

mixing time (MIX), 3.0 s; acquisition time (AT), 269 ms; spectral window (SW) in F1 and F2 domains, 1902.2 Hz; size, 1024 data points; number of increments,  $2 \times 256$  employing the States-Haberkorn-Rueben hypercomplex data collection;<sup>20</sup> quadrature detection with line broadening (LB and LB2), 0.1 Hz, and apodization (AF and AF2), 0.135 s in both dimensions; zero-filled to 2048 data points in both  $t_1$  and  $t_2$ .

**HETCOR (<sup>1</sup>H, <sup>13</sup>C-heteronuclear shift correlation):**<sup>17</sup> direct (<sup>1</sup>J<sub>CH</sub>) correlation; sequence D1-90(H)- $t_{1/2}$ -180(H,C) $t_{1/2}$ -90(H)-90(C)-acquire; relaxation delay (D1), 1.0 s; J1XH, 140 Hz; PW90<sub>H</sub> (PP), 17.5  $\mu$ s; PW90<sub>C</sub>, 12.5  $\mu$ s; acquisition time (AT), 85 ms; spectral window (SW)<sub>H</sub> in F1, 2089.4 Hz; spectral window (SW)<sub>C</sub> in F2, 12019.2 Hz; size, 1024 data points in F2; number of increments (NI), 256 zero-filled to 1024 data points in  $t_1$ ; quadrature detection with pseudoecho (absolute value, AV display) weighting in both dimensions. **Long-range HETCOR** data collection was performed as above except that J1XH = 6.0 Hz. Data processing was performed as above except that the weighting functions (RE, RE2, AF, AF2) were optimized by using the interactive weighting feature of the Varian software.

**DEPT spectral editing:**<sup>16</sup> sequence D1-90(H)-D3-(90)-(180)(90)(H), 90(C)-D3-T(H), (90)(180)(90)(C)-D3-acquire, where D3 =  $1/2J$  and  $T = 45^\circ, 90^\circ, 135^\circ$ ; relaxation delay (D1), 3.0 s; D3 delay; 2.57 ms; pulse widths, decoupler pulse width (PP), 17.5  $\mu$ s, and PW90 (C), 12.5  $\mu$ s; acquisition time (AT), 1.0 s; spectral window (SW), 26000 Hz; size, 16000 data points zero-filled to 32K data points with 1.0-Hz line broadening; number of transients (NT), 1024.

**$T_1$  Measurements.** Both proton (<sup>1</sup>H) (Table I) and carbon (<sup>13</sup>C) (Table II)  $T_1$  data were collected by using the inversion-recovery sequence: D1-(180)-D2-(90)-acquire. The standard Varian software calculated the  $T_1$  data by using a three-parameter exponential-least-squares fit of the peak amplitudes as a function of the D2 delay, which was an arrayed parameter of 11 values. The acquisition time (AT) was 3.7 s, zero-filled to 65K data points for the  $T_1$  calculation.

**X-ray Structure Analysis of Savinin.** The compound crystallized with difficulty from a very low concentration in hexane (0.05 mg in 1 mL) with slow evaporation at room temperature to afford disordered bunches of transparent crystals. From one of these crystals was cut a suitable piece of crystal (0.4  $\times$  0.2  $\times$  0.1 mm) for X-ray structure analysis. Preliminary unit cell and space group information was obtained from oscillation and

Weissenberg photographs. The final unit cell constants were determined by centering 25 reflections on a Nicolet R3m diffractometer and by least-squares refinement. Crystal data:  $a = 11.605$  (2)  $\text{\AA}$ ,  $b = 11.902$  (1)  $\text{\AA}$ ,  $c = 12.354$  (2)  $\text{\AA}$ ,  $\beta = 77.04$  (1) $^\circ$ , density measured by flotation in KI/H<sub>2</sub>O = 1.36 g cm<sup>-3</sup>,  $d_{\text{calc}} = 1.40$  g cm<sup>-3</sup>,  $Z = 4$ , space group monoclinic  $P2_1$  with two molecules in the asymmetric unit, four in the unit cell.

The intensity data of 2374 unique reflections (2182 observed with  $I < 3\sigma(I)$ ) were measured by using Ni-filtered Cu K $\alpha$  radiation,  $\omega$ -scan with scan speed  $2^\circ/\text{min}$  up to  $(2\theta)_{\text{max}} = 114^\circ$ . The data were scaled by Wilson plot and corrected for Lorentz and polarization effects in the usual way. Absorption correction, empirical method, was applied ( $\mu = 8.3$  cm<sup>-1</sup>).

The structure was solved by direct methods using SHELXTL.<sup>28</sup> An  $E$  map with the best phase set from the N-Quest criterion revealed 60% of the atoms of the two molecules in the asymmetric unit. Partial structure expansion and subsequent difference Fourier synthesis led to the complex structure. The positions of the hydrogens were calculated from the C atoms to which they are bound. Final cycles of anisotropic refinement (with the non-hydrogen atoms only) converged at  $R = 4.3\%$  (unit weights). The atomic parameters and bond lengths and angles are deposited at the Cambridge Crystallographic Data Centre.

**Molecular Force Field Calculations.** The molecular model of savinin was generated from the Build and Edit options of the CHEMLAB-II program.<sup>21</sup> In the study of the different conformations of the rotation along the bonds C1'-C $\alpha'$ , C $\alpha'$ -C $\beta'$ , and C1-C $\alpha$ , the energy maps were generated by scanning these three bonds between  $0^\circ$  and  $360^\circ$  in  $10^\circ$  increments. The minimal steric energy of each conformation was calculated by the MMFF option of the program. X-ray crystallographic data<sup>24</sup> of savinin were initially used to create the conformation which corresponded to savinin in the solid state.

