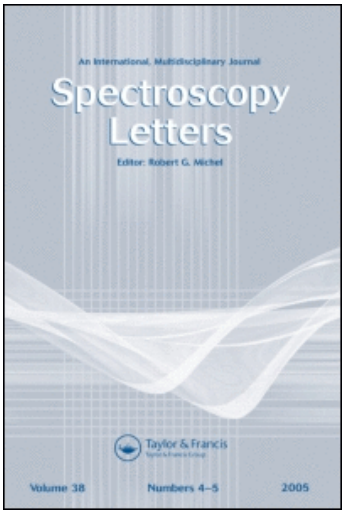


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# Proton and Carbon-13 NMR Studies of the Phencyclone Adducts of Medium Alkyl Chain-Length *N*-*n*-Alkylmaleimides. Hindered Rotations and Magnetic Anisotropic Effects. Ab initio Calculations for Optimized Structures

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## ABSTRACT

The Diels–Alder adducts, **3a–e**, of phencyclone, **1**, have been prepared from a series of *N*-*n*-alkylmaleimides, **2**, with medium chain-length

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*n*-alkyl groups. The maleimides were obtained by cyclodehydration of the *N*-*n*-alkylmaleamic acids, **4**, formed from reaction of maleic anhydride with the corresponding *n*-alkylamines. The five adducts prepared included derivatives from *n*-heptyl, **3a**; *n*-octyl, **3b**; *n*-nonyl, **3c**; *n*-decyl, **3d**; and *n*-dodecyl, **3e**. The NMR spectra of the adducts were studied in $CDCl_3$ at ambient temperatures at 300 MHz for proton and 75 MHz for carbon-13, with full proton assignments achieved by high-resolution COSY45 spectra for the aryl and the alkyl regions. Slow exchange limit (SEL) spectra were observed for both $^1H$ and $^{13}C$ spectra showing slow rotation on the NMR timescales of the unsubstituted bridgehead phenyl groups. Endo Diels–Alder adduct stereochemistry was supported by striking magnetic anisotropic shielding effects in the $^1H$ spectra of the alkyl groups, with the $NCH_2CH_2$ signal of each adduct appearing upfield of tetramethylsilane (TMS) at ca. −0.32 ppm. Proton NMR spectra for precursor maleamic acids and maleimides are reported, with some solvent effects found ($CDCl_3$ vs. $d_6$-acetone) for the carbon-bound HC═CH protons of **4**. Ab initio molecular modeling calculations at the Hartree-Fock level using the 6-31G* basis set have been performed for two key conformers of the phencyclone adduct of *N*-*n*-octylmaleimide, as a representative structure for these hindered adducts, to estimate geometric parameters for the adduct. A syn conformer, with the alkyl chain directed into the adduct cavity, was found to be ca. 0.23 kcal/mol lower energy than an anti conformer (in which the alkyl chain was directed away from the phenanthrenoid moiety).

*Key Words:* Dynamic NMR; One- and two-dimensional NMR; Homonuclear chemical shift correlation NMR; COSY; Restricted rotation; $^1H$ and $^{13}C$ NMR; Stereochemistry; Maleamic acids; Maleimides, Hartree-Fock/6-31G*.



## INTRODUCTION

Phencyclone, **1**, serves as a potent Diels–Alder diene.[1] Previous studies of a number of adducts of phencyclone (and analogs) have confirmed a remarkable degree of steric hindrance.[2–7] Simple inspection of phencyclone adduct models[8] indicates that the bridgehead phenyl ortho protons, H-2′ and 6′, have a potential closest approach distance of as little as 0.1–0.2 Å with the phenanthrenoid moiety protons, H-1 and 8. Our NMR results have suggested that this steric congestion leads to the observed slow exchange limit (SEL) spectra for the unsubstituted bridgehead phenyls at ambient temperatures with medium field spectrometers, e.g., 200 or 300 MHz for $^1H$ and 50 or 75 MHz for $^{13}C$. The bridgehead phenyls may thus be forced into a

conformation which reduces repulsions with proximal groups. The adducts previously studied have exhibited some striking magnetic anisotropic effects consistent with this proposed structure. We report here the preparation and NMR spectral data for the adducts, **3a–e**, respectively, of phencyclone with *N-n*-heptylmaleimide, **2a**; *N-n*-octylmaleimide, **2b**; *N-n*-nonylmaleimide, **2c**; *N-n*-decylmaleimide, **2d**; and *N-n*-dodecylmaleimide, **2e** (see Fig. 1 for structures). Rotations about the $C-C_6H_5$ bonds are evaluated based on the

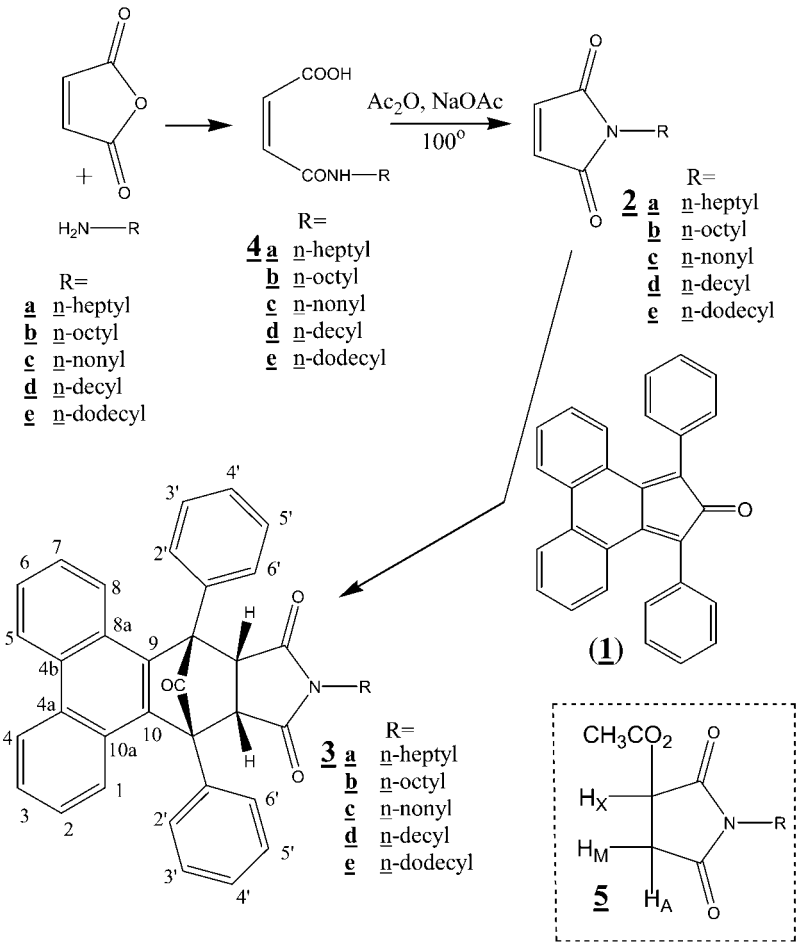


***Figure 1.*** Structures of key compounds (with atom numbering) and summary of synthetic pathways.

potential SEL or fast exchange limit (FEL) proton or carbon-13 NMR spectra. Possible magnetic anisotropic effects that might result from the phenanthrenoid or carbonyl moieties are also examined by studies of proton chemical shifts for the *n*-alkyl groups, to try to map out these effects along the length of the alkyl chain. Ab initio molecular modeling calculations have been performed for the phencyclone adduct of *N*-*n*-octylmaleimide, as a representative structure for these hindered adducts. These optimizations were performed at the Hartree-Fock level using the 6-31G* basis set, to estimate geometric parameters for the adduct in two key conformations. These combined experimental and computational studies have broad basic significance concerning hindered molecular motions, crowded molecules, and spatial aspects of magnetic anisotropy.



