atom via an aziridinium intermediate cannot occur. Since the aminomercuration is a reversible process,[10] especially in a strong acid media, the β-elimination is a much more favorable process.

Experimental Section

General Procedures. Melting points were determined in an open capillary on a Büchi hot-stage apparatus and are uncorrected. Optical rotations were recorded at room temperature on a Perkin-Elmer Model 241 polarimeter. ^1H (300-MHz) and ^{13}C NMR (75-MHz) spectra were recorded on a Brücker AC-300 spectrometer with tetramethylsilane as internal standard. GC-Mass spectra were recorded on a Hewlett-Packard 5930 A mass spectrometer. Microanalyses were performed on a Perkin-Elmer Model 240 instrument.

General Procedure for Preparation of 1,2-Diaminocyclohexanes (4). To a THF solution (20 mL) of limonene (1.36 g, 10 mmol) and the corresponding arylamine (50 mmol) was added dropwise a water solution of HgO (2.1 g, 10 mmol) and HBF_4 (4.05 mL, 40% v/v, 20 mmol). The reaction mixture was stirred for 30 min at −20 °C, and then it was heated to reflux for 5 h, during which time the yellow solution changed to red and Hg^0 was formed. The flask was then cooled to room temperature, and the Hg^0 was filtered off (1.8 g, 90%). The organic layer was poured into 3 M NaOH (20 mL) and extracted with ether (3 × 20 mL). The ethereal layer was washed with water (2 × 20 mL), dried (Na_2SO_4), and evaporated at reduced pressure. The excess of amine was eliminated at 10^{-2} Torr, and the resulting oil was distilled at 10^{-6} Torr. A mixture of monoamines 5 and 6 distilled at 120–130 °C, while diamines 4 were collected at 150–160 °C as a viscous yellow-orange oil in 45–50% yield. **4a** crystallized on standing and was then recrystallized from ethanol, giving a white crystalline solid; mp 101–102 °C.

(−)-(1*R*,2*R*,4*R*)-*N*,*N*′-Diphenyl-1-methyl-4-(1-methylethenyl)-1,2-diaminocyclohexane (4a): $[\alpha]_D$ −54.6° (*c* 1.00, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.2–1.5 (m + s, 5 H), 1.7–1.9 (m + s, 6 H), 2.1 (m, 2 H), 2.3 (m, 1 H), 3.5 (s, 2 H, NH), 4.8 (s, 2 H), 7.2–6.8 (m, 10 H, Ar); ^{13}C NMR ($CDCl_3$) δ 17.2, 20.6, 27.5, 33.6, 38.0, 43.8, 56.8, 59.6, 108.7, 114.2, 118.0, 119.8, 120.3, 128.5, 129.1, 145.6, 147.4, 148.3 MS *m*/*z* 320 (M^+). Anal. Calcd for $C_{22}H_{28}N_2$: C, 82.50; H, 8.75; N, 8.75. Found: C, 82.45; H, 8.75; N, 8.70. Anal. Calcd for $C_{22}H_{28}N_2$: C, 82.50; H, 8.75; N, 8.75. Found: C, 82.45; H, 8.75; N, 8.70.

(−)-(1*R*,2*R*,4*R*)-*N*,*N*′-Bis(*p*-chlorophenyl)-1-methyl-4-(1-methylethenyl)-1,2-diaminocyclohexane (4b): $[\alpha]_D$ −38.3° (*c* 1.00, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 17.5, 20.7, 27.5, 33.6, 37.9, 43.8, 57.1, 59.7, 108.9, 115.3, 121.7, 122.6, 125.0, 128.5, 129.0, 144.1, 145.9, 148.2; MS *m*/*z* 388 (M^+). Anal. Calcd for $C_{22}H_{26}N_2Cl_2$: C, 67.86; H, 6.68; N, 7.19; Cl, 18.25. Found: C, 67.78; H, 6.61; N, 7.11; Cl, 18.17.

