proceed via an enzyme–ADP–metal ion complex as suggested.[45]

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Registry No. PCOP, 125830-06-0; PCOP(hydrochloride), 125830-05-9; Cu^{2+}, 15158-11-9; Ni^{2+}, 14701-22-5; Co^{2+}, 22541-53-3; Zn^{2+}, 23713-49-7; Mg^{2+}, 22537-22-0; Ca^{2+}, 14127-61-8; 1,10-phenanthroline-2-carboxylic acid chloride hydrochloride, 37067-11-1; orthophosphoric acid, 7664-38-2.

Stereoelectronic Effects on Chemoselectivity in the Free Radical Bromination of Arylcyclopropanes

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Abstract: The reaction of atomic bromine with several arylcyclopropanes has been investigated. For systems where the aryl moiety is phenyl or α- or β-naphthyl, the expected S_H2 pathway leading to cyclopropane ring cleavage is observed. In the case of 9-cyclopropylanthracene, however, an unprecedented hydrogen atom abstraction reaction is observed. These observations are explicable on stereoelectronic grounds. For the 9-anthryl system, the lowest energy perpendicular conformation finds the α-C–H bond aligned with the π-system, and consequently hydrogen abstraction is facile. In this conformation, the α-C–C bonds are deactivated toward bromine atom attack. For phenyl- and β-naphthylcyclopropane, the bisected conformation is preferred and ring opening predominates. The ground-state conformation of α-cyclopropylnaphthalene is unique in that it is midway between bisected and perpendicular. Although cyclopropane ring opening is the only detected process, quantitative data are presented which demonstrate that the *rate* of this process is diminished because of unfavorable stereoelectronic factors. Analysis of this reaction system with the Curtin–Hammett principle leads to a general statement of the requirements for α-hydrogen abstraction from cyclopropylarenes by bromine atom.

Introduction

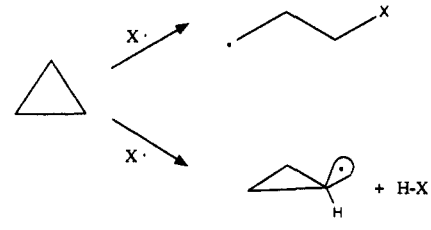
The reaction of a free radical with cyclopropane results in hydrogen abstraction and/or ring opening (Scheme I), the observed chemoselectivity being dependent on the nature and identity of the attacking radical. Imidyl[1,2] and *tert*-butoxy[3] radicals yield exclusively hydrogen abstraction products. Chlorine atom[3,4] yields both hydrogen abstraction and ring-opened products, the product ratio being temperature dependent. Bromine atom produces ring-opened products exclusively.[5-7]

The free radical bromination of alkylcyclopropanes has been studied in considerable detail and shown to involve the backside attack of bromine atom on the least-hindered position of the cyclopropane (with inversion of configuration), resulting in formation of the most-stable radical (Scheme II).[5,6] This S_H2 process represents a formal carbon atom abstraction by Br• and derives its thermodynamic driving force from the relief of cyclopropane ring strain.

For arylcyclopropanes, free radical bromination also yields ring-opened products.[8-10] The effect of substituents on the aromatic ring has been examined, and the reaction is found to correlate with σ^+ ($\rho = -1.84$).[10] This substituent effect is remarkably similar to that observed for hydrogen abstraction from substituted toluenes by bromine atom (correlation to σ^+, $\rho = -1.76$),[10] which is not unreasonable because both processes involve formation of a benzyl radical (presumably via a polar transition state).

Irrespective of the substituents present on the cyclopropyl ring, there are no reported examples of abstraction of a cyclopropyl

Scheme I



Scheme II

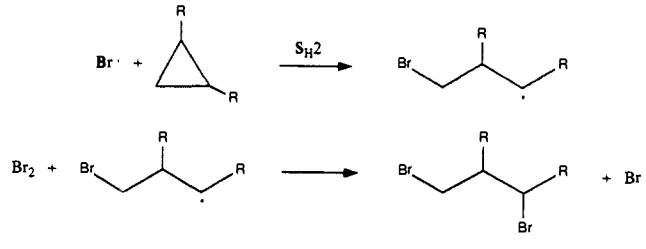


Table I. Bromination of Phenylcyclopropane under a Variety of Conditions

entry	brominating agent/ conditions	time, min	temp, °C	% $PhCHBrCH_2CH_2Br$
1	$Br_2/CCl_4/h\nu$[a]	5	15	100
2	$Br_2/CH_2Cl_2/h\nu$[a]	5	−78	100
3	Br_2/CCl_4/dark[b]	5	15	0[c]
4	Br_2/CH_2Cl_2/dark[b]	5	−78	0[c]
5	NBS/Bz_2O_2/CCl_4[d]	90	80	0[c]

[a] Irradiated with a 400-W medium pressure mercury-arc lamp at a distance of 1–2 ft through Pyrex. [b] Nondegassed solution, protected from light. Excess Br_2 quenched with a suitable olefin before analysis. [c] >95% recovered starting material. [d] NBS = *N*-bromosuccinimide; Bz_2O_2 = 2–3% benzoyl peroxide.

(1) Traynham, J. C.; Lee, Y.-S. *J. Am. Chem. Soc.* **1974**, *96*, 3590.
(2) Tanko, J. M.; Skell, P. S.; Seshadri, S. *J. Am. Chem. Soc.* **1988**, *110*, 3221.
(3) Walling, C.; Fredricks, P. S. *J. Am. Chem. Soc.* **1962**, *84*, 3326.
(4) Roberts, J. D.; Dirstine, P. H. *J. Am. Chem. Soc.* **1945**, *67*, 1281.
(5) Maynes, G. G.; Applequist, D. E. *J. Am. Chem. Soc.* **1973**, *95*, 856.
(6) Shea, K. J.; Skell, P. S. *J. Am. Chem. Soc.* **1973**, *95*, 6728.
(7) The gas-phase photobromination of cyclopropane with a Br_2/Cl_2 mixture yields ca. 10% cyclopropyl bromide, undoubtedly with Cl• serving as H-abstractor. When Cl_2 is omitted, only 1,3-dibromopropane is formed. Dedio, E. L.; Kozak, P. J.; Vinogradov, S. N.; Gunning, H. E. *Can. J. Chem.* **1962**, *40*, 820.
(8) Kuivila, H. G.; Caywood, S. C.; Boyce, W. F.; Langevin, F. L., Jr. *J. Am. Chem. Soc.* **1955**, *77*, 5175.
(9) LaLonde, R. T.; Ferrara, P. B.; Debboli, A. D., Jr. *J. Org. Chem.* **1972**, *37*, 1094.
(10) Applequist, D. E.; McKenzie, L. F. *J. Org. Chem.* **1976**, *41*, 2262.

