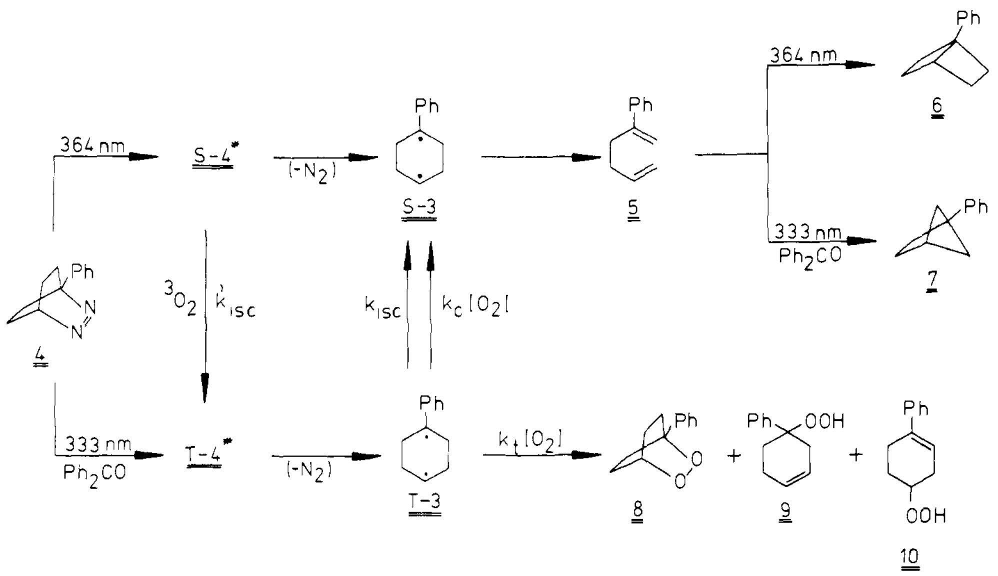
Scheme I

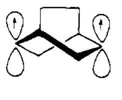


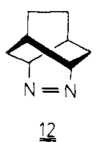
$$\frac{1}{X_P} = \frac{1}{1-X_H} = \frac{1}{T_f} + \frac{1}{k_t\tau_T[O_2]} \quad (1)^a$$

[a] X_P = mole fraction of peroxide (trapped product); X_H = mole fraction of hydrocarbons (untrapped product); $T_f = k_t/(k_t + k_c)$ is the trapping factor; k_t = rate constant for oxygen trapping; k_c = rate constant for spin-catalyzed intersystem crossing; $\tau_T = 1/k_{ISC}$ is the triplet lifetime; k_{ISC} = rate constant for inherent intersystem crossing.

The phenyl-substituted triplet 1,4-cyclohexadiyl **T-3** ($\tau_T \sim 300$ ns) is several 1000-fold longer lived than the parent triplet diradical **T-1** ($\tau_T \sim 0.1$ ns). Stabilization by phenyl conjugation alone can hardly account for such a massive effect, as evidenced by Norrish type II triplet diradicals[13] or by 1,5-diradicals.[14] We suggest that Salem's orbital orientation rule[3] is the reason for this large differentiation in the triplet lifetimes.[2] On photoextrusion of the nitrogen from the bicyclic azoalkane precursor, the 1,4-cyclohexadiyl is initially born in the boat conformation. In the absence of stabilization of the radical centers, efficient spin-orbit coupling[3] in the boat conformation of the parent triplet diradical **1a** leads to significant amounts (ca. 33%) of bicyclo[2.2.0]hexane as product. However, phenyl stabilization of the radical site in **3a** increases its lifetime and therewith provides sufficient time for the species to relax to the preferred twist-boat conformation **3b**, as suggested by theoretical work on tetramethylene.[4] Intersystem crossing is now slow because the parallel arrangement of the radical lobes in **3b** is not conducive for spin-orbit coupling.[3] Molecular distortions to the chair conformation induces spin inversion, but the resulting singlet exclusively fragments into the 1,5-hexadiene **5** rather than cyclizing to the bicyclo[2.2.0]hexane **6**. The intervening σ-bond is better aligned for fragmentation in the chair than in the twist-boat conformation **3b**.

It is of interest to report that the triplet 1,4-cyclohexadiyl **11**, derived from the known[15] azoalkane **12**, can be trapped with $^3O_2$.