(−)-(1*R*,2*R*,4*R*)-*N*,*N*′-Di-*p*-tolyl-1-methyl-4-(1-methylethenyl)-1,2-diaminocyclohexane (4c): $[\alpha]_D$ −36.2° (*c* 1.00, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 17.4, 20.0, 20.2, 20.5, 27.4, 33.5, 37.9, 43.7, 56.8, 59.6, 108.5, 114.4, 121.7, 126.9, 128.9, 129.0, 129.4, 129.6, 142.6, 145.0, 148.3; MS *m*/*z* 348 (M^+). Anal. Calcd for $C_{24}H_{32}N_2$: C, 82.76; H, 9.19: N, 8.04. Found: C, 82.68; H, 9.07; N, 7.96.

(−)-*N*-α-Terpinyl-*N*-phenylamine (9). To a THF solution (20 mL) of limonene (1.36 g, 10 mmol) and aniline (4.7 g, 50 mmol) was added $Hg(OAc)_2$ (3.18 g, 10 mmol) and the mixture stirred at room temperature for 30 min. Then, NaOH (20 mL, 0.5 M) and $NaBH_4$ (0.38 g, 10 mmol)/NaOH (10 mL, 3 M) were consecutively added. After 2 h, diethyl ether (20 mL) was added and the solution washed with water (3 × 20 mL) (Hg^0, 1.9 g, 95%). The organic layer was dried with Na_2SO_4 and concentrated under vacuum and the residual oil purified by flash column chromatography with CH_2Cl_2 as the eluent: yield 1.48 g, 65%; yellowish oil; [α] −12° (*c* 1, $CHCl_3$): ^1H NMR ($CDCl_3$) δ 1.2–2.0 (m, 16 H), 3.4 (br, 1 H), 5.4 (s, 1 H), 7.2–6.8 (m, 5 H); ^{13}C NMR δ 23.0 (q), 24.0 (t), 24.8 (q), 25.3 (q), 26.5 (t), 31.0 (t), 41.7 (d), 55.6 (s), 116.5 (d), 117.4 (d), 120.7 (d), 128.5 (d) 133.3 (s), 146.5 (s); MS *m*/*z* 229 (M^+). Anal. Calcd for $C_{16}H_{23}N$: C, 83.84; H, 10.04; N, 6.11. Found: C, 83.80; H, 10.00; N, 6.06.

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Supplementary Material Available: X-ray data for compound 4 (8 pages). Ordering information is given on any current masthead page.

C-N Rotational Barriers in Ferrocenecarboxamides

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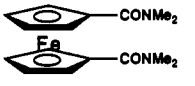
Introduction

The barrier to rotation about the C-N bond of amides is lowered by the presence of electron-donating groups attached to the amide carbonyl.[1-3] For example, the ΔG^* for C-N bond rotation in *N*,*N*-dimethyl-4-methoxybenzamide is 14.5 kcal mol^{-1}, while the corresponding barrier in *N*,*N*-dimethyl-4-nitrobenzamide is 16.4 kcal mol^{-1}.[2,3] This effect has been attributed to competitive delocalization (cross-conjugation) whereby electron donation diminishes the C-N bond order relative to a more electron-deficient system. In view of the striking facility for electron donation exhibited by ferrocenes,[4] the rotational barriers for ferrocenecarboxamides might be expected to be rather low in comparison to other arenecarboxamides. Specifically, one might expect comparatively free rotation of the NR_1R_2 group in the fulvene-like resonance for **2a** shown in Scheme I. Though ferrocenecarboxamides have been known for some time,[5] we know of no study of their rotational barriers. We find that the ΔG^* for C-N bond rotation in the simple ferrocenecarboxamides **3** and **4** is also about 14.4 kcal mol^{-1}. These results and a possible explanation are recounted below.