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Table II. Bromination of α- and β-Cyclopropylnaphthalene under a Variety of Conditions

entry	isomer	brominating agent/ conditions	time, min	temp, °C	results
1	α	Br_2(dil)/CCl_4/$h\nu$[a]	30	10	95% $C_{10}H_7CHBrCH_2CH_2Br$
2	α	Br_2/CCl_4/dark/O_2[b]	1440	10	85% $C_{10}H_6Br$-c-C_3H_5 5% $C_{10}H_7$-c-C_3H_5 2% $C_{10}H_7CHBrCH_2CH_2Br$
3	α	NBS/Bz_2O_2/CCl_4[c]	90	80	95% $C_{10}H_7$-c-C_3H_5 5% $C_{10}H_7CHBrCH_2CH_2Br$
4	β	Br_2(dil)/CCl_4/$h\nu$[a]	30	10	93% $C_{10}H_7CHBrCH_2CH_2Br$

[a] "Dilute" Br_2 delivery (see Experimental Section); irradiated with a 400-W medium-pressure mercury-arc lamp at a distance of 1–2 ft through Pyrex. [b] Air-saturated solution, protected from light. [c] NBS = *N*-bromosuccinimide; Bz_2O_2 = 2–3 mol·% benzoyl peroxide.

Table III. Bromination of 9-Bromo- and 9-Chloro-10-cyclopropylanthracene in CCl_4 under a Variety of Conditions

entry	cyclopropylarene	brominating agent/ conditions	time, min	reaction product; % yield
1	**1b**	$Br_2/h\nu$[a]	5	**2b**; 95
2	**1b**	Br_2/dark/O_2[b]	60	**3b**; 100
3	**1c**	$Br_2/h\nu$[a]	5	**2c**; 95
4	**1c**	Br_2/dark/O_2[b]	60	**3c**; 100

[a] Irradiated with a 400-W medium-pressure mercury-arc lamp at a distance of 1–2 ft through two Pyrex layers. [b] Nondegassed solution, protected from light.

hydrogen by bromine atom. This observation is readily rationalized in view of the difference in the bond strengths of the C–H and C–C bonds in cyclopropane, 106[11] and 61[12] kcal/mol, respectively.

We have examined the free radical bromination of a variety of arylcyclopropanes and report the first example of abstraction of a cyclopropyl hydrogen by bromine atom. Further, it is shown that the observed chemoselectivity (hydrogen vs carbon atom abstraction) is a consequence of stereoelectronic factors on the reactivity of the α-C–C and α-C–H bond.

Results

A. Phenylcyclopropane. Irradiation of a degassed solution of Br_2 and phenylcyclopropane in CCl_4 results in rapid (<5 min) discharge of bromine color. The reaction is quantitative, resulting in the exclusive formation of 1,3-dibromo-1-phenylcyclopropane (Table I, entries 1 and 2).

The possible occurrence of an electrophilic pathway giving rise to the ring-opened 1,3-dibromide was rigorously excluded in our reactions by the observation that no reaction occurs for an unirradiated/undegassed mixture in an equivalent time period (Table I, entries 3 and 4). No reaction was observed in the attempted Ziegler bromination (*N*-bromosuccinimide/CCl_4)[13] of phenylcyclopropane (Table I, entry 5).[14]

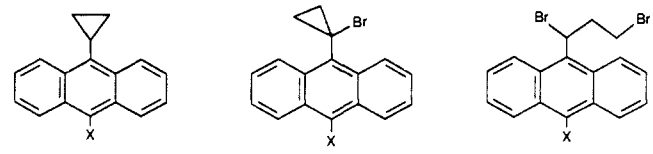
B. α- and β-Cyclopropylnaphthalene. Studies of the free radical bromination of α- and β-cyclopropylnaphthalene were carried out with the use of a specialized delivery system that ensured an even and low concentration of Br_2 during the course of the reaction (vide infra). This procedure produced the corresponding 1,3-dibromides in high yields (Table II) and dramatically curtailed the intervention of competing electrophilic aromatic substitution (EAS) processes. The contribution of an ionic pathway to the total cyclopropane ring-opened dibromide is insignificant in our reactions, because for the reaction of α-cyclopropylnaphthalene with Br_2 in a purely electrophilic pathway, the products are 4-bromo-1-cyclopropylnaphthalene and 1-(α-naphthyl)-1,3-dibromopropane in a 45:1 ratio (Table II).

Table IV. Cyclopropylarene/Methylarene Competitions for Bromine Atom in CCl_4

aryl group	$k_{cyclopropyl}/k_{methyl}$	temp, °C	ref
α-naphthyl	0.17 ± 0.01	10	this work
β-naphthyl	1.0 ± 0.08	10	this work
phenyl	1.61 ± 0.04	40	this work
p-chlorophenyl[a]	1.90 ± 0.04	20	10

[a] CS_2 solvent.

C. 9-Cyclopropylanthracene (and Derivatives). As with the cyclopropylnaphthalenes, the attempted bromination of 9-cyclopropylanthracene is complicated by a competing electrophilic aromatic substitution process (i.e., **1a** + Br_2 → **1c**). However, a variety of bromination procedures were successful in eliminating this electrophilic aromatic substitution process.



1 (a, X = H) (b, X = Cl) (c, X = Br) 2 3

"Dilute" Bromination of 9-Cyclopropylanthracene. Utilization of the "dilute" bromination procedure minimizes the amount of EAS product formed in the free radical bromination of 9-cyclopropylanthracene. Thus, treatment of 9-cyclopropylanthracene (in CCl_4) with Br_2 (dilute) results in the formation of >70% 1-(9-anthryl)cyclopropyl bromide (**1a** → **2a**).

