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^{1}H, ^{13}C, and ^{19}F NMR studies of phencyclone adducts of *N*-(polyhalophenyl)maleimides: evidence for dynamic NMR in maleamic acids Ab initio calculations for optimized structures

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Abstract

NMR methods, including one- and two-dimensional techniques (at 7.05 T) for ^{1}H, ^{13}C and ^{19}F, have been applied to studies of hindered rotations and magnetic anisotropy in some crowded Diels–Alder adducts of phencyclone (**1**). Symmetrically substituted *N*-aryl maleimides (**2**) bearing numerous halogens on the *N*-aryl ring, were employed as dienophiles to form the target adducts (**3**). The maleimides included: *N*-(4-bromo-2,6-difluorophenyl)maleimide (**2a**); *N*-(2,3,5,6-tetrafluorophenyl)maleimide (**2b**); *N*-(4-bromo-2,3,5,6-tetrafluorophenyl)maleimide (**2c**); *N*-(2,3,4,5,6-pentachlorophenyl)maleimide (**2d**); and *N*-(2,4,6-tribromophenyl)maleimide (**2e**). Maleimides (**2a**–**2c**) were prepared from the precursor *N*-aryl maleamic acids (**5a**–**5c**). Ambient temperature fluorine-19 NMR of these maleamic acids in d_6-acetone showed substantial unusual peak broadening consistent with intermediate exchange rate processes, which may correspond to the *N*-aryl rotation process. Maleimides (**2d**) and (**2e**) were produced in one step from pentachloroaniline or 2,4,6-tribromoaniline, respectively, and maleic anhydride with anhydrous $ZnCl_2$ at ca. 200 °C. For the adducts (**3**), we observed slow exchange limit spectra on the ^{1}H, ^{13}C, [and ^{19}F, for (**3a**–**3c**)] NMR timescales for the rotation of the *unsubstituted* bridgehead phenyls about the C(sp^3)–C(sp^2) bonds, and for the rotations of the *N*-aryl rings about the N(sp^2)–C(aryl sp^2) bonds. Ab initio calculations for geometry optimizations at the Hartree–Fock level with 6-31G* (or LACVP*) basis sets were performed for the adducts. We believe that this is the first report of detailed ^{1}H, ^{13}C, and ^{19}F NMR data for a substantial collection of *N*-aryl maleamic acids, maleimides and their phencyclone adducts bearing multiple fluorines or other halogens directly on the *N*-aryl ring, together with complementary quantitative geometric parameters from high-level HF/6-31G* (or LACVP*) calculations.

Keywords: Hindered rotations; Magnetic anisotropy; Dynamic NMR; One- and two-dimensional (1D and 2D) NMR; COSY; HETCOR; Hartree–Fock; Molecular modeling

1. Introduction

This report presents the first compilation of the results of ab initio calculations (Hartree–Fock level) together with multinuclear NMR studies of hindered systems derived from phencyclone (**1**), by Diels–Alder additions with symmetrically substituted halogen-containing *N*-aryl maleimides, bearing multiple fluorine, chlorine and/or bromine atoms directly on the *N*-aryl ring. Phencyclone is well known as an effective diene component for Diels–Alder cycloaddition reactions [1] and *N*-substituted maleimides (**2**), are excellent

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dienophiles with (**1**) [2]. The normally expected *endo* stereochemistry for the Diels–Alder adducts (**3**), results in highly hindered systems. (Fig. 1 shows the relevant structures and synthetic pathways.) Slow exchange limit (SEL) ^{1}H and ^{13}C NMR spectra at ambient temperatures were observed for hindered rotations about the C(sp^2)–C(sp^3) bonds to the *unsubstituted* bridgehead phenyls in the adducts, using medium field strength NMR spectrometers, e.g., ca. 200–300 MHz for proton and 50–75 MHz for carbon-13 [3–7]. When the adducts are formed from *N*-aryl maleimides, potential hindered rotations about the N(sp^2)–C(aryl sp^2) bonds in the *N*-aryl moieties could be examined [8]. With the *endo* adduct stereochemistry, striking examples of magnetic anisotropic shielding effects may be observed as a result of proximity of the *N*-aryl substituent to the phenanthrenoid group of the adduct [9,10]. Modern molecular modeling software for ab initio calculations of optimized adduct structures has been used to gain insight into adduct geometries [10,11]. When fluorine atoms are incorporated into the *N*-aryl substituent, NMR studies of (**3**) can be extended to a third nucleus, ^{19}F [12]. These present and ongoing studies are broadly aimed at obtaining a better understanding of molecular motions (especially hindered rotations) and the geometric aspects of magnetic anisotropic effects.

2. Experimental

General NMR and other techniques were described earlier [2,13]. Spectra were obtained on a Bruker ACF300 NMR spectrometer (7.05 T magnet) at 300 MHz for ^{1}H, 75 MHz for ^{13}C, and 282 MHz for ^{19}F, using the QNP (quad nuclear probe) and Aspect 3000 data system. Acquisitions were performed at ambient temperatures in $CDCl_3$ unless otherwise noted, e.g., d_6-acetone for maleamic acids. Proton shifts were referenced to internal tetramethylsilane, TMS, at 0.0 ppm. Carbon-13 shifts were referenced to the center line of the $CDCl_3$ triplet at 77.0 ppm (or to internal TMS at 0.0 ppm with other solvents). Fluorine spectra were referenced to internal $CFCl_3$ at 0.0 ppm. Standard Bruker microprograms were routinely used for two-dimensional (2D) ^{1}H–^{1}H and ^{19}F–^{19}F homonuclear chemical shift correlation NMR by COSY45, and for the 2D ^{1}H–^{13}C heteronuclear HETCOR. NMR signal multiplicities are abbreviated as: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Q refers to quaternary non-protonated aryl carbon signals. High resolution COSY spectra for the aryl proton regions typically employed 256 increments in the t_1 dimension with spectral widths of ca. 600 Hz, e.g., the regions from about 6.8–8.8 ppm. In listing the ^{1}H NMR data, we generally show gross multiplicities, d or t, for signals of the bridgehead phenyls and phenanthrenoid moieties, without explicitly listing the observed vicinal splittings, which were in the normal range, ca. 8 Hz (or the smaller long-range splittings that could be seen). For routine one-dimensional (1D) spectra, we used relaxation delays (RD) of 1 s for ^{1}H, 3 s for ^{13}C, and 5 s for ^{19}F. Because of extensive splitting of some carbon signals by fluorine, not all non-protonated carbons produced positively observable absorptions, even though we routinely used 15,000–17,000 FID acquisitions (i.e., number of scans, NS) for the 1D ^{13}C NMR. For two of the adducts (**3d**) and (**3e**), 1D ^{13}C NMR spectra were obtained, using RD values of 1, 5 and 60 s, and the number of scans was as high as 27,000. [*Note*: Further details regarding interpretations and assignments of the NMR spectra are presented in the Section 3 for most compounds, including maleamic acids (**5a**–**5c**); maleimides (**2d**) and (**2e**); and adducts (**3a**–**3e**), and should be consulted in conjunction with the brief summary details that are included below in this Section 2.] Solvents and reagents were obtained from Aldrich Chemical (Milwaukee, WI) and were used without further purification. Melting points were obtained on Mel-Temp apparatus (Laboratory Devices, Cambridge, MA) and are uncorrected. Infrared (IR) spectra for two of the adducts, were obtained on Type 61 (polyethylene) 3M Disposable IR Cards; only stronger peaks are reported, and peaks in the 2800–3000 cm^{-1} region in which the cards absorb strongly have been omitted. Spectra were acquired on a Perkin-Elmer 1640 instrument with DTGS detector, using 4 cm^{-1} resolution. For computational studies, Spartan '04 for Windows (full version, v.1.0.0 ©1991–2003; 17 September 2003) or Spartan '04 Essential (v.2.0.0 ©1991–2003; 8 October 2003) was obtained from Wavefunction Inc., Irvine, CA and installed on Dell Pentium 4 platforms with processor speeds of 2.26 or 3.06 GHz, using 512 or 1024 MB memory. Calculation parameters included turning symmetry OFF and convergence ON.

2.1. Syntheses of maleamic acids

The maleamic acids (**5a**–**5c**) were prepared by similar procedures, from maleic anhydride and the corresponding substituted anilines (**4a**–**4c**), as shown in Fig. 1. Details of the synthesis of (**5a**) are given as an illustrative procedure (see Section 3 for further details regarding NMR spectra of compounds (**5a**–**5c**)).

2.2. *N*-(4-Bromo-2,6-difluorophenyl)maleamic acid (*5a*)

A solution of 4-bromo-2,6-difluoroaniline (1.024 g, 4.924 mmol) in ca. 30 mL CH_2Cl_2 was added dropwise with magnetic stirring to a suspension of maleic anhydride (0.490 g, 4.997 mmol) in 30 mL CH_2Cl_2. After 30 min at room temperature, solvent removal gave the crude maleamic acid as an off-white crystalline solid (1.340 g, 89% yield, mpr 170–172 °C), used without further purification (see Section 3 for further details of NMR). ^{1}H NMR (d_6-acetone, ppm): 10.14 (1H, br s, NH); 7.46 (2H, approx. d, apparent ^{3}J(HCCF) = 7.14, aryl H); 6.78 (1H, d, ^{3}J = 12.71, half of AB

