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Supplementary Material Available: Tables of bond distances, bond angles, and refined temperature factor expressions for carbazole-TCNE 1:2 complex (3 pages); table of structure factors (5 pages). Ordering information is given on any current masthead page.

Thermodynamic Basicity vs Kinetic Basicity of Diazoles (Imidazoles and Pyrazoles)

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The intrinsic basicity of 24 azoles (pyrazoles, indazoles, imidazoles, benzimidazoles) and 7-methylazaindole was determined by mass spectrometry techniques, ion cyclotron resonance (ICR) and/or chemical ionization (CI) in conjunction with tandem mass spectrometry (MS/MS). A reasonably good agreement ($r^2 = 0.967$) is found between both methods (15 compounds). Thus, it is possible to use CI/MS/MS to determine the intrinsic basicity of compounds not measurable by ICR for purity or volatility reasons. Some anomalies are interpreted in terms of entropy and steric effects. The basicity data are also discussed by using empirical models (σ_α, σ_R) and chelation and annelation effects.

Introduction

In the study of the intrinsic basicity of azoles, we have used both ion-cyclotron-resonance (ICR) spectrometry[1-3] and chemical ionization (CI) mass spectrometry.[4,5] These techniques analyze processes (1) and (2) respectively:

$$B + B_0H^+ \rightleftarrows BH^+ + B_0 \quad (1)$$

$$[B_0HB^+]^* \rightarrow B_0 + HB^+ \text{ (or } B + HB_0^+) \quad (2)$$

Both processes measure the relative basicity between B_0 and B bases. However, the first one is an equilibrium and, consequently, depends only on the energies of reagents and products, whereas the second one corresponds to the breaking of a hydrogen bond. This kinetic process will depend on the potential energy curve connecting the complex $[B_0HB^+]^*$ to its fragments. Consequently, while the firts one (1) is, in general, insensitive to steric effects,[6] the second one (2) seems to be sensitive to these effects.[7] It is the aim of this paper to compare these methods using an homogeneous set (pyridine-like nitrogen basic center, five-membered rings) of 25 compounds, most of them pyrazoles, imidazoles, and their benzo derivatives; 19 compounds were studied by ICR, 21 by chemical ionization, and 15 by both methods. Chart I contains the 25 structures.

Cooks, the discoverer of the mass spectrometric kinetic method,[8] discusses its advantages over the equilibrium method, which is hardly efficient in several circumstances (low volatility of the samples for instance).[9] In the present case, for 1*H*-benzimidazole (**11**), only an approximate value can be obtained by ICR (about 13 kcal mol^{-1} more basic than pyrazole) and the proton affinity of 1-*n*-butyl-1*H*-imidazole (**14**), 1-*tert*-butyl-1*H*-imidazole (**15**), and 1-(adamant-1-yl)-1*H*-imidazole (**20**) cannot be measured by ICR since the R^+ ion cleaves off.

Experimental Section

The synthesis of the compounds can be found in the following references: 1*H*-pyrazole (**1**) (commercial), 1*H*-indazole (**2**) (com-

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0022-3263/91/1956-0179$02.50/0