## EXPERIMENTAL

General NMR and other techniques were described earlier.[2,3] Spectra were obtained on a Bruker ACF300 NMR spectrometer (7.05 Tesla) at 300 MHz for $^{1}H$ and 75 MHz for $^{13}C$, equipped with quad nuclear probe (QNP) and Aspect 3000 data system, at ambient temperatures in $CDCl_3$ unless otherwise noted. Proton shifts were referenced to internal tetramethylsilane (TMS) at 0.0 ppm. For carbon-13 spectra, shifts were referenced to the center line of the $CDCl_3$ triplet at 77.0 ppm. WALTZ16 was used for composite pulse decoupling of protons during normal carbon-13 NMR. For carbon-13 spectra, relaxation delays of 3 sec were routinely used, resulting in peak areas that were roughly proportional to the numbers of protonated carbons. For 1D NMR, peak multiplicities are abbreviated as: singlet, s; doublet, d; triplet, t; quartet, q; multiplet, m; Q refers to quaternary non-protonated carbons (usually aryl). Other abbreviations include: sl (slight), v (very), br (broad), and app (approximate). Observed proton NMR splittings are given in Hz. Standard Bruker microprograms were routinely employed for proton–proton (2D) homonuclear chemical shift correlation spectra. Typical "high-resolution" COSY45 spectra for aryl proton regions covered a sweep width of ca. 2 ppm (or less) with 256 increments in $t_1$ and 8 or 16 transients for each increment; crosspeaks corresponding to $^{3}J$, $^{4}J$, and $^{5}J$, for H–H couplings were usually seen. Separate COSY45 spectra were acquired for the upfield proton regions of the n-alkyl groups, covering a sweep width of ca. 3.5 ppm, with 128 increments in $t_1$; crosspeaks were seen for vicinal couplings [see Fig. 2(a) and (b) for representative COSY spectra of the aryl and alkyl regions, respectively, of an adduct]. IR data were obtained using Type 61 (polyethylene) Disposable IR Cards (3M) on Perkin Elmer 1640 or Midac M2000 spectrophotometers, with DTGS detectors and wavenumber

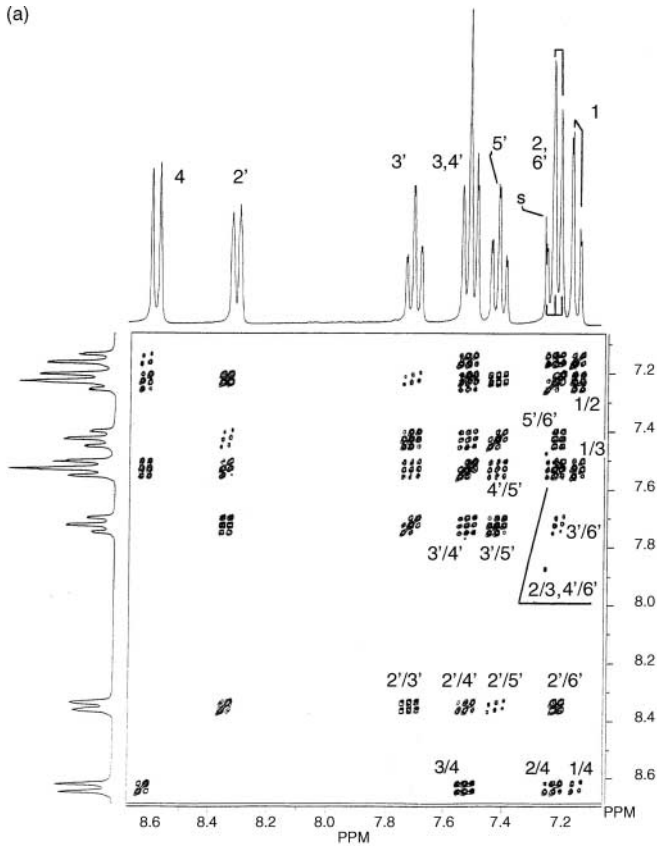


***Figure 2.*** The 300 MHz $^1$H NMR spectra for adduct **3a** (in $CDCl_3$, ambient temperature) shown as projections for the COSY45 spectra. The 2H singlet at 4.41 ppm for the bridgehead methines is not shown. (a) High-resolution COSY45 spectrum for the aryl proton region. $CHCl_3$ solvent impurity is noted S. The spectral width in $F_2$ was 488 Hz, acquired in 1024 complex data points, with no zero-filling. In $F_1$, 256 $t_1$ increments were taken, zero-filling once. For each increment, two dummy scans and 16 acquisitions were used. Data were processed with unshifted sine-bell apodization in both dimensions. The magnitude mode spectrum is unsymmetrized. (b) The COSY45 spectrum for the upfield region. The water impurity is marked W, TMS is labeled T, and unidentified impurities are noted I. Alkyl chain signals are labeled as: $\alpha$, $\beta$, $\gamma$, $\delta$, $\varepsilon$, $\zeta$, and $\omega$. In the $F_1$ dimension, 128 $t_1$ increments were obtained, each with two dummy scans and eight acquisitions, zero-filling once. The $F_2$ spectral width was 1029 Hz, using 512 complex data points, with no zero-filling. Unshifted sine-bell apodization in both dimensions was applied and the final magnitude mode spectrum has been symmetrized. *Note*: Different chemical shift and amplitude scales are used in (a) and (b).

*(continued)*

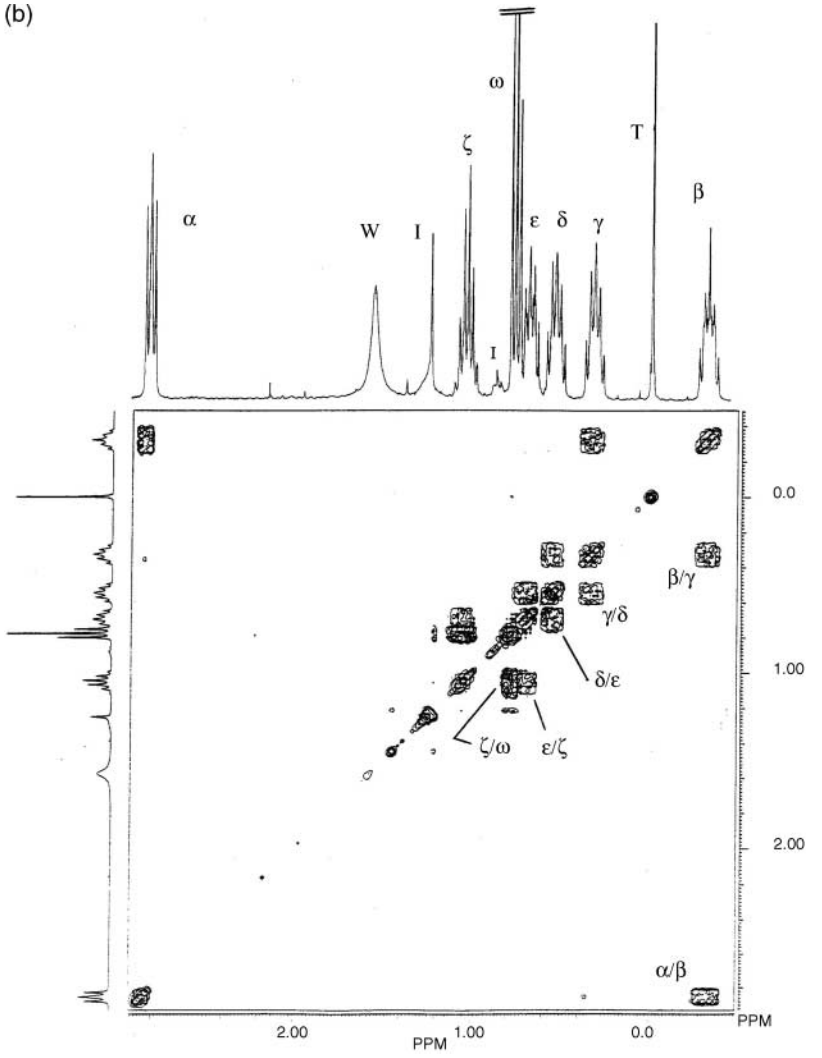


***Figure 2.*** Continued.

resolution of $4\,cm^{-1}$; 16 scans were usually acquired. The IR peaks listed here include most of the peaks that were medium (m), strong (s), or very strong (vs) in intensity. A weak (w) shoulder or peak may be noted. [Note that the IR card manufacturer suggested that, because of strong absorption by polyethylene in the aliphatic CH [stretch] region from $2800-3000\,cm^{-1}$, observed bands in

this region may not be useful. Much weaker bands of polyethylene occur ca. 1460 ($CH_2$ scissoring bend) and ca. 720 $cm^{-1}$ ($CH_2$ rocking). In fact, absorptions in each of these regions are expected for all of our reported compounds as a consequence of the medium-length alkyl chains. We have chosen, therefore, to include significant peaks seen in these regions in the listings of IR absorptions presented here.] Reported melting points are uncorrected. Reagents and solvents were obtained from Aldrich Chemical (Milwaukee, WI) or Lancaster Synthesis (Windham, NH) and were used without further purification. Since we have previously described[2] detailed procedures for syntheses of the *n*-hexyl analogs for the maleamic acid, maleimide, and phencyclone adduct, we present here a full description for preparation only of the corresponding *n*-heptyl analogs, as being representative of the series (see Discussion). Full $^1H$ and $^{13}C$ NMR data, and IR absorption peaks, are given for each of the phencyclone adducts, which we believe are reported for the first time. (The comparative proton NMR data and assignments for the adducts, **3**, are separately shown in Table 1.) Synthesis, characterization, and relevant data for the other alkylmaleamic acids and alkylmaleimides are generally available in the literature (see Discussion). Since the maleamic acids, **4a**–**e**, and the maleimides, **2a**–**e**, were prepared by us strictly as intermediates (which did not require or receive extensive purification) for preparation of the target phencyclone adducts, **3**, we have characterized these materials only by proton NMR and IR, listing these data in this Experimental section. Melting point data are included here, except for some maleimides that were obtained only as oils or semi-solids. Typical crude yields were: maleamic acids, ca. 60–95%; maleimides, 15–40%; phencyclone adducts, 30–90%.