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**Registry No.** Savinin, 493-95-8.

(28) Sheldrick, G. M. SHELXTL (Release 4.1), A program for crystal Structure Determination, Cambridge, England, 1983.

## Kinetic vs Thermodynamic Factors in $\alpha$ -Hydrogen Atom Abstractions from Alkyl Aromatics

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The relative reactivities of several 9-alkylanthracenes toward bromine atom have been determined. Whereas for alkylbenzenes it is observed that isopropyl > ethyl > methyl, an inverted reactivity order was observed in the 9-anthryl system: methyl (1.00) > cyclopropyl (0.33) > ethyl (0.063)  $\gg$  isopropyl (<0.001), per  $\alpha$ -hydrogen at 80  $^\circ\text{C}$ . Stereoelectronic factors, specifically the alignment of the  $\alpha$ -C-H bond with the anthryl  $\pi$ -system, are implicated as bearing primary responsibility for this unusual reactivity order. In a general context, the relative importance of stereoelectronic effects vs the stability of the incipient radical in hydrogen atom abstractions from alkyl aromatics is discussed.

### Introduction

The selectivity of a free radical in hydrogen atom abstractions from carbon can generally be correlated to the "nature" of the attacking radical and the strength of the C-H bond. Thus, the familiar reactivity order,  $3^\circ > 2^\circ > 1^\circ$ , observed for a variety of abstracting radicals can be

directly related to the thermodynamic stability of the resulting free radical. This correlation between carbon radical stability and transition-state energetics was recognized over a half-century ago by Evans and Polanyi<sup>1</sup> and

(1) Evans, M. G.; Polanyi, M. *Trans. Faraday Soc.* 1938, 34, 11.

provides a classic and early example of the application of linear free-energy relationships to free-radical chemistry.

There are a few examples in the literature where this "natural" reactivity order has been perturbed. Such anomalies have been discussed in the context of (a) steric inhibition to resonance, in cases where the resulting radicals are conjugated, (b) stereoelectronic and/or steric effects, and (c) polar effects.<sup>2</sup> In this paper, we provide quantitative data for hydrogen abstractions from 9-alkylanthracenes by bromine atom and, using semiempirical MO theory and molecular mechanics calculations, discuss the relative importance of these two factors in hydrogen atom abstractions from alkyl aromatics.

### Literature Overview

Tolbert and Khanna have recently provided evidence for the importance of stereoelectronic effects in the biomimetic oxidation of 9,10-dialkylanthracenes.<sup>3</sup> It was argued that the rate of deprotonation of an ethyl group at the 9-position of an anthracene radical cation was diminished (relative to methyl) because of unfavorable stereoelectronic factors. Specifically, steric interactions between the *peri*-hydrogens and the ethyl group result in a conformation where the CH<sub>2</sub>-CH<sub>3</sub> bond is perpendicular to the aromatic plane, placing the  $\alpha$ -C-H bonds out of alignment with the adjacent  $\pi$ -system. In contrast, in its lowest energy conformation, the 9-methyl derivative has a C-H bond aligned with the  $\pi$ -system, and consequently, deprotonation is facile.<sup>4</sup>

A similar discrepancy in the "natural" reactivity order was noted by Gleicher et al. nearly a decade earlier.<sup>5</sup> These workers found that rates of addition of trichloromethyl radical to 9-substituted anthracenes correlate to Brown's  $\sigma^+$  substituent constants. However, 9-alkyl-substituted anthracenes exhibit substantial deviation from the line, in the order CH<sub>3</sub> > CH<sub>2</sub>CH<sub>3</sub> > CH(CH<sub>3</sub>)<sub>2</sub>. It was argued that a competing hydrogen abstraction was responsible and that the preceding order reflected the relative reactivity of each alkyl group toward  $\cdot\text{CCl}_3$ . Steric inhibition to resonance in the resulting radical was deemed the factor responsible for this unusual reactivity order.<sup>5</sup>

Our interest in this problem arose from the observation that the free-radical bromination of 9-cyclopropylanthracene results in the formation of an unprecedented hydrogen abstraction product, in lieu of the normal cyclopropane ring opening (S<sub>H</sub>2) process.<sup>6</sup> The lowest energy conformation of this molecule was such that the  $\alpha$ -C-H and  $\alpha$ -C-C bonds were activated and deactivated, respectively, toward bromine atom attack because of stereoelectronic factors. Competitive brominations of several cyclopropyl arenes established that C-C bond reactivity varied as a function of the conformation of the cyclopropyl group with respect to the aromatic ring. In this paper, we examine the effect of conformation on C-H bond reactivity and assess the relative importance of stereoelectronic factors and incipient radical stability in hydrogen atom abstractions from alkyl aromatics.

**Table I. Relative Reactivities of 9-Alkylanthracenes toward Bromine Atom at Different Temperatures**

R	relative reactivity <sup>a</sup> as a function of temperature (°C)					
	12.0 <sup>b</sup>	40.0 <sup>c</sup>	60.0 <sup>c</sup>	80.0 <sup>c</sup>	100.0 <sup>c</sup>	120.0 <sup>c</sup>
CH <sub>3</sub>	1.00	1.00	1.00	1.00	1.00	1.00
<i>c</i> -CH(CH <sub>3</sub> ) <sub>2</sub>	0.15	0.21	0.27	0.33	0.43	0.53
CH <sub>2</sub> CH <sub>3</sub>	0.047	0.051	0.055	0.063	0.069	
CH(CH <sub>3</sub> ) <sub>2</sub>	virtually unreactive (<0.0001)					

<sup>a</sup> Per-hydrogen vs 9-methylanthracene. <sup>b</sup> Initiated photolytically with a 400-W medium-pressure Hg arc lamp through Pyrex. <sup>c</sup> Initiated thermally with benzoyl peroxide.