Table I. Intrinsic Basicity, ΔG (kcal mol^{-1}), of Diazoles

compound	$\delta\Delta G^0$(obs)	$\Delta G^{0\,a}$	$\Delta\Delta G^{0\,b}$	ref
1		−9.1 ± 0.2	0.0	2, 3
2		−11.0 ± 0.2	−1.9	2
3		−12.1 ± 0.1	−3.0	3
4		−12.4 ± 0.1	−3.3	3
5		−13.2 ± 0.2	−4.1	3
6		−15.6 ± 0.2	−6.5	2
7		−18.3 ± 0.1	−9.2	3
8		−18.4 ± 0.2	−9.3	3
9		−19.9 ± 0.2	−10.8	3
10		−20.3 ± 0.1	−11.2	2
12		−23.8 ± 0.2	−14.7	3
13		−25.6 ± 0.2	−16.5	2
17		−29.4 ± 0.1	−20.3	3
18	−1.3 ± 0.1[c]	−30.1 ± 0.4	−20.9	
	1.0 ± 0.1[d]			
	2.1 ± 0.1[e]			
21		−32.7 ± 0.4	−23.6	13
22	−1.1 ± 0.1[f]	−17.2 ± 0.1	−8.1	
	1.1 ± 0.1[g]			
23	−2.5 ± 0.1[h]	−22.8 ± 0.1	−13.7	
	1.3 ± 0.4[i]			
24	−1.3 ± 0.1[f]	−17.0 ± 0.4	−7.9	
	1.5 ± 0.2[g]			
	−0.8 ± 0.2[j]			
25	1.3 ± 0.1[k]	−24.7 ± 0.5	−15.6	
	0.2 ± 0.1[i]			
	0.5 ± 0.2[l]			

[a] Relative to ammonia (PA = 204.0 kcal mol^{-1}). [b] Relative to 1*H*-pyrazole. [c] Reference base: triethylamine (−29.3). [d] Reference base: tri-*n*-propylamine (−31.3). [e] Reference base: diisopropylethylamine (−31.8). [f] Reference base: neopentylamine (−16.3). [g] Reference base: 2-methoxypyridine (−18.2). [h] Reference base: 3-methylpyridine (−20.3). [i] Reference base: di-*n*-propylamine (−24.1). [j] Reference base: 4-methoxycarbonylpyridine (−16.0). [k] Reference base: diisopropylamine (−26.4). [l] Reference base: *N*-methylpyrrolidine (−25.5).

Table II. Chemical Ionization Experiments, CID Values (Corrected)

exp	pair of compounds (M_r)	K	exp	pair of compounds (M_r)	K
1	**1** (68)/**2** (118)	3.9	19	**9** (68)/**11** (118)	7.5
2	**1** (68)/**3** (82)	3.2	20	**9** (68)/**12** (82)	4.4
3	**1** (68)/**4** (82)	2.9	21	**11** (118)/**12** (82)	1.4
4	**1** (68)/**5** (82)	5.4	22	**11** (118)/**17** (96)	4.5
5	**2** (118)/**3** (82)	2.2	23	**12** (92)/**13** (132)	1.5
6	**1** (68)/**8** (96)	8.5	24	**12** (92)/**14** (124)	2.4
7	**1** (68)/**6** (132)	64	25	**13** (132)/**16** (146)	1.9
8	**1** (68)/**10** (132)	73	26	**14** (124)/**16** (146)	1.1
9	**2** (118)/**6** (132)	4.2	27	**14** (124)/**17** (96)	2.3
10	**3** (82)/**8** (96)	2.4	28	**14** (124)/**18** (174)	2.4
11	**4** (82)/**8** (96)	2.6	29	**15** (124)/**16** (146)	1.0
12	**5** (92)/**8** (96)	3.9	30	**15** (124)/**17** (96)	1.7
13	**6** (132)/**9** (68)	2.1	31	**15** (124)/**18** (174)	2.4
14	**6** (132)/**7** (96)	3.8	32	**17** (96)/**20** (202)	2.6
15	**6** (132)/**8** (96)	3.7	33	**17** (96)/**19** (174)	1.2
16	**8** (96)/**10** (132)	2.7	34	**18** (174)/**20** (202)	3.2
17	**9** (68)/**10** (132)	1.4	35	**20** (202)/**21** (132)	3.6
18	**10** (132)/**11** (118)	2.0			