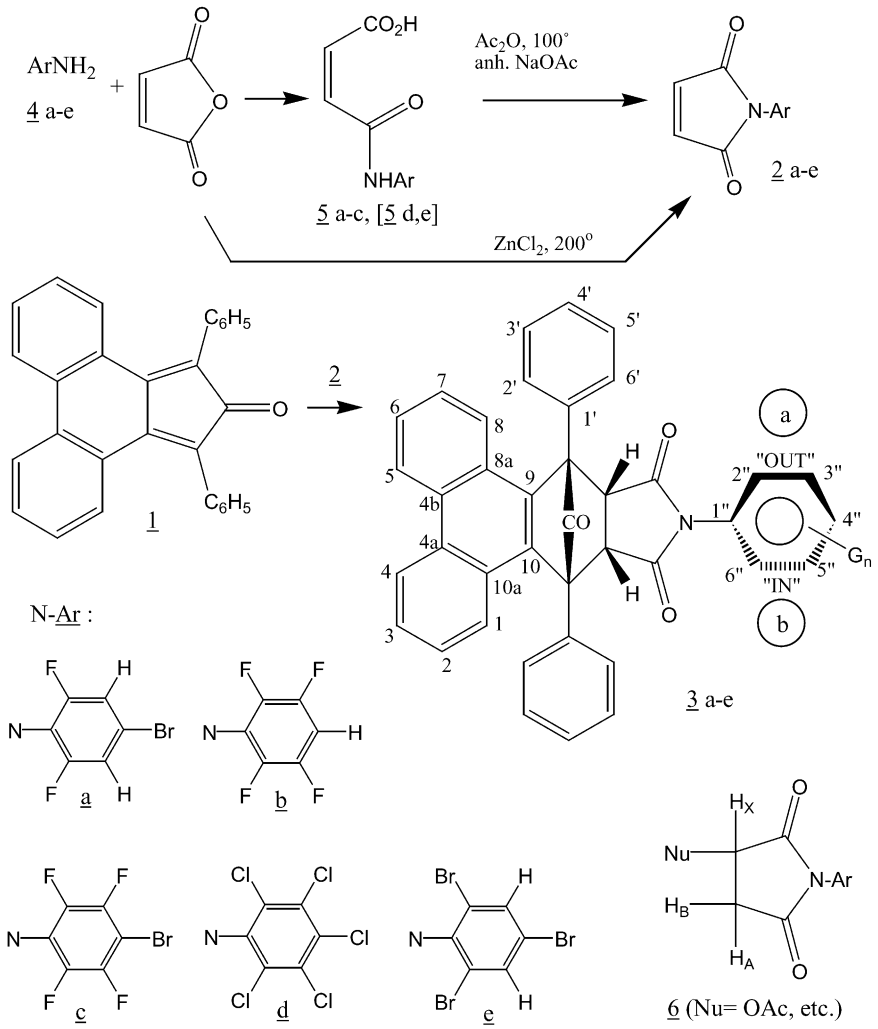

Fig. 1. Summary of synthetic routes with general compound structures and atom numbering. Syntheses of the maleamic acids and maleimides are shown at the top. Formation of the adducts (**3a**–**3e**), from phencyclone with the respective maleimide, together with atom numbering for the adducts, is shown across the center of the Figure. The halogen substitution patterns of the *N*-aryl rings in each series of compound (**a**–**e**) is shown at the lower left of the Figure. The general structure of the acetoxypyrrolidinone impurities (**6**), observed by NMR in some samples of the maleimides (**2a**–**2c**), appears at the bottom right.

q, *cis* HC=CH); 6.47 (1H, d, ^3J = 12.69, half of AB q, *cis* HC=CH). ^{19}F NMR (d_6-acetone): −114.87 (slightly broadened apparent d, ^3J = 8.29).

2.3. N-(2,3,5,6-Tetrafluorophenyl)maleamic acid (5b)

Prepared analogously to (**5a**), above, the crude maleamic acid was washed with hexane and dried to give pure white crystals of the maleamic acid (mpr 117–119.5 °C, lit. mp 121 °C [14]). On standing, a second crop was obtained, collected by vacuum filtration, washed with cold hexane, and dried, to give a tan solid (combined total 61% yield; see Section 3 for further details of NMR). ^{1}H NMR (d_6-acetone): 10.25 (1H, br s, NH); 7.55 (1H, tt, J = 10.46 and 7.33, aryl H); 6.76 (1H, d, *cis* ^3J = 12.58, half of AB q, HC=CH); 6.46 (1H, d, *cis* ^3J = 12.59, half of AB q, HC=CH). ^{19}F NMR (d_6-acetone): −140.25 (2F, q, J = 10.5); −144.99 (2F, br s).

2.4. N-(4-bromo-2,3,5,6-tetrafluorophenyl)maleamic acid (5c)

Prepared analogously to (**5a**), above, after standing at ambient temperature (1 week) with slow evaporation of solvent, the crude maleamic acid crystals were obtained (97% yield) mpr 129–135 °C, used directly for conversion to the maleimide (see Section 3 for further details of NMR). ^{1}H NMR (d_6-acetone): 10.27 (1H, very broad s, NH); 6.75 (1H, d, ^3J = 12.52, *cis*, HC=CH, half of AB q); 6.47 (1H, d, ^3J = 12.53, *cis*, HC=CH, half of AB q). ^{19}F NMR (d_6-acetone): −135.01 (2F, slightly broadened symmetrical complex m, −143.18 (2F, very broad d, apparent J = 18.3).

2.5. Syntheses of maleimides

The maleimides (**2a**–**2c**) were prepared by similar procedures, from the respective maleamic acids (**5a**–**5c**),

by reaction in acetic anhydride (boiling water bath), promoted with anhydrous NaOAc. The illustrative procedure for (**2a**) is given in detail. For maleimides (**2d**) and (**2e**), direct one-step high-temperature reactions (ca. 200 °C) were used, with the corresponding anilines (**4d**) or (**4e**), in maleic anhydride as solvent, promoted by anh. $ZnCl_2$. The detailed procedure for preparation of (**2d**) is given below (see Section 3 for further details regarding NMR spectra of compounds (**2d**) and (**2e**)).

2.6. *N-(4-Bromo-2,6-difluorophenyl)maleimide (**2a**)*

The crude maleamic acid (**5a**) (565.3 mg, 1.847 mmol), acetic anhydride (20 g), anhydrous sodium acetate (20 mg) and 2,6-di-*t*-butyl-4-methylphenol (BHT, ca. 3 mg) were placed in a flask fitted with reflux condenser topped by a drying tube and heated in a boiling water bath for 1.2 h. The dark reddish-brown mixture was cooled and quenched with ice water, extracted with CH_2Cl_2 and washed repeatedly with water, 5% $NaHCO_3$, and brine. The organic layer was separated and dried, and solvent was removed (rotary evaporator). The resulting solid was recrystallized from toluene to give light tan needles of the maleimide (210 mg, 39.5% yield, mpr 107.5–112 °C), which was used for subsequent reaction with phencyclone. ^{1}H NMR ($CDCl_3$, ppm): 8.05 (1H, very br s, NH); 7.23–7.29 (2H, complex symmet. m, aryl H); 6.94 (2H, s, HC=CH). Note trace of acetoxypyrrolidinedione with three equal area dd signals: 5.66 (dd, ^3J = 5.3 and ^3J = 9.0, H_X); 3.40 (dd, ^2J = 18.75, ^3J = 8.82, H_B); 2.95 (dd, ^2J = 18.75, ^3J = 5.15, H_A). ^{19}F NMR: −115.16 (s, aryl F).

2.7. *N-(2,3,5,6-Tetrafluorophenyl)maleimide (**2b**)*

Prepared analogously to (**2a**), above. The crude maleamic acid (**5b**) (1.910 g, 7.26 mmol), anh. sodium acetate (243 mg, 2.96 mmol) and acetic anhydride (ca. 2.5 mL) were heated in a boiling water bath for 30 min, becoming dark reddish-black, and allowed to cool to room temperature and stand for 3 days. The mixture was transferred to a separatory funnel with water (25 mL) and CH_2Cl_2 (25 mL), and the organic layer was repeatedly washed with water, aqueous $NaHCO_3$ and water. After drying (anh. $MgSO_4$), solvent removal from the organic layer gave the crude maleimide as an off-white solid (1.206 g, 67% crude yield) mpr 124–132 °C, lit. mp 137° [14], used directly for adduct formation. ^{1}H NMR: 7.23 (1H, tt, J = 9.69 and 7.25, aryl H); 6.98 (2H, s. HC=CH). Also present were signals consistent with ca. 35% of the acetoxypyrrolidinedione: 5.67 (1H, dd, ^3J = 8.92 and 5.20, H_X); 3.44 (1H, dd, ^2J = 18.55, ^3J = 8.95, H_B); 3.00 (1H, dd, ^2J = 18.59, ^3J = 5.21, H_A); 2.22 (3H, s, OAc). ^{19}F NMR: −138.11 (2F, complex mult.); −143.98 (2F, complex mult.); plus impurity peaks.

2.8. *N-(4-Bromo-2,3,5,6-tetrafluorophenyl)maleimide (**2c**)*

Prepared analogously to (**2a**), above. The crude maleamic acid (**5c**) (1340 mg, 3.918 mmol) prepared above, was combined with anh. sodium acetate (90 mg, 1.10 mmol) and ca. 4 mL acetic anhydride. After heating in a boiling water bath for 30 min, the dark reddish-brown mixture was cooled and transferred to a separatory funnel with 50 mL H_2O and 50 mL CH_2Cl_2. After extensive washings as above, the yellowish solution was treated with decolorizing carbon, and filtered through a Celite pad. Solvent removal gave the crude beige maleimide (557 mg, 1.72 mmol, 44% yield) mpr 80–90 °C, used for adduct formation. ^{1}H NMR: 6.99 (2H, s, HC=CH). In addition to the maleimide signal, three dd resonances were observed, consistent with ca. 8% impurity acetoxypyrrolidinedione: 5.65 (1H, dd, ^3J = 8.95 and 5.20, AcOC*H*, H_X); 3.44 (1H, dd, ^2J = 18.58, ^3J = 8.97, H_B); 3.01 (1H, dd, ^2J = 18.60, ^3J = 5.22, H_A). ^{19}F NMR: −132.04 (2F, complex symmetr. m [eight lines]); −142.50 (2F, complex symmetr. m [eight lines]). Each eight-line multiplet was sharp, and the two multiplets were essentially identical.

2.9. *N-(2,3,4,5,6-Pentachlorophenyl)maleimide (**2d**)*

2,3,4,5,6-Pentachloroaniline (1.3254 g, 5.00 mmol), maleic anhydride (2.5196 g, 25.69 mmol) and anhydrous $ZnCl_2$ (350.2 mg, 5.270 mmol) were combined in a test tube and maintained at ca. 200 °C for 65 min, using a thermometer to monitor the temperature and provide mixing. After cooling to room temperature, the material was transferred with ca. 100 mL boiling water to an erlenmeyer flask, heated further (steam bath) and allowed to cool and crystallize. The resulting crude light beige maleimide had mpr 138–153 °C, lit. 152° [15], 1.546 g, 4.48 mmol, 89.6% yield (see Section 3 for further details of NMR). ^{1}H NMR: 6.96 (H–C=C–H). ^{13}C NMR: 167.00 (imide C=O); 134.88 (H–C=C–H); 135.85 very weak (Q); 133.82 (Q); 132.52 (Q); 127.95 very weak (Q).