## Preparation of *N*-*n*-Heptylmaleamic Acid, 4a

*n*-Heptylamine (5.688 g, ca. 7.3 mL, 49.4 mmol) in $CH_2Cl_2$ (6 mL) was added dropwise with cooling (ice slush) and stirring to a pre-chilled slurry of freshly powdered maleic anhydride (4.845 g, 49.4 mmol) in $CH_2Cl_2$ (12 mL). The initially undissolved maleic anhydride went into solution upon amine addition. After ca. 20 min, product maleamic acid crystals formed, and were allowed to stand an additional 20 min, then collected by vacuum filtration, washed with cold $CH_2Cl_2$, and dried, to give the crude *N*-*n*-heptylmaleamic acid, 5.598 g, 98% yield, mp 65–70°C, lit. mp 74–75°C.[9a] IR ($cm^{-1}$): 3242.6, 3076.6, 2958.6, 2922.2, 2915.6, 2847.7, 1707.2, 1640.8, 1526.2, 1469.9, 1404.5, 1374.6, 1299.5, 1241.7, 1191.1, 1152.2, 1060.9, 959.5, 851.8, 634.0. $^1H$ NMR ($CDCl_3$): 7.66 (1H, br t, NH); 6.45 (1H, d, $J = 12.82$, half of AB q, HC═CH); 6.32 (1H, d, $J = 12.81$, half of AB q, HC═CH); 3.37 [2H, app. q, $J = 6.79$ (note coupling to NH), $NCH_2$]; 1.60

***Table 1.*** Proton NMR shifts for phencyclone adducts of *N*-*n*-alkyl maleimides, in ppm (with observed coupling constants in Hz).

| Nucleus | *n*-Heptyl, **3a** | *n*-Octyl, **3b** | *n*-Nonyl, **3c** | *n*-Decyl, **3d** | *n*-Dodecyl, **3e** |
|---|---|---|---|---|---|
| H-1,8 | 7.15 (8.40) | 7.15 (8.38) | 7.15 (8.34) | 7.15 (8.35) | 7.15 (8.35) |
| H-2,7 | 7.23 (7.29) | 7.22 (ca. 7.7) | 7.22 (8.10) | 7.22 (7.54) | 7.22 (7.03) |
| H-3,6 | 7.53 (7.7) | 7.52 (7.56) | 7.52 (7.49) | 7.52 (7.47) | 7.52 (7.52) |
| H-4,5 | 8.63 (8.39) | 8.62 (8.38) | 8.62 (8.39) | 8.62 (8.37) | 8.62 (8.40) |
| H-2′ | 8.35 (7.81) | 8.34 (7.85) | 8.34 (7.79) | 8.34 (7.76) | 8.34 (7.79) |
| H-3′ | 7.72 (7.61) | 7.72 (7.58) | 7.71 (7.53) | 7.72 (7.60) | 7.71 (7.50) |
| H-4′ | 7.53 (7.7) | 7.52 (7.56) | 7.52 (7.49) | 7.52 (7.47) | 7.52 (7.52) |
| H-5′ | 7.42 (7.59) | 7.42 (7.54) | 7.42 (7.59) | 7.42 (7.57) | 7.42 (7.38) |
| H-6′ | 7.21 (7.29) | 7.21 (7.05) | 7.21 (7.07) | 7.20 (7.07) | 7.21 (7.03) |
| $NCH_2$ (1) | 2.85 (7.72) | 2.85 (7.70) | 2.84 (7.68) | 2.85 (7.66) | 2.84 (7.67) |
| $CH_2$ (2) | −0.321 (7.80) | −0.313 (7.78) | −0.313 (7.76) | −0.315 (7.77) | −0.314 (7.76) |
| $CH_2$ (3) | 0.326 (7.53) | 0.321 (7.56) | 0.320 (7.55) | 0.318 (7.53) | 0.317 (7.53) |
| $CH_2$ (4) | 0.544 (7.33) | 0.536 (7.39) | 0.536 (7.36) | 0.533 (7.35) | 0.533 (7.35) |
| $CH_2$ (5) | 0.693 | 0.718 (7.48) | 0.710 (7.35) | 0.708 (7.39) | 0.71 (7.38) |
| $CH_2$ (6) | 1.06 (7.33) | 1.01 (7.40) | 1.03 (7.35) | 1.019 (7.21) | 1.02 (6.93) |
| CH (7) | 0.78 (7.27) | 1.16 (7.40) | ca. 1.13 | ca. 1.17 | ca. 1.18 |
| CH (8) | | 0.83 (7.22) | 1.23 (6.69) | ca.1.17 | ca. 1.1–1.35 |
| CH (9) | | | 0.87 (7.01) | 1.27 (6.86) | ca. 1.1–1.35 |
| CH (10) | | | | 0.88 (7.11) | ca. 1.1–1.35 |
| CH (11) | | | | | ca. 1.26 |
| CH (12) | | | | | 0.89 (6.75) |
| Bridgehead | 4.41 | 4.40 | 4.39 | 4.40 | 4.39 |

*Notes*: Approximate observed coupling constants are shown in parentheses, and refer only to the gross vicinal ($^3J$) couplings. Fine splitting from long range couplings have been omitted, but were often seen for aryl proton signals. Gross multiplicities for the aryl protons (d or t) were consistent with the numbers of vicinal proton neighbors (one or two, respectively).

(2H, app. quintet, $J = 7.15$, $NCH_2CH_2$); ca. 1.31 (m, $[CH_2]_4$); 0.88 (3H, skew t, $J = 6.75$, $CH_3$). In selective homodecoupling experiments, irradiation at 1.60 ppm collapsed the signal at 3.37 ppm to a doublet with $J = 5.8$, presumably the vicinal HNCH splitting. Irradiation at 3.37 ppm caused collapse of the 1.60 ppm quintet to a triplet, and collapsed the NH triplet to a singlet. This material was used directly for conversion to the maleimide.

## Preparation of *N*-*n*-Heptylmaleimide, 2a

A mixture of 5.397 g (25.3 mmol) *N*-*n*-heptylmaleamic acid (prepared as above), anh. sodium acetate (0.822 g, 10.0 mmol) and acetic anhydride (8.80 g) was heated in a boiling water bath for 40 min, during which time the clear colorless solution gradually darkened to a deep reddish-brown. After standing 1 week at room temperature, the mixture had become a semi-solid slurry, to which 50 mL $H_2O$ was added. The mixture was extracted with two portions of diethyl ether (total 60 mL) and the combined ether extracts were washed with 2% aq. KOH ($3 \times 40$ mL) and 40 mL $H_2O$. After drying (anh. $MgSO_4$), solvent removal on a rotary evaporator (aspirator pressure, bath ca. 50°) gave a residue of red oil [lit. bp 118°/2.2 Torr[9a]] which partially crystallized on standing, to give 1.767 g (35.8%) of the crude maleimide, **2a**; this was satisfactory for preparation of the phencyclone adduct. IR ($cm^{-1}$): 3095.5, 2928.4, 2915.7, 2856.7, 1708.2 vs, 1657.4 s, 1633.8 s, 1556.4 s, 1441.5 vs, 1407.7 vs, 1372.4 s, 1288.5, 1224.7 s, 1116.6, 830.1 s, 696.0 vs. $^1H$ NMR ($CDCl_3$): 6.69 (2H, s, HC═CH); 3.51 (2H, t, $J = 7.33$, $NCH_2$); 1.58 (2H, app. quintet, $J = 7.20$, $NCH_2CH_2$); 1.27 (app. br s, $[CH_2]_4$); 0.87 (3H, app. skew t, $J = 6.76$, $CH_3$).

