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Nucleophilic Reactivities and Lewis Basicities of 2-Imidazolines and Related **N-Heterocyclic Compounds**

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The nucleophilicity parameters N and s_{N_l} as defined by the linear free-energy equation $\log k(20 \text{ °C}) = s_N(N + E)$, of the 2imidazolines **1a-d** and the related N-heterocyclic compounds 2-5 have been determined by studying the rates of their reactions with differently substituted benzhydrylium ions in dichloromethane at 20 °C by stopped-flow or laser flash photolysis techniques. It is demonstrated that the N and s_N parameters thus obtained can be used to reliably predict the

rate constants for their reactions with Michael acceptors of known electrophilicity E. A comparison of the nucleophilicity parameters of the imidazoline derivatives 1 with other commonly used nucleophilic organocatalysts shows that they are 10 to 10³ times less nucleophilic than PPh₃, 1,8-diazabicyclo[5.4.0]undec-7-ene, or 4-(dimethylamino)pyridine. The structure-reactivity relationships of these heterocycles are discussed.

Introduction

Imidazolines, oxazolines, and thiazolines are important building blocks in natural products and pharmaceuticals,^[1,2] and are often used as ligands in coordination chemistry and homogeneous catalysis.^[3] Chiral imidazolines have been employed as organocatalysts^[4] in asymmetric Diels-Alder, Friedel-Crafts, and Michael reactions.^[5] Recently, Lectka and co-workers reported sulfonated analogues of 4,5-dihydro-1H-imidazole to be efficient nucleophilic catalysts in diastereoselective Staudinger β -lactam synthesis by activating in situ generated ketenes.^[6] In 2006, Tan and coworkers used chiral imidazolines as catalysts in asymmetric Morita-Baylis-Hilman reactions.^[7,8]

It has been reported in numerous publications that the rate constants $(\log k)$ for the reactions of nucleophiles with carbocations and Michael acceptors can be described by the linear free-energy relationship (1),^[9] in which electrophiles are characterized by the solvent-independent electrophilicity parameters E and nucleophiles are characterized by two solvent-dependent parameters, the nucleophilicity parameter N and the sensitivity parameter $s_{\rm N}$.

$$\log k(20 \text{ °C}) = s_{\rm N}(N+E) \tag{1}$$

In this work we have used the benzhydrylium methodology to characterize the nucleophilicity parameters of the 2-

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imidazolines 1a-d, 2-methylthiazoline (2), and 2-methyloxazoline (3), and to compare their reactivities with those of the homologous tetrahydropyrimidines 4a,b, dihydropyrrole 5, and previously characterized nucleophilic organocatalysts (Scheme 1).^[10]



Scheme 1. Nitrogen-containing heterocycles 1-5 and DABCO and DMAP.

Results and Discussion

Reaction Products

The addition of a dichloromethane solution of 1a or 1b to an equimolar amount of (dma)₂CH⁺BF₄⁻ in dichloromethane gave a mixture of monosubstituted 6a,b and disub-

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Scheme 2. Products obtained from the reaction of 1a,b with $(dma)_2CH^+BF_4^-$.

stituted products 7a,b in a ratio of around 1:3 as well as 1a-H⁺ and 1b-H⁺ (Scheme 2; the abbreviations used to describe the benzhydrylium ions are defined in Table 1). The formation of the disubstituted products 7a,b can be explained by the subsequent reactions of the deprotonated (by a second molecule of 1a or 1b) monosubstituted products **6a**,**b** with $(dma)_2CH^+BF_4^-$. Although we were unable to isolate the monosubstituted products, the disubstituted imidazolinium tetrafluoroborates 7a,b-BF₄ were isolated by subsequent aqueous work-up and crystallization. Crystals of 7b-BF₄ suitable for single-crystal X-ray structure analysis were grown by diffusion of *n*-pentane vapor into a dichloromethane/ethyl acetate solution (10:1) of 7b-BF₄ (Figure 1).^[11] For details of the experimental procedures and characterization of the products, see the Supporting Information.



Figure 1. Crystal structure of **7b**-BF₄. The ellipsoids are drawn at the 50% probability level.^[11]

The higher homologue of **1a**, 2-methyl-1,4,5,6-tetrahydropyrimidine (**4a**), however, readily reacted with (dma)- $CH^+BF_4^-$ to give only the 1:1 adduct **8** in 92% yield (Scheme 3).



Scheme 3. Formation of 8 by the reaction of 4a with $(\mbox{dma})_2\mbox{-} CH^+BF_4^-.$

Compounds 1c, 2, and 3 did not react with $(dma)_2$ -CH⁺BF₄⁻ when an equimolar amount of the nucleophile was mixed with $(dma)_2$ CH⁺BF₄⁻ in CH₂Cl₂ at room temperature. However, mixing of 1c or 2 with an equimolar amount of substituted benzhydryl chloride or bromide gave the addition products 9–11 in yields greater than 90%, as determined in situ by NMR spectroscopy (Scheme 4).