2.10. *N-(2,4,6-Tribromophenyl)maleimide (**2e**)*

Prepared analogously to (**2d**), above. 2,4,6-Tribromoaniline (2.6528 g, 8.04 mmol), maleic anhydride (5.0085 g, 51.08 mmol) and anhydrous $ZnCl_2$ (686.4 mg, 5.037 mmol) were maintained at ca. 190–200 °C for 75 min, using a thermometer to monitor the temperature and provide occasional mixing. (A bath of boiling ethylene glycol, bp 196–198°, was used to provide a stable heat source.) Following workup as for (**2d**), the resulting crude tan maleimide had mpr 129–135 °C, lit. 142° [15], 2.9562 g, 7.21 mmol, 89.7% yield (see Section 3 for further details of NMR). ^{1}H NMR: 7.82 (2H, s, aryl H); 6.91 (2H, s, HC=CH). Ca. 3% or less of pyrrolidinedione impurities were seen based on small dd resonances at: 4.85 (1H, dd, ^3J = 8.47, 3.83, H_X); 3.56 (1H, dd, ^2J = 18.89, ^3J = 8.66, H_B); 3.17 (1H, dd, ^2J = 18.92, ^3J = 3.77, H_A). ^{13}C NMR: 167.34 (approx. t, J = 9.49, imide); 135.05 (2 × CH, dd, ^1J = 175.57, ^3J = 6.21, aryl H3,5); 134.66 (2 × CH, dd, ^1J = 185.13, ^2J = 2.34, HC=CH); 129.84 (very weak, t, ^3J = 7.73, *ipso* NC1); 125.73

(weak, t, ^2J = 2.27, 2 × CBr, C2,6); 124.73 (very weak, t, ^2J = 4.09, 1 × CBr, C4).

2.11. Syntheses of phencyclone adducts

Similar procedures were used for the five adducts (**3a**–**3e**), and illustrative details are provided for (**3a**) and (**3b**) with noteworthy differences cited for the other adducts (see Section 3 for further details regarding NMR spectra of compounds (**3a**–**3e**)).

2.12. N-(4-Bromo-2,6-difluorophenyl)maleimide adduct (3a)

An excess of the crude 4-bromo-2,6-difluorophenylmaleimide (114.3 mg, 0.397 mmol) and phencyclone (76.4 mg, 0.200 mmol) were refluxed in 25 mL toluene. The dark green–black phencyclone color was discharged in 20 min to give a clear yellow solution. Solvent removal by rotary evaporator gave the crude adduct which was recrystallized from ethanol to give white solid (45 mg, 34% yield), mpr 273–280 °C (dec. with darkening and gas evoln., see Section 3 for further details of NMR). ^{1}H NMR ($CDCl_3$, ppm): 8.67 (2H, d, H4,5); 8.31 (2H, d, H2′); 7.71 (2H, t, H3′); 7.53 (4H, t, H4′ and H3,6); 7.43 (2H, t, H5′); 7.12–7.23 (6H, m, including H6′ at 7.22, H2,7 at 7.19, H1,8 at 7.14); 7.01 (1H, d, ^{3}J(HCCF) = 8.57, H3″); 6.59 (1H, d, ^3J(HCCF) = 8.08, H5″); 4.69 (2H, s, sp^3). ^{13}C NMR: 195.92 (ketone); 171.62 (imide); 157.50 (dd, C2″); 157.23 (dd, C6″); 133.56 (Q); 133.18 (Q); 131.72 (Q); 131.00 (C6′); 129.40 (C3′); 128.94 (C2′); 128.66 (C5′); 128.50 (C4′ or 3,6); 127.03 (C3,6 or 4′); 126.48 (C2,7); 126.21 (Q); 125.77 (C1,8); 123.37 (t, C1″); 123.00 C4,5); 116.10 (C3″); 115.69 (C5″); 103.58 CBr); 63.55 (C_6H_5–*C*); 45.54 (2 × sp^3). Two weak apparent dd patterns appear at low field, ca. 159.1 and 155.6 ppm. ^{19}F NMR: −115.705 (1F, s); −115.816 (1F, s).

2.13. N-(2,3,5,6-Tetrafluorophenyl)maleimide adduct (3b)

The crude maleimide (**2b**), produced as above, was used in excess. Thus, 904 mg (3.69 mmol) of the maleimide and 318 mg (0.832 mmol) of phencyclone were combined with a magnetic stirbar in a small screw-cap vial with Teflon®-lined cap, with sufficient CH_2Cl_2 (ca. 15 mL) to bring the level of the reaction mixture to within 2–3 mm of the vial lip. After tightly capping the vial and stirring at ambient temperature for 3 days, the intense green–black color of the phencyclone was discharged. The resulting light-colored solid was collected by vacuum filtration, washed with hexane and dried to give the crude adduct (471 mg, 90% yield); a portion recrystallized from ethanol had mpr 262–268 °C (dec., gas evoln.). IR (cm^{-1}): 1793.8; 1731.5; 1521.8; 1498.5; 1448.0; 1347.6; 1262.0; 1179.4; 940.2; 775.7; 753.4; 724.0; 698.3; 633.3 (see Section 3 for further details of NMR). ^{1}H NMR: 8.68 (2H, d, H4,5); 8.28 (2H, d, H2′); 7.71 (2H, approx. t, H3′); 7.53 (4H, approx. t, H4′ and 3,6); 7.43 (2H, approx. t, H5′); 7.11–7.24 (6H, m, including H6′ at 7.23, H2,7 at 7.20, H1,8 at 7.13); 6.88 (1H, tt, *J* = ca. 9.7 and 7.1, C_6F_4H); 4.69 (2H, 2 × sp^3). ^{13}C NMR: 195.74 (ketone C=O); 171.30 (imide NC=O); weak multiplets ca. 147.19, 143.84 and 140.38; 135.24 very weak (assigned to trace impurity of maleimide HC=CH); 133.39 (Q); 133.07 (Q); 131.73 and 131.71 (poss. split peak? Q); 130.96 (2 × CH); 129.40 (2 × CH); 128.82 (2 × CH); 128.68 (2 × CH); 128.54 (2 × CH); 127.14 (2 × CH); 126.53 (2 × CH); 126.08 and 126.07 (poss. split peak? Q); 125.61 (2 × CH); 123.12 (2 × CH); very weak multiplet ca. 111.1; 107.27 (1 × CH, t, *J* = 22.6, C4″); 63.51 (C_6H_5–*C*); 45.67 (2 × CH, sp^3). ^{19}F NMR: −137.77 (1F, dd, *J* = 21.85 and 11.52); −138.69 (1F, dd, *J* = 21.87 and 11.75); −144.15 (1F, ddd, *J* = 21.83, 11.59, 5.34); −144.57 (1F, ddd, *J* = 21.83, 11.59, 5.34).

2.14. N-(4-Bromo-2,3,5,6-tetrafluorophenyl)maleimide adduct (3c)

Similar to the procedure for (**3b**), phencyclone (114 mg. 0.298 mmol), excess crude maleimide (207 mg, nominal 0.639 mmol), and CH_2Cl_2 (ca. 15 mL) were combined in a screw-cap vial and stirred overnight. The intense dark green–black phencyclone color was discharged to give a pale yellow supernatant and some solid. Partial solvent removal, filtration, washings with ice-cold hexanes and drying gave the crude adduct as a white solid (90.6 mg, 30.4%) mpr 260–262 °C (gas evoln. and dec.) IR (cm^{-1}): 1793.6 (strained ketone C=O); 1731.3; 1497.3; 1448.2; 1351.5; 1268.6; 1219.7; 1176.4; 978.2; 777.1; 756.0; 724.7; 698.6 (see Section 3 for further details of NMR). ^{1}H NMR: 8.69 (2H, d, H4,5); 8.28 (2H, d, H2′); 7.72 (2H, t, H3′); 7.54 (4H, t, overlap of H3,6 and H4′); 7.44 (2H, t, H5′); 7.11–7.23 (6H, complex m, including H6′ at 7.23, H2,7 at 7.20 and H1, 8 at 7.14); 4.73 (2H,s, 2 × sp^3). ^{13}C NMR: 195.65 (ketone C=O); 171.12 (imide NC=O); four very weak multiplets at ca. 146.3, 144.1, 143.0 and 140.6; 133.33 (Q); 133.04 (Q); 131.72 and 131.71 (tentative split peak, apparent *J* = 0.86, Q); 130.96 (2 × CH); 129.43 (2 × CH); 128.77 (2 × CH); 128.71 (2 × CH); 128.58 (2 × CH); 127.21 (2 × CH); 126.56 (2 × CH); 126.04 (Q); 125.62 (2 × CH); 123.13 (2 × CH); 109.90 (tentative, very weak possible t, apparent *J* ca. 16, possible C1″); 102.02 (t, *J* ca. 22, C4″); 63.53 (C_6H_5–*C*); 45.73 (2 × CH). ^{19}F NMR: −131.68 (1F, ddd, *J* = 22.58, 9.11 and 4.20); −132.61 (1F, ddd, *J* = 22.67, 9.34 and 4.20); −142.69 (1F, ddd, *J* = 22.67, 9.10 and 5.77); −143.03 (1F, ddd, *J* = 22.53, 9.30 and 5.74).