### Results

**A. Reactivity Studies. Relative Reactivity of 9-Alkylanthracenes.** The reactivity of several 9-alkylanthracenes toward bromine atom were assessed via competition experiments using *N*-bromosuccinimide (NBS) in CCl<sub>4</sub> as the brominating agent.<sup>7</sup> Because of limited solubility of the alkylanthracenes in CCl<sub>4</sub>, it was not possible to achieve a 10-fold excess of each hydrocarbon. (Typically, NBS was the limiting reagent with a 1- to 2-fold excess of alkylanthracene.) The reaction mixtures were analyzed by 270-MHz <sup>1</sup>H NMR, and relative rate constants were calculated by  $k_A/k_B = \ln(A_o/A_f)/\ln(B_o/B_f)$ , where the subscripts "o" and "f" refer to the initial and final concentrations, respectively, of the starting alkyl aromatics. Integrations of the NMR spectrum were performed in quadruplicate, and mass balances were near 100% in virtually all experiments (a small amount of elimination products was detected for 9-ethylanthracene at reaction temperatures exceeding 100 °C). The raw data, including initial and final concentrations of all starting materials and products, are available as supplementary material. The results are summarized in Table I.

**Absolute Rate Constants for H Abstraction.** In order to estimate *absolute* rate constants for the abstraction of hydrogen from the 9-alkylanthracenes, competition experiments pitting 9-methylanthracene against cumene were performed. Brominations were carried out at 40 °C using NBS/CCl<sub>4</sub> and 2 mol % benzoyl peroxide as initiator. Competitions were performed in triplicate, reaction mixtures were analyzed by both quantitative <sup>1</sup>H NMR and GLC, and the full results are available as supplementary material. 9-Methylanthracene was determined to be 18.7 (±0.7) times more reactive (per molecule) than cumene toward bromine atom. Further, the absolute rate constant for abstraction of hydrogen from toluene by Br<sup>•</sup> is  $2 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$  at 40 °C.<sup>8</sup> Cumene is reported to be 57.5 times more reactive than toluene toward Br<sup>•</sup> per hydrogen, or 19.2 times per molecule.<sup>9,10</sup> These values allow us to estimate a rate constant on the order of  $10^8 \text{ M}^{-1} \text{ s}^{-1}$  for the abstraction of hydrogen from 9-methylanthracene.

**H/D Isotope Effect.** The effect of isotopic substitution on the rate of hydrogen atom abstraction from 9-cyclopropylanthracene was briefly examined. Deuterated analogue **2** was prepared by LiAlD<sub>4</sub> reduction of the corresponding cyclopropyl bromide (eq 1). A competition pitting **2** vs 9-methylanthracene (NBS/CCl<sub>4</sub>) found the

(2) Russell, G. A. In *Free Radicals*, Vol. I; Kochi, J. K., Ed.; Wiley: New York, 1973; pp 275-331.

(3) Tolbert, L. M.; Khanna, R. K. *J. Am. Chem. Soc.* 1987, 109, 3447.

(4) This simultaneous discussion of radical cation deprotonation and hydrogen atom abstraction by radicals is reasonable because both processes lead to the same products, and proceed via transition states whose charge and composition are identical. Consequently, similar structural effects on reactivity are anticipated.

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(6) Tanko, J. M.; Mas, R. H.; Suleman, N. K. *J. Am. Chem. Soc.*, in press.

(7) The Ziegler conditions (NBS/CCl<sub>4</sub>) are generally accepted as the best experimental method for determining bromine atom selectivities. For a review, see: Poutsma, M. L. In *Free Radicals*, Vol. II; Kochi, J. K., Ed.; Wiley: New York, 1973; pp 159-229.

(8) Based upon an activation energy of 7.6 kcal/mol and  $\log(A) = 13.5$  ( $\text{cm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ ): Anderson, H. R., Jr.; Scheraga, H. A.; VanArtsdalen, E. R. *J. Chem. Phys.* 1953, 21, 1258.

(9) Friedrich, S. S.; Friedrich, E. C.; Andrews, L. J.; Keefer, R. M. *J. Org. Chem.* 1969, 34, 900.

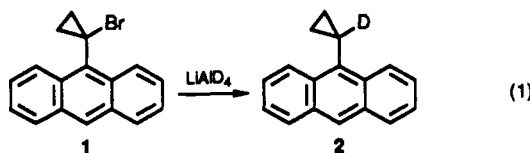
(10) Russell, G. A.; Desmond, K. A. *J. Am. Chem. Soc.* 1963, 85, 3139.

Table II. Lowest Energy Conformations of 9-Alkylanthracenes

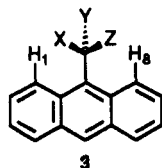
alkyl group	structure	$\theta$ , deg <sup>a,b</sup>
CH <sub>3</sub>		90, 30
c-C <sub>3</sub> H <sub>5</sub>		90
CH <sub>2</sub> CH <sub>3</sub>		33
CH(CH <sub>3</sub> ) <sub>2</sub>		16

<sup>a</sup> Calculated (molecular mechanics). <sup>b</sup> H-C-C<sub>Ar</sub>-C<sub>Ar</sub> dihedral angle.

latter to be 23.6 ( $\pm 0.9$ ) times more reactive (per molecule) towards bromine atom at 80 °C. Division of this value into the relative rate constant for the undeuterated analogue (Table I) yields  $k_H/k_D = 2.6$ .