11



12

This is the *first* bicyclic, localized triplet diradical that could be trapped with molecular oxygen![2] Presumably its appreciable lifetime derives from its essentially rigid twist-boat conformation, as confirmed by molecular mechanics calculations.[16]

Acknowledgment. We are grateful to the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the Stiftung Volkswagenwerk for generous financial support.

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[13] Caldwell, R. A.; Majima, T.; Pac, C. *J. Am. Chem. Soc.* **1982**, *104*, 629.

[14] (a) Barton, D. H. R.; Charpiot, B.; Ingold, K. U.; Johnston, L. J.; Motherwell, W. B.; Scaiano, J. C.; Stanforth, S. *J. Am. Chem. Soc.* **1985**, *107*, 3607. (b) Zimmt, M. B.; Doubleday, C., Jr.; Gould, I. R.; Turro, N. J. *J. Am. Chem. Soc.* **1985**, *107*, 6724.

[15] Askani, R.; Schwertfeger, W. *Chem. Ber.* **1977**, *110*, 3046.

[16] Molecular Mechanics (MMPMI) from Serena Software, Bloomington, IN. We thank K. E. Gilbert and J. J. Gajewski, for making this program available to us.

Radical Anions in Hydrocarbon Media. Interaction between Unsolvated and/or Solvated Radical Anions and Metal Alkoxides. Evidence for Cation-Dependent Clustering of Ketyl Anions at High Concentrations

Constantinos G. Screttas* and Maria Micha-Screttas

Institute of Organic Chemistry
The National Hellenic Research Foundation
Athens 116 35, Greece

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Almost all the chemistry of radical anions (RA) can be understood on the basis of their ability to donate an electron plus a metal cation and as such can be considered as homogeneous sources of metals. It is this property which makes them increasingly useful reagents in organic and organometallic synthesis.[1] A serious problem associated with their employment in organometallic preparations, however, is the instability of the organometallic products in the ethereal solvents[2] which are necessary for the preparation of RA.[3] We now report a method of solubilizing unsolvated RA in hydrocarbon media thus broadening their synthetic and catalytic potentials. We also present physical evidence concerning the state of aggregation of RA at concentrations which, perhaps, are not accessible by other relevant techniques.[4] Previously, only dilute solutions of unsolvated

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[1] For a recent review, see: Cohen, T. *Tetrahedron* **1986**, *42*, 2803.

[2] Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: Oxford, 1974, p 8.

[3] Coates, G. E.; Green, M. L. H.; Wade, K. *Organometallic Compounds, The Main Group Elements*, Methuen: London, 1969; Vol. 1, p 59.

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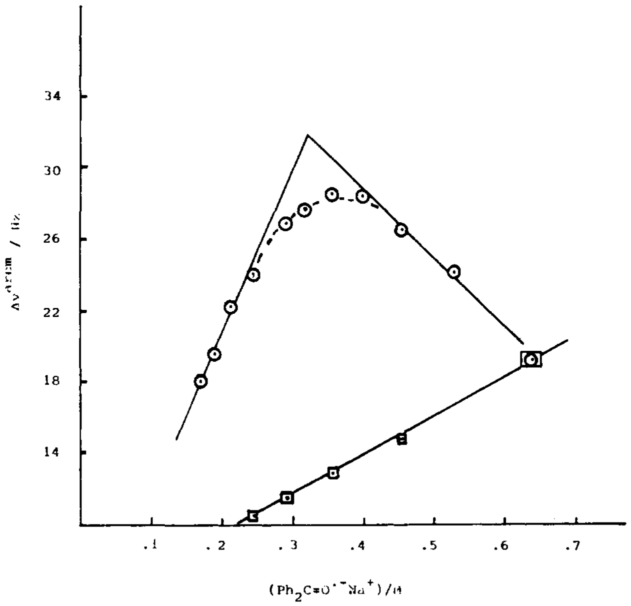

Figure 1. Relationship between paramagnetic NMR shift of aromatic protons ($PhCH_3$) and the formal concentrations of $Ph_2C{=}O^{\bullet-}Na^+$: squares, dilution with toluene; circles, dilution with 2 M $LiOCH_2CH_2OEt$ in toluene.

fluorenone radical anion, $FlO^{\bullet-}$, in aromatic hydrocarbons had been obtained by the use of complex cations of the onium type.[5]