2.15. N-(2,3,4,5,6-Pentachlorophenyl)maleimide adduct (3d)

As for (**3b**) above, in a small screw-cap vial with Teflon®-lined cap was placed phencyclone (382.1 mg, 0.999 mmol), CH_2Cl_2 (ca. 15 mL) and a slight excess of the pentachlorophenylmaleimide (prepared as above, 362.7 mg, 1.051 mmol). The vial was capped and stirred at ambient

temperature for 3 days. The intense dark green–black phencyclone color had decolorized to give a light yellow solution. After partial solvent removal, the resulting solid was collected, washed with cold CH_2Cl_2 and dried to give the crude tan adduct (680.2 mg, 93.4% yield), mpr 267–270 °C (early shrinkage, gas evoln. and dec, see Section 3 for further details of NMR). ^{1}H NMR: 8.69 (2H, d, H4,5); 8.32 (2H, d, H2′); 7.72 (2H, approx. td, H3′); 7.56 (H3,6) overlapped with 7.54 (H4′) to give a 4H approx. t; 7.43 (2H, approx. td, H5′); 7.14–7.25 (6H, m, including H2,7 at 7.21, H6′ at 7.20, and H1,8 at 7.16); 4.74 (2H, s, 2 × sp^3). ^{13}C NMR: 195.31 (ketone C=O); 171.41 (imide NC=O); 135.52 (very weak, Q, CX); 134.86 (very weak, trace impurity of maleimide HC=CH); 133.425 (2Q); 133.402 (2Q); 132.84 (very weak, Q, CX); 132.37 (very weak, Q, CX); 131.91 (very weak, Q, CX); 131.73 (2Q); 131.40 (very weak, Q, CX); 130.94 (2 × CH); 129.42 (2 × CH); 128.93 (2 × CH); 128.65 (2 × CH); 128.55 (2 × CH); 128.27 (very weak, Q, CX); 127.33 (2 × CH); 126.74 (2 × CH); 126.57 (2Q); 125.91 (2 × CH); 122.99 (2 × CH); 63.59 (C_6H_5–*C*); 45.61 (2 × sp^3 CH).

2.16. N-(2,4,6-Tribromophenyl)maleimide adduct (*3e*)

As for the preparation of (**3d**), phencyclone (382.0 mg, 0.999 mmol), a slight excess of the tribromophenylmaleimide (prepared as above, 430.7 mg, 1.051 mmol), and CH_2Cl_2 were stirred at ambient temperature for 7 days in a small capped vial. The intense dark green–black phencyclone color was largely discharged to give a light beige solution. After partial solvent removal, the resulting solid was collected, washed with cold CH_2Cl_2 and dried to give the crude pale tan adduct (706.5 mg, 89.0% yield), mpr 224–234 °C (early shrinkage, gas evoln. and dec, see Section 3 for further details of NMR). ^{1}H NMR: 8.63 (2H, d, H4,5); 8.36 (2H, d, H2′); 7.72 (2H, td, H3′); 7.64 (1H, d, ^4J = 1.98, ''outer'' H of *N*-aryl); 7.53 (4H, approx. t, overlap of H3,6 and H4′); 7.42 (2H, approx. td, H5); 7.16–7.24 (7H, complex m, including ''inner'' H of *N*-aryl at 7.23; H2,7 at 7.21; H6′ at 7.20; H1,8 at 7.19); 4.71 (2H, s, 2 × CH, sp^3). Traces of maleimide and pyrrolidinedione impurities appeared to be present. ^{13}C NMR: 195.36 (ketone); 171.65 (imide); 134.90 (1 × CH); 134.43 (1 × CH); 133.64 (2Q); 133.55 (2Q); 131.85 (2Q); 130.93 (2 × CH); 130.45 (1Q); 129.39 (2 × CH); 129.09 (2 × CH); 128.59 (2 × CH); 128.48 (2 × CH); 127.21 (2 × CH); 126.86 (2Q); 126.69 (2 × CH); 126.14 (2 × CH); 124.43 (1Q); 124.40 (1Q); 123.48 (1Q); 122.74 (2 × CH); 63.58 (C_6H_5–*C*); 45.53 (2 × CH, sp^3).

3. Results and discussion

3.1. Syntheses and NMR interpretation

(Note that specific discussions, where appropriate, of NMR interpretation (and rationales for assignments) for most of the compounds prepared here are presented below in this Section 3. The discussions of the selected compounds are arranged in the same order as for their syntheses in the Section 2, with the maleamic acids (**5**), first; followed by the maleimides (**2**); and the phencyclone adducts (**3**), last.)

The desired maleimides (**2**), are generally accessible according to Fig. 1. The top of Fig. 1 shows the reaction of maleic anhydride with the appropriately substituted anilines (**4a**–**4e**). (Specific substitution patterns of the aniline *N*-aryl rings are shown at the lower left of the Figure.) In the more standard two-step approach, the substituted aniline (**4**), is condensed with maleic anhydride at mild temperatures to give the corresponding maleamic acids, e.g. (**5a**–**5c**), as isolated intermediates. A separate cyclodehydration step, as with anh. sodium acetate in acetic anhydride at ca. 90–100 °C, converts the maleamic acids (**5a**–**5c**), to the maleimides (**2a**–**2c**). With anilines of low basicity or reduced reactivity, direct reaction at high temperature (ca. 180–200 °C) of, e.g. (**4d**) or (**4e**), with maleic anhydride (without solvent, in the presence of an acid catalyst, e.g., anh. $ZnCl_2$) can give (**2d**) or (**2e**) directly, in one step, without isolation of the maleamic acids (**5**). In the two-step method, using NaOAc/Ac_2O for the cyclodehydration, we frequently found a common impurity in the crude product maleimides. This impurity (**6**) (shown at the bottom right of Fig. 1), characterized by NMR, would formally correspond to an acetic acid addition product of (**2**), an acetoxypyrrolidinedione [16]. In the absence of acetic anhydride/sodium acetate, other nucleophiles could potentially add to maleimides to give corresponding pyrrolidinediones.

Infrared (IR) spectra of two representative phencyclone adducts were obtained to confirm the presence of the sharp band ca. 1794 cm^{-1}, attributed to the strained ketone carbonyl stretch. This band would imply that undesired decarbonylation of the C=O has not occurred during the reactions or workup procedures. Phencyclone adducts at elevated temperatures can potentially undergo decarbonylation, retro-Diels–Alder reactions, etc. We did not see NMR spectral evidence for the potential stereoisomer, i.e., the *exo* adducts, in our isolated products. Recent X-ray studies of some phencyclone adducts have confirmed the *endo* configuration normally preferred for Diels–Alder adducts [17–19].

The presence of fluorine in a molecule potentially complicates the ^{1}H and ^{13}C NMR spectra because of the spin–spin couplings, *J*(HF) or *J*(CF). For ^{13}C NMR, this splitting by ^{19}F can be especially problematic because the splitting leads to lower signal-to-noise ratios for each component of the resulting carbon multiplet signal; particularly for [normally weak] signals of non-protonated carbons, signal detection is more difficult. (Our NMR spectrometer system does not allow for fluorine decoupling.) Adding to this problem was the rather low $CDCl_3$ solubility of most of the adducts. (Note that precursor maleamic acids also exhibited low $CDCl_3$ solubility; d_6-acetone was often a better solvent.)

The key NMR experiments for evaluating bridgehead phenyl rotations were the high resolution two-dimensional (2D) COSY45 spectra for homonuclear (^{1}H–^{1}H) chemical shift correlation. Under our conditions, routine detection of crosspeaks for ^3J, ^4J and even ^5J couplings in the phenanthrenoid and bridgehead phenyl systems was generally possible. It was possible to map out the $(CH)_4$ and $(CH)_5$ spin systems for the phenanthrenoid and phenyl systems, respectively, allowing full proton assignments even when numerous signal overlaps occurred in the one-dimensional (1D) ^{1}H spectra. With slow phenyl rotation on the NMR timescale, five 2H intensity signals are expected for the two bridgehead phenyls, and four 2H intensity signals for the phenanthrenoid moiety (in the absence of accidental overlaps) in the aryl proton regions of adducts of (**1**). (If protons are present on the *N*-aryl rings of the adducts, additional signals or overlaps would be expected.) If the bridgehead phenyls rotated rapidly on the NMR timescale, the resulting fast exchange limit (FEL) spectra would show one 4H signal for the *ortho* phenyl protons, one 4H signal for the *meta* protons, and one 2H signal for the *para* protons. The above analyses assume that the adducts (**3**), exhibit an effective mirror symmetry plane on the NMR timescale. For the 1D ^{13}C NMR spectra with proton decoupling, the SEL regime for bridgehead phenyl rotation would predict signals for nine pairs of aryl methines, including five from the phenyls and four from the phenanthrenoid, plus signals of four pairs of non-protonated (quaternary, Q) aryl carbons from these groups. Potential complications and additional aryl carbon signals result from the *N*-aryl groups and possible splitting by ^{19}F. Using a standard 3 s relaxation delay (RD) for the 1D ^{13}C spectra resulted in peak areas from signals of protonated carbons being roughly proportional to the numbers of these carbons. Carbon-13 NMR spectra can directly support slow bridgehead phenyl rotations as well as slow rotations for the *N*-aryl ring. Assignments for the protonated carbons can be straightforward by use of the 2D heteronuclear chemical shift correlation spectra (HETCOR) in the absence of accidental proton signal overlaps, but the non-protonated aryl (quaternary, Q) carbons may not be readily assigned. If severely split by fluorines, these non-protonated aryl carbons may not always be observable above baseline noise. In some cases, we have made tentative assignments based on chemical shift arguments or expected C–F coupling constants. In compounds with fluorine, ^{19}F NMR spectra were acquired, first with coarse digital resolution with $CFCl_3$ as internal reference, and then with fine digital resolution (narrow spectral width) to resolve complex fluorine signal multiplicities.

With highly fluorinated *N*-aryl rings in the adducts (**3**), ^{19}F–^{19}F COSY spectra have been employed to rigorously identify vicinal pairs of fluorines. With symmetrical 2,3,5,6-tetrafluoro substitution on the *N*-aryl ring, observation of four separate fluorine signals in the ^{19}F NMR shows slow rotation of the *N*-aryl group (on the fluorine NMR timescale), attributed to hindered rotation about the N(sp^2)–C(aryl sp^2) bond due to repulsions between the imide carbonyl oxygens and the *ortho* substituents (i.e., 2″,6″ attachments) on the *N*-aryl. (Adduct structures and atom numbering are shown in Fig. 1.) These repulsions force the *N*-aryl to twist away from coplanarity with the imide system of the pyrrolidinedione ring. The equilibrium dihedral angle between the pyrrolidinedione and *N*-aryl ring can approach 90° for bigger 2″,6″-substituent groups on the *N*-aryl. This conformation results in one edge (the b edge) of the *N*-aryl ring being directed ''into'' the cavity of the adduct (**3**), and therefore ''towards'' the phenanthrenoid moiety. Substituents on these inner positions might experience buttressing effects and magnetic anisotropic shielding from the proximal phenanthrenoid. Substituents on the opposite, or outer edge (the a edge) of the *N*-aryl ring are directed ''away'' from the phenanthrenoid, and would not experience these effects; the chemical shifts of substituents aimed ''out of'' the adduct cavity would show relatively normal NMR chemical shifts.