**B. Conformations of 9-Alkylanthracenes.** The conformations of the 9-alkylanthracenes were studied using molecular mechanics (MM2/ $\pi$ )<sup>11</sup> and semiempirical (AM1) MO theory.<sup>12</sup> The lowest energy conformations for each compound and the angle  $\theta$  (defined by the  $\alpha$ -C-H bond with respect to the aromatic plane) are summarized in Table II. The dominant factor to be considered in the conformational analysis of these compounds involves interactions between substituents attached to C-15 (X, Y, and Z in 3) and the *peri*-hydrogens (H-1 and H-8). The lowest energy conformation tends to be the rotamer which maximizes the distance between the largest substituent(s) at C-15 and the *peri*-hydrogens.



**9-Methylanthracene.** There are three degenerate conformations for 9-methylanthracene in which one  $\alpha$ -C-H bond is perpendicular to the aromatic plane ( $\theta = 90^\circ$ ).

**9-Ethylanthracene.** As suggested by Tolbert and Khanna,<sup>3</sup> the lowest energy conformation of 9-ethylanthracene finds the CH<sub>2</sub>-CH<sub>3</sub> perpendicular to the aromatic plane, with  $\theta = 33^\circ$ . This conformation places the CH<sub>3</sub> group farthest from the *peri*-hydrogens and is similar to the conformation of 9-*n*-propylanthracene, whose X-ray crystal structure has been reported.<sup>13</sup> Another confor-

Table III. AM1-Calculated Bond Dissociation Energies of 9-Alkylanthracenes<sup>a</sup>

R	BDE, kcal/mol	R	BDE, kcal/mol
CH <sub>2</sub> CH <sub>2</sub> CH	83.0	CH <sub>2</sub> CH <sub>3</sub>	80.3
CH <sub>3</sub>	[81.8] <sup>b</sup>	CH(CH <sub>3</sub> ) <sub>2</sub>	75.9

<sup>a</sup> MOPAC v. 5.0 (QCPE 455). <sup>b</sup> Reference 19.

Table IV. AM1-Calculated and Experimental Bond Dissociation Energies of Various Alkanes and Alkylbenzenes

compound	BDE, kcal/mol	
	calculated <sup>a</sup>	experimental <sup>b</sup>
c-C <sub>3</sub> H <sub>8</sub>	107.2	106.3
CH <sub>3</sub> CH <sub>3</sub>	[98.2]	98.2
CH <sub>3</sub> CH <sub>2</sub> CH <sub>3</sub>	93.7	95.1
(CH <sub>3</sub> ) <sub>2</sub> CH	89.3	93.2
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	[88.0]	88.0
C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>3</sub>	83.1	85.4
C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> ) <sub>2</sub>	80.2	84.4

<sup>a</sup> MOPAC v. 5.0 (QCPE 455); see text for explanation. <sup>b</sup> Reference 19.

mation in which  $\theta = 66^\circ$  was also found, but both AM1 and MM2/ $\pi$  estimate the conformer to be about 7 kcal/mol higher in energy.

**9-Isopropylanthracene.** The lowest energy conformation of 9-isopropylanthracene shows  $\theta = 16^\circ$ . No other conformation was found for which  $\theta$  was greater than  $16^\circ$ , undoubtedly because the steric interaction between the two methyl groups and the *peri*-hydrogens is energetically prohibitive. (However, both MM2/ $\pi$  and AM1 locate a conformation of slightly higher energy (<1 kcal/mol) in which  $\theta$  was between 3 and  $4^\circ$ .) These conclusions are analogous to those reached by Harvey and co-workers for 9,10-dialkyl-9,10-dihydroanthracenes.<sup>14,15</sup> Using <sup>1</sup>H NMR (NOE), these workers report that the  $\alpha$ -C-H bond of a bulky substituent, such as an isopropyl group, tends to be oriented towards one of the *peri*-hydrogens.

**9-Cyclopropylanthracene.** Both AM1 and MM2/ $\pi$  show the lowest energy conformation of 9-cyclopropylanthracene to be "perpendicular", with  $\theta = 90^\circ$ . This result is also confirmed by the X-ray crystal of the 10-chloro derivative.<sup>16</sup> An alternative "bisected" conformation ( $\theta = 0^\circ$ ) is calculated to be 6.3 and 9.7 kcal/mol higher in energy by AM1 and MM2/ $\pi$ , respectively.

**C. Bond Dissociation Energies of 9-Alkylanthracenes.** Deconvolution of the relative importance of stereoelectronic vs thermodynamic factors in these hydrogen atom abstractions requires some knowledge of the  $\alpha$ -C-H bond dissociation energies of the 9-alkylanthracenes. These values were obtained using semiempirical molecular orbital theory (AM1 approximation)<sup>12</sup> to calculate the heats of formation of the starting alkyl aromatics and corresponding free radicals pertinent to this study. For the radicals, geometries were optimized using the UHF approximation. In order to place the calculated  $\Delta H_f^\circ$ 's on the same scale as for the closed-shell species, a single-point calculation on the UHF-optimized geometry using the HE approximation was performed. This procedure has been recommended by Dewar and Rzepa<sup>17</sup> and

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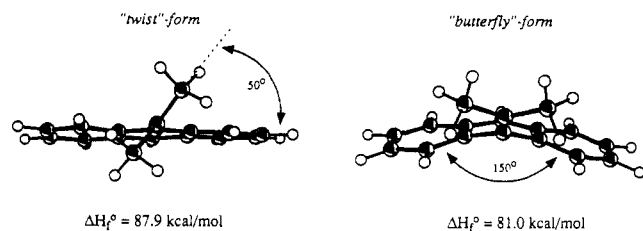
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**Figure 1.** AM1-optimized geometries for the 2-(9-anthryl)-2-propyl radical.