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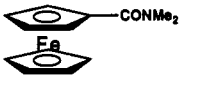

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Results and Discussion

Ferrocenecarboxamides **3** and **4** were prepared without incident from their corresponding acid chlorides by exposure to the appropriate amines in dichloromethane,

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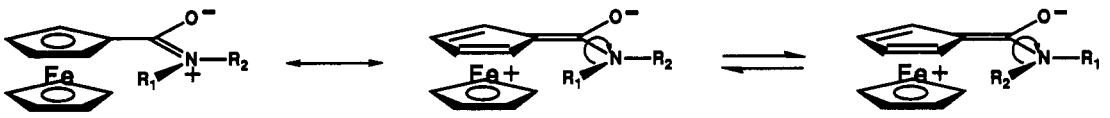
0022-3263/91/1956-2932$02.50/0

Scheme I



1 2a 2b

Table I. Activation Parameters for C–N Rotation in Ferrocenecarboxamides at 298 K

amide	$\Delta G^{\ddagger}$ [a]	$\Delta H^{\ddagger}$ [a,b]	$\Delta S^{\ddagger}$ [b,c]	ref
3	14.4	9.6 ± 0.74	−16.2 ± 2.6	this work
4	14.3	4.68 ± 0.66	−32.5 ± 2.4	this work
N,N-dimethyl-4-methoxybenzamide	14.6	15.0	+1.4	2
N,N-dimethyl-4-methylbenzamide	14.9	19.7	+16.3	3

[a] kcal-mol^{-1}. [b] Uncertainty is ±2σ. [c] cal deg^{-1} mol^{-1}.

chromatographic purification, and subsequent recrystallization. All of their physical and spectroscopic properties are consistent with the assigned structures.

^{1}H NMR spectra (300 MHz) were obtained for each compound at various temperatures (1.0 mg mL^{-1} in CD_2Cl_2 with a trace of pyridine to suppress acid-catalyzed isomerization). The coalescence temperature (T_c) for the interconversion of the syn and anti methyl groups was 295 K for 3 and 293 K for 4. Unimolecular rate constants for isomerization were calculated by measuring $\Delta\nu$ at slow exchange[6] (283–293 K for 3 and 263–289 K for 4). The slow exchange limit was determined by lowering the temperature of the sample until the width at half height ($\nu_{1/2}$) of the syn and anti methyl group resonances reached a minimum (~3.4 Hz); separation of the syn and anti methyl resonances at this temperature afforded $\Delta\nu_0$ = 62.6 Hz at 263 K for 3 and $\Delta\nu_0$ = 87.4 Hz at 253 K for 4. Arrhenius plots afforded linear graphs with correlations coefficients ≥0.990; the activation parameters derived from these plots are shown in Table I. The uncertainty in the activation parameters[7] was determined by assuming an error in the measurement of frequency by the NMR spectrometer of twice the hertz/point resolution and then determining the maximum error in ln (k) by propagating the error through the equations for the calculation of the rate constants. These errors were then used to determine the maximum probable error in the slope and y intercept of the Arrhenius plots. The uncertainty reported for the activation parameters is ± two standard deviations. There is very little error associated with determinations of $\Delta G^{\ddagger}$.[7a]

There is much evidence to indicate that ferrocene is a powerful electron donor. The pK_{R+} value for the hydration of the ferrocenylcarbinyl cation is −1.28,[8] indicating greater stability for this cation than for the triphenylmethyl cation (pK_{R+} −6.44).[9] Rapid solvolysis at centers adjacent to ferrocene, studied by Richards,[10] Traylor,[11] Ugi,[12] and others,[13] is attributed to the electron-releasing capacity of ferrocene. Moreover, acetylferrocene is significantly more basic (pK_a −2.8 for carbonyl protonation)[14] than other aryl ketones (e.g., acetophenone, pK_a −7.82).[15] Taken together, these observations encourage the expectation that ferrocenecarboxamides should extend the trends described by Jackman[2] and Fong[3] and exhibit low rotational barriers. However, the $\Delta G^{\ddagger}$ for C–N rotation in ferrocenecarboxamides 3 and 4 is about 14.4 kcal mol^{-1}, indistinguishable from the corresponding value in *N,N*-dimethyl-4-methoxybenzamide. The activation enthalpies for rotation in 3 and 4 (9.7 and 6.3 kcal mol^{-1}, respectively) are significantly lower than for substituted *N,N*-dimethylbenzamides (see the table), which is consistent with this expectation in that the electronic effect should be largely reflected in $\Delta H^{\ddagger}$. Also consistent with this is the observation that the amide with the more electron deficient opposing Cp ring (3) has the higher $\Delta H^{\ddagger}$.[10d]