mercial), 4-methyl-1*H*-pyrazole (**3**),[3] 3(5)-methyl-1*H*-pyrazole (**4**),[3] 1-methyl-1*H*-pyrazole (**5**)[3], 1-methyl-1*H*-indazole (**6**),[5] 1,3-dimethyl-1*H*-pyrazole (**7**),[3] 1,5-dimethyl-1*H*-pyrazole (**8**),[3] 1*H*-imidazole (**9**) (commercial), 2-methyl-2*H*-indazole (**10**),[5] 1*H*-benzimidazole (**11**) (commercial), 1-methyl-1*H*-indazole (**12**),[3] 1-methyl-1*H*-benzimidazole (**13**),[2], 1-*n*-butyl-1*H*-imidazole (**14**),[10] 1-*tert*-butyl-1*H*-imidazole (**15**),[11] 1-ethyl-1*H*-benzimidazole (**16**),[12] 1,2-dimethyl-1*H*-imidazole (**17**),[3] 1-*tert*-butyl-1*H*-benzimidazole (**18**),[11] 1-*n*-butyl-1*H*-benzimidazole (**19**),[13] 1-adamantyl-1*H*-imidazole (**20**),[14] 7-methylazaindole (**21**),[15] 1-*n*-butyl-1*H*-pyrazole (**22**),[16] 1-adamantyl-1*H*-pyrazole (**23**),[14] bis(pyrazol-1-yl)methane (**24**),[17] and bis(pyrazol-1-yl)-1,2-ethane (**25**).[18]

Table III. Differences in Basicity (in ln K Units) Relative to Pyrazole

compd	$\Sigma\Delta$ ln K	compd	$\Sigma\Delta$ ln K
1	0	**12**	4.91
2	1.07	**13**	5.26
3	1.55	**14**	5.72
4	1.30	**15**	5.83
5	1.41	**16**	5.85
6	2.51	**17**	6.47
7	3.85	**18**	6.57
8	2.50	**19**	6.65
9	3.26	**20**	7.58
10	3.88	**21**	8.86
11	4.85		

Table IV. Predicted $\Delta\Delta G$ Values of Diazoles

compd	$\Delta\Delta G$ (kcal mol^{-1})	compd	$\Delta\Delta G$ (kcal mol^{-1})
11	−14.2	**19**	−19.5
14	−16.7	**20**	−22.3
15	−17.1	**21**	−26.1
16	−17.1		

The ICR procedure (Irvine) has been throughly described.[1-3] Only for new proton affinity (PA) values are the reference bases given in Table I.

The mass spectrometry studies (Mons) have been performed on a Varian MAT 311A reversed geometry instrument modified for the introduction of a collision gas between the two sectors.[5] Chemical ionization of mixtures of samples was performed with methane as the reagent gas. A 30% attenuation of the main beam was used. Of the two possibilities of fragmentation of the protonated dimers, MIKE (mass-analyzed ion kinetic energy, unimolecular reactions) or CID (collision-induced dissociations), the second one was selected for sensitivity reasons. The relative rate constants, k_{BH}/k_{B_0H} of Table II have been corrected for mass differences.[8b]

Results and Discussion

Chemical Ionization Results. The values of Table II provided a ladder anchored on pyrazole. To calculate the differences in basicity (expressed in ln K = ln (k_B/k_{B_0}) units), we have proceeded in the following way. A presence (1)–absence (0) matrix, similar to those known as Free–Wilson matrices,[19] was built up. The matrix contains 20 independent variables, $x_1, x_2, ..., x_{20}$, corresponding to the 20 adjacent pairs **1/2**, **2/3**, ..., **20/21**, and 36 dependent variables, corresponding to the 35 experiments reported in Table II plus the 1/1 pair (ln K = 0). A regression analysis (r^2 = 0.82 shows that two experiments, nos. 7 and 15, deviate twice as much as the other experiments. If these points are excluded, the regression coefficient improves (r^2 = 0.92) and the worst result is obtained for experiment 19 with an acceptable agreement [ln K(exp) = 2.015, ln K(calc) = 1.58]. For the excluded experiments the calculated values are far from the experimental ones:

(10) Dou, H. J. M.; Metzger, J. *Bull. Soc. Chim. Fr.* **1976**, 1861.
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(16) Dou, H. J. M.; Elguero, J.; Espada, M.; Hassanaly, P. *An. Quim.* **1978**, *74*, 1137.
(17) Claramunt, R. M.; Hernández, H.; Elguero, J.; Juliá, S. *Bull. Soc. Chim. Fr.* **1983**, *II*, 15.
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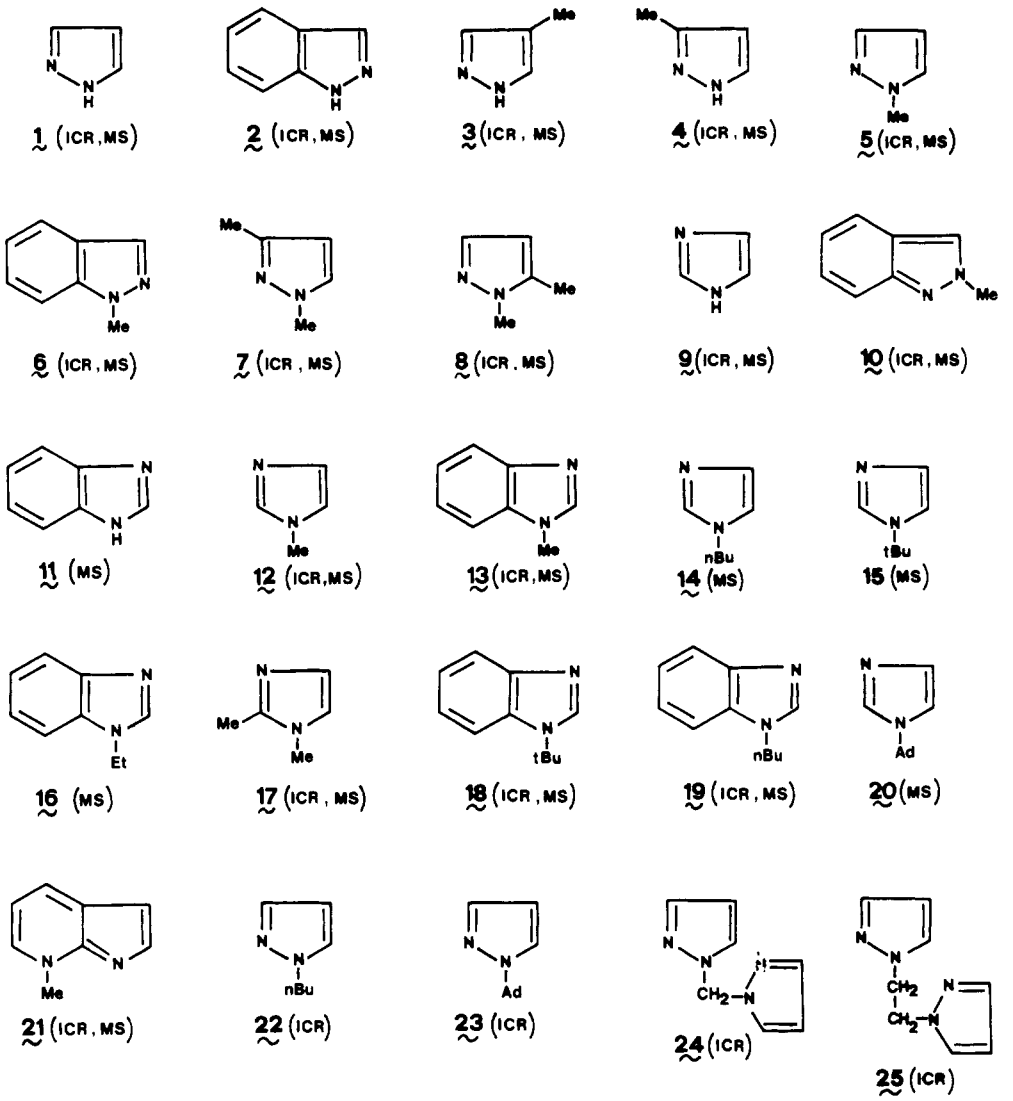
(19) Cativiela, C.; Lafuente, J. A. G.; Laureiro, J. I. G.; Elguero, J. *Gazz. Chim. Ital.* **1989**, *119*, 41.