9-Cyclopropyl-10-haloanthracenes. Introduction of a halogen atom at the 10-position of cyclopropylanthracene effectively shuts down the competing EAS process. Thus, irradiation of a solution containing Br_2 and 9-cyclopropyl-10-chloro- or 9-cyclopropyl-10-bromoanthracene (**1b**, **1c**) results in rapid discharge of the bromine color. The reaction products, formed in nearly quantitative yields, are the corresponding cyclopropyl bromides (**2b**, **2c**), arising from abstraction of the cyclopropyl methine hydrogen by bromine atom (Table III, entries 1 and 3).

In contrast, when carried out in the dark, a slower electrophilic process occurs, resulting in formation of the cyclopropane ring-opened 1,3-dibromides **3b** and **3c** (Table III, entries 2 and 4). Thus, in the 9-anthryl system, distinction between the electrophilic and free radical pathways is straightforward because each gives rise to a different product.

Ziegler Bromination of 9-Cyclopropylanthracene. Treatment of 9-cyclopropylanthracene with *N*-bromosuccinimide (NBS/CCl_4), initiated either photochemically or thermally with benzoyl peroxide, results in high (>95%) yields of the hydrogen abstraction product **2a**. The yields for the photoinitiated process tend to be slightly lower because of light-induced decomposition of the reaction product.[15]

(11) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493.

(12) Berson, J. A.; Pedersen, L. D.; Carpenter, B. K. *J. Am. Chem. Soc.* **1976**, *98*, 122.

(13) Lüning, U.; Seshadri, S.; Skell, P. S. *J. Org. Chem.* **1986**, *51*, 2071 and references therein.

(14) In retrospect, this result is not surprising because under Ziegler conditions (NBS/CCl_4), Br· is the chain carrier. As such, NBS serves only as an HBr scavenger, yielding succinimide and regenerating Br_2. However, because no H-abstraction from phenylcyclopropane occurs, a mechanism for maintaining a low steady-state concentration of Br_2 is not available.

(15) Evidence that bromine atom (not imidyl radical) is the hydrogen abstractor in this system is provided by the photointiated reaction of 9-cyclopropylanthracene with 3,3-dimethyl-*N*-bromoglutarimide in CH_2Cl_2, conditions conducive to imidyl radical chains.[13] The major product of the reaction (as deduced from ^1H NMR analysis of the crude product) arises from addition of imidyl radical to the aromatic nucleus.

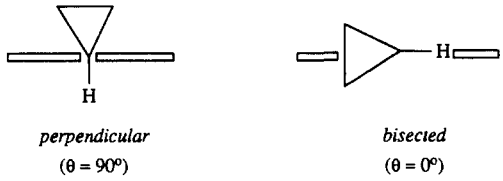


Figure 1. Conformations of cyclopropylarenes.

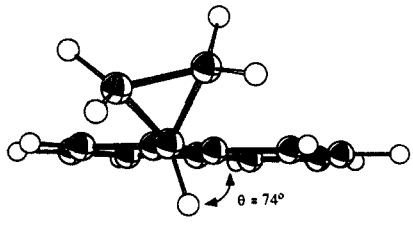


Figure 2. ORTEP plot of α-cyclopropylnaphthalene (AM1-optimized geometry).

D. Cyclopropylarene/Methylarene Competitions for Bromine Atom. Competitive brominations between the cyclopropylarene (Ar-c-C_3H_5) and corresponding methylarene (Ar-CH_3) were performed for Ar = phenyl and α- and β-naphthyl. The results are summarized in Table IV. By using the results obtained for the phenylcyclopropane/toluene competition (the former is 1.6× more reactive toward Br•) and the reported rate constant for abstraction of hydrogen from toluene (2×10^5 M^{-1} s^{-1}),[16] the absolute rate constant for the S_H2 process is estimated to be ca. 3×10^5 M^{-1} s^{-1}.

Discussion

A. Stereoelectronic Effects on α-C–C and α-C–H Bond Reactivity in Cyclopropylarenes. The free radical bromination of phenylcyclopropane, as well as α- and β-cyclopropylnaphthalene, yields the expected cyclopropane ring-opened 1,3-dibromides. In contrast, free radical bromination of 9-cyclopropylanthracene (and its 10-substituted derivatives) results in exclusive formation of the corresponding cyclopropyl bromide, arising from the unexpected abstraction of the cyclopropyl methine hydrogen by bromine atom. These unusual observations are readily explained on kinetic grounds, namely a stereoelectronic effect on the reactivity of α-C–C and α-C–H bonds.

Cyclopropylarenes exist in either one of two possible conformations, bisected and perpendicular (Figure 1, where θ represents the angle defined by the cyclopropyl methine C–H bond with respect to the aromatic plane). For cyclopropylarenes in general, the bisected conformation is usually preferred because of favorable interactions between the cyclopropyl HOMO and aromatic LUMO in this conformation.[17-19]

A variety of experimental probes including ^{1}H NMR[20-22] and X-ray crystallography[23,24] have demonstrated that phenylcyclopropane exists in the bisected conformation. Estimates based upon ^{1}H NMR indicate the alternative perpendicular conformation is about 1.4 kcal/mol higher in energy.[20]

Molecular mechanics calculations suggest that the lowest energy conformer of α-cyclopropylnaphthalene is in-between a purely bisected and perpendicular conformation (θ = 67°). The bisected conformation is 1.2 kcal/mol higher in energy, with a 1.4 kcal/mol barrier to interconversion.[24] AM1 calculations agree with this assessment, but predict θ = 74° (Figure 2). These calculational results agree with the X-ray crystal structure of 4-cyclopropyl-1-naphthalenecarboxylic acid, a closely related derivative of α-cyclopropylnaphthalene, which indicates θ = 54°.[24]

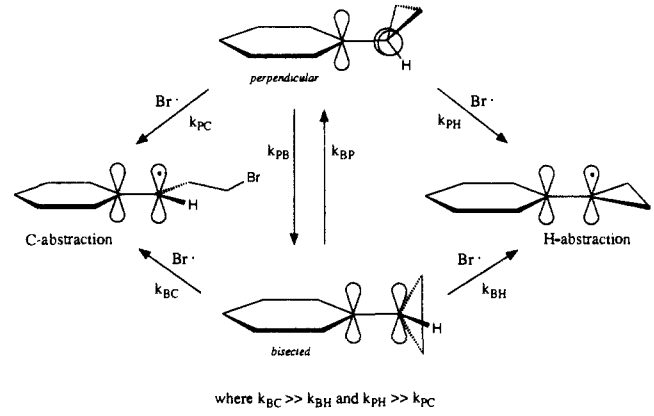


Figure 3. Effect of conformation on the reactivity of cyclopropylarenes toward bromine atom.