Clark<sup>18</sup> for comparing the energies of open- and closed-shell species.

Table III lists the calculated bond dissociation energies (BDE's) for the compounds utilized in this study. The values were obtained by calculating  $\Delta H_{\text{rxn}}$  for the hydrogen-exchange process  $\text{AnCH}_3 + \text{AnCHR}_2 \cdot \rightarrow \text{AnCH}_2 \cdot + \text{AnCHR}_2$  using AM1-derived heats of formations, where  $\Delta H_{\text{rxn}} = \text{BDE}(\text{AnCH}_3) - \text{BDE}(\text{AnCHR}_2)$ . The experimental bond dissociation energy for 9-methylanthracene, the standard upon which these values are based, is 81.8 kcal/mol.<sup>19</sup>

In order to assess the reliability of this procedure, BDE's of various alkanes and alkylbenzenes whose experimental values are available were similarly calculated (Table IV). For the simple alkanes,  $\text{CH}_3\text{CH}_3$  was chosen as the reference compound. For the alkylbenzenes, toluene was the reference. In all cases, the calculated values reproduce the trends in the experimental data, although the effect of increasing  $\alpha$ -alkyl substitution on the BDE tends to be overestimated by about 2.0 kcal/mol.

## Discussion

**A. Possible Structure of the 2-(9-Anthryl)-2-propyl Radical.** Unfavorable steric interactions between the methyl groups and *peri*-hydrogens of the 2-(9-anthryl)-2-propyl radical make a planar geometry unlikely. To reduce this interaction, we anticipated that  $\text{C}_{\text{Ar}}-\text{C}^{\cdot}$  bond rotation might occur to remove the methyl groups from the aromatic plane. Conjugation between the radical center and anthryl  $\pi$ -system, and consequently radical stability, would be diminished.

AM1 molecule orbital calculations on this radical found two optimized geometries (Figure 1). One geometry, as expected, finds the methyls twisted 50° out of the aromatic plane. For the other geometry, the anthryl ring system attains a "butterfly" structure, for which the planes containing the outer rings define a 150° angle.

This alternative "butterfly" structure is more stable by 7 kcal/mol. The intriguing feature of this structure is that steric interactions are effectively minimized while still maintaining good overlap between the radical center and the anthryl  $\pi$ -system.

**B. Stereoelectronic Effects vs Radical Stability.** At all temperatures examined, the 9-alkylanthracenes show an inverted reactivity order toward bromine atom,  $1^\circ > \text{cyclopropyl} > 2^\circ > 3^\circ$ . This reactivity order does not correlate with the AM1-calculated bond dissociation energies of these compounds, but is instead a function of the conformation of the starting alkylaromatic (Table V).

From the variable temperature selectivity data in Table I, it is possible to evaluate differences in Arrhenius parameters for hydrogen abstraction from the 9-alkyl-

**Table V. Relative Rates of  $\alpha$ -Hydrogen Abstraction from 9-Alkylanthracenes by Bromine Atom at 80 °C**

R	relative reactivity <sup>a</sup>	$\theta$ , deg <sup>b</sup>
$\text{CH}_3$	1.00	90
<i>c</i> - $\text{C}_3\text{H}_5$	0.33	90
$\text{CH}_2\text{CH}_3$	0.063	33
$\text{CH}(\text{CH}_3)_2$	<0.0001	<16

<sup>a</sup> Per  $\alpha$ -hydrogen. <sup>b</sup>  $\text{H}-\text{C}-\text{C}_{\text{Ar}}-\text{C}_{\text{Ar}}$  dihedral angle determined from molecular mechanics calculations on the lowest energy conformation.

**Table VI. Arrhenius Parameters for Abstraction of Hydrogen from 9-Alkylanthracenes by Bromine Atom**

R	$E_a(\text{R}) - E_a(\text{CH}_3)$ , kcal/mol	$\log(A_{\text{R}}/A_{\text{CH}_3})^a$
$\text{CH}_3$	0.00	0.00
<i>c</i> - $\text{C}_3\text{H}_5$	2.6	1.2
$\text{CH}_2\text{CH}_3$	0.9	-0.6

<sup>a</sup> Per-hydrogen.

anthracenes by bromine atom. The Arrhenius plots are available as supplementary material; the derived results are summarized in Table VI. Because 9-isopropylanthracene is virtually inert under the reaction conditions, only data for 9-methyl-, 9-ethyl-, and 9-cyclopropylanthracene are available.

The difference in reactivity between 9-methyl- and 9-ethylanthracene is reflected in a difference in activation energy for these substrates. (The activation energy for 9-methylanthracene is 0.9 kcal/mol lower.) The surprisingly high reactivity of 9-cyclopropylanthracene is found not to arise from a low activation energy, per se, but rather a more favorable Arrhenius *A* factor. However, because of the intrinsic structural differences between a cyclopropyl group and a freely rotating alkyl group (e.g., likely differences in rotational and vibrational entropies of activation), we are reluctant to attach any particular significance to this observation.