3.2. *N*-(4-Bromo-2,6-difluorophenyl)maleamic acid (**5a**)

Note that the fluorine NMR for the *N*-(4-bromo-2,6-difluorophenyl)maleamic acid showed an apparent broadened doublet when acquired with proton decoupling (see Fig. 2a). This doublet was incompletely resolved, with valley height about 64% of the average height of the two peaks. The full width of the doublet measured at half-height (i.e., somewhat below the valley) was ca. 14.9 Hz. If this maleamic acid exhibited fast rotation about the *N*-aryl bond, the two fluorines should be rendered chemically equivalent (isochronous). With decoupling of protons, a singlet should be observed for the ^{19}F signal. With *N*-aryl amides, two possible important bond rotation processes may be envisioned [20–22]. One process involves rotation about the N–C=O bond, which would interconvert *syn* and *anti* amide conformers. The second process would be the *N*-aryl rotation. The former process, N–C=O rotation, is generally found to be slow at ambient temperatures on typical proton or carbon-13 NMR timescales. In the ^{1}H NMR for the crude maleamic acid, only a single set of sharp signals is observed for the AB q of the HC=CH portion, implying just one predominant amide conformer. (If both *syn* and *anti* amide conformers were present in appreciable amounts under a slow exchange limit (SEL) regime, two sets of AB q signals would be expected.) This implies that N–C=O rotation is not a factor in the observed pair of broad lines in the fluorine NMR. If *N*-aryl rotation was slow and the aryl group was effectively near-coplanar with the amide group, the two fluorines are non-equivalent. They could produce two singlets in the ^{19}F NMR if the ^4J(FCCCF) magnitude is very small, or an AB q pattern (approaching a pair of doublets, depending on the difference in chemical shifts of the fluorines) if the ^4J coupling is appreciable. With intermediate *N*-aryl rotation rates, chemical exchange broad-

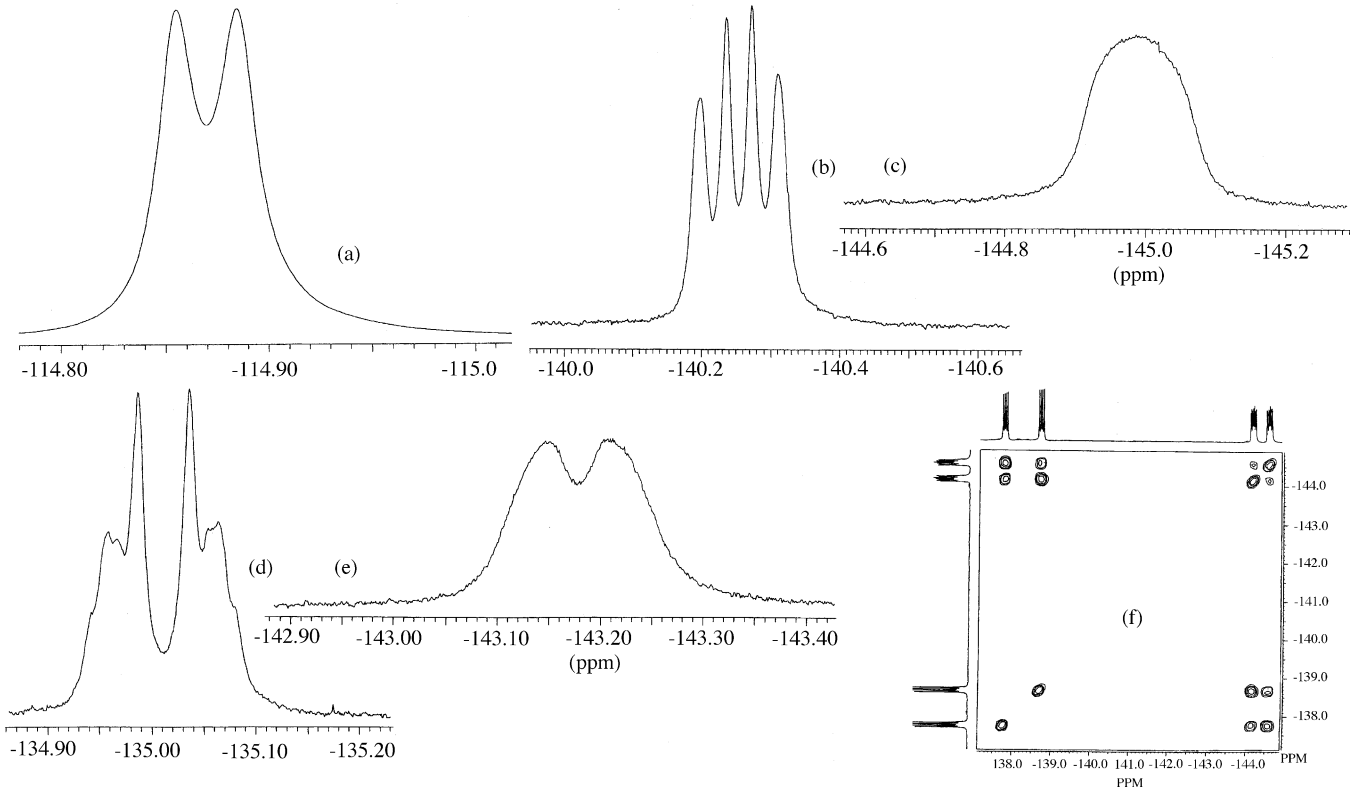

Fig. 2. Fluorine-19 NMR spectra, 282 MHz, at ambient temperatures. Chemical shifts are in ppm relative to $CFCl_3$ at 0.0 ppm. Spectra were acquired with proton decoupling. For the maleamic acids, spectra were recorded in d_6-acetone. Trace (a) (top left) is *N*-(4-bromo-2,6-difluorophenyl)maleamic acid (compound (**5a**)). Traces (b and c) (upper middle and right) show the spectrum for *N*-(2,3,5,6-tetrafluorophenyl)maleamic acid (compound (**5b**)). The spectrum of compound (**5c**), *N*-(4-bromo-2,3,5,6-tetrafluorophenyl)maleamic acid is seen in traces (d and e) (bottom left and middle). Spectral traces (b and c) are displayed with identical horizontal and vertical scales and represent equal area peaks; this applies also to traces (d and e). The symmetrized ^{19}F–^{19}F COSY45 spectrum, *f* (bottom right), corresponds to the phencyclone adduct (**3b**), of *N*-(2,3,5,6-tetrafluorophenyl)maleimide (compound (**5b**)), in $CDCl_3$. The spectral window ran from −137 to −145 ppm, using two dummy scans and four transients at each of 64 t_1 increments.

ening can be expected, which might obliterate F–F splittings or the ^{19}F chemical shift differences ($\Delta\nu$), depending on the kinetic rate and the magnitudes of couplings and $\Delta\nu$. We believe that this is the explanation for the broad doublet ^{19}F NMR signal.

[A trivial alternative explanation is possible; if proton decoupling were incomplete, then even with fast *N*-aryl rotation, the fluorine resonance could be a gross doublet due to vicinal ^3J(HCCF) coupling. This is not the case, as is indicated by the following. The proton NMR of the crude maleamic acid showed the presence of about 11% of the starting material, 4-bromo-2,6-difluoroaniline, based on the presence of the sharp complex multiplet, ca. 7.05–7.15 ppm, for the absorption signal of the aryl protons of this material. (This aryl proton multiplet was found to be identical to a reference ^1H NMR spectrum in d_6-acetone for the pure starting aniline.) In the fluorine NMR of the crude maleamic acid, a sharp singlet at −130.66 ppm is seen, ca. 12% of the area of the lower field doublet. This singlet may be assigned to the bromodifluoroaniline; the width at half-height was only 2.8 Hz. For the fluorine resonance of the aniline to be such a sharp singlet clearly shows that: (a) full proton decoupling was effective, and (b) the downfield doublet assigned to the maleamic acid was abnormally broadened.] We also point out that the aryl proton NMR spectrum shows a sharp resonance for the *meta* aryl protons, H3,5. We believe that the ^1H NMR for these protons is effectively FEL on the proton timescale, with the chemical shifts of these protons essentially sharply averaged, and the observed near-doublet signal showing spacing consistent with an approximate vicinal ^3J H–F coupling. This may be deceptively simple, since the maleamic acid's bromodifluorophenyl ring is an AA′XX′ spin system. The aryl proton spectrum can be in the FEL regime, showing a sharply averaged multiplet, while the ^{19}F NMR may only be at an intermediate exchange regime, if there is a small $\Delta\nu$ for the protons and a larger $\Delta\nu$ magnitude for the fluorines.

3.3. *N*-(2,3,5,6-Tetrafluorophenyl)maleamic acid (**5b**)

The fluorine-19 NMR spectrum appears to be a striking example of a dynamic NMR spectrum with an intermediate exchange rate. (Throughout this paper, we use the term

"dynamic NMR" in its broadest sense for describing our studies, that is, use of NMR spectra to gain insight regarding possible kinetic rate processes, to judge whether a particular system might be characterized as exhibiting an SEL or FEL spectrum, or [of special interest] whether the spectrum suggests a system at some intermediate exchange rate, as suggested by significant signal broadening. Thus, simple observation of the numbers of spectral absorption signals, and their integrated areas, may directly suggest, e.g., aryl ring rotation rates as being slow, fast or intermediate [on the respective NMR time scales] even without explicit use of variable-temperature studies or line-fitting analyses aimed at explicit determination of process rates or barriers to interconversions.) For the specific case of (**5b**), the fluorine-19 NMR is shown in Fig. 2b and c. Two equal-area signals are seen, with one being a sharp apparent quartet, and the other being a broad, featureless signal. Our explanation is that the favored conformation can be visualized as having the *N*-aryl roughly coplanar with the amide and alkene moieties, so that the environments of F2 and F6 are not the same, the F3 and F5 pair also being non-equivalent. Fast *N*-aryl rotation would render the *ortho* F2 and F6 chemically equivalent (isochronous), and the *meta* F3 and F5 pair would also be a chemically equivalent (isochronous) pair; two sharply exchange-averaged multiplets would be expected (one for each pair of fluorines). With *N*-aryl rotation at the slow exchange limit, four discrete sharp multiplets might be seen. An intermediate rate for the *N*-aryl rotation can cause partial averaging and broadening of the splittings and chemical shift differences. Note that the ^{1}H NMR spectrum for the *para* proton of the tetrafluorophenyl ring shows a sharp tt pattern, and we believe that there is only one significant amide conformer present. This proton lies on the rotation axis for the *N*-aryl rotation, so its chemical shift would not be affected by the aryl ring rotation. Splitting of the proton by the four fluorines is potentially complex, since the system would be considered AA′MM′X, but moderate *N*-aryl rotation rates may be sufficient to sharply average the H–F couplings, to give a deceptively simple tt pattern expected from an A_2M_2X system.