The conformations of 9-cyclopropylanthracene have also been explored by X-ray crystallography and molecular mechanics calculations.[24] In this system, the normally preferred bisected conformation is destabilized by unfavorable steric interactions between the *peri*-hydrogen and the *cis*-hydrogens of the cyclopropyl group, and the cyclopropane ring adopts the perpendicular conformation.

We propose that the observed chemoselectivity depends on the conformation of the cyclopropylarene. For compounds in the bisected conformation (e.g., phenylcyclopropane, β-cyclopropylnaphthalene), the cyclopropyl methine C–H bond is orthogonal to the π-system, and therefore not activated for abstraction by bromine atom. In contrast, the π-component of the vicinal C_1–C_2 and C_1–C_3 bonds is perfectly aligned with the aromatic π-system, and the carbon atom abstraction process is facilitated by benzylic stabilization in the transition state (Figure 3).

For compounds in the perpendicular conformation (e.g., 9-cyclopropylanthracene), it is the C–H bond that is aligned with the π-system; abstraction of hydrogen by Br• leads to a transition state in which full benzylic stabilization can be realized. Thus, although the carbon atom abstraction process is thermodynamically favored (vide infra), hydrogen abstraction prevails because of kinetic control.

B. Curtin–Hammett Analysis. The above results are amenable to analysis with use of the Curtin–Hammett (C–H) principle, which can be applied to Figure 3 under the following boundry conditions:[25] condition 1, if the rates of reaction are slower than the rate of conformational interconversion (k_{BP}, $k_{PB} \gg k_{BC}$[Br•], k_{PH}[Br•], the product ratio H-abstr/C-abstr will be a function of the difference in free energy of the transition states, but not of the relative populations of the two conformers; condition 2, at the other extreme, if conformational interconversion is slow relative to reaction rates k_{BC}[Br•], k_{PH}[Br•] $\gg k_{PB}$, k_{BP}) and making the usual assumption that the reaction with Br• is irreversible, then the product ratio reflects the relative population of the two conformers and the rate constant ratio k_{PH}/k_{BC}.

Condition 1 reflects the generally recognized statement of the C–H principle. Condition 2 is less general because few reaction rates exceed the rate of conformational interconversion, particularly when the interconversion involves rotation about a C–C single bond.

There is little double that the transition state for the ring-opening process from the bisected conformation (k_{BC}) is lower in energy than that for hydrogen abstraction from the perpen-

(16) On the basis of an activation energy of 7.6 kcal/mol and log (A) = 13.5 ($cm^3 \cdot mol^{-1} \cdot s^{-1}$); Anderson, H. R., Jr.; Scherage, H. A.; VanArtsdalen, E. R. *J. Chem. Phys.* **1953**, *21*, 1258.
(17) Hoffmann, R. *Tetrahedron Lett.* **1970**, 2907. Hoffmann, R.; Davidson, R. B. *J. Am. Chem. Soc.* **1971**, *93*, 5699.
(18) Jorgensen, W. C.; Salem, L. *The Organic Chemist's Book of Orbitals*; Academic Press: New York, 1973.
(19) Clark, T.; Spitznagel, G. W.; Klose, R.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1984**, *106*, 4412.
(20) Closs, G. L.; Klinger, H. B. *J. Am. Chem. Soc.* **1966**, *88*, 3265.
(21) Kusuyama, Y.; Dyllick-Brenzinger, C.; Roberts, J. D. *Org. Magn. Reson.* **1980**, *13*, 372.
(22) Jason, M. E.; Kurzweil, P. R.; Leonard, K. E. *J. Org. Chem.* **1986**, *51*, 2551.
(23) de Boer, J. S. A. M.; Loopstra, B. O.; Stam, C. H. *Recl. Trav. Chim. Pays-Bas* **1987**, *106*, 537.
(24) Drumright, R. E.; Mas, R. H.; Merola, J. S.; Tanko, J. M. *J. Org. Chem.* In press.
(25) For reviews of the Curtin-Hammett principle, see: Seeman, J. I. *J. Chem. Educ.* **1986**, *63*, 42. Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83.

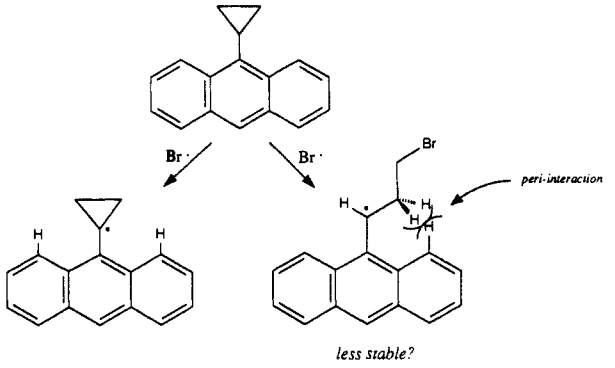


Figure 4. Steric inhibition to resonance as a possible explanation for the variation in chemoselectivity.

dicular conformation. Although both enjoy "benzylic" stabilization, the former benefits from partial relief of cyclopropane ring strain, while the latter suffers additional strain as the hybridization is changing from sp^3 to sp^2.

For 9-cyclopropylanthracene, the perpendicular conformation is calculated to be about 9.7 kcal/mol lower in energy, with a 12 kcal/mol barrier to interconversion.[24] The rate constant for hydrogen atom abstraction is estimated to be about 10^7–10^8 $M^{-1}s^{-1}$.[26] Extrapolation of our phenylcyclopropane/toluene competition results to the 9-anthryl system suggests that k_{BC} is on the same order of magnitude. It thus seems reasonable to conclude that conformational interconversion is slower than the reaction rates,[27] and that the product ratio reflects the predominance of the preferred conformer (i.e., condition 2 kinetics).

Similarly, the C–H principle explains the chemiselectivity found for α-cyclopropylnaphthalene, whose ground-state conformation is midway between perpendicular and bisected (Figure 3), with an essentially freely rotating cyclopropyl group within a 180° arc.[24] Given the molecular mechanics calculated barrier to rotation is only 1.4 kcal/mol, condition 1 kinetics applies. The product distribution therefore reflects the relative energies of the two transition states.