Chart I



no. 7, ln K(exp) = 4.159 (K = 64), ln K(calc) = 2.51 (K = 12.3); no. 15, ln K(exp) = 1.308 (K = 3.7), ln K(calc) = −0.015 (K = 0.985). We shall discuss later these abnormal experiments.

The coefficients β of the model $\eta = \beta_0 + \beta_1 x_1 + \ldots + \beta_{20} x_{20}$ are the differences in basicity between two adjacent bases, $\Sigma\Delta$ ln K, expressed in ln K units. We have transformed, by simple addition, these values into differences in basicity relative to pyrazole, $\Sigma\Delta$ ln K, and reported them in Table III.

It is now possible to compare these values with the $\Delta\Delta G$ values (kcal mol^{-1}) of Table I (Figure 1). The regression line (eq 3) is fitted to the data by the method of least squares:

$$\Delta\Delta G = 0.26 - 2.97\Sigma\Delta \ln K \quad (3)$$

$$n = 15,\ r^2 = 0.967$$

The slope of eq 1 corresponds to an effective temperature[8,9] of almost 1500 K. Equation 1 and the $\Sigma\Delta$ ln K values of Table III yield Table IV $\Delta\Delta G$ values for compounds not measurable (**11**, **14**, **15**, **20**) or not measured (**16**, **19**) by ICR. The value for benzimidazole, −14.2 kcal mol^{-1}, is near the value estimated from ICR (−13 kcal mol^{-1}).

We have also calculated that the proton affinity of 7-methylazaindole, which corresponds to the CI experiment no. 35 (Table II) and to the $\Sigma\Delta$ ln K value of Table III, should be −26.1 kcal mol^{-1} relative to pyrazole (ICR value: −23.6 kcal mol^{-1}).[15] In the quoted reference[15] there was described the experimental N 1s electron binding energies of some compounds related to 7-methylazaindole (Els = 398.83 eV): imidazo[1,2-*a*]pyridine (399.18 eV, δPA = 25.9 kcal mol^{-1} relative to ammonia at 204.0 kcal mol^{-1}), benzoxazole (399.94 eV, δPA = 7.6 kcal mol^{-1}), and 2-methylbenzoxazole (399.72 eV, δPA = 11.9 kcal mol^{-1}). For the last three compounds, there exists a linear relationship between both series of values:

$$\mathrm{PA} = 9776.4 - 24.4\mathrm{Els} \quad (4)$$

$$n = 3,\ r^2 = 0.996$$

With this equation and the Els value of 7-methylazaindole, a value of δPA = −34.0 kcal mol^{-1} relative to ammonia can be calculated, which corresponds to −24.9 kcal mol^{-1} relative to pyrazole. This is an indication that ICR underestimates the basicity of 7-methylazaindole, or there is a larger than normal error in the CI measurement here.

Anomalies in the CI Method. The two experiments that have been excluded from the multiple regression (nos. 7 and 15) involve 1-methyl-1*H*-indazole (**6**); relative to 1*H*-pyrazole (**1**) (expt. no. 7), it appears too basic (K = [**6**]/[**1**], K(exp) = 64, K(calc) = 12.3), whereas relative to 1,5-dimethyl-1*H*-pyrazole (**8**) (K = [**8**]/[**6**], K(exp) = 3.7 K(calc) = 0.985), it behaves as a too weak base.