## Preparation of the Adduct, 3a, from Phencyclone and *N*-*n*-Heptylmaleimide

In a screw-cap vial (ca. 20 mL capacity) were placed a magnetic stirbar, 1.070 g (nominal 5.48 mmol) of the crude *N*-*n*-heptylmaleimide (prepared above), phencyclone (0.942 g, 2.47 mmol), and sufficient $CH_2Cl_2$ to bring the mixture volume to within 5 mm of the vial brim. The vial was capped (Teflon® liner) and the nearly-opaque green–black mixture was stirred at room temperature. In ca. 10 min, the intense phencyclone color was almost completely discharged, giving a pale lime-green solution. Solvent was removed (rotary evaporator) to about one-quarter volume, giving an oil. Addition of ca. 50 mL hexane eventually resulted in crystals that were collected by vacuum filtration, washed with more hexane, and dried, giving

the desired adduct as an off-white solid, 1.376 g (96%), mp 190–193°C, dec., gas evolution. IR ($cm^{-1}$): 3088.0, 3059.9, 3032.2, 2930.7, 2918.9, 2855.2, 1791.6 vs (strained ketone C═O), 1772.8 w shoulder, 1702.5 vs (imide C═O), 1498.4, 1447.7, 1436.8, 1395.7, 1369.5, 1346.4, 1288.1, 1269.9, 1241.9, 1222.4, 1169.4, 1137.9, 1070.2, 1044.1, 1034.4, 778.7, 754.8, 724.1, 698.6. $^{13}C$ NMR ($CDCl_3$): 196.79 (ketone), 174.25 (imide), 133.84 (Q), 133.31 (Q), 131.26 (Q), 130.91, 129.33, 129.12, 128.60, 128.38, 127.00, 126.60, 126.35 (Q), 125.83, 122.90, 63.35 ($C$–$C_6H_5$), 44.42 (2 × CH), 38.75 ($NCH_2$), 30.87, 28.23, 26.34, 25.77, 22.44, 13.93 ($CH_3$). This material was used for full NMR studies.

**N-n-Octylmaleamic acid** (**4b**): mp 79–83°C [lit. 79–81°C;[9a] 84–85°C;[9b] 84–86°C;[9c] 80–82°C;[9d,9e] 74.5°C[9f]]. $^1H$ NMR ($CDCl_3$): 7.63 (1H, v. br t, NH); 6.44 (1H, d, $J = 12.82$, half of AB q, HC═CH); 6.31 (1H, d, $J = 12.80$, half of AB q, HC═CH); 3.37 [2H, app. q, $J = 6.79$ (note coupling to NH), $NCH_2$]; 1.60 (2H, app. quintet, $J = 7.0$, $NCH_2CH_2$); ca. 1.29 (m, $[CH_2]_5$); 0.88 (3H, skew t, $J = 6.7$, $CH_3$). $^1H$ ($d_6$-acetone): 8.63 (1H, br s, NH); 6.55 (1H, d, $J = 12.86$, half of AB q, HC═CH); 6.26 (1H, sl. br d, $J = 12.84$, half of AB q, HC═CH); 3.36 [2H, complex m, (note coupling to NH), $NCH_2$]; 1.60 (2H, app. br quintet, $J = 7.1$, $NCH_2CH_2$); ca. 1.30 (m, $[CH_2]_5$); 0.88 (3H, skew t, $CH_3$).

IR ($cm^{-1}$): 3068.9, 2916.4, 2850.4, 1702.2, 1638.8, 1577.9, 1465.8, 1403.9, 1289.9, 1256.9, 1228.7, 1183.0, 1147.9, 1066.2, 850.0, 629.8.

**N-n-Octylmaleimide** (**2b**): Lit. bp 142°/5 Torr;[9b] lit. mp 36–37°C;[9a] 36–38°C;[9c] 37–37.5°C;[9d] 42.5°C.[9f] $^1H$ NMR ($CDCl_3$): 6.68 (2H, s, HC═CH); 3.50 (2H, m, $NCH_2$); 1.40–1.60 (2H, br m, $NCH_2CH_2$); 1.27 (br m, $[CH_2]_5$); 0.87 (3H, app. skew t, $CH_3$). IR ($cm^{-1}$): 2926.9, 2915.4, 2855.6, 1752.6, 1708.8 vs, 1658.1, 1441.2, 1407.7 s, 1371.8, 830.2, 696.0.

**N-n-Octylmaleimide adduct** (**3b**) *from phencyclone*: mp 168–176°C (dec., gas evoln.); $^{13}C$ NMR ($CDCl_3$): 196.79 (ketone), 174.25 (imide), 133.84 (Q), 133.31 (Q), 131.26 (Q), 130.90, 129.33, 129.11, 128.59, 128.37, 127.00, 126.59, 126.34 (Q), 125.82, 122.90, 63.34 ($C$–$C_6H_5$), 44.42 (2 × CH), 38.75 ($NCH_2$), 31.69, 28.54, 28.41, 26.36, 25.83, 22.53, 14.08 ($CH_3$). IR ($cm^{-1}$): 3060.2, 2922.5, 2913.5, 2848.0, 1792.0 vs, 1703.1 vs, 1498.5, 1461.5, 1447.6, 1436.7, 1395.5, 1368.0, 1346.4, 778.7, 754.0, 723.8, 698.2.

**N-n-Nonylmaleamic acid** (**4c**): mp 77.5–79°C [lit. 78–80°C;[9a] 74–76°C[9c]]. $^1H$ NMR ($CDCl_3$): 7.15 (1H, br s, NH); 6.34 (2H, app. s, HC═CH, essentially isochronous. The expected AB q has collapsed to a single central peak with no trace of valley, but with very small residual outer peaks still detectable, $J$ = ca. 12.9); 3.38 [2H, q, (note coupling to NH), $NCH_2$]; 1.60 (2H, app. quintet, $J = 6.94$, $NCH_2CH_2$); ca. 1.27 (m, $[CH_2]_6$); 0.88 (3H, skew t, $J = 6.62$, $CH_3$). $^1H$ ($d_6$-acetone): 8.64 (1H, br s, NH); 6.55 (1H, d, $J = 12.9$, half of AB q, HC═CH); 6.26 (1H, d,

$J = 12.9$, half of AB q, HC═CH); 3.37 [2H, app. q, $J = 6.7$ (note coupling to NH), $NCH_2$]; 1.61 (2H, app. quintet, $J = 7.1$, $NCH_2CH_2$); ca. 1.29 (m, $[CH_2]_6$); 0.88 (3H, skew t, $J = 6.7$, $CH_3$). IR ($cm^{-1}$): 3235.3, 2913.8, 2846.1, 1708.6 s, 1642.0, 1518.6, 1470.4, 1409.0, 1284.1, 1223.1, 1042.0, 849.9 vs, 793.4, 754.6, 718.1, 631.0, 597.0.

**N-n-Nonylmaleimide** (**2c**): mp 44–49.5°C [lit. 45–47°C[9a,c]]. $^1H$ NMR ($CDCl_3$): 6.68 (2H, s, HC═CH); 3.51 (2H, t, $J = 7.33$, $NCH_2$); 1.58 (2H, m, $J =$ ca. 6.5, $NCH_2CH_2$); 1.26 (app. br s, $[CH_2]_6$); 0.88 (3H, skew t, $J = 6.5$, $CH_3$). IR ($cm^{-1}$): 3297.4, 3094.4, 2926.2, 2913.9, 2852.5, 1752.5 s, 1706.2 s, 1658.8, 1441.3, 1407.5, 1371.7, 1224.4, 116.3, 829.2 s, 696.0 s.

**N-n-Nonylmaleimide adduct** (**3c**) *from phencyclone*: mp 186–194°C (dec., gas evoln.); $^{13}C$ NMR ($CDCl_3$): 196.79 (ketone), 174.25 (imide), 133.85 (Q), 133.31 (Q), 131.26 (Q), 130.91, 129.32, 129.12, 128.59,128.36, 126.99, 126.59, 126.35 (Q), 125.83, 122.90, 63.34 ($C$–$C_6H_5$), 44.42 (2 × CH), 38.75 ($NCH_2$), 31.75, 29.12, 28.69, 28.59, 26.36, 25.83, 22.63, 14.10 ($CH_3$). IR ($cm^{-1}$): 3060.0, 3031.9, 2927.6, 2913.7, 2853.6, 1792.0 vs, 1702.9 vs, 1605.3, 1498.6, 1447.7, 1436.8, 1395.6, 1367.8, 1347.0, 1222.3, 1165.4, 1137.8, 1044.0, 778.7, 754.1, 723.9, 698.3.