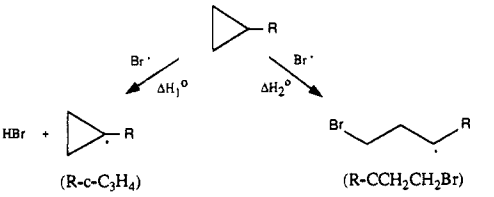
This analysis leads to the general prediction that for hydrogen abstraction to occur, the cyclopropylarene must prefer the perpendicular conformation and, equally as important, there must exist a high barrier for its conversion to the bisected form.

C. Thermochemical Considerations. We have examined the merits of an alternative explanation involving steric inhibition to resonance in the incipient radical to explain α-hydrogen abstraction from 9-cyclopropylanthracene and have found this argument to be untenable. For the radical arising from ring opening of 9-cyclopropylanthracene, unfavorable steric interactions with the *peri*-hydrogens may force a distortion from planarity, thereby decreasing the stability of the ring-opened radical (Figure 4). In contrast, for the corresponding cyclopropyl radical (arising from H-abstraction), encapsulation in a 3-membered ring may pull the CH_2's sufficiently far from the *peri*-hydrogens so that the planar form can be achieved with nominal steric problems (although with a compensatory increase in ring strain relative to the ring-opened radical).

In order to assess this "radical stability" argument, information regarding the difference in enthalpy of reaction for the H-abstraction and ring-opening process ($\Delta\Delta H°$) was required. These data were obtained by using calculated heats of formation for the pertinant radicals (obtained from semiempirical MO calculations by using the AM1 approximation,[28] Table V).

These calculations indicate that for all classes of arylcyclopropanes examined, the ring-opening process is thermodynamically favored by at least 30 kcal/mol.[29] Thus, it is unlikely that the unusual chemoselectivity observed in the 9-anthryl system has its roots in the relative stabilities of the radicals arising from ring opening and hydrogen abstraction.[30]

Table V. AM1-Calculated Difference in Enthalpy of Reaction ($\Delta\Delta H°$) for Hydrogen Abstraction and Ring Opening of Substituted Cyclopropanes by Bromine Atom



R	$\Delta\Delta H°$,[a] kcal/mol
H	37.6
phenyl	36.2
α-naphthyl	33.4
β-naphthyl	35.9
9-anthryl	31.1

[a] $\Delta\Delta H° = \Delta H_1° - \Delta H_2° = \Delta H_f°(R\text{-}c\text{-}C_3H_4) + \Delta H_f°(HBr) - \Delta H_f°(R\text{-}CCH_2CH_2Br)$.

D. Effect of Conformation on the *Rate* of C-Atom Abstraction. In order to assess the effect of conformation on C–C bond reactivity, the relative rates of S_H2 processes for cyclopropylarenes adopting differing conformations were obtained. In order to eliminate the varying influence of the different aryl moieties on the stability of the incipient radicals, these experiments were carried out via competition of Br· for the cyclopropylarene and the corresponding methylarene.

The results of these experiments are summarized in Table IV. For the phenyl system, our results are in close agreement with those of Applequist et al.,[10] who found the S_H2 process in (4-chlorophenyl)cyclopropane to be about 2 times faster than H-atom abstraction from the corresponding toluene. Our competition, based on the 4-H system, yields within experimental error the same relative rate constant and confirms the validity of the premise that the relative stabilizing abilities of the various aryl moieties can be corrected for. β-Cyclopropylnaphthalene, with its purely bisected conformation, exhibits a reactivity similar to that of phenylcyclopropane. However, the α-naphthyl system, whose conformation is not purely bisected (θ = 54–74°),[24] suffers a diminution of the rate of the S_H2 process by at least a factor of 6. These results demonstrate the stereoelectronic requirements for the S_H2 attack of bromine atom on cyclopropylarenes and further strengthen the arguments presented in Figure 3.

Summary

We have established that the free radical bromination of arylcyclopropanes can proceed via α-hydrogen abstraction, in

(26) Tanko, J. M.; Mas, R. H. *J. Org. Chem.* Accepted for publication.

(27) The reaction of Br· with toluene is 2–3 orders of magnitude slower, and has an E_a of only 7.2 kcal/mol.[16] It is therefore reasonable to expect an even *lower* activation energy for 9-cyclopropylanthracene.

(28) Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

(29) In the series R = H, phenyl, β-naphthyl, α-naphthyl, and 9-anthryl, $\Delta\Delta H°$ decreases slightly. This trend undoubtedly arises from a saturation effect, reflecting the fact that in terms of abilities to stabilize a radical center, 9-anthryl > α-naphthyl > β-naphthyl > phenyl > H.

(30) Some indication of the reliability of these calculated $\Delta\Delta H°$'s can be obtained from thermochemical data by estimation of the C–H bond dissociation energy of phenylcyclopropane.

C–H BDE(Ph-c-C_3H_5) =
BDE(PhCH(CH_3)$_2$)+ [BDE(C_3H_6) − BDE(C_5H_{10})] = 96.2 kcal/mol

The term in brackets, reflecting the difference in BDE between cyclopentane and cyclopropane, should account for the effect of increased ring strain associated with the phenylcyclopropyl radical. Similarly, an estimate of the C–C BDE of phenylcyclopropane can be obtained by adjusting the C–C bond dissociation of ethylbenzene to account for relief of cyclopropane ring strain

C–C BDE(Ph-c-C_3H_5) = BDE(PhCH$_2$–CH_3) − 27.5 kcal/mol =
48.3 kcal/mol

Given the BDE's of a primary alkyl bromide and HBr are 69 and 87.5 kcal/mol, respectively, $\Delta\Delta H°$ is estimated to be on the order of 29.4 kcal/mol for phenylcyclopropane. This value compares favorably to the AM1-derived value of 36.2 kcal/mol.

addition to the more commonly observed ring-opening reaction. The chemoselectivity depends both on conformation (bisected vs perpendicular) and on the magnitude of the barrier to conformational interconversion. We have also presented evidence for similar stereoelectronic control on the rate of the ring-opening (S_H2) process.

