction, diene hydroboration as presented here provides only a partial solution to the general problem of remote stereocontrol. The most serious synthetic limitation is that relative asymmetric induction operates here only in a mechanistic sense, since the first, controlling asymmetric center is produced in the same overall reaction which subsequently creates the second. The key point, however, is that the stereochemistry associated with the intramolecular hydroboration step can be efficiently controlled by a remote chiral center. We believe that the generality of the cyclization approach to remote asymmetric induction is now firmly established and that examination of other intramolecular reactions in this context will reveal similar stereochemical controls.[28]

(24) Dihydromyoporone: ^1H NMR ($CDCl_3$) δ 8.00 (br s, 1 H), 7.40 (t, 1 H, J = 1.7 Hz), 6.74 (br s, 1 H), 3.75 (m, 1 H), 2.75 (br t, 2 H, J = 6 Hz), 2.0-1.1 (m), 0.89 (m, 9 H). ^{13}C NMR ($CDCl_3$) δ 195.6, 147.0, 144.1, 108.6, 67.4, 47.0, 45.5, 37.8, 30.0, 29.1, 24.5, 23.4, 22.0, 20.3. Epidihydromyoporone: ^{13}C NMR ($CDCl_3$) δ 195.4, 147.0, 144.1, 108.6, 67.7, 47.7, 45.1, 38.0, 32.0, 29.2, 25.9, 24.6, 23.2, 18.8. We wish to thank Dr. L. T. Burka at Vanderbilt University for a sample of authentic dihydromyoporone.

(25) Authentic optically active **18** (for ^{13}C NMR identification of *dl*-**18**) was prepared by Wurtz-like dimerization of (*R*)-$BnOCH_2CH(CH_3)CH_2Br$ (Mg, Li_2CuCl_4, THF) followed by deprotection (Li/NH_3). Authentic *meso*-**20** was prepared by a dithiane alkylation sequence: (1) 2-lithiodithane, THF, (*S*)-$THPOCH_2CH(CH_3)CH_2Br$; (2) *sec*-BuLi, (*R*)-$BnOCH_2CH(CH_3)CH_2Br$, THF; (3) RaNi, EtOH; (4) H_2O-HOAc; (5) Li/NH_3.

(26) **18**: IR (neat) 3300, 2920, 1480, 1400, 1050, 1000, 950 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.48 (d, 4 H, J = 6 Hz), 1.75-1.1 (m), 0.90 (d, 6 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 67.3, 35.6, 30.0, 16.5 (cf. *dl*-**18**: 67.5, 35.7, 30.2, 16.4). **20**: IR (neat) 3300, 2920, 1460, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.45 (dd, 4 H, J = 6, 2 Hz), 1.75-1.1 (m), 0.90 (d, 6 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 67.9, 35.5, 33.3, 24.1, 16.5 (cf. *dl*-**20**: 68.0, 35.4, 33.2, 24.0, 16.4).

(27) We wish to thank Dr. N. Cohen at Hoffmann-La Roche, Nutley, NJ, for a sample of authentic (±)-**2**.

(28) This work was supported by grants from the National Science Foundation (NSF CHE7801769) and the National Institutes of Health (RO1 HL 25634).

(29) Fellow of the Sloan Foundation, 1978-1980.

W. Clark Still,*[29] Kevin P. Darst

Department of Chemistry, Columbia University
New York, New York 10027

Received June 23, 1980

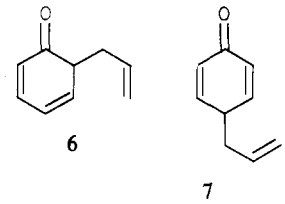
Ultraviolet Photoelectron Spectrum of the Phenoxy Radical

Sir:

We believe we have measured the ultraviolet photoelectron (UPE) spectrum of phenoxy radical (**1**) and, with the aid of MNDO[1] calculations, assigned the bands below 12 eV. To our knowledge this would be the first time that the UPE spectrum of a complex organic radical has been assigned in detail.

The MNDO calculations were carried out by both the spin-unrestricted[2] (UMNDO) and "half-electron"[3] (MNDO/HE) versions. Using Koopmans' theorem,[4] MNDO/HE gives good estimates of the first ionization energies of radicals while UMNDO gives first ionization energies that are usually larger by ~1 eV, due to the overestimation of correlation. Analogous results may be expected for the higher ionizations.

Phenoxy radical was obtained by thermolysis of allyl phenyl ether (**2**).[5] Comparisons for known compounds indicated the absolute values for IPs to be correct to ±0.02 eV. The resolution (Ar) was 20-30 meV. Spectra for several radicals (Et, *t*-Bu, allyl, $PhCH_2$) closely resembled those reported by Beauchamp et al.[6] Full experimental details will be given elsewhere. Besides ally radical (**3**), the only other products that might normally be expected under our conditions are phenol (**4**) (from **1**), 1,5-hexadiene (**5**), the dienones **6** and **7**, and *o*-allylphenol (**8**) (**2** → **6** → **7** or



6 7

8). The bands in our spectrum (Figure 1) do not correspond to

(1) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899, 4907.
(2) Pople, J. A.; Nesbet, R. H. *J. Chem. Phys.* **1954**, *22*, 571.
(3) (a) Longuet-Higgins, H. C.; Pople, J. A. *Proc. Phys. Soc., London* **1955**, *68*, 591; (b) Dewar, M. J. S.; Hashmall, J. A.; Venier, C. G. *J. Am. Chem. Soc.* **1968**, *90*, 1953.
(4) Koopmans, T. *Physica (Utrecht)* **1935**, *1*, 104.
(5) Fisher, I. P.; Palmer, T. F.; Lossing, F. P. *J. Am. Chem. Soc.* **1964**, *86*, 2742. Electron impact IP for **1**, 8.84 eV.
(6) (a) Houle, F. A.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 3290; (b) *Ibid.* **1979**, *101*, 4069.

0002-7863/80/1502-7387$01.00/0