By stirring an aromatic ketone ($Ar_2C{=}O$) or hydrocarbon (ArH) in 2 M $LiOCH_2CH_2OEt$ (**1**) in toluene or methylcyclohexane with an alkali metal a rapid reduction too place, and solutions of 0.3–1.0 M of RA were obtained.[6] Radical anions of $Ar_2C{=}O$ appeared to form more readily, and they were more soluble than $(ArH)^{\bullet-}$. In the case where the alkali metal in RA was other than the metal in the alkoxide no or very slow exchange was observed with the exception of potassium naphthalenide. A marked difference between the formal concentration[6] and the concentration of unpaired spins was noticed. Especially, solutions of $Ph_2C{=}O^{\bullet-}M^+$, M = Li, Na, were feebly paramagnetic, with 15% of the reducing electrons of the solution being unpaired,[7] entries 1–2, Table I. Interestingly, dilution of concentrated solutions of $Ph_2C{=}O^{\bullet-}M^+$ with **1** in toluene caused a spectacular change of the color of the solution from a greenish-blue to pure blue with a simultaneous increase of paramagnetism. In Figure 1 is shown the behavior of $Ph_2C{=}O^{\bullet-}Na^+$. The curved line represents the change of paramagnetism with respect to dilution with **1**, whereas the straight line corresponds to the respective change as a function of dilution with *pure toluene*. The curved line resembles a titration curve from which an equivalence point can be estimated. These stoichiometries of interaction between $Ph_2C{=}O^{\bullet-}M^+$, M = Li, Na, K, and **1** are given in Table I, and they agree to within 3–9% with 1/7, 1/5, and 1/4, respectively. The observed stoichiometries, which reflect the corresponding alkoxide demand, seem to correlate with the relevant increase of the concentration of the unpaired spins at, or beyond, the stoichiometric point, Table I. These observations are indicative of the existence in solution of species which are diamagnetic and unstable and that their stabilization in the paramagnetic form(s) require a certain number of alkoxide molecules per molecule of $Ph_2C{=}O^{\bullet-}M^+$. The latter number depends strongly on M^+. The most alkoxide-demanding $Ph_2C{=}O^{\bullet-}Li^+$ is the least stable, a fact which is manifested also by its tendency to undergo disproportionation to a reddish-purple dianion within 3–4 days at room temperature. A different behavior is exhibited by $(ArH)^{\bullet-}M^+$ with respect to dilution. Namely, unlike $Ar_2C{=}O^{\bullet-}M^+$, dilution either with pure toluene or toluene solution of **1** has exactly the same effect, e.g., Figure 2. This dichotomy between $Ar_2C{=}O^{\bullet-}$ and $(ArH)^{\bullet-}$ most probably arises from the presence of the electronegative[8] oxygen in ketyls which, in turn, can attain coordination numbers as high as 6.[9] This allows them to behave like ordinary alkoxides which are known to undergo clustering in solution.[10] Close proximity between ketyl entities in a cluster may allow spin pairing, hence the diamagnetic character at high concentrations. Addition of **1** produces mixed alkoxide–ketyl clusters, e.g., displacement of an alkoxide molecule from the edge of a $(ROLi)_n$ polyhedron by a molecule of $Ar_2C{=}O^{\bullet-}M^+$ should lead to $(ROLi)_{n-1}(Ar_2\dot{C}{-}O^-M^+)$. In the latter species spin pairing should be less probable, hence the observed increase of paramagnetism on adding **1**.

Table I. Stoichiometries of Interaction between Radical Anions and Lithium 2-Ethoxyethoxide in Toluene and Relevant Data

entry no.	RA	M	(RA)/ (ROLi)	molar param solvent NMR shift[a] (ppm/mol)	unpaired spins[b] (%) *c*	*d*
1	$(Ph_2C{=}O)^{\bullet-}M^+$	Li	1/6.84	1.85	15	73
2	$(Ph_2C{=}O)^{\bullet-}M^+$	Na	1/4.64	0.97	15	38
3	$(Ph_2C{=}O)^{\bullet-}M^+$	K	1/3.66	1.37	40	54
4	$(PhCH{=}CHPh)^{\bullet-}M^+$	Li		1.77	69	69
5	$(PhCH{=}CHPh)^{\bullet-}M^+$	Na		1.50	59	59
6	$(anthracene)^{\bullet-}M^+$	Li		1.76	69	69

[a] Referred to the CH_3 proton band of toluene at the stoichiometric point. It is 3–10% smaller than the shift referred to the aromatic protons. Reasonably, hyperfine interactions contribute very little to the observed shift. Namely, it reflects the macroscopic paramagnetism. [b] See footnote 7. [c] Before adding $LiOCH_2CH_2Et$ at the stoichiometric point. [d] After adding $LiOCH_2CH_2OEt$ at the stoichiometric point.