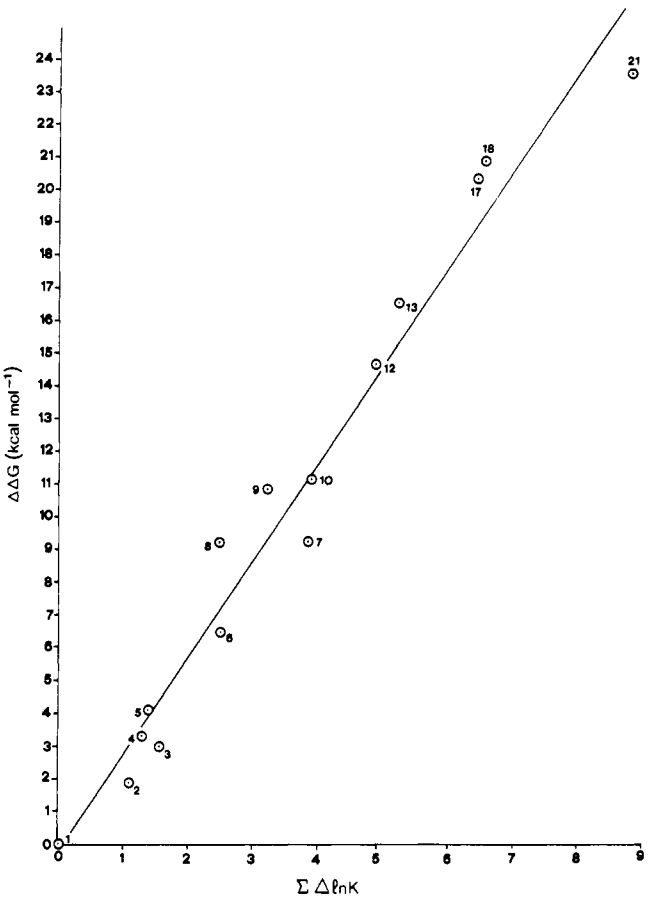
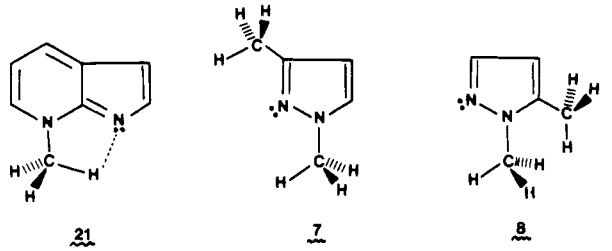


Figure 1. Plot of $\Delta\Delta G$ (in kcal mol^{-1}) vs $\Sigma\Delta$ ln K.

Chart II



21 7 8

Some anomalies of Figure 1 could be related to steric and entropic effects[20,21] since the cell temperature in ICR, 320 K,[22,23] is much lower than the "effective" temperature (about 1500 K) found in the CI experiments. These effects appear when the methyl groups near the lone pair are in a fixed (or, at least, in a highly populated) conformation in ICR and freely rotate in CI experiments. For instance, in compound **21** there is an intramolecular hydrogen bond (IMHB) (Chart II)[15] that stabilizes the neutral form. Since the IMHB disappears at 1500 K, this will result in an increase of the CI determined basicity, although this increase would not explain the 2.5 kcal mol^{-1} deviation of **21** in Figure 1. On the contrary the *N*-methyl group of a compound like **8** with a geared conformation (Chart II) cannot rotate in the [B–H··B]$^+$ complex and its basicity, as determined by CI, appears lower than that of its isomer,

Table V. Polarizability and Resonance Contributions to Gas-Phase Basicities

substituent	σ_α	σ_R	pyrazoles		imidazoles		benzimidazoles	
H	0	0	**1**	0	**0**	−10.8	**11**	−14.2
methyl	−0.35	−0.08	**5**	−4.1	**12**	−15.0	**13**	−16.8
ethyl	−0.49	−0.07		(−6.6)		(−16.1)	**16**	17.4
n-butyl	−0.57	−0.07	**22**	−8.1	**14**	−17.0	**19**	−19.8
tert-butyl	−0.75	−0.07		(−10.6)	**15**	−17.4	**18**	−21.2
adamantyl	−0.95	−0.06	**23**	−13.7	**20**	−22.6		(−23.6)

pyrazoles: $\Delta\Delta G = 15.43\sigma_\alpha - 14.21\sigma_R$, $n = 4$, $r^2 = 0.999$ (6)

imidazoles: $\Delta\Delta G = -10.9 + 11.69\sigma_\alpha - 7.63\ \sigma_R$, $n = 5$, $r^2 = 0.938$ (7)

benzimidazoles: $\Delta\Delta G = -14.2 + 11.12\sigma_\alpha - 18.76\ \sigma_R$, $n = 5$, $r^2 = 0.958$ (8)

1,3-dimethyl-1*H*-pyrazole (**7**). Finally, the ICR value for 1*H*-imidazole (**9**) (−10.8) in Figure 1 appears too large. Mautner's value (−9.3)[3,24] lies in the line of regression.