(We note that a referee has suggested that NMR line broadening may not necessarily be an indication of an intermediate exchange-rate process, such as a hindered rotation, but may reflect other factors affecting relaxation rates or resulting from extensive unresolved coupling. However, we strongly favor intermediate exchange rates of the *N*-aryl rotations for the maleamic acids (**5a**), (**5b**) and (**5c**) (discussed below) as the most reasonable explanation in the present case, since line-broadening in the ^{19}F NMR of the maleamic acids is seen here for three different *N*-aryl ring substitution patterns (2,4,6; 2,3,5,6; and 2,3,4,5,6). If the earlier case of *N*-(pentafluorophenyl)maleamic acid is also considered [8,12], for which varying line broadening of signals in the ^{19}F NMR spectrum was observed *when temperature was varied*, we would have *four different N*-(polyhalophenyl) maleamic acids, encompassing three different *fluorine* substitution patterns (2,6; 2,3,5,6; and 2–6), all of which exhibit fluorine-19 NMR signals broadened to a greater or lesser extent. That these are all *N*-aryl amides, for which hindered *N*-aryl rotations are known to be potentially significant on various NMR timescales, would seem to be very suggestive that we are, indeed, observing the effects of intermediate exchange rate ^{19}F NMR spectra for these maleamic acids. All four of these maleamic acids possess fluorines at both the 2- and 6-positions [i.e., *ortho* to nitrogen] of the *N*-aryl rings, where the effects on the *N*-aryl rotation rates would most largely be determined, and we would therefore suspect that the four compounds should have similar energy barriers to the *N*-aryl rotations. This would be fully consistent with the fact that NMR line broadenings for all four maleamic acids were observable at the same temperature, ca. 298 K, on our NMR.)

3.4. *N*-(4-Bromo-2,3,5,6-tetrafluorophenyl)maleamic acid (**5c**)

The fluorine NMR spectrum for the maleamic acid is consistent with an intermediate exchange rate for *N*-aryl rotation, causing some exchange-broadening, much more severe in the higher field absorption (see Section 3 above for (**5b**)) The fluorine-19 NMR is shown in Fig. 2d and e.

3.5. *N*-(2,3,4,5,6-Pentachlorophenyl)maleimide (**2d**)

This compound's carbon-13 NMR was obtained using a relaxation delay (RD) of 60 s with 1230 transients acquired. The long RD provided enhanced response for the weak signals of the non-protonated aryl carbons (relative to the protonated vinyl carbons). The two signals at 135.85 and 127.95 ppm were each about half the area of the signals at 133.82 and 132.52 ppm, and we attribute the weaker pair of signals to the single carbons C1 (N–C, *ipso*) and C4 (*para*), with the higher field signal tentatively assigned to the N–C carbon. Note that the *ipso* and *para* carbons of an aryl ring are often found to exhibit shorter T_1 relaxation times than the *ortho* or *meta* carbons (if similarly substituted), because the *ipso* and *para* carbons, lying on the rotation axis of the aryl ring, have slower effective motions, longer correlation times, and (for relatively small molecules) shorter T_1. The *ortho* or *meta* carbons, lying off the rotation axis of the aryl ring, would have faster effective motions and shorter correlation times [23]. However, *this would only be applicable for aryl rings that are rotating rapidly.* For the *N*-aryl rings in the maleimides and phencyclone adducts described in this paper, the point is that these rings are essentially prevented from fast rotation about the *N*-aryl bonds because of the *ortho* substituents. If this is the case, we would not expect appreciable T_1 differences for on-axis versus off-axis *N*-aryl ring carbons (due to this effect), and carbon-13 NMR peak areas might more closely reflect the

numbers of each type of carbon [23]. We make the presumption of slow *N*-aryl rotation in the maleimides, as well as in the adducts, because the expected interatomic repulsions of *ortho N*-aryl ring substituents with the imide carbonyls should be grossly similar for the maleimides and the adducts. In the maleimides, however, since the two faces of the maleimide ring are identical, we cannot observe different NMR chemical shifts for the two *ortho* (C2,6) positions of the *N*-aryl ring (and likewise for the two *meta* (C3,5) positions). In the phencyclone adducts, slow rotations of the *N*-aryl rings are readily demonstrable because the two faces of the pyrrolidinedione ring are quite different from one another.

3.6. *N*-(2,4,6-Tribromophenyl)maleimide (**2e**)

Some clarification for carbon assignments was obtained by acquiring the *proton coupled* spectrum with RD = 60 s in addition to the usual proton decoupled spectrum. Carbon signal multiplicities and observed splittings are shown in the Section 2. Assuming that the magnitudes for the aryl ring vicinal ^{3}J(CH) couplings with ca. 180° dihedral angles are greater than the geminal ^{2}J couplings in these systems, we have made the indicated tentative assignments [21]. Signals attributed to the individual non-protonated aryl carbons C1 and C4 had areas about half or less than those assigned to the pair of *ortho* CBr carbons.

3.7. 4-(Bromo-2,6-difluorophenyl)maleimide adduct (**3a**)

In the proton NMR, triplets for H4′ and for H3,6 were essentially isochronous, giving a 4H t signal. A complex 6H multiplet from 7.12 to 7.23 ppm included H6′, H2,7 and H1,8. Approximate shifts were estimated from the COSY spectrum. Note that higher field 1H doublets were seen at 7.01 and 6.59 ppm, assigned to the ''outer'' H3″ and the ''inner'' H5″, respectively.

In the ^{13}C NMR, two weak apparent dd patterns appear at low field, ca. 159.1 and 155.6 ppm. Fluorine is strongly deshielding for directly bonded aryl carbon. We tentatively assign these signals to the CF carbons at the 2″ and 6″ positions of the *N*-aryl ring, with each carbon showing the large ^{1}J(CF) direct coupling and a smaller ^{3}J(CCCF) coupling. The most consistent interpretation of the observed couplings suggests the following assignments, with the higher field carbon being designated as the ''inner'' carbon, C6″, on the ''b'' edge of the *N*-aryl. C2″ resonates at 157.50 ppm, ^{1}J = 258 Hz, ^{3}J = 4.8 Hz. C6″ resonates at 157.23 ppm, ^{1}J = 262.8 Hz, ^{3}J = 5.1 Hz. The very weak singlet at 103.58 ppm is assigned to C4″, the CBr, shielded by the heavy-atom effect of the directly bonded bromine. An extremely weak approximate triplet is centered at 123.37 ppm, assigned to the *ipso* carbon, CN, C1″, showing geminal ^{2}J splitting by the two fluorines of ca. 11.2 Hz. A strong set of peaks is centered at ca. 115.9 ppm, with total area consistent with two methines. The absorption appears as eight equal lines, with a central double doublet and a pair of flanking doublets. We cannot be certain whether this represents a pair of adjacent dd patterns or whether the dd patterns overlap. These are assigned to the C3″ and C5″ carbons on the *N*-aryl ring, with long range ^{4}J(CF) coupling ca. 3.9 Hz, and ^{2}J(CCF) couplings ca. 22.8 Hz (or 31.1 Hz). Using the smaller values for the geminal couplings, and assigning higher field position to the ''inner'' carbon, C5″, we would have C5″ at 115.69 ppm and the ''outer'' C3″ at 116.10 ppm. Protonated carbons on the bridgehead phenyls and the phenanthrenoid groups are rigorously known from the HETCOR spectrum, which shows nine crosspeaks for the aryl methine pairs. We could not observe the crosspeaks for the C3″ and C5″ methines, which absence we attribute to inadequate signal-to-noise ratios as a result of the splitting of the signals of these carbons into dd patterns by the fluorines.

The proton decoupled fluorine spectrum showed two sharp singlets, separated by 0.11 ppm, with peak widths at half-height ca. 3.1 Hz, implying negligible ^{4}J(FF) coupling magnitude.

3.8. *N*-(2,3,5,6-Tetrafluorophenyl)malemide adduct (**3b**)

Several uncertainties in the ^{13}C NMR spectrum assignments may be attributed to substantial splitting by fluorine, with the resulting high multiplicity for the carbon signals causing poor signal-to-noise ratios, despite acquisition of more than 15,000 accumulated transients. These uncertain features include the following: (a) The weak complex multiplets ca. 147.2, 143.8 and 140.4 ppm appear roughly as a 1:2:1 triplet, with spacings between adjacent pairs of these multiplets of ca. 253 and 261 Hz. These spacings are consistent with the direct ^{1}J(CF) couplings for aryl fluorides [23], and we believe that the apparent triplet pattern is the result of overlap of two gross doublets for fluorine-bearing carbons; the centers of these doublets would be 145.5 and 142.1 ppm, assigned to either the *ortho* or the *meta* pair of CF carbons of the tetrafluorophenyl group. This would account for two of the four aryl CF groups; we are not confident of the location for the other pair. (b) The signal at 135.24 ppm is exceedingly weak, and we have assigned it to the HC=CH absorption from a trace impurity of the precursor maleimide. A small sharp singlet is seen in the proton NMR of the adduct at ca. 6.94 ppm, attributable to the HC=CH of the maleimide. [The absence of a corresponding peak in the carbon spectrum of the adduct of the brominated analog described below would suggest that this weak peak is, in fact, not part of the adduct.] Only four of these aryl Q carbon signals are expected for the bridgehead phenyl and phenanthrenoid moieties, and related phencyclone adducts [from *N*-phenylmaleimide and *N*-*n*-alkylmaleimides] have generally shown three signals at relatively low field, i.e., 131–134 ppm, with a higher field Q signal at ca. 126 ppm, and peaks of seven of the nine intense aryl methine pairs appearing within the 126–131 ppm window [10,24]. (c) Our sample showed two absorptions consistent with these aryl Q

signals ca. 131.7 and 126.1 ppm, each of which appeared as a doublet with slightly split peaks; the apparent splittings were 1.35 Hz for the 131.7 ppm signal and 0.86 Hz for the 126.1 ppm signal. If these observed splittings were real, and not artifactual, we could not account for them as being the result of through-bond coupling (*J* coupling, spin–spin coupling) with a fluorine on the *N*-aryl group; the fluorines are just too many bonds removed. We have speculated that this might represent a through-space dipolar coupling effect resulting from the unusual proximity of the ''inner'' *ortho* fluorine to quaternary carbons of the phenanthrenoid system, but this is not certain. (d) An extremely weak multiplet was seen at 111.1 ppm as a possible triplet of multiplets; the spacing between the three branches was about 15 Hz, which could be consistent with ^{3}J(FCCC) or ^{2}J(FCC) for the tetrafluorophenyl ring; we might tentatively assign this as the *N*-aryl C1″. The one carbon assignment for the C_6F_4H ring which is firm is for the protonated carbon, C4″, appearing as a clean triplet with $J = 22.6$ Hz, exhibiting peak area consistent with a single methine. Note that the simple triplet appearance means that the carbon is split by only one pair of fluorines.