The results found for hydrogen atom abstractions from the 9-alkylanthracenes are in stark contrast to those observed for the corresponding alkylbenzenes ( $\text{C}_6\text{H}_5\text{R}$ ), whose relative reactivities toward bromine atom,  $(\text{CH}_3)_2\text{CH}$  (57.0) >  $\text{CH}_3\text{CH}_2$  (25) >  $\text{CH}_3$  (1.0) per-hydrogen at 80°,<sup>9,10</sup> can be directly correlated to the strengths of the benzylic C-H bonds: 84.4, 85.4, and 88.0 kcal/mol for cumene, ethylbenzene, and toluene, respectively.<sup>19</sup> Although the dominant factor underlying the reactivity of alkylbenzenes toward bromine atom is the thermodynamic stability of the resulting radical, it has been suggested that these substrates may also be subject to some degree of stereoelectronic control. For example, the enhanced reactivity of indan toward bromine atom (1.7 times more reactive than ethylbenzene per  $\alpha$ -hydrogen) has been ascribed to better alignment of the benzylic C-H bond with the  $\pi$ -system.<sup>10,20</sup> (For indan, the lowest energy conformation is one in which one set of  $\alpha$ -C-H bonds are parallel to the  $\pi$ -system.) However, in these systems, stereoelectronic factors are far less important than the thermodynamic stability of the resulting benzylic radicals, and the "natural" reactivity order is retained.

We suggest that this difference in the reactivity order of the phenyl and 9-anthryl systems may be ascribed to the location of the transition state along the reaction coordinate. The abstraction of hydrogen from toluene (by bromine atom) is approximately thermoneutral ( $\Delta H = +0.5$  kcal/mol),<sup>22</sup> suggesting a transition state symmetri-

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cally located between reactants and products. Hydrogen abstraction from the 9-alkylanthracenes may involve earlier, more reactant-like transition states. This proposition is supported by the following: (a) Hydrogen abstractions from 9-alkylanthracenes are considerably more exothermic than for the corresponding alkylbenzenes.<sup>23</sup> (b) Reaction rates for the 9-alkylanthracenes are at least 3 orders of magnitude faster than for the alkylbenzenes. (c) The free-radical bromination of toluene exhibits a primary H/D isotope effect near 7. The H/D isotope effect for 9-cyclopropylanthracene is diminished ( $k_H/k_D = 2.5$ ).<sup>24-28</sup>

Because  $\alpha$ -hydrogen abstractions from 9-alkylanthracenes by bromine atom proceed via earlier transition states than the corresponding phenyl derivatives, we propose the former are therefore more sensitive to starting material conformation (stereoelectronic effects) than the stability of the resulting radical. The degree of alignment of the  $\alpha$ -C-H bond of the 9-alkylanthracene with the adjacent  $\pi$ -system profoundly perturbs substrate reactivity, and these stereoelectronic factors bear primary responsibility for the inverted reactivity order.

### Experimental Section

**General Considerations (Theoretical).** Molecular mechanics calculations were performed using MMX, Serena Software, Bloomington, IN 47402-3076. This program is derived from MM2 (QCPE 395) with  $\pi$ -routines from MMP1 included and was run on either an IBM PS/2 Model 50 or DEC VAX 8800. Semiempirical MO calculations were performed using the AM1 approximation developed by Dewar et al.<sup>12</sup> 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 using UHF, followed by a single-point calculation using the half-electron approximation.<sup>17,18</sup>

**General Considerations (Experimental).** Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Nuclear magnetic resonance (<sup>1</sup>H and <sup>13</sup>C) spectra were obtained on a 270-MHz Bruker FT NMR spectrometer. All chemical shift values are reported in  $\delta$  units relative to Me<sub>4</sub>Si ( $\delta$  0.00 ppm). Infrared spectra were recorded on a Perkin-Elmer Mode 710B spectrometer. IR bands were calibrated with the 1601.8 cm<sup>-1</sup> band of polystyrene and are reported in cm<sup>-1</sup>. Samples were prepared as KBr pellets. 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  $\times$  0.25 mm) or on an HP-1 (methyl silicone gum) instrument test column (5 m  $\times$  0.53 mm). Mass spectra data were obtained from a Varian MAT 112 magnetic instrument operating at either 10 or 70 eV. The following materials (99% gold label or HPLC grade) were purchased from Aldrich Chemical Co. and used as received (unless otherwise noted): 9-methylanthracene, anthrone, hexamethyldisiloxane, chlorobenzene, benzyl chloride, benzyl bromide, 1,1,2,2-tetrachloroethane, methyl bromide, ethyl bromide, isopropyl bromide, cyclopropyl bromide, magnesium ribbon, methylcyclohexene, 1,1,2-trichloroethene, diphenyl ether, benzoyl peroxide, cumene, iodine, CDCl<sub>3</sub>, lithium aluminium deuteride, anhydrous potassium carbonate, anhydrous sodium

sulfate, anhydrous magnesium sulfate, anhydrous sodium bisulfite, neutral alumina, acetonitrile, and ethanol. *N*-Bromosuccinimide (NBS) was recrystallized from water and dried extensively in vacuo. Carbon tetrachloride and dichloromethane were slurried with potassium hydroxide for 24 h, decanted, and fractionally distilled from phosphorus pentoxide. The middle portion of each solvent was stored over molecular sieves. Tetrahydrofuran, benzene, and toluene were distilled fresh from sodium or potassium metal (using benzophenone as an indicator), while diethyl ether was distilled fresh from lithium aluminum hydride before use.