Discussion of the Basicity Data. We have now a collection of 24 diazoles with known proton affinities, determined either by ICR, by dissociation of proton-bound dimers, or by both methods (Tables I and IV, $\Delta\Delta G$ values).

To discuss these values, we will use the same approach that gives satisfactory results in the case of pyridines.[25] Thus, the variation of the standard free-energy changes of an acid–base equilibrium in the gas phase can be described by eq 5 for *N*-alkyl substituents.

$$\Delta\Delta G = a + \rho_\alpha\sigma_\alpha + \rho_R\sigma_R \qquad (5)$$

We have gathered in Table V the σ values from the literature[26] for six substituents on the nitrogen together with the $\Delta\Delta G$ values corrected by 0.4 kcal mol^{-1} to account for symmetry variations between NH and NR azoles.[27] There is no symmetry difference between the NH and NMe indazoles.

The results of the multiple regression range from excellent (eq 6) to good (eqs 7 and 8). In the case of imidazoles, only 1-*tert*-butyl-1*H*-imidazole (**15**) deviates significantly ($\Delta\Delta G$(calc) = −19.1 kcal mol^{-1}). The calculated values, in parentheses, are good approximations to the still unknown experimental values.

If we assume that compounds **24** and **25** are similar to *N*-benzyl ($\sigma_\alpha = -0.70$, $\sigma_R = -0.07$) and *N*-phenethyl ($\sigma_\alpha = -0.65$, $\sigma_R = -0.07$)[26] pyrazoles, then eq 6 yields $\Delta\Delta G$(**24**) = −9.8 kcal mol^{-1} and $\Delta\Delta G$(**25**) = −9.0 kcal mol^{-1}, respectively.

The values, when compared with Table I results (corrected for symmetry),[27] −8.2 and −15.9 kcal mol^{-1}, respectively, show a fair agreement in the case of bis(pyrazolyl)methane (**24**) but a large discrepency for bis(pyrazolyl)ethane (**25**). We propose that in the last compound, a chelation of the protonated form by the second pyrazole intervenes, which results in a stabilization of the cation and in a subsequent increase of basicity. For geometrical reasons, this chelation is not possible in the bis(pyrazolyl) cation, where the distance between pyridine-like nitrogens is too large (2.9 Å).[28]

Comparison of eqs 4, 5, and 6 shows that polarizability effects are more important in pyrazoles than in imidazoles and benzimidazoles whereas the resonance effects are more erratic due to their small variation in the alkyl series.

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The last comment concerns the annelation effect, i.e., the difference in basicity between azoles and benzazoles.[2] Using the data of pyrazole/indazole, 1-methylpyrazole/1-methylindazole, and the imidazole/benzimidazole pairs of Table V, the following equation can be calculated, always taking into account the symmetry effect:

$$\Delta\Delta G(\text{benzazole}) = -2.5 - 0.96\Delta\Delta G(\text{azole})$$

$$n = 7,\ r^2 = 0.989$$

For other related compounds we have found[2] a similar slope (0.93). To 1-*tert*-butyl-1*H*-benzimidazole (**18**) (-21.2) should correspond a value of -19.4 kcal mol^{-1} for 1-*tert*-butyl-1*H*-imidazole (**15**). The value, -17.1 (uncorrected) of Table IV seems again underestimated.

In conclusion, both methods (CI/MS/MS and ICR) yield comparable results. Part of the scatter in Figure 1 is expected due to the fundamental difference of process (1) and (2).