**N-n-Decylmaleamic acid 4d**: mp 83–86°C [lit. 87–88°C;[9a] 81–82°C;[9c] 83–84°C;[9d] 80°C[9f]]. $^1H$ NMR ($CDCl_3$): 7.0 (1H, br unsymm. s, NH); 3.38 [2H, app. q, $J = 6.8$ (note coupling to NH), $NCH_2$]; 1.60 (2H, app. br quintet, $J = 7.0$, $NCH_2CH_2$); ca. 1.26 (br m, $[CH_2]_7$); 0.88 (3H, skew t, $J = 6.7$, $CH_3$). Note: the expected AB q for the HC═CH appeared heavily distorted and asymmetrical due to severe leaning and to substantial broadening (possibly caused by the proximal NH) of the upfield half; estimated shifts were 6.35 ppm ($J = 12.83$) and 6.32 ppm ($J = 12.94$). Small broad shoulders on the upfield half of the AB q may have been impurities or the result of the amide CO-NH conformer. $^1H$ ($d_6$-acetone): 8.62 (1H, br s, NH); 6.55 (1H, d, $J = 12.9$, half of AB q, HC═CH); 6.26 (1H, d, $J = 12.8$, half of AB q, HC═CH); 3.37 [2H, app. q, $J = 6.7$ (note coupling to NH), $NCH_2$]; 1.60 (2H, app. br quintet, $J = 7.1$, $NCH_2CH_2$); ca. 1.29 (br m, $[CH_2]_7$); 0.88 (3H, skew t, $J = 6.7$, $CH_3$). IR ($cm^{-1}$): 3295.6, 2916.3, 2848.7, 1713.3, 1638.6, 1540.6, 1472.8, 851.9.

**N-n-Decylmaleimide** (**2d**): mp 46–53°C [lit. 47–48°C;[9a] 48–49°C;[9c] 46.5–48°C;[9d] 43.5°C[9f]]. $^1H$ NMR ($CDCl_3$): 6.68 (2H, s, HC═CH); 3.51 (2H, t, $J = 7.33$, $NCH_2$); 1.57 (2H, app. br quintet, $NCH_2CH_2$); 1.15–1.35 (app. br s, $[CH_2]_7$); 0.88 (3H, skew t, $CH_3$). IR ($cm^{-1}$): 3088.0, 2922.2, 2915.3, 2848.3, 1751.3, 1708.2 vs, 1542.2, 1464.3, 1447.1, 1406.5, 1370.3, 829.8, 719.8, 694.6.

**N-n-Decylmaleimide adduct** (**3d**) *from phencyclone*: mp 166–169°C (dec., gas evoln.); $^{13}C$ NMR ($CDCl_3$): 196.80 (ketone), 174.25 (imide), 133.87 (Q), 133.33 (Q), 131.27 (Q), 130.92, 129.33, 129.13, 128.59,

128.37, 127.00, 126.60, 126.37 (Q), 125.85, 122.90, 63.36 (*C*–$C_6H_5$), 44.44 (2 × CH), 38.76 ($NCH_2$), 31.87, 29.43, 29.19, 28.75, 28.59, 26.38, 25.85, 22.68, 14.10 ($CH_3$). IR ($cm^{-1}$): 3060.8, 2920.6, 2913.6, 2848.0, 1792.4 vs, 1703.1 vs, 1447.6, 1395.7, 1346.2, 778.6, 753.6, 723.7, 698.0.

**N-n-Dodecylmaleamic acid** (**4e**): mp 94–95°C [lit. 92–94°C;[9d] 81.5°C [9f]]. $^1$H NMR ($CDCl_3$): 7.65 (1H, br t, NH); 6.45 (1H, d, $J = 12.8$, half of AB q, HC═CH); 6.32 (1H, d, $J = 12.7$, half of AB q, HC═CH); 3.37 [2H, app. q, $J = 6.8$ (note coupling to NH), $NCH_2$]; 1.60 (2H, app. br quintet, $NCH_2CH_2$); 1.20–1.37 (br m, $[CH_2]_9$); 0.88 (3H, skew t, $CH_3$). $^1$H ($d_6$-acetone): 8.66 (1H, br s, NH); 6.56 (1H, d, $J = 12.9$, half of AB q, HC═CH); 6.26 (1H, d, $J = 12.9$, half of AB q, HC═CH); 3.36 [2H, complex m, (note coupling to NH), $NCH_2$]; 1.60 (2H, app. br quintet, $NCH_2CH_2$); 1.22–1.41 (br m, $[CH_2]_9$); 0.88 (3H, skew t, $CH_3$). IR ($cm^{-1}$): 3229.6, 3066.9, 2917.7, 2848.2, 1707.9, 1641.5, 1576.7, 1465.1 s, 1403.3, 1375.9, 1254.4, 1231.4, 1149.0, 849.9.

**N-n-Dodecylmaleimide** (**2e**): mp 49–52°C [lit. 54.5–56°C;[9d] 55°C;[9f] 54–54.5°C;[9g] 56–57°C[9h]]. $^1$H NMR ($CDCl_3$): 6.69 (2H, s, HC═CH); 3.51 (2H, t, $J = 7.33$, $NCH_2$); 1.42–1.62 (complex m, $NCH_2CH_2CH_2$); 1.18–1.39 (app. br s, $[CH_2]_8$); 0.88 (3H, skew t, $CH_3$). IR ($cm^{-1}$): 3445.2, 3314.4, 3104.9, 2954.1, 2924.4, 2913.1, 2848.1, 1752.7, 1702.8 vs, 1633.3 s, 1538.6, 1469.0, 1452.0, 1423.7, 1374.9, 1127.8, 840.1 s, 699.8 s.

**N-n-Dodecylmaleimide adduct** (**3e**) *from phencyclone*: mp 153–162°C (dec., gas evoln.); $^{13}$C NMR ($CDCl_3$): 196.78 (ketone), 174.24 (imide), 133.87 (Q), 133.33 (Q), 131.27 (Q), 130.92, 129.32, 129.13, 128.59, 128.36, 126.99, 126.59, 126.37 (Q), 125.85, 122.90, 63.36 (*C*–$C_6H_5$), 44.44 (2 × CH), 38.76 ($NCH_2$), 31.91, 29.61, 29.54, 29.48, 29.34, 28.75, 28.59, 26.37, 25.84, 22.67, 14.09 ($CH_3$). IR ($cm^{-1}$): 3060.2, 3032.1, 2927.5, 2913.7, 2853.1, 1792.2 vs, 1772.9 w shoulder, 1703.5 vs, 1498.5, 1447.7, 1436.7, 1395.7, 1346.3, 778.7, 753.6, 723.7, 698.2.

## RESULTS AND DISCUSSION

Preparation of the desired *N-n*-alkylmaleimides, **2a**–**2e**, was achieved by sodium acetate-promoted cyclodehydration in acetic anhydride (at 90–100°) of the respective maleamic acids, **4a**–**4e**; these acids were derived from condensation of maleic anhydride with the corresponding n-alkylamine (see Fig. 1) The *N-n*-alkylmaleamic acids generally formed rapidly and cleanly, in reasonably good yields, but would not necessarily crystallize readily. Solvent removal from their respective product mixtures often gave the crude maleamic acids as oils, which would crystallize on standing. The key feature in the proton NMR spectra for these compounds was the (expected)

AB quartet associated with the non-equivalent vinyl hydrogens, HC═CH, exhibiting the observed vicinal coupling, ca. 12.8 Hz, for cis geometry.[10] For several of the maleamic acids, e.g., the nonyl, **4c**, and decyl, **4d**, this spectral region, with $CDCl_3$ solvent, was complicated by nearly isochronous chemical shifts for these vinyl protons, with some broadening of half of the AB q (attributed to long-range *J* coupling or quadrupolar broadening from the amide nitrogen). For the compounds **4b**–**4e**, the spectra were also acquired in $d_6$-acetone, which provided the virtue of consistently better dispersion of the two vinyl proton signals, with a resulting clear AB q pattern. The significant solvent effect for these carbon-bound protons was somewhat unexpected; changes in the amide NH chemical shift and NH signal appearance were also seen. The $NCH_2$ resonance routinely exhibited vicinal coupling to the NH proton, as reflected in the approximate quartet (or higher) multiplicity of the $NCH_2$ signal, and by the homodecoupling experiment performed for **4a**.