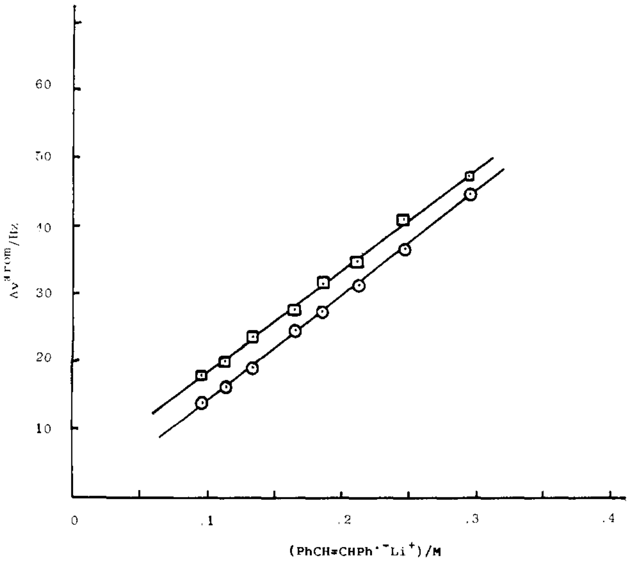

Figure 2. See caption, Figure 1.

Solvated $Ar_2C{=}O^{\bullet-}M^+$ do interact with metal alkoxides. For example, addition of a concentrated solution of $Mg(OCH_2CH_2OEt)_2$, **2**, in tetrahydrofuran (THF) to a THF solution of $FlO^{\bullet-}Li^+$ causes a rapid drop of paramagnetism to almost complete disappearance of the latter. By plotting, Figure 3, the results in the form of a magnetic titration the stoichiometry of

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(4) We employed NMR spectroscopy: de Boer, E.; Grotens, A. M.; Smid, J. *J. Am. Chem. Soc.* **1970**, *92*, 4742. Screttas, C. G.; Micha-Screttas, M. *J. Org. Chem.* **1981**, *46*, 993. ESR and ENDOR techniques might miss the concentration-dependent phenomena that are reported in this work.

(5) Cazianis, C. T.; Screttas, C. G. *Tetrahedron* **1983**, *39*, 165.

(6) The concentration of the radical anions was taken equal to the reducing power of the solution. The latter was determined by reacting an aliquot with an excess of 1,2-dibromoethane and titrating the liberated Br^-.

(7) Estimated from the deviation of the observed molar paramagnetic solvent shift and the theoretical value, 2.55 ppm/mol at 35 °C. The latter is given by the Dickinson–Langevin equation: de Boer, E.; MacLean, C. *J. Chem. Phys.* **1966**, *44*, 1334. Dickinson, W. C. *Phys. Rev.* **1951**, *81*, 717.

(8) Mao, S. W.; Nakamura, K.; Hirota, N. *J. Am. Chem. Soc.* **1974**, *96*, 5341 and references therein.

(9) Weiss, E. *Helv. Chim. Acta* **1963**, *46*, 2051.

(10) Bradley, D. C.; Mehrotra, R. C.; Gaur, D. P. *Metal Alkoxides*; Academic Press: London, 1978; p 74.

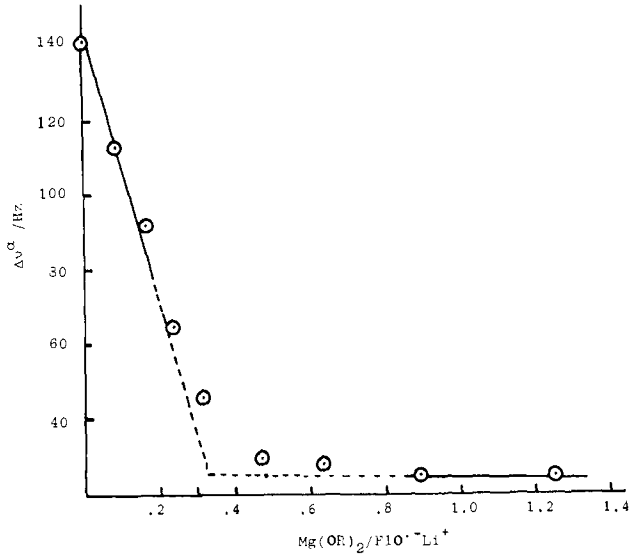

Figure 3. Magnetic titration of ca 1 M $\mathrm{FlO^{\bullet-}Li^+}$ against 1.65 M of $\mathrm{Mg(OCH_2CH_2OEt)_2}$ in THF (The indicated shift is referred to the α-proton band of THF.).