Compensating negative activation entropies (−16 and −27 eu) account for the relatively high rotational barriers in 3 and 4. Amides typically exhibit $\Delta S^{\ddagger} > 0$ for C–N rotation,[1] indicating greater rotational freedom in the amide as it approaches a transition state in which the C–N bond order approximates unity. The implication of our results is that compounds 3 and 4 undergo a net loss in degrees of freedom as the transition state for rotation is approached. The carbonyl carbon becomes more electron deficient in the transition state, so it is possible that C–N rotation is accompanied by puckering of the carboxamide–Cp ligand to distribute the transient electron deficiency through the ferrocene. Thus, C–N rotation would be coupled to a larger molecular reorganization. Though the structure of ferrocenylcarbinyl cations has been the subject of considerable controversy,[4,10–13,16] such a puckered structure is supported both by calculations[17] and X-ray analysis.[18] However, ferrocenecarboxaldehyde[19] and 1,1′-diacetylferrocene[20] betray no significant distortion of this sort.

An alternative explanation relies on the prediction from molecular models that the transition state will suffer from steric repulsion between the endo methyl group and the

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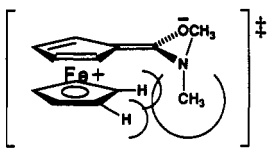
opposite Cp ring (transition state 5). Compounds 3 and 4 are thus complementary to ortho-substituted *N,N*-dimethylbenzamides in which steric strain is relieved upon proceeding to the transition state.[21] The ferrocene nucleus may relieve steric congestion in the transition state by tilting the offending Cp ring relative to the central axis (transition state 6), which may in turn be accompanied by an interruption of Cp–Cp rotation. If this is so, ferrocenes 3 and 4 serve as examples of dynamic gearing[22] in which C–N and Cp–Cp rotations and Cp–Cp angle could all be coupled in a highly ordered activation process. This process is reminiscent of Streitwieser's suggestion[23] that hindered rotation of opposing pair of *tert*-butyl groups in 1,1',3,3'-tetra-*tert*-butylferrocene as they pass each other may account for the observed $\Delta S^{\ddagger}$ of −5 eu for Cp rotation. Jackman et al.[24] have discussed the utility of activation entropy as a criterion for correlated rotations.



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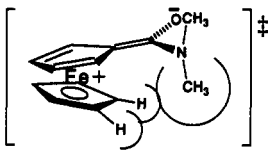

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Experimental Section

General Methods. ^{1}H NMR spectra were obtained using Bruker AM-300 and AF-300 instruments; chemical shifts are reported relative to internal TMS. IR samples were prepared by spreading a chloroform solution on a NaCl plate and allowing the chloroform to evaporate. Melting points are uncorrected. Dichloromethane was distilled from CaH_2. EtOAc and hexanes for chromatography were both distilled. Flash chromatography[25] was performed with Kieselgel 60 SiO_2 (230–400 mesh) from E. Merck. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

***N,N,N',N'*-Tetramethylferrocene-1,1'-dicarboxamide (3).** 1,1'-Bis(chlorocarbonyl)ferrocene (0.340 g, 1.09 mmol) was dissolved in 25 mL of dry CH_2Cl_2 containing 0.25 mL of triethylamine. Dimethylamine gas was bubbled through the solution for 15 min, followed by N_2. The reactions mixture was concentrated, and the residue was purified by flash chromatography to give 0.200 g (0.610 mmol, 56% yield) of an orange solid: mp 130 °C; R_f 0.12 (4:1 EtOAc/hexanes on SiO_2); ^{1}H NMR (300 MHz, 16 °C, $CDCl_3$) δ 4.67 (s, 4 H), 4.37 (s, 4 H), 3.14 (br s, 6 H), 3.03 (br s, 6 H) ppm; ^{13}C NMR (75 MHz, 23 °C, $CDCl_3$) δ 170.0, 80.0, 72.5, 71.5, 39.0 (br), 36.3 (br) ppm; IR (thin film) ν 3088, 2925, 1610 (C=O), 1396, 1107 cm^{-1}; UV ($CHCl_3$) λ_{max} 243 nm (ϵ 12 200); MS (EI) m/z 328 (100, M$^+$), 284 (15), 257 (21), 241 (16), 192 (42), 121 (52) amu; HRMS m/z calcd for $C_{16}H_{20}N_2O_2Fe$, 328.0874, m/z observed 328.0874. Anal. Calcd for $C_{16}H_{20}N_2O_2Fe$: C, 58.54; H, 6.10; N, 8.54; Fe, 17.07. Found: C, 58.36; H, 6.01, N, 8.36; Fe, 16.66.