Experimental Section

General Considerations (Theoretical). All computations reported in this paper were performed with use of the AM1 approximation developed by Dewar et al.[28] and implemented through MOPAC, V.5.0 (QCPE 455). Full geometry optimizations were performed on the parent hydrocarbons. For the open-shell species, geometries were optimized with UHF, followed by a single-point calculation using the half-electron approximation.[31]

General Considerations (Experimental). Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. ^1H and ^{13}C nuclear magnetic resonance spectra were obtained on a 270-MHz Bruker FT NMR spectrometer. All chemical shift values are reported in δ units relative to Me_4Si (δ 0.00 ppm). Infrared spectra were recorded on a Perkin-Elmer Model 710B spectrometer. Elemental analyses were obtained from Multichem Laboratories Inc., Lowell, MA. Gas chromatographic analyses were performed on a Hewlett-Packard HP 5890A instrument equipped with both FID and TCD detectors and an HP 3393A reporting integrator. Analyses were accomplished either on an Alltech RSL-200 (nonpolar) capillary column (30 m × 0.25 mm) or on an HP-1 (Methyl Silicone Gum) Instrument Test column (5 m × 0.53 mm). Mass spectral data were obtained on a Varian MAT 112 magnetic instrument operating at either 10 or 70 eV.

Materials. The following materials (99% gold label or HPLC grade) were purchased from Aldrich Chemical Co. and used as received: phenylcyclopropane, benzoyl peroxide, and bromine. *N*-Bromosuccinimide (Aldrich) was recrystallized from water and dried in vacuo. α- and β-cyclopropylnaphthalene,[32] 9-cyclopropylanthracene,[33] 9-chloro-10-cyclopropylanthracene,[24] and 3,3-dimethyl-*N*-bromoglutarimide[13] were prepared according to published procedures. The following solvents, obtained from Aldrich Chem Co., were purified before use: carbon tetrachloride and dichloromethane were slurried with potassium hydroxide for 24 h, decanted, and fractionally distilled from phosphorus pentoxide; benzene and toluene were distilled from K^+/benzophenone ketyl.

^1H NMR Analysis. At least four integrations were carried out on selected proton absorption reactants, products, and internal standards. Integral amplitudes were maximized to obtain the highest possible accuracy. The average deviation of individual integrations from the mean was generally on the order of 1%.

Bromination of Phenylcyclopropane. Phenylcyclopropane was brominated under the following conditions. The results are summarized in Table I.

a. Photobromination. Phenylcyclopropane (15 μL, 0.13 mmol), anhydrous potassium carbonate (20.0 mg, 0.14 mmol), and 5.0 mL of dichloromethane were combined in a 30-mL pressure tube (sealed with an O-ringed Teflon needle valve) and degassed 4 times by the freeze–pump–thaw (FPT) method. Bromine (6.5 μL, 0.13 mmol) was degassed and distilled (via vacuum line) into the reaction mixture at −198 °C. The reaction mixture was warmed to the desired reaction temperature (−78 or 15 °C) and irradiated with a 400-W medium-pressure Hg-arc lamp at a distance of 2 ft through two Pyrex layers. Complete discharge of bromine color occurred within 5 min. The contents of the pressure tube were filtered and evaporated to dryness under reduced pressure at room temperature and analyzed by ^1H NMR and GLC.

b. "Dark" Bromination. The above procedure was followed except the pressure tubes were carefully wrapped with aluminum foil to exclude light, the reaction mixtures were not degassed, and after 5 min excess methylcyclohexene or 1,1,2-trichloroethene was added to scavenge unreacted Br_2.

c. Ziegler Bromination. Phenylcyclopropane (15.0 μL, 0.130 mmol), NBS (23.5 mg, 0.132 mmol), and benzoyl peroxide (1.0 mg, 0.0041 mmol) in 5 mL of CCl_4 were combined in a pressure tube and FPT degassed. The mixture was heated and maintained at 80.0 °C for 1 h. Afterward, the reaction mixture was analyzed by GLC and ^1H NMR.

Phenylcyclopropane/Toluene Competitive Bromination. Br_2 was FPT degassed on the vac-line and distilled directly into a FPT-degassed solution of toluene, phenylcyclopropane, and anhydrous K_2CO_3 (to scavenge HBr) in 5 mL of CCl_4 at −198 °C. The reaction mixture was placed in a thermostatically maintained water bath (40 °C) and irradiated with a 400-W medium-pressure mercury-arc lamp through two Pyrex layers. Complete discharge of Br_2 took place within 5–10 min. The experiment was performed in quadruplicate, and reaction mixtures were analyzed by GLC and ^1H NMR. In all cases the mass balances were quantitative. The results are summarized in Table IV.

General Procedure for "Dilute" Bromination. With use of a steady stream of an inert carrier gas (argon or nitrogen), Br_2 vapor was conducted from a reservoir containing degassed Br_2 (liquid) through a 3-way stopcock into a CCl_4 solution containing the substrate(s) (with concurrent irradiation). This procedure ensured a low concentration of Br_2 during the course of the reaction, thereby eliminating any competing electrophilic processes. Typically, the reactants and solvent (approximately 0.1 mmol of substrate in 10 mL of CCl_4) were placed in a Pyrex reaction vessel equipped with a dry-ice condenser, thoroughly degassed via bubbling argon, and irradiated for 10–30 min through two Pyrex layers with a 400-W medium-pressure Hg lamp, placed 12–30 in. from the flask during delivery of Br_2. The reaction was maintained at constant temperature by the circulation of a transparent fluid through the jacketed flask.

Dilute Bromination of α- and β-Cyclopropylnaphthalene. α- and β-cyclopropylnaphthalene were brominated according to the procedure outlined above. After reaction, the product mixture was concentrated (reduced pressure/room temperature) and analyzed by ^1H NMR. The results are summarized in Table II.

Cyclopropylnaphthalene/Methylnaphthalene Competitions. For these competitions, the dilute Br_2 delivery system was employed, with the added precaution of terminating the Br_2 delivery at approximately 50–70% conversion of the reactants. Quantitation was carried out by ^1H NMR and mass balances were quantitative. The results are summarized in Table IV.