Four separate sharp multiplets for the ^{19}F absorptions are consistent with the SEL *N*-aryl rotation causing different chemical shifts for the ''inner'' versus the ''outer'' positions (relative to the cavity of the adduct). Two dd signals appeared at lower field, ca. −138.2 ppm, and two ddd multiplets (each consisting of eight near-equal intensity lines) appeared at higher field, ca. −144.4 ppm. If the nitrogen is shielding for *ortho* fluorines (as it is for *ortho* protons), the high field ddd multiplets would be F2 and F6. The ^{19}F–^{19}F COSY45 spectrum, seen in Fig. 2f, showed stronger crosspeaks, suggesting vicinal orientation, for the lower field dd signal with the higher field ddd absorption, and a comparable crosspeak correlated the higher field dd resonance with the lower field ddd signal. Thus, any effect from the phenanthrenoid moiety on the fluorines in the cavity of the adduct appears to have opposite influence on the vicinal pair of fluorines, moving their resonances in opposite directions. See below for discussion of the spectra for the brominated analog with the 4-bromo-2,3,5,6-tetrafluorophenyl ring.

3.9. *N*-(4-Bromo-2,3,5,6-tetrafluorophenyl)maleimide adduct (**3c**)

Over 17,000 transients were acquired for the carbon-13 NMR spectrum of this adduct. Nevertheless, extensive splitting of carbon signals by fluorine caused difficulty in assignments for the halogenated aryl ring. Several salient points: (a) In the 140–147 ppm region, four roughly equal intensity complex multiplets were recognizable, potentially being either two adjacent gross doublets or two overlapped gross doublets. For the *N*-(2,3,5,6-tetrafluorophenyl)maleimide adduct described above, an approximate 1:2:1 triplet was seen in a similar chemical shift region, and was interpreted as a pair of doublets with ^{1}J(CF) ca. 250–260 Hz. If the four multiplets in the bromotetrafluoro analog are considered to be overlapping doublets, approximate direct one-bond C–F couplings of ca. 250 Hz (for a doublet centered at ca. 144.8 ppm) and ca. 260 Hz (for a doublet centered at ca. 142.4 ppm) can be estimated. Interpreting the four multiplets as two adjacent doublets would imply approximate direct one-bond C–F couplings of ca. 166 and 176 Hz, which are less likely [21]; we favor the former rationale. These two gross doublets, then, could be assigned to a pair of non-equivalent carbons on the C_6BrF_4 ring, either the *ortho* C2″ and C6″, or the *meta* C3″ and C6″. If these two doublets represent one of these carbon pairs, the signals for the other pair of fluorine-bearing carbons are not obvious, as was the case for the non-brominated C_6F_4H ring in the analog described earlier. (b) In the case of the C_6BrF_4 ring, as was seen for the non-brominated C_6F_4H ring in the preceding analog, one of the weak Q signals appeared as a slightly split peak, ca. 131.7 ppm. We had tentatively postulated that this might result from a through-space dipolar C–F coupling. In the less hindered 4-bromo-2,6-difluorophenyl system, no such splittings of any quaternary aryl carbon signals were seen, suggesting that such splitting may require very crowded, ''buttressed'' systems, i.e., the two tetrafluorophenyl systems. (c) At higher field for aryl carbon absorptions, a few exceedingly weak peaks were observed ca. 109.9 ppm, which we tentatively ascribe to the aryl CN, C1″, appearing as a possible triplet. (d) A more secure assignment is for the triplet at 102.02 ppm (*J* ca. 22 Hz). We believe that this is the signal for CBr, C4″, based (in part) on the expected shielding by bromine for directly bonded carbon; the observed splitting could be either ^{2}J or ^{3}J.

In the ^{19}F NMR spectrum, the four sharp, highly resolved fluorine multiplets confirm that the *N*-aryl rotation is at the SEL, and that each fluorine is in a distinct environment. Because of similarities of coupling constants, we assume that the lower field pair of signals arise from one pair of fluorines, either the *ortho* 2″, 6″ or the *meta* 3″, 5″ pair, with the higher field signals assigned to the other pair. The homonuclear fluorine–fluorine COSY45 experiment was performed on this compound. Strong crosspeaks, signifying vicinal couplings, were seen between the lowest field and the highest field absorptions, i.e., −131.7 and −143.0 ppm (and also between −132.6 and −142.7 ppm signals), as was the case for the non-brominated tetrafluorophenyl analog described above. For both of these compounds (with similar fluorine substitution patterns), we tentatively suggest that the lower field pair of fluorine-19 NMR signals may be assigned to the *ortho* pair of fluorines at the 2″ and 6″ positions because they exhibit a larger $\Delta\delta$, ca. 0.9 ppm, than the higher field pair of signals which exhibit a magnitude of $\Delta\delta$ ca. 0.3–0.4 ppm. It would be reasonable that a larger difference in environments for ''inner'' versus ''outer'' positions on the *N*-aryl ring would be experienced by the *ortho* than by the *meta* (3″, 5″) fluorines, and this could express itself in the chemical shift differences.

3.10. N-(2,3,4,5,6-Pentachlorophenyl)maleimide adduct (**3d**)

With the 4-bromo-2,6-difluorophenyl, 2,3,5,6-tetrafluorophenyl, and 4-bromo-2,3,5,6-tetrafluorophenyl as the *N*-aryl moieties in the phencyclone adducts, a qualitative sense of the *N*-aryl rotation rates can potentially be obtained by NMR of a sensitive nucleus, either proton (for adduct (**3a**)) or fluorine-19 for adducts (**3a**), (**3b**) or (**3c**). However, for the pentachlorophenyl system of adduct (**3d**), the problem is more difficult, since the *N*-aryl ring has no sensitive nucleus attached. It is still possible to answer the question if carbon-13 NMR is used. This requires a rather pure sample of (**3d**) to avoid impurities with interfering carbon signals, and a very high number of scans (NS) to obtain adequate signal intensity to detect the expected exceedingly weak responses from the non-protonated carbons. We used up to 27,000 scans with a 1 s relaxation delay (RD) and compared the resulting spectrum to that acquired with RD = 60 s (NS = 3954). Except for a trace peak of the precursor maleimide (HC=CH signal at 134.86 ppm), the ^{13}C spectra were very clean, and have allowed, we believe, firm identification of all six carbon signals for the NC_6Cl_5 ring. For each of the six single non-protonated carbon signals expected for the SEL spectrum of the adduct, weak (but similar intensity) signals were seen. Five of the six signals were at even lower field than the lowest field peak (at 130.94 ppm) of the methine pairs, consistent with direct attachment of an electronegative atom, i.e., chlorine. The sixth of these weak peaks was seen at 128.27 ppm, possibly the *ipso* N–C, C1″. With RD = 1 s and NS = 27,157, the average intensity of each of these six weak peaks was 7.81 integral units (range from 5.96 to 9.49) compared to an average of 22.67 integral units per carbon (range from 13.45 to 32.80) for the quaternary pairs of carbons from the bridgehead phenyls and phenanthrenoid moieties, i.e., C1′, C4a,4b; C8a,10a; and C9,10. This suggests extremely long relaxation times for the NC_6Cl_5 carbons, consistent with their considerable distance from protons, which might assist in relaxation. For comparison, each of the protonated aryl methines had an average peak area of 90.25 integral units (per carbon). Using RD = 60 s and NS = 3954, with the protonated aryl methines exhibiting an average peak area of 90.25 integral units per carbon for their signal peaks, the quaternary pairs now showed average peak areas of 54.89 integral units (per carbon) but the six single carbon signals of the NC_6Cl_5 ring were only 36.18 integral units (range 28.34 for the peak at 128.26 ppm, to 48.27). This implies exceedingly long relaxation times for the NC_6Cl_5 carbons, even when compared to the other quaternary pairs. (Note that these samples were not degassed in any way.) Thus, slow rotation of the NC_6Cl_5 ring on the carbon-13 NMR timescale is demonstrated.

3.11. N-(2,4,6-Tribromophenyl)maleimide adduct (**3e**)

The carbon spectra were acquired with RD = 1 s (NS = 20,328) and 60 s (NS = 2670) to aid in distinction and assignments of the single methine and the non-protonated quaternary carbons. Thus, with the short 1 s relaxation delay, the areas of protonated carbon signals are quite closely proportional to their numbers, while non-protonated carbon signals are much weaker; even the pairs of aryl Q carbons have areas that are barely half that for a single CH. With RD = 5 s, the strongest signal for a quaternary pair, 2Q, at 133.55 ppm, actually has area greater than either single methine peak. But the four 1Q signals of the *N*-aryl ring each still have substantially less area than the peaks of the 2Q signals. With the long RD = 60 s (NS = 2670), enhanced response for quaternary aryl carbons of the adduct provided very favorable signal-to-noise ratio, so that the required 19 aryl carbon signals are unambiguously defined: nine methine pairs and four quaternary pairs from the bridgehead phenyls and the phenanthrenoid moieties, plus two unique methines and four single quaternary carbons from the brominated *N*-aryl. We have clearly demonstrated slow rotations and SEL spectra on both proton and ^{13}C NMR timescales for both the bridgehead phenyls and the *N*-aryl ring.