The shorter chain-length *N*-*n*-alkylmaleimides have low reported mp ranges, e.g., Mehta and coworkers[9b] reported only reduced pressure boiling points for the *n*-butyl-, *n*-hexyl-, and *n*-octylmaleimides. Kalgutkar et al.[9c] reported mp ranges for the maleimides as: *n*-octyl (36–38°C); *n*-nonyl (45–47°C); and *n*-decyl (48–49°C). Coleman and coworkers[9d] gave mp values for the maleimides as: *n*-octyl (37–37.5°C); *n*-decyl (46.5–48°C); *n*-dodecyl (54.5–56°C), with yields of 15%, 20%, and 24%, respectively. Their relatively low yields may be attributed to the use of very high reaction temperatures (170–180°C) and product distillation to pot temperatures of 210°C. Gonzales Ramos et al.[9f] have synthesized an extensive series of the *N*-*n*-alkylmaleimides, and gave IR and NMR data. These workers presented IR data based on KBr pellets, and reported 60 MHz proton NMR data using $d_6$-dimethyl sulfoxide solvent for the maleamic acids and $CCl_4$ for the maleimides; our data, therefore, complement this earlier work. Heitz and coworkers[9a] and Blicq et al.[9i] have also described maleimide syntheses. For our present purposes, we were primarily interested in the preparation of the clean phencyclone adducts from the maleimides, and these adducts are readily isolated in good purity (based on proton and carbon-13 NMR, see below), even from rather crude maleimides. The phencyclone essentially serves as a derivatizing agent for the maleimides, with the Diels–Alder additions producing highly crystalline, readily isolated products for the NMR studies. It is an important virtue of these reactions that clean adducts (for the key target NMR studies) are obtainable even from maleimides of only modest purity. We have earlier described detailed procedures and characterizations for the analogous *N*-*n*-hexylmaleamic acid and *N*-*n*-hexylmaleimide.[2] The simple unhindered *N*-*n*-alkylmaleimides act as effective electron-deficient Diels–Alder dienophiles with phencyclone. Based on their proton NMR spectra, the maleimides used here were not formed in

particularly high yield or high purity, but the crude maleimides proved completely satisfactory for conversion to clean adducts from phencyclone. Increments of crude product maleimides could be added to the phencyclone until the decolorization of the intense green–black color of **1** was achieved, indicating the complete consumption of **1**. Alternatively, a nominal molar excess (e.g., two-fold) of crude maleimide could be provided at the outset and allowed to react with **1**, to assure that excess **2** was present. The desired phencyclone adducts, **3a–3e**, because of their high melting points and low solubilities, would readily separate from the reaction mixtures, leaving excess maleimides and associated impurities remaining in the mother liquors. Washing the initially collected adducts with solvent served to further remove unreacted excess maleimides. The proton and carbon-13 NMR spectra of the adducts confirmed that these compounds were clean and free of **2**.

A significant impurity for each of the crude maleimides, based on proton NMR, appeared to be the compounds **5**, acetoxypyrrolidinedione derivatives of the maleimides, formally resulting from acetic acid addition to the HC═CH group of **2**. Thus, $CDCl_3$ spectra for **2a–2e** all exhibited three "double doublet" (dd) patterns attributed to an approximate AMX system. The $H_X$ proton, $CH_3CO_2CH$, deshielded by the acetoxy group and resonating at ca. 5.41 ppm, showed observed vicinal splittings of ca. 4.8 and 8.8 Hz from the diastereotopic pair of $CH_2$ protons which make up the $H_A$ and $H_M$ parts of the spectral system. The $H_M$ signal appeared near 3.15 ppm with observed $^3J = 8.8$ Hz and $^2J = 18.4$ Hz, and the $H_A$ portion was seen at ca. 2.65 ppm, with $^3J = 4.8$ Hz and $^2J = 18.4$ Hz. Additional spectral signals required for these acetoxy derivatives (for the alkyl chain and acetoxy group) contributed to the spectral complexity and signal overlaps in the $^1H$ NMR spectra for the crude maleimides. The structure of compounds **5** is shown in Fig. 1. These acetoxypyrrolidinedione derivatives have been discussed by Wang.[11]

For small scale reactions with **1**, we have found it convenient to run the reactions in screw-cap vials, leaving minimal headspace to reduce the amount of oxygen that might lead to undesired side-reactions, such as air oxidation of **1** to 9,10-dibenzoylphenanthrene by oxidative decarbonylation. (Small amounts of the free-radical trap, BHT, have sometimes been added to the reaction mixtures in an effort to suppress this oxidation and the possible free radical additions or polymerizations of maleimides, but BHT was not used for this present work.[2,3]) Potential formation of the dibenzoylphenanthrene from **1** after reaction at elevated temperatures with atmospheric oxygen has been discussed recently by Marchand et al.[12] Since the unhindered *n*-alkylmaleimides employed by us here react rapidly with **1** under mild conditions, the oxidative side reaction is not a problem.

In our hands, the isolated adducts seemed to be predominantly or exclusively single stereoisomers, presumably normal endo addition products

expected from the Diels–Alder reaction.[1,13–16] Infrared spectra for all adducts were extremely similar, with the spectrum of each adduct showing a strong band near 1790 $cm^{-1}$, consistent with the strained bridging ketone carbonyl of the adducts, implying that loss of this carbonyl had not occurred during adduct preparation or workup. Thermal decarbonylation, retro-Diels–Alder or other decomposition reactions of the phencyclone adducts are possibilities at elevated temperatures. The endo adduct stereochemistry would be consistent with the large magnetic anisotropic effects reported here for the N-alkyl protons.

The key proton NMR experiments for characterization of the adducts, **3a–3e**, were the high-resolution COSY45 spectra. For the aryl proton regions, it was possible to fully map out and assign the $(CH)_4$ system for the phenanthrenoid moiety, with H-4,5 appearing at lowest field, due to a buttressing effect and to combined anisotropic deshielding from the three rings of this aromatic system. For the unsubstituted bridgehead phenyl groups, the COSY45 spectra allowed the clear delineation of the $(CH)_5$ spin systems, unambiguously demonstrating that these phenyl rings exhibit slow rotation on the NMR timescale. The aryl protons produce nine 2H intensity signals with some partial overlaps in the 1D spectra, but the second dimension of the COSY spectra provides separated crosspeaks to confirm nine kinds of aryl protons. Crosspeaks appeared for $^3J$, $^4J$, and even $^5J$ couplings, with crosspeak intensity and "tilting" serving to confirm assignments. The 1D carbon-13 spectra for all adducts exhibited nine roughly equal intensity signals ($9 \times 2CH$) for the aryl methine pairs, confirming that bridgehead phenyl rotation is in the SEL on the $^{13}C$ NMR timescale (75 MHz) as well as on the $^1H$ NMR timescale (300 MHz). For the upfield signals of the n-alkyl groups, the $^{13}C$ NMR spectra of the phencyclone adducts were completely free from overlaps. In the $^1H$ NMR, some overlaps for the alkyl signals occurred for the chain lengths of nine or longer, and where this overlap was severe, signal complexity near the diagonal prevented precise chemical shift assignments from the COSY spectra. Full proton NMR assignments of the adducts are summarized in Table 1. Figure 2(a) and (b) shows the COSY45 spectra for the aryl and alkyl proton regions, respectively, of adduct **3a**.

Significant examples of magnetic anisotropic effects are seen for several sets of protons. For example, chemical shifts for the bridgehead phenyl protons range from about 7.20 to 8.35 ppm, a wide range for a $C_6H_5$ group connected to a bridgehead $sp^3$ carbon and bearing no substituent groups. We believe that a substantial contribution to the anisotropic effects on the phenyls is derived from the imide carbonyls. The relative shielding of H-1,8 and H-2,7 of the phenanthrenoid is largely attributed to anisotropic shielding by the bridgehead phenyls. But the most dramatic anisotropic effects in the adducts is certainly the considerable shielding of the $NCH_2\mathit{CH_2}$ protons of

the alkyl chain, with these protons absorbing at ca. −0.32 ppm, upfield of TMS. For the phencyclone adducts of the maleimides, the anisotropic shielding of the *n*-alkyl chain results in enhanced dispersion of the proton NMR shifts, so that all seven or eight of these signals are essentially distinguishable for **3a** and **3b**. With longer chain lengths, overlaps of the $CH_2$ resonances occur, from the seventh methylene outwards from the nitrogen. The observed results of anisotropic shielding in the *n*-alkyl groups of the adducts presented here are fully consistent with data observed earlier for the shorter chain systems of *n*-propyl,[4] *n*-butyl,[5] and *n*-hexyl.[2] The main significance of the current studies with longer chains is the added ability to follow the anisotropic shielding magnitudes further out in space, while avoiding or minimizing contributions from the actual chain terminus to the observed shielding magnitudes. With the corresponding maleimides, only the shifts of protons alpha to the nitrogen, i.e., $NCH_2$, and beta, i.e., $NCH_2CH_2$, can accurately be resolved; the gamma protons, $NCH_2CH_2CH_2$, already begin to form part of an envelope of absorption. Because of the chemical shift uncertainties in the maleimides, it is difficult to determine accurate estimates of the shieldings in the analogous adducts, **3**. Approximate values might be: $NCH_2$ (0.66 ppm); $NCH_2CH_2$ (1.89 ppm); $NCH_2CH_2CH_2$ (0.95 ppm), for the differences in the chemical shifts between corresponding protons in the phencyclone adducts and the maleimides. Less accurate values might be based on assuming a reference chemical shift value of ca. 1.20 ppm for the $CH_2$ groups more remote from the nitrogen, and subtracting the observed shifts seen in **3e**, to give shielding values of: $N(CH_2)_3CH_2$ (0.67 ppm); $N(CH_2)_4CH_2$ (0.49 ppm); $N(CH_2)_5CH_2$ (0.18 ppm); $N(CH_2)_6CH_2$ (0.02 ppm).