**Synthesis of 9-Alkylanthracenes.** 9-Cyclopropyl-, 9-ethyl-, and 9-isopropylanthracene were prepared according to a modified version of the procedures reported by Mosnaim<sup>29</sup> et al. and by Bauld.<sup>30</sup> Grignard reagents were prepared by mixing appropriate alkyl bromides with magnesium ribbon in the presence of catalytic amount of iodine. Typically, anthrone (5–10 g) was dissolved in tetrahydrofuran (1 g of anthrone per 20 mL of THF), and the solution was added dropwise to an appropriate Grignard reagent (5–10% molar excess compared to the amount of anthrone used). The reaction mixture was refluxed for 2–3 h. Afterward, the reaction mixture was cooled in an ice bath for 10 min and gradually acidified with concentrated HCl. The acidified mixture was extracted twice with dichloromethane, and the combined extracts were washed with a saturated solution of sodium bisulfite and dried over Na<sub>2</sub>SO<sub>4</sub>. Crude product was obtained by evaporating the solvent with a rotary evaporator. Preliminary purification was done by percolating the product through a column of neutral alumina with large amount of hexane-dichloromethane (95:5). Pure product was obtained by recrystallization from either ethanol or acetonitrile. Typical yield of pure product samples ranged from 40% to 70%.

**9-( $\alpha$ -Deuteriocyclopropyl)anthracene (2).** A 30-mL pressure tube was charged with 9-cyclopropylanthracene (242.1 mg, 1.11 mmol), NBS (218.0 mg, 1.22 mmol), benzoyl peroxide (3.0 mg, 0.012 mmol), and 10 mL of carbon tetrachloride. The reaction mixture was degassed four times by the freeze-pump-thaw method and heated to 80.0 °C in a constant-temperature bath for 2 h. The contents of the pressure tube were filtered directly into a clean 100-mL round-bottom flask. (Note: GLC analysis was performed to assure complete conversion of 9-cyclopropylanthracene to the corresponding cyclopropyl bromide, 1.) Solvent was removed in vacuo (1–2 h) give a yellow residue; 50 mL of dry benzene and 84.0 mg (2.00 mmol) of LiAlD<sub>4</sub> were added, and the flask was equipped with a refluxing condenser, nitrogen inlet, and magnetic stirring bar. The contents of the flask were refluxed for 48 h, 20–30 mL of cold deionized water was added cautiously to quench the excess LiAlD<sub>4</sub>, and 25 mL of diethyl ether was added, and the organic layer was separated, dried over MgSO<sub>4</sub>, and evaporated. Column chromatography of the crude residue over neutral alumina using a 97:3 mixture of hexane-dichloromethane as solvent afforded 130.0 mg (yield 54%) of white powder of An-c-CD(CH<sub>2</sub>)<sub>2</sub> (2). Recrystallization from ethanol gave crystalline material with a melting point of 132–133 °C: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  0.81 (m, 2 H, *cis*-cyclopropylmethylene hydrogens), 1.48 (m, 2 H, *trans*-cyclopropylmethylene hydrogens), 7.44–7.53 m, 4 H, 2-, 3-, 6-, and 7-H anthryl hydrogens), 8.00 (m, 2 H, 4- and 5-H anthryl hydrogens), 8.36 (s, H, 10-H anthryl hydrogen), 8.73 (m, 2 H, 1- and 8-H anthryl hydrogens); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  9.10 and 9.86 (cyclopropyl carbons), 124.78, 124.97, 125.96, 126.42, 128.88, 131.66, 131.81, and 134.63 (anthryl carbons); IR (cm<sup>-1</sup>) 3077, 3051, 3000, 1621, 1440, 1366, 1036, 1018, 1005, 892, 867, 847, 823, 795, 771, 734, 697, 624, 562; MS (EI, 10 eV) *m/e* (relative intensity) 221 (2.0), 220 (19.0), 219 (100, M<sup>+</sup>), 218 (53.4), 217 (13.6), 216 (27.7), 215 (6.9), 205 (7.6), 204 (45.7), 203 (48.6), 202 (14.6), 192 (7.9), 191 (4.2), 190 (13.4), 189 (5.1), 110 (5.1), 109 (5.2), 102 (5.5).

**Competition Experiments.** Competitive brominations were carried out as follows: At temperatures of 40.0 °C and above, each of the alkyl aromatics was weighed into a 30-mL pressure tube (equipped with a Teflon-coated magnetic stir bar and an O-ring

(22) Based upon the bond dissociation energies of toluene (ref 19) and HBr (ref 21).

(23) 9-An-CH<sub>3</sub> + Br<sup>•</sup> → 9-An-CH<sub>2</sub><sup>•</sup> + HBr is 5.7 kcal/mol exothermic based upon the bond dissociation energies of 9-methylanthracene (ref 19) and HBr (ref 21).

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Teflon needle valve) containing a weighed amount of NBS and benzoyl peroxide (2 mol %) and 5–7 mL of  $\text{CCl}_4$  added. The mixture was degassed four to five times by the freeze–pump–thaw technique and placed in a controlled-temperature bath. When the reaction was completed (1–2 h), a weighed quantity (0.100–0.200 mmol) of one or two appropriate internal standards for NMR analysis (benzyl chloride, benzyl bromide, 1,1,2,2-tetrachloroethane, or hexamethyldisiloxane) was added. A 0.25-mL sample of the liquid portion of the reaction mixture was then transferred to an NMR tube containing 0.25 mL of  $\text{CDCl}_3$ .  $^1\text{H}$  NMR analysis of the solution was performed as soon as possible (generally, in less than 10 min) so as to avoid significant degradation of the  $\alpha$ -brominated products. For the competitive bromination of 9-cyclopropylanthracene versus cumene, excess 9-cyclopropylanthracene and its corresponding  $\alpha$ -brominated product were analyzed by  $^1\text{H}$  NMR, while unreacted cumene was analyzed by GLC. The internal standard used for GC analysis was chlorobenzene, added to the mixture along with the NMR internal standard (benzyl chloride) after the completion of the reaction. At the reaction temperature of 12.0 °C, the reaction mixture was irradiated with a 400-W medium-pressure mercury arc lamp (at a distance of 2 ft and through two layers of Pyrex) for 20–30 min. During this time, about 50–75% of the initial amount of NBS was consumed. Longer irradiation times led to decomposition of the primary reaction products.