***N,N*-Dimethylferrocenecarboxamide (4).** (Chlorocarbonyl)ferrocene (0.270 g, 1.09 mmol) was dissolved in 25 mL of dry CH_2Cl_2 containing 0.25 mL of triethylamine. While cooling the reaction flask, dimethylamine was bubbled through the solution for 30 min. Flushing with N_2, concentration in vacuo, and purification by flash chromatography afforded 0.138 g (0.537 mmol, 49% yield) of an orange solid: mp 108–109 °C; ^{1}H NMR (300 MHz, 10 °C, $CDCl_3$) δ 4.62 (s, 2 H), 4.31 (s, 2 H), 4.22 (s, 5 H), 3.23 (br s, 3 H), 3.04 (br s, 3 H) ppm; ^{13}C NMR (75 MHz, 23 °C, $CDCl_3$) δ 170.6, 78.29, 70.51, 69.65, 69.20, 38.53 (br), 36.42 (br) ppm; IR (thin film) ν 3081, 2943, 1613 (C=O), 1391, 1107, 1022 cm^{-1}; UV ($CHCl_3$) λ_{max} 242 nm (ϵ 9400); MS (EI) m/z 257 (100, M$^+$), 213 (43, M$^+$ − N(CH$_3$)$_2$), 185 (37, M$^+$ − CON(CH$_3$)$_2$), 121 (35, $C_5H_5Fe^+$) amu; HRMS m/z calcd for $C_{13}H_{15}NOFe$, 257.0503, m/z observed 257.0504. Anal. Calcd for $C_{13}H_{15}NOFe$: C, 60.70; H, 5.84; N, 5.45; Fe, 21.79. Found: C, 59.87; H, 5.73; N, 5.20; Fe, 20.96.

Acknowledgment. We thank the National Institutes of Health (GM39816) for financial support.

Supplementary Material Available: Data and plots of Arrhenius analysis (3 pages). Ordering information is given on any current masthead page.

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A Relationship between Experimentally Determined pK_as and Molecular Surface Ionization Energies for Some Azines and Azoles

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Acidities of organic compounds have played a key role in the development and understanding of physical organic chemistry.[1-8] For example, the Hammett[1-3] and Taft[2,4,5] equations have been based largely on aqueous acidities of substituted benzoic and acetic acids. A working knowledge of relative acidities and basicities is particularly important in organic synthesis; while a considerable amount of this involves nonaqueous media, acidities are nevertheless most often discussed in terms of pK_as.[5,7,8] With the increasing number of organic molecules being designed and prepared, there exists a need to develop methodology for predicting their aqueous acidities.

In this work we present a relationship between the measured pK_as of a series of azines (1–4) and azoles (5–10) and the average local ionization energy, $\bar{I}(\mathbf{r})$, on the molecular surface. We will show that this relationship provides a basis for reliable estimates of pK_a values within these classes of compounds (Chart I).

$\bar{I}(\mathbf{r})$ has recently been introduced as a useful property for analyzing chemical reactivity;[9,10] it is rigorously defined within the framework of self-consistent-field molecular orbital (SCF-MO) theory by eq 1.

$$\bar{I}(\mathbf{r}) = \sum_i \frac{\rho_i(\mathbf{r})|\epsilon_i|}{\rho(\mathbf{r})} \qquad (1)$$

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