Molecular modeling calculations were initially performed using TITAN, version 1.0.5 (Wavefunction, Inc., 1999) on a Dell Pentium 4 PC with 1.4 GHz processor speed and 256 MB RAM. We have also used Spartan ′04 ESSENTIAL (v. 2.0.0, Wavefunction, Inc. ©1991–2003; October 8, 2003) on Dell Pentium 4 platforms with 2.4 (or 3.06) GHz processor speeds and 1024 MB memory. These systems potentially allow up to 200 atoms or 2000 basis functions (for the TITAN Hartree-Fock module). The calculations were run several times with each different software package to confirm reproducibility or locate the lowest energy optimized structures. Data presented here reflect the lowest energy calculations, regardless of the software or platform used.

Examination of the fully optimized structure for **3b** appears to raise a question. With the n-octyl chain oriented in a fully extended conformation away from ("anti" to) the phenanthrenoid moiety, it would seem that the protons at the "odd-numbered" positions on the alkyl chain, i.e., alpha, gamma, epsilon, etc., $NCH_2CH_2CH_2CH_2CH_2\ldots$, would be closer to the perpendicular axis of the central aryl ring of the phenanthrenoid system and thus more likely to be anisotropically shielded. It does not seem intuitively

clear that the shielding for the beta protons (relative to the maleimide nitrogen) in the adduct should be greater magnitude than for the alpha protons of the $NCH_2$. We therefore considered the alternative conformation corresponding to a structure resulting from ca. 180° rotation about the $NCH_2$ bond, so that the octyl is still fully extended but now much closer to the phenanthrenoid system. In this "syn" conformer, it would seem that the beta protons, $NCH_2CH_2$, would be optimally situated for anisotropic shielding from the phenanthrenoid group. Presumably, the actual observed NMR chemical shifts reflect a time-weighted average of the different existing conformers. It could be possible that even if this "syn" conformer is a minor contributing structure, the very high degree of anisotropic shielding for the beta protons in this structure could dominate the observed spectrum. Interconversion of the syn and anti (and other possible) conformers are expected to be fast on the NMR timescales, so that a FEL system would be seen. We have separately optimized the syn conformer at HF/6-31G* and determined that its energy was actually 0.0003622 au (0.227 kcal/mol) below that of the anti. Thus, the lowest energy fully converged structures for the anti adduct had −1853.2686667 au and for the syn adduct had −1853.2690289 au, where the calculated energies are expressed in atomic units (hartrees) [1 hartree = 627.5 kcal/mol]. Surprisingly, the syn conformer was actually slightly more stable than the anti. In view of this result, the relative anisotropic shielding magnitudes along the *n*-alkyl chain appear understandable. The significant point is that the calculated energy difference between the two conformers is very small, ca. 0.23 kcal/mol. This implies comparable contributions from both the syn (slightly predominant) and the anti conformers. Neither conformer by itself is fully consistent with experimentally observed anisotropic shielding magnitudes, which increase from the alpha to the beta alkyl protons, and monotonically decrease on going further out along the chain. Rapid interconversion of the contributing syn and anti conformers provides a straightforward way to account for observed shielding along the alkyl chain. For adduct **3b**, the optimized structures of anti and syn conformers are shown in Fig. 3(a) and (b), respectively.

Molecular modeling results for **3b**, the phencyclone adduct of *N*-*n*-octylmaleimide, showed the effects of severe repulsions of the ortho protons, H-2′,6′, of the bridgehead phenyls with: (a) the phenanthrenoid H-1,8; (b) the ketone and imide carbonyls; and (c) the bridgehead methine C*H*. These interactions must largely determine the orientations of the bridgehead phenyls. Relevant geometric parameters (distances, angles, and dihedral angles) are summarized in Tables 2 and 3. Selected interatomic distances and distances from specified atoms to defined points in the phenanthrenoid group are used to characterize the structures. "Point 1" was defined as the midpoint of the line joining C-8a and C-10a, and was regarded as the "center" of the middle ring of the phenanthrenoid system. "Point 2" was the midpoint

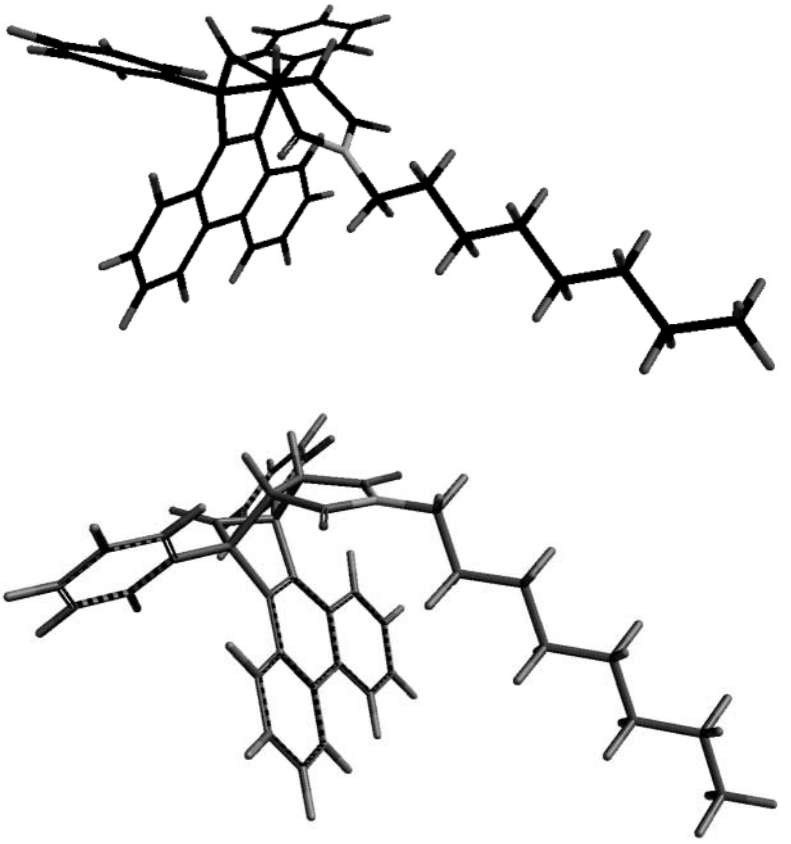

*Figure 3.* Selected HF/6-31G* optimized structures for adduct **3b**, from reaction of phencyclone with *N-n*-octylmaleimide. Upper: (a) Anti conformer of adduct **3b**. Lower: (b) Syn conformer of adduct **3b**. (*View this art in color at www.dekker.com.*)

of the bond joining C-9 and C-10. "Point 3" was the midpoint of the bond of C-4a to C-4b. "Point 4" was the midpoint of the line joining phenanthrenoid H-2 and H-7. The distance between Points 3 and 4 was an approximate indicator of the extent of puckering of the phenanthrenoid ring system; these distances were 0.273 and 0.275 Å for the anti and syn conformers, respectively. For the adduct, dihedral angles of the bridgehead phenyl groups are defined with C-2′ arbitrarily designated as proximal to the bridging ketone carbonyl. We have tabulated not only the distances from each of the hydrogens of the alkyl groups to Points 1 and 2, but also the angles defined by Point 2, Point 1, Hydrogen. These angles provide a rough measure of how close the

***Table 2.*** Geometric parameters calculated for adduct **3b**, anti and syn conformers. Distances (Å) from hydrogens of alkyl chain to reference points in phenanthrenoid system. Angles (°) from Point 2, to Point 1, to specified hydrogen.