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Stereospecific Friedel–Crafts Alkylation of Aromatic Compounds: Synthesis of Optically Active 2- and 3-Arylalkanoic Esters[1]

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The alkylation of aromatic compounds, such as benzene, toluene, chlorobenzene, and naphthalene, with optically active (*S*)-alkyl 2-(sulfonyloxy)propionates and (*R*)-alkyl 3-(sulfonyloxy)butanoates in the presence of $AlCl_3$ afforded optically active (*S*)-alkyl 2-arylpropionates and (*S*)-alkyl 3-arylbutanoates in fair to good chemical yields (40–84%) and in good to excellent optical yields (61–97%). As usually occurs in Friedel–Crafts alkylation reactions, poor regioselectivity was observed.

We have recently reported the synthesis of (*S*)-methyl and (*S*)-ethyl 2-phenylpropionate as first examples of a Friedel–Crafts alkylation reaction with acyclic alkylating reagents, proceeding with good chemical yields (70–80%) and high stereospecificity (>97%) with inversion of configuration.[2] As an extension of these findings, we now report the results obtained in a detailed investigation on the synthetic usefulness and limitation of this alkylation reaction: using sulfonyloxy derivatives of optically active hydroxy esters **1** as the alkylating reagents, under $AlCl_3$ catalysis, the reaction afforded fair to good chemical and optical yields of the corresponding arylalkanoic esters **3** (Scheme I). In order to gain insight on the regioselectivity of the reaction, we have extended this study to the alkylation of some substituted benzenes and naphthalene.

Scheme I[a]

$$\underset{\mathbf{1}}{CH_3{}^*CH(OX)(CH_2)_nCOOR} + \underset{\mathbf{2}}{ArH} \xrightarrow{AlCl_3} \underset{\mathbf{3}}{CH_3{}^*CH(Ar)(CH_2)_nCOOR}$$

[a] **1a**: $n = 0$, X = SO_2CH_3, R = CH_3. **1b**: $n = 0$, X = SO_2CH_3, R = C_2H_5. **1c**: $n = 0$, X = SO_2Cl, R = CH_3. **1d**: $n = 0$, X = SO_2Tol, R = CH_3. **1e**: $n = 0$, X = SO_2Tol, R = C_2H_5. **1f**: $n = 0$, X = SO_2CF_3, R = C_2H_5. **1g**: $n = 1$, X = SO_2CH_3, R = CH_3. **1h**: $n = 1$, X = SO_2CH_3, R = C_2H_5. **1i**: $n = 1$, X = SO_2Tol, R = C_2H_5. **2a**: Ar = C_6H_5. **2b**: Ar = $CH_3C_6H_4$. **2c**: Ar = $C_{10}H_7$. **2d**: Ar = Cl-C_6H_4. **3a**: $n = 0$, Ar = C_6H_5, R = CH_3. **3b**: $n = 0$, Ar = C_6H_5, R = C_2H_5. **3c**: $n = 1$, Ar = C_6H_5, R = CH_3. **3d**: $n = 1$, Ar = C_6H_5, R = C_2H_5. **3e**: $n = 0$, Ar = *o*-, *m*-, and *p*-$CH_3C_6H_4$, R = C_2H_5. **3f**: $n = 1$, Ar = *o*-, *m*-, and *p*-$CH_3C_6H_4$, R = C_2H_5. **3g**: $n = 0$, Ar = 1- and 2-$C_{10}H_7$, R = CH_3. **3h**: $n = 0$, Ar = *o*-, *m*-, and *p*-ClC_6H_4, R = C_2H_5. **3i**: $n = 1$, Ar = *o*-, *m*-, and *p*-ClC_6H_4, R = C_2H_5.

Results

Alkylation of Benzene. We first examined the influence of the leaving group in the $AlCl_3$-mediated alkylation of benzene (**2a**), taken as a model reaction; in the previous report,[2] we employed, as alkylating reagents, (*S*)-methyl

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