interaction could be estimated. The stoichiometries $(\mathrm{FlO^{\bullet-}M^+})/(\mathbf{2})$ for M = Li, Na, and K, respectively, were 3.00/1, 2.94/1, and 1.92/1. Again, we observe a cation-dependent stoichiometry, being 3/1 for $\mathrm{Li^+}$ and $\mathrm{Na^+}$ and 2/1 for $\mathrm{K^+}$. If disappearance of paramagnetism takes place by a spin-pairing mechanism, then six molecules of $\mathrm{FlO^{\bullet-}Li^+}$ and $\mathrm{FlO^{\bullet-}Na^+}$ interact with two molecules of **2** at the stoichiometric point, whereas two of four $\mathrm{FlO^{\bullet-}K^+}$ interact with one or two molecules of **2**, respectively. These results could indicate the existence of tetrameric and exameric paramagnetic $\mathrm{FlO^{\bullet-}M^+}$ clusters. Hirota[8] besides identifying triple and quadruple ions[11] identified higher clusters and proposed structures for tetrameric and pentameric alkali metal fluorenone ketyls.

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(11) Russell, G.; Gerlock, J. L. *J. Am. Chem. Soc.* **1974**, *96*, 5838. Hirota, N. *Ibid.* **1967**, *89*, 32. Biloen, P.; Prins, R.; van Voorst, J. D. M. *J. Chem. Phys.* **1967**, *46*, 4149. Hirota, N.; Weissman, S. I. *J. Am. Chem. Soc.* **1964**, *86*, 2538; **1961**, *83*, 3533.

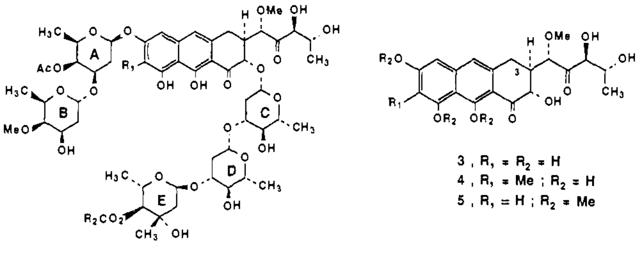
A Highly Stereoselective Total Synthesis of the Natural Enantiomer of Olivin

William R. Roush,*[1] Michael R. Michaelides, Dar Fu Tai, and Wesley K. M. Chong

Department of Chemistry, Indiana University
Bloomington, Indiana 47405
Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Received August 13, 1987

The aureolic acid antibiotics are a group of clinically effective antitumor agents.[2] As illustrated by **1** and **2** below, these compounds are structurally complex, each having a di- and a trisaccharide attached to a central aglycone, either olivin (**3**) or chromomycinone (**4**). While two syntheses of tri-*O*-methylolivin (**5**) have been reported,[3] no syntheses of the natural, *unprotected* aglycones have yet appeared.[4] As a continuation of our work on the total synthesis of olivomycin A (**1**),[5] we have completed and are pleased to report here the first total synthesis of olivin in the naturally occurring enantiomeric form.



1, R_1 = H; R_2 = iPr olivomycin A
2, R_1 = R_2 = Me chromomycin A_3

3, R_1 = R_2 = H
4, R_1 = Me; R_2 = H
5, R_1 = H; R_2 = Me

The synthesis (see Scheme I) commenced with the reaction of threonine-derived aldehyde **6**[5a] with in situ generated[6] dimethyl (*Z*)-γ-methoxyallylboronate [prepared from 2.2 equiv of methyl allyl ether, 2.2 equiv of *n*-BuLi–TMEDA, and 2.2 equiv of $\mathrm{FB(OMe)_2}$] that provided **7**, mp 61–62 °C, in 75–83% yield following chromatographic purification. After protection of **7** as the TBDMS ether, the vinyl unit was cleaved by ozonolysis, and the resulting aldehyde condensed with 1.2 equiv of $\mathrm{Ph_3P{=}CHCHO}$ in benzene at reflux (5 h) to give unsaturated aldehyde **8** in 55% yield after one recycle of recovered saturated aldehyde.[8] The critical C(3) stereocenter of **3** was next introduced with very high stereoselection (>20:1) and in excellent yield by treatment of **8** with $\mathrm{(CH_2{=}CH)_2CuLi}$ in an ether–THF mixture containing TMS-Cl.[5b,9,10] It is notable that use of the corresponding unsaturated ester as in our original studies[5b] gave highly variable yields and that very poor results were obtained on attempted scale up. By comparison, the conversion of **8** to **9** has proven to be highly reproducible, and multigram quantities of **9** are easily prepared in this way.