| | Pt. 1: midpoint C-8a/C-10a line | | Pt. 2: midpoint C-9/C-10 bond | | Angles (°) | |
|---|---|---|---|---|---|---|
| Alkyl H | anti | syn | anti | syn | anti | syn |
| H-1 | 4.546, 4.547 | 5.384, 5.388 | 4.564, 4.565 | 5.168, 5.171 | 83.08, 83.09 | 73.31, 73.35 |
| H-2 | 6.405, 6.406 | 3.794, 3.799 | 6.002, 6.003 | 4.140, 4.144 | 65.57, 65.58 | 97.51, 97.60 |
| H-3 | 7.062, 7.064 | 6.255, 6.259 | 7.087, 7.089 | 6.526, 6.529 | 86.18, 86.20 | 97.22, 97.27 |
| H-4 | 8.765, 8.766 | 5.568, 5.573 | 8.485, 8.486 | 6.286, 6.289 | 72.88, 72.89 | 120.58, 120.65 |
| H-5 | 9.592, 9.593 | 7.890, 7.894 | 9.621, 9.621 | 8.453, 8.455 | 87.65, 87.66 | 113.21, 113.24 |
| H-6 | 11.207, 11.208 | 7.796, 7.799 | 10.998, 10.999 | 8.662, 8.664 | 77.10, 77.10 | 131.48, 131.53 |
| H-7 | 12.138, 12.138 | 9.928, 9.930 | 12.168, 12.168 | 10.653, 10.655 | 88.52, 88.52 | 123.21, 123.24 |
| H-8 | 13.728, 13.728 | 10.221, 10.224 | 13.566, 13.566 | 11.159, 11.161 | 79.88, 79.88 | 137.41, 137.44 |

*Notes*: Point 1 is defined as the midpoint of the line from C-8a to C-10a, and marks the approximate center of the middle ring of the phenanthrenoid system. Point 2 is the midpoint of the C-9/C-10 bond. Distances (and angles) are shown for each hydrogen of the alkyl chain, except for H-8 (of the methyl group) for which the data given refer only to the two proximal protons. Angle parameters refer to the angles defined from Point 2, Point 1, to the designated proton. Data refer to optimized geometries from HF/6-31G*calculation on the adduct of *N*-*n*-octylmaleimide. See Discussion.

***Table 3.*** Geometric parameters calculated for adduct **3b**, anti and syn conformers. Interatomic distances (Å) and dihedral angles (°) for the bridgehead phenyls.

| | anti | syn |
|---|---|---|
| Distances | | |
| O═C ketone to H-2′ | 2.724, 2.724 | 2.720, 2.724 |
| NC═O imide to H-6′ | 2.559, 2.562 | 2.556, 2.562 |
| H-1/8 to H-2′ | 3.416, 3.416 | 3.414, 3.417 |
| H-1/8 to H-6′ | 3.056, 3.057 | 3.056, 3.060 |
| H-6′ to bridgehead CH | 2.281, 2.282 | 2.283, 2.284 |
| Dihedral angles | | |
| O═C–C–C(ipso)-C-2′ | 51.92, −51.90 | 51.77, −51.93 |
| Phenanthrenoid pucker[a] | 0.273 | 0.275 |
| N pyramidalization[b] | 0.003 | 0.010 |

*Notes*: Measurements refer to atoms or groups on each side of the molecule. Signs for the dihedral angles reflect the local axial chirality, as measured. See Discussion and notes for Table 2 and for this table.

[a]Pucker is measured as the distance (angstroms) from the midpoint of the C-4a–C-4b bond (Point 3) to the midpoint of the line joining phenanthrenoid H-2 and H-7 (Point 4).

[b]Pyramidalization at the nitrogen is expressed as the distance of the nitrogen from the plane defined by the three carbons directly bonded to nitrogen.



alkyl protons are (with respect to angular measure) to the approximate perpendicular axis of the central phenanthrenoid ring, i.e., an angle of 90° would indicate that the proton lies close to the axis, where it should receive maximum anisotropic shielding with respect to the angular part of this shielding. This approximation should be valid since the hydrogens of the n-alkyl groups lie close to a plane which: (a) is perpendicular to the central ring of the phenanthrenoid system, (b) bisects the bond from C-9 to C-10, and (c) passes through Point 1 (the center of the ring). Note that the signs of the tabulated dihedral angles may reflect the sense of the axial chirality in selected portions of the structures, as optimized. Data in Tables 2 and 3 indicate considerable similarity in the anti and syn conformers with respect to the aromatic ring portions of the structures. Table 2 data show that the beta alkyl protons, $NCH_2CH_2$, are especially close to Point 1 (3.8 Å) and also lie near the perpendicular axis through Point 1 (ca. 97.5° angle) for the syn conformer, which factors would contribute to the large anisotropic shielding of these protons.

Our present ab initio HF/6-31G* calculations appear to be the highest level that has been applied to these compounds. The 6-31G basis set expresses each inner-shell basis function in terms of six Gaussians, with each valence-shell basis function split into two parts, expressed by three and one Gaussians,

respectively; this 6-31G basis set is thus a split-valence basis set.[17–19] Supplementation of the 6-31G basis set for non-hydrogen atoms by use of d-type Gaussians provides the 6-31G* basis set, a polarization basis set. In our hands, we encountered some difficulty in obtaining consistent convergence for the geometry optimizations of the phencyclone adduct with TITAN, with numerous calculations resulting in "stuck optimizations." For the anti structure, five of six calculations were "stuck" using TITAN, and for the syn conformer, two of five calculations were "stuck" when completed. In contrast, all calculations run in Spartan ′04 Essential converged smoothly and yielded lower energy final structures than the TITAN results, i.e., four calculations for anti and two for syn. Spartan results were also extremely reproducible, to within $10^{-5}$ au. The results presented here, therefore, were based on the Spartan ′04 software. [Calculation parameters included the disabling of symmetry, turning convergence ON, and (for TITAN) specifying highest accuracy cutoffs for the SCF (IACC = 1), as suggested by Wavefunction, Inc.] That these calculations for the phencyclone adducts are non-trivial is suggested by the typical CPU calculation times for these runs, ca. 25–38 hr or more, for each calculation, with no other applications running. For the adduct **3b**, 749 basis functions were involved in the optimizations. It is suggested that at least part of the convergence difficulties here are associated with rather flat energy surfaces over which slightly different rotational isomers are interconverted, making it difficult to locate true global energy minima. A few general observations that we made include: (a) some non-planarity ("puckering") of the phenanthrenoid moiety is seen in the optimized adduct structures; if this three-ring aromatic portion is regarded as having a "butterfly-like" structure, then the outer rings ("wings") are slightly folded toward the *N*-alkyl chain; (b) almost no pyramidalization at the nitrogen is seen, with the nitrogen lying within 0.003 and 0.010 Å of the plane defined by the three directly bonded carbons for the anti and syn conformers, respectively; (c) the conformations of the bridgehead phenyls relative to the ketone carbonyl is in good agreement with ab initio HF/6-31G* calculations performed on some phencyclone adducts derived from *N*-arylmaleimides,[20] ca. 52° for the O=C–C–C(ipso)–C > (2′) dihedral angle magnitudes. A reviewer has suggested low-temperature NMR or nuclear Overhauser effect (NOE) experiments as potentially informative to gain further insight into the adduct structures and behavior.



## CONCLUSIONS

The hindered Diels–Alder adducts, **3**, from phencyclone, **1**, have been prepared using a series of *N*-*n*-alkylmaleimides, with n-alkyl chain lengths

ranging from heptyl to dodecyl. Ambient temperature NMR spectra for $CDCl_3$ solutions of the adducts showed slow rotation of the unsubstituted bridgehead phenyl groups on both the proton NMR timescale (300 MHz) and the carbon-13 NMR timescale (75 MHz), with SEL $^1H$ and $^{13}C$ NMR spectra. Full aryl proton assignments in the adducts were achieved using high-resolution COSY45 spectra; extensive assignments in the alkyl portions were also achieved, limited only by a small amount of signal overlaps for the longest chains. Estimates of anisotropic shielding magnitudes of the alkyl groups in the adducts were obtained by comparing $^1H$ chemical shifts for corresponding alkyl protons in the maleimides and their phencyclone adducts. Maximum shielding magnitude was found for the alkyl protons beta to the nitrogen, with the $NCH_2CH_2$ protons in the adducts appearing about 1.89 ppm to higher field (i.e., at ca. −0.32 ppm, upfield of TMS) than in the maleimides. Ab initio molecular modeling calculations for the *N-n*-octylmaleimide adduct of phencyclone were performed to allow estimates of geometric parameters in this adduct, and results indicated that the syn conformation (of alkyl relative to phenanthrenoid) was actually 0.23 kcal/mol lower in energy than the anti conformer (in which the chain was directed away from the phenanthrenoid moiety).



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