**Quantitation by GLC.** After reaction, unconsumed alkyl aromatics were analyzed vs an appropriate internal standard. Analyses were performed in triplicate.

**Quantitation by  $^1\text{H}$  NMR Analysis.** At least four integrations were carried out on selected proton absorptions of  $\alpha$ -brominated products, excess competitors, 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%. The average chemical shift values ( $\delta$  in parts per million downfield from TMS) are as follows: benzyl chloride, 4.6 (s, 2 H,  $\text{CH}_2\text{Cl}$ ); benzyl bromide, 4.4 (s, 2 H,  $\text{CH}_2\text{Br}$ ); 1,1,2,2-tetrachloroethane, 5.9 (s, 2 H,  $\{\text{CHCl}_2\}_2$ ); hexamethyldisiloxane, 0.07 (s, 18 H,  $(\text{CH}_3)_3 \times 2$ ); toluene, 2.4 (s, 3 H,  $\text{CH}_3$ ); 9-methylanthracene, 3.1 (s, 3 H,  $\text{CH}_3$ ); 9-ethylanthracene, 1.4 (t, 3 H,  $J = 7.6$  Hz,  $\text{CH}_3$ ), 3.6 (q, 2 H,  $J = 7.6$  Hz,  $\text{CH}_2$ ); 9-isopropylanthracene, 1.8 (d, 6 H,  $J = 7.4$  Hz, 2  $\text{CH}_3$ ), 4.6 (h, 1 H,  $J = 7.4$  Hz, CH); 9-cyclopropylanthracene, 0.8 (m, 2 H, *cis*-cyclopropylmethylene), 1.5 (m, 2 H, *trans*-cyclopropylmethylene), 2.5 (m, 1 H, cyclopropylmethine); 9-( $\alpha$ -bromomethyl)anthracene, 5.5 (s, 2 H,  $\text{CH}_2\text{Br}$ ); 9-( $\alpha$ -bromoethyl)anthracene, 2.3 (d, 3 H,  $J = 7.3$  Hz,  $\text{CH}_3$ ), 6.7 (q, 1 H,  $J = 7.3$  Hz, CHBr); 9-vinylanthracene, 5.6 and 5.9 (dd, 2 H,  $J = 2.0$  Hz and  $J = 15.6$  Hz, *cis*- and *trans*-olefinic protons of  $\text{CH}_2$ ), 7.4 (dd, 1 H, CH); 9-( $\alpha$ -bromocyclopropyl)anthracene, 1.5 (m, 2 H, *cis*-cyclopropyl H's), 2.1 (m, 2 H, *trans*-cyclopropyl H's). All absorptions used in the computations of relative reactivities were clean and well resolved.

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**Supplementary Material Available:** Detailed experimental data for the studies of the relative reactivity of 9-alkylanthracenes toward bromine atom (initial and final concentrations of reactants and products) and an Arrhenius plot of the data in Table I (5 pages). Ordering information is given on any current masthead page.

## Experimental and Theoretical Study of the Reactivity of Primary and Secondary Enaminones toward Diphenylketene. A Comparison of AM1 and HAM/3 Semiempirical Methods

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Diazodiphenylethanone (1) reacts with acyclic enamino ketones 2 and enamino esters 3 to form products of electrophilic attack of diphenylketene at  $\text{C}_\alpha$  (5) and nitrogen (6 and 7). The relative reactivity of the different enaminones was shown to be consistent with HOMO energies determined by the HAM/3 semiempirical method. However, this approach could not completely explain the reactivity of the cyclic enamino ketones 4, which, by HAM/3, show a high-energy second HOMO corresponding to the nonbonded pair of electrons on oxygen.

### Introduction

Our interest in understanding the reactivity of enaminones has led us to attempt to correlate experimental results with theoretical studies in the case of the reactions of primary and secondary enaminones with diphenylketene. According to perturbation theory, the major contributions to bond making when two reagents approach each other involve opposite charge attractions at the reaction sites and the interactions between the filled orbitals of one reagent and the unfilled orbitals of the other, with HOMO's and LUMO's corresponding to the most important interactions because of the proximity of their energy levels. When the HOMO/LUMO interaction is the major factor governing differential reactivity, the reaction is said to be frontier-orbital controlled.<sup>1</sup> Thus, a molecular orbital method which calculates reliable energy levels of frontier

orbitals as well as electron density at each atom is needed in reactivity studies.

The semiempirical molecular orbital method called HAM/3 (hydrogenic atoms in molecules, version 3) was parameterized to calculate mainly ionization potentials, excitation energies, and electron affinities.<sup>2–4</sup> The quality of this method has been tested. Average absolute deviation in ionization potentials for molecules are in the range 0.3–0.4 eV.<sup>5</sup> The method has been successfully used to analyze photoelectron spectra of molecules.<sup>6–9</sup> The ac-

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