With a highly selective and efficient solution to the major stereochemical problems well in hand, we turned our attention to the construction of the anthracenone nucleus of **3**. Naphthoate

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(1) Current address: Indiana University.

(2) For reviews, see: (a) Remers, W. A. *The Chemistry of Antitumor Antibiotics*; Wiley-Interscience: New York, 1979; Chapter 3. (b) Skarbeck, J. D.; Speedie, M. K. *Antitumor Compound Natural Origin: Chemistry and Biochemistry*; Aszalos, A., Ed.; CRC Press: 1981; Chapter 5.

(3) (a) Dodd, J. H.; Starrett, J. E.; Weinreb, S. M. *J. Am. Chem. Soc.* **1984**, *106*, 1811. (b) Franck, R. W.; Bhat, V.; Subramaniam, C. S. *Ibid.* **1986**, *108*, 2455.

(4) For other studies directed toward the synthesis of olivin, see: (a) Thiem, J.; Wessel, H. P. *Liebigs Ann. Chem.* **1981**, 2216. (b) Kraus, G. A.; Hagen, M. D. *J. Org. Chem.* **1983**, *48*, 3265. (c) Rama Rao, A. V.; Dhar, T. G. M.; Gujar, M. K.; Yadav, J. S. *Indian J. Chem.* **1986**, *25B*, 999.

(5) (a) Roush, W. R.; Harris, D. J.; Lesur, B. M. *Tetrahedron Lett.* **1983**, *24*, 2227. (b) Roush, W. R.; Lesur, B. M. *Ibid.* **1983**, *24*, 2231. (c) Roush, W. R.; Straub, J. A. *Ibid.* **1986**, *27*, 3349.

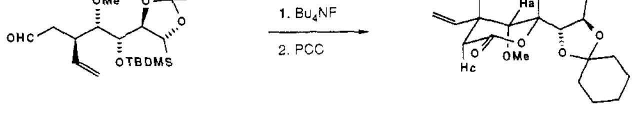
(6) (a) Wuts, P. G. M.; Bigelow, S. *J. Org. Chem.* **1982**, *47*, 2498. (b) Fujita, K.; Schlosser, M. *Helv. Chim. Acta* **1982**, *65*, 1258.

(7) The spectroscopic properties of all new compounds are fully consistent with the assigned structures.

(8) This reaction also produced substantial quantities (6–25%, depending on reaction conditions and stoichiometry) of the corresponding diene aldehyde. For large scale work, therefore, it was preferable to perform the RCHO to $\mathrm{RCH{=}CHCHO}$ conversion by a three-step operation: (i) $\mathrm{Ph_3PCHCO_2Me}$, $\mathrm{CH_2Cl_2}$, 23 °C; (ii) DIBAL-H, $\mathrm{Et_2O}$, −78 °C; (iii) PCC, $\mathrm{CH_2Cl_2}$. The overall yield of **8**, a 4:1 mixture of *E*-*Z* isomers, from **7** was 55–60%. The presence of (*Z*)-**8** did not noticeably influence the stereoselectivity of the subsequent cuprate reaction.

(9) The yield is 75% if TMS-Cl is omitted. For other studies on the use of TMS-Cl in organocuprate conjugate additions, see: (a) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6015, 6019. (b) Alexakis, A.; Berlan, J.; Besace, Y. *Ibid.* **1986**, *27*, 1047. (c) Horiguchi, Y.; Matsuzawa, S.; Nakamura, E.; Kuwajima, I. *Ibid.* **1986**, *27*, 4025. (d) Nakamura, E.; Matsuzawa, S.; Horiguchi, Y.; Kuwajima, I. *Ibid.* **1986**, *27*, 4029.

(10) The stereochemistry of the vinylcuprate addition was established as shown below. The stereochemical outcome is identical with that reported previously for reactions of the corresponding enones and unsaturated esters (ref 5b). For other examples of high diastereoface selectivity in organocuprate conjugate additions, see: Bernardi, A.; Cardani, S.; Poli, G.; Scolastico, C. *J. Org. Chem.* **1986**, *51*, 5041.



$\mathrm{H_a}$: br t, J = 2 Hz
$J_{b,c}$ = 10 Hz