Bromination of 9-Cyclopropylanthracene with *N*-Bromosuccinimide (NBS). 9-Cyclopropylanthracene (0.47 g, 2.16 mmol), NBS (0.77 g, 4.32 mmol), benzoyl peroxide (0.0030 g, 0.022 mmol), and 30 mL of anhydrous carbon tetrachloride were placed in a 100-mL round-bottomed flask equipped with a Teflon-coated magnetic stirring bar, nitrogen inlet, and refluxing condenser. The reaction mixture was bubbled with dry nitrogen for 15 min and then refluxed for 1 h. After the mixture was cooled to 15 °C, succinimide and excess NBS were filtered off and the filtrate concentrated under reduced pressure at room temperature. The resulting viscous brown liquid was dissolved in 50 mL of hexane, chilled in an ice bath, and filtered. The filtrate was washed consecutively with 15 mL of $NaHCO_3$ (saturated) and 15 mL of $Na_2S_2O_3$ (saturated) and dried over anhydrous Na_2SO_4. The hexane solution was then concentrated and chilled in an ice bath. After about 30 min, 0.58 g (90% yield) of 9-(α-bromocyclopropyl)anthracene was isolated: mp 113–115 °C; ^1H NMR ($CDCl_3/CCl_4$) δ 1.48 (m, 2 H, *cis*-cyclopropylmethylene hydrogens), 2.06 (m, 2 H, *trans*-cyclopropylmethylene hydrogens), 7.49 (m, 2 H, 3- and 6-H anthryl hydrogens), 7.64 (m, 2 H, 2- and 7-H anthryl hydrogens), 8.02 (m, 2 H, 4- and 5-H anthryl hydrogens), 8.47 (s, H, 10-H anthryl hydrogen), 8.78 (m, 2 H, 1- and 8-H anthryl hydrogens); ^{13}C NMR ($CDCl_3$) δ 20.31 and 27.90 (cyclopropyl carbons), 125.37, 126.11, 128.93, 128.99, 129.78, 130.17, 131.73, 133.30, and 134.20 (anthryl carbons); MS (EI, 70 eV) *m/e* (rel intensity) 298 (21.5, M^+, ^{81}Br), 296 (22.0, M^+, ^{79}Br), 217 (100), 215 (77), 202 (82), 189 (40), 176 (15), 163 (18), 150 (10), 108 (15). Anal. Calcd for $C_{17}H_{13}Br$: C, 68.71; H, 4.38; Br, 26.91. Found: C, 68.34; H, 4.49; Br, 25.63. Reduction of this compound with tri-*n*-butyltin hydride yields 9-cyclopropylanthracene.

Photoinitiated Reaction of 9-Cyclopropylanthracene with *N*-Bromo-3,3-dimethylglutarimide (33DMNBG). 9-cyclopropylanthracene (150.0 mg, 0.688 mmol) and 33DMNBG (160.0 mg, 0.727 mmol) were dissolved in 5 mL of dichloromethane in a 30-mL pressure tube (sealed with an O-ringed Teflon needle valve). The solution was degassed 4 times by the freeze–pump–thaw method, placed in a 20 °C water bath, and then irradiated with a 400-W medium-pressure mercury-arc lamp (through two layers of Pyrex at a distance of 1.5 ft) for 1 h. ^1H NMR and GLC analysis found no evidence for the formation of 9-(α-bromocyclopropyl)anthracene. Inspection of the aromatic region of the ^1H NMR spectrum revealed that aromatic substitution likely occurred. The exact structure of this product was not determined.

Photobromination of 9-Chloro-10-cyclopropylanthracene. A mixture of 9-chloro-10-cyclopropylanthracene (55.0 mg, 0.22 mmol), anhydrous potassium carbonate (61.0 mg, 0.44 mmol), and 5 mL carbon tetrachloride in a 30-mL pressure tube (sealed with an O-ringed Teflon needle valve and equipped with a Teflon-coated magnetic stirring bar) was degassed 4 times by FPT technique. Bromine (11.0 μL, 0.22 mmol) was degassed on the vac-line and distilled directly into the reaction mixture at −196 °C. The mixture was warmed to 15 °C and irradiated with a

(31) Dewar, M. J. S.; Rzepa, H. S. *J. Am. Chem. Soc.* **1978**, *100*, 784.
(32) Hahn, R. C.; Howard, P. H.; Kong, S.-M.; Lorenzo, G. A.; Miller, N. L. *J. Am. Chem. Soc.* **1969**, *91*, 3558.
(33) Bauld, N. L.; McDermed, J. D.; Hudson, C. E.; Rim, Y.-S.; Zoeller, J., Jr.; Gordon, R. D.; Hyde, J. S. *J. Am. Chem. Soc.* **1969**, *91*, 6666.

400-W medium-pressure mercury-arc lamp (placed 2 ft from the pressure tube) through two layers of Pyrex. Bromine was completely consumed in 5 min. ^{1}H NMR analysis of this solution showed that 9-chloro-10-(α-bromocyclopropyl)anthracene was formed in 95% yield. The remaining 5% was comprised of 1,3-dibromo-1-(9-chloroanthryl)propane (3%) and unidentified products (2%). Spectral data for 9-chloro-10-(α-bromocyclopropyl)anthracene: ^{1}H NMR ($CDCl_3/CCl_4$) δ 1.45 (m, 2 H, *cis*-cyclopropylmethylene hydrogens), 2.06 (m, 2 H, *trans*-cyclopropylmethylene hydrogens), 7.57–7.71 (m, 4 H, 2-, 3-, 6-, and 7-H anthryl hydrogens), 8.56 (m, 2 H, 1- and 8-H anthryl hydrogens), 8.81 (m, 2 H, 4- and 5-H anthryl hydrogens); ^{13}C NMR ($CDCl_3$) δ 20.30 and 28.00 (cyclopropyl carbons), 125.00–136.00 (m, anthryl carbons). Repeated attempts to isolate pure 9-chloro-10-(α-bromocyclopropyl)anthracene by column and thin-layer chromatography were unsuccessful due to the rapid decomposition of the compound.

Photobromination of 9-Bromo-10-cyclopropylanthracene. This reaction was carried out at 15 °C by using the same procedure described for 9-chloro-10-cyclopropylanthracene. The yield of 9-bromo-10-(α-bromocyclopropyl)anthracene was determined by ^{1}H NMR analysis to be 95%. ^{1}H NMR ($CDCl_3/CCl_4$) δ 1.47 (m, 2 H, *cis*-cyclopropylmethylene hydrogens), 2.08 (m, 2 H, *trans*-cyclopropylmethylene hydrogens), 7.44–7.69 (m, 4 H, 2-, 3-, 6-, and 7-H anthryl hydrogens), 8.61 (m, 2 H, 1- and 8-H anthryl hydrogens), 8.81 (m, 2H, 4- and 5-H anthryl hydrogens).