Table 1
Calculated parameters for phencyclone adducts of polyhalophenylmaleimides

Adduct	Optimized energies (au)[a]	Dihedral angle O=*C*–C–C–C2′[b]	Dihedral angle O=*C*–N–C–C6″ (inner)[c]	Distance of *N*-Ar C6″ substituent to phenanthrenoid[d]	*N* pyramidalization[e]	Phenanthrenoid pucker[f]
(**3a**)	−1980.574906	51.77	76.04	3.473	0.004	0.289
(**3b**)	−2165.904533	52.56	90.67	3.431	0.010	0.277
(**3c**)	−2178.247712	51.97	73.69	3.490	0.005	0.284
(**3d**)	−4064.980568	52.26	92.49	3.539	0.034	0.294
(**3e**)	−1807.572845	51.53	93.07	3.720	0.042	0.331

[a] Energies in atomic units (1 au = 627.5 kcal/mol).
[b] Dihedral angles in degrees. The magnitude of the average dihedral angles for the two bridgehead phenyls is given. C2′ is arbitrarily designated as the carbon proximal to the ketone carbonyl.
[c] Dihedral angles in degrees. The magnitude of the dihedral angle is given as measured to the closer imide carbonyl.
[d] Distance in angstroms, measured from the ''inner'' substituent at C6″ of the *N*-aryl ring to the midpoint of the line joining C8a and C10a, the ''center'' of the middle ring of the phenanthrenoid moiety.
[e] Pyramidalization expressed as distance (Å) of nitrogen from the plane defined by the three directly bonded atoms.
[f] Pucker defined as the distance (Å) between the midpoints of the lines joining C4a–C4b and H2–H7.

3.12. Ab Initio geometry optimizations

Ab initio geometry optimizations for the adducts have been performed at the Hartree–Fock level with 6-31G* basis set (or LACVP* for bromine-containing compounds), using Spartan '04 for Windows (full version) or Spartan '04 Essential (Wavefunction Inc., Irvine, CA) [25–28]. To conserve space, our summary data (shown in Table 1) for these computational results is limited to: optimized energies; dihedral angles of bridgehead phenyls relative to the ketone; dihedral angles of the *N*-aryl rings relative to the imide; closest approach distances (angstroms) of the inner *ortho* substituent atom of the *N*-aryl ring to the center of the middle ring of the phenanthrenoid moiety; pyramidalization at nitrogen expressed as the distance (angstroms) of the nitrogen from the plane defined by the three directly-bonded atoms; and puckering of the phenanthrenoid system. The latter parameter is defined as the distance between the midpoints of: (a) the line joining H2 and H7, and (b) the C4a–C4b bond. We have defined the center of the

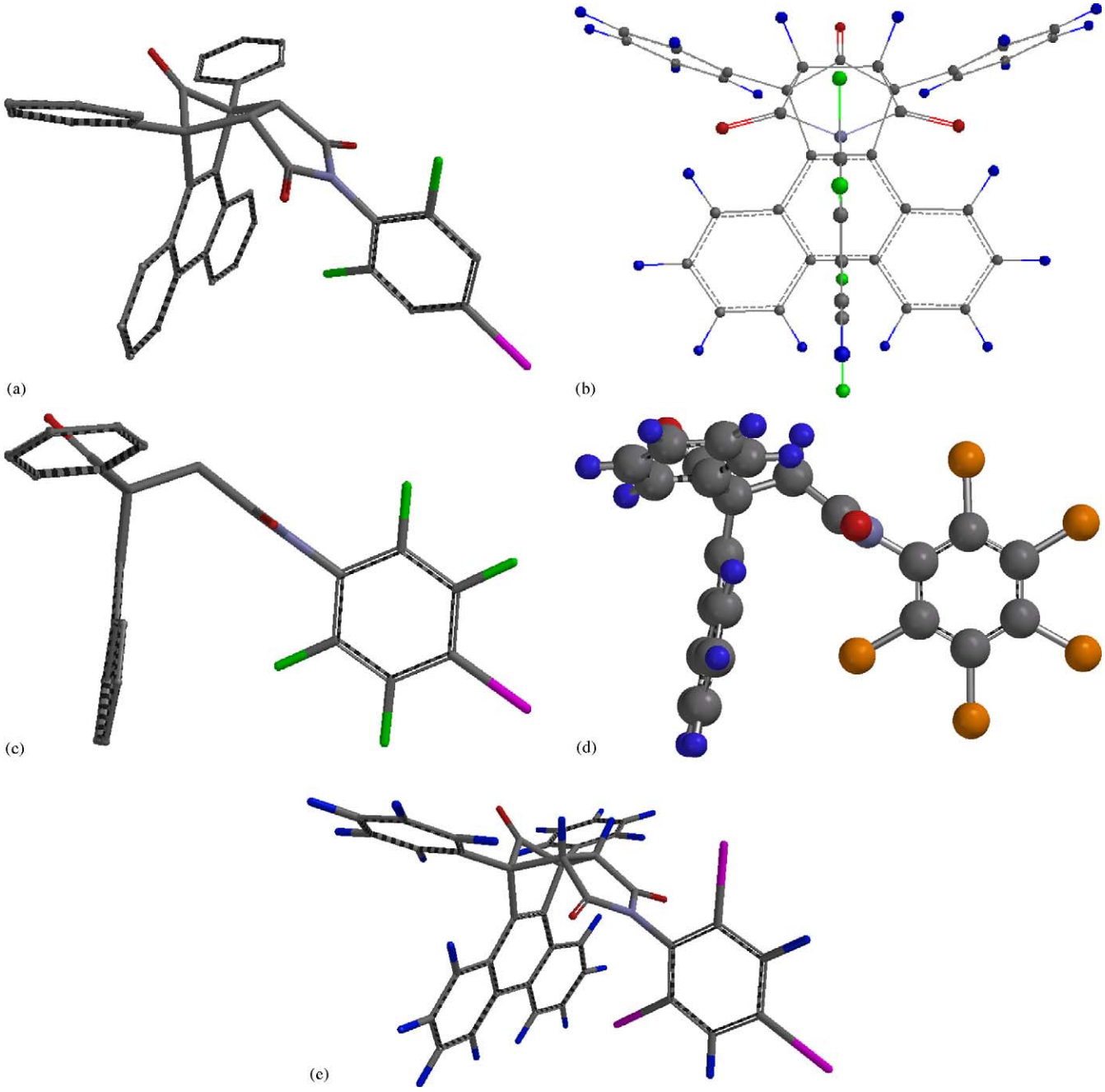

Fig. 3. Representative views of calculated structures for phencyclone adducts. In some cases, the hydrogens are "hidden" for clarity. (a) Compound (**3a**), from 4-bromo-2,6-difluorophenylmaleimide; (b) compound (**3b**), from 2,3,5,6-tetrafluorophenylmaleimide; (c) compound (**3c**), from 4-bromo-2,3,5,6-tetrafluorophenylmaleimide; (d) compound (**3d**), from pentachlorophenylmaleimide; and (e) compound (**3e**), from 2,4,6-tribromophenylmaleimide.

phenanthrenoid middle ring as the midpoint of the line from C8a to C10a. All five adducts had similar dihedral angles for the bridgehead phenyls, ca. 52°. For adducts (**3a**) and (**3c**), these dihedrals differed by about 0.5° between the phenyl on one side of the adduct and the phenyl on the other side, although for the other adducts, the dihedrals differed by less than 0.15°. It is also striking that for the same adducts (**3a**) and (**3c**), the *N*-aryl ring was found to form a dihedral angle of ca. 75° relative to the imide, much less symmetrical than for the other adducts, for which the *N*-aryl ring was nearly perpendicular to the imide. The adducts (**3a**) and (**3c**) both possess a pair of *ortho* 2″,6″ fluorines and a *para* bromine on the *N*-aryl ring, but it is not obvious why these compounds should deviate as they do in their calculated values. Nitrogen pyramidalization is notably greater for adducts (**3d**) and (**3e**), in which larger, lower row atoms, i.e., Cl and Br, occupy the crowded *ortho* ''inner'' positions on C6″ of the *N*-aryl ring, such that the *N*-aryl tips away from the phenanthrenoid system. This is also reflected for (**3e**) in which there is appreciably more puckering of the phenanthrenoid moiety. If this system is regarded as ''butterfly-like'' in shape, the outer rings (i.e., the butterfly wings) are folded towards the *N*-aryl, while the central ring of the phenanthrenoid is relatively more remote, to reduce hindrance. Fig. 3 shows representative calculated structures for some of the adducts.

4. Conclusions

We have prepared, and presented NMR data for, phencyclone adducts from five *N*-arylmaleimides (**2**), including: (**2a**), *N*-(4-bromo-2,6-difluorophenyl)maleimide; (**2b**), *N*-(2,3,5,6-tetrafluorophenyl)maleimide; (**2c**), *N*-(4-bromo-2,3,5,6-tetrafluorophenyl)maleimide; (**2d**), *N*-(2,3,4,5,6-pentachlorophenyl)maleimide; and (**2e**), *N*-(2,4,6-tribromophenyl)maleimide. Maleimides (**2a**–**2c**) were prepared in two steps, with isolation of intermediate *N*-aryl maleamic acids (**5**). The corresponding maleamic acids (**5a**–**5c**), each showed signal broadening in their ambient temperature fluorine-19 NMR spectra (at 282 MHz) consistent with an intermediate exchange regime, which we have ascribed to the process involving *N*-aryl rotation. In the phencyclone adducts (**3a**–**3e**), proton and carbon-13 NMR (at 300 and 75 MHz, respectively) showed SEL spectra for rotation of the bridgehead phenyls about the $C(sp^2)$–$C(sp^3)$ bonds. Adducts (**3a**–**3c**) displayed SEL spectra for the *N*-aryl rotations based on, e.g., ^1H, ^{13}C and fluorine-19 NMR. For adducts (**3d**) and (**3e**), slow *N*-aryl rotation was shown by ^1H or ^{13}C NMR. Significant magnetic anisotropic effects were seen for protons on the *N*-aryl rings of adducts (**3a**) and (**3e**), depending on their orientation ''into'' or ''out of'' the adduct cavity; with the ''inner'' orientation, the nuclei are directed towards, and shielded by, the phenanthrenoid moiety. Ab initio geometry optimizations for the five phencyclone adducts, performed at the Hartree–Fock level, using the 6-31G* or LACVP* basis sets, resulted in calculated structures that reflected considerable hindrance, and were consistent with observed slow rotation rates (on the NMR timescales) for the *unsubstituted* bridgehead phenyl and *N*-aryl rings.

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