Dark Bromination of 9-Bromo-10-cyclopropylanthracene. 9-Bromo-10-cyclopropylanthracene (70.0 mg, 0.23 mmol), NBS (20.5 mg, 0.12 mmol), and 5 mL of CCl_4 were placed in a 30-mL pressure tube that was equipped with a magnetic stirring bar and carefully wrapped with aluminum foil. Bromine (5.8 μL, 0.11 mmol) was distilled into the pressure tube via a vac-line. The pressure tube was sealed with an O-ringed Teflon needle valve and immersed in a water bath maintained at 15 °C. After 1 h, the contents of the pressure tube were evaporated to dryness under reduced pressure. ^{1}H NMR analysis indicated the presence of only one product, 1,3-dibromo-1-(9-bromoanthryl)propane. ^{1}H NMR ($CCl_4/CDCl_3$) δ 2.8 (m, 1 H), 3.4–3.5 (m, 2 H), 3.7 (m, 1 H), 7.5–7.7 (m, 4 H, 2-, 3-, 6-, and 7-H anthryl hydrogens), 8.4 (d, 1 H, J = 9 Hz, 4-H anthryl hydrogen), 8.7 (dd, 2 H, 1- and 8-H anthryl hydrogens), 8.8 (d, 1 H, J = 10 Hz, 5-H anthryl hydrogen). Reduction of a reaction residue with an excess amount of n-Bu_3SnH in benzene afforded only 9-propylanthracene.

Dark Bromination of 9-Chloro-10-cyclopropylanthracene. This experiment was carried out in an analogous manner as the dark bromination of 9-bromo-10-cyclopropylanthracene. Only one product, 1,3-dibromo-1-(9-chloroanthryl)propane, was obtained after 1 h of reaction time. ^{1}H NMR ($CCl_4/CDCl_3$) δ 2.77 (m, 1 H), 3.38–3.49 (m, 2 H), 3.66 (m, 1 H), 7.65–7.54 (m, 4 H, 2-, 3-, 6-, and 7-H anthryl hydrogens), 8.36 (d, 1 H, J = 8.7 Hz, 4-H anthryl hydrogen), 8.60 (dd, 2 H, 1- and H-8 anthryl hydrogens), 8.79 (d, 1 H, J = 9.8 Hz, 5-H anthryl hydrogen). ^{13}C NMR (CDCl) δ 31.24, 41.65 and 45.79, 123.08–131.8.

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Comparative Analysis of Diastereoselection Levels Attainable during Controlled Exo and Endo Addition of Chiral Cyclopentenyl Organometallics to Optically Pure and Racemic 1-Vinylnorbornan-2-ones

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Abstract: The levels of diastereoselection attainable during endo addition to (+)-**8** and of exo addition to (−)-**9** and (±)-**10** have been tested with five differently substituted cyclopentenyl anions. The extent of intermolecular recognition reaches useful levels when an endo attack is involved. In contrast, diastereomeric differentiation is significantly reduced when an exo trajectory is followed. These data are concisely rationalized in terms of an essentially coplanar arrangement of the reactants with appropriate stacking during the endo face-selective process. In contrast, a knife-edge alignment is adopted by the cyclopentenyl species as exo attack on the norbornanone carbonyl group begins. Structural assignments to the product alcohols were realized by direct X-ray crystallographic analysis of these or their anionic oxy-Cope products. The balance of the structural information evolved from diagnostic ^{1}H NMR correlations involving the cyclopentenyl olefinic proton and those of the vinyl group when recorded in benzene-d_6 solution. In each example, oxy-Cope rearrangement took place stereospecifically to deliver a single product. Whereas an endo chair transition state was followed by the exo alcohols, an exo boat arrangement was adopted in the endo norbornanol series.

The determination of diastereoselection levels attainable during nucleophilic capture of chiral β,γ-unsaturated ketones by chiral vinyl organometallics has gained increasing significance in recent years.[2] The interest accorded these condensations has been spurred by the considerable practical import that such processes can bring to the stereospecific synthesis of natural products via subsequent anionic oxy-Cope rearrangement.[3] Since the level of preferred C–C bond formation is recognized to hinge on the subtle interplay of several factors, a deeper understanding of individual controlling influences is essential for more rational utilization of the protocol.

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(2) (a) Paquette, L. A.; Learn, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 7873. (b) Paquette, L. A. In *Organic Synthesis: Modern Trends*; Chizhov, O., Ed.: Blackwell Scientific Publictions: Oxford, 1988; pp 1–12. (c) Paquette, L. A.; Learn, K. S.; Romine, J. L. *Tetrahedron* **1987**, *43*, 4989. (d) Paquette, L. A.; Learn, K. S.; Romine, J. L.; Lin, H.-S. *J. Am. Chem. Soc.* **1988**, *110*, 879. (e) Paquette, L. A.; DeRussy, D. T.; Cottrell, C. E. *Ibid.* **1988**, *110*, 890. (f) Paquette, L. A.; DeRussy, D. T.; Gallucci, J. C. *J. Org. Chem.* **1989**, *54*, 2278. (g) Paquette, L. A.; He, W.; Rogers, R. D. *Ibid.* **1989**, *54*, 2291.

(3) (a) Paquette, L. A.; Andrews, D. R.; Springer, J. P. *J. Org. Chem.* **1983**, *48*, 1148. (b) Paquette, L. A.; Colapret, J. A.; Andrews, D. R. *Ibid.* **1985**, *50*, 201. (c) Paquette, L. A.; Romine, J. L.; Lin, H.-S. *Tetrahedron Lett.* **1987**, *28*, 31. (d) Paquette, L. A.; Macdonald, D.; Anderson, L. G.; Wright, J. *J. Am. Chem. Soc.* **1989**, *111*, 8037. (e) Oplinger, J. A.; Paquette, L. A. *Tetrahedron Lett.* **1987**, *28*, 5441. (f) Paquette, L. A.; Poupart, M.-A. *Tetrahedron* **1989**, *45*, 107. (g) Paquette, L. A.; Poupart, M.-A. *Tetrahedron Lett.* **1988**, *29*, 273. (h) Poupart, M.-A.; Paquette, L. A. *Ibid.* **1988**, *29*, 269 and relevant references cited in these papers.

0002-7863/90/1512-5562$02.50/0