Scheme 4. Products obtained from the reactions of 1c and 2 with benzhydryl derivatives.

Kinetics

Most of the reactions of the nucleophiles 1-5 with benzhydrylium ions (Table 1) were investigated photometrically in CH₂Cl₂ at 20 °C by using stopped-flow techniques as

 $-d[\operatorname{Ar_2CH^+}]/dt = k_2[\operatorname{Ar_2CH^+}][\operatorname{Nu}]$

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described previously.^[9] The kinetics of the reactions of **4a** with benzhydrylium ions were also studied in CH₃CN and DMSO.

Table 1. Abbreviations and the electrophilicity parameters E for the benzhydrylium ions used in this work.





For the fast reactions $(k > 10^6 \text{ m}^{-1} \text{ s}^{-1})$, the benzhydrylium ions were generated by laser flash photolysis (7 ns pulse, 266 nm) of substituted benzhydryltriphenylphosphonium tetrafluoroborates in the presence of **2** and **3**, as described previously.^[12] In all cases, an excess of the heterocyclic nucleophiles (more than 10 equiv.) over the electrophiles was used to achieve pseudo-first-order conditions. The pseudo-first-order rate constants k_{obs} were obtained by a least-squares fit of the exponential decay of the absorbances of Ar₂CH⁺ to the expression $A = A_0 e^{-k_{obs}t} + C$. The plots of k_{obs} against nucleophile concentration were linear with negligible intercepts, as shown in Figure 2b, which indicates a second-order rate law [Equation (2)]. The slopes of these correlation lines yielded the second-order rate constants k, which are presented in Table 2.

Nucleophilicity Parameters

When the logarithms of the second-order rate constants (Table 2) for the reactions of the nucleophiles 1-5 with the



Figure 2. a) Exponential decay of the absorbance A at 622 nm during the reaction of **1b** $(1.28 \times 10^{-4} \text{ M})$ with $(\text{mpa})_2\text{CH}^+\text{BF}_4^ (1.00 \times 10^{-5} \text{ M})$ in CH₂Cl₂ at 20 °C ($k_{\text{obs}} = 10.7 \text{ s}^{-1}$). b) Determination of the second-order rate constant $k = 8.12 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ from the dependence of k_{obs} on the concentration of **1b**.

reference electrophiles Ar_2CH^+ were plotted against the empirical electrophilicity parameters E of Ar_2CH^+ (Table 1), linear correlations were obtained, as shown for some representative examples in Figure 3 (see the Supporting Information for all reaction series investigated). As described above, the kinetics of the reactions of the nucleophiles **2** and **3** with benzhydrylium ions were measured by two different techniques, the stopped-flow method and laser flash photolysis. Linear correlations (as shown for **2** in Figure 4) between the logarithms of the rate constants k measured by the two methods and the electrophilicity parameters E reflect the consistency of our measurements.

According to Equation (1), the slopes of the correlation lines give the nucleophile-specific sensitivity parameters s_N and the intercepts on the abscissa give the nucleophilicity parameters N for 1–5; these values are listed in Table 2.^[9]

Relationship between Structures and Nucleophilicities

The similarities of the slopes of the correlation lines in Figure 3 (and Figure 4), which are numerically expressed by the sensitivity parameters s_N in Table 2, indicate that the relative nucleophilicities of the N-heterocycles 1–5 depend only slightly on the nature of the electrophiles.

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Table 2. Second-order rate constants for the reactions of benzhydrylium ions (Ar₂CH⁺) with the nucleophiles 1–5 in dichloromethane at 20 °C.

Nucleophile	$N, s_{\rm N}^{[a]}$	Benzhydrylium ion ^[b]	$k [\mathrm{M}^{-1}\mathrm{s}^{-1}]$	Method ^[c]
N	12.92, 0.77	(dma) ₂ CH ⁺	3.73×10^4	SF
Me N		(pyr) ₂ CH ⁺	1.04×10^4	SF
H 1a		$(tha)_2 CH^+$	3.75×10^{3}	SF
		$(ind)_2 CH^+$	1.76×10^{3}	SF
− N,	12.31.0.77	$(mpa)_2CH^+$	8.12×10^{4}	SF
Ph		$(dma)_2CH^+$	1.26×10^{4}	SF
Ĥ 1b		(pyr) ₂ CH ⁺	3.25×10^{3}	SF
		$(thq)_2 CH^+$	1.42×10^{3}	SF
		(ind) ₂ CH ⁺	5.22×10^2	SF
⊂ ^N	10.03, 0.75	$(mfa)_2 CH^+$	$4.91 imes 10^4$	SF
Me N		$(dpa)_2 CH^+$	8.81×10^3	SF
Ac 1c		$(mor)_2 CH^+$	2.25×10^3	SF
		(mpa) ₂ CH ⁺	1.48×10^3	SF
N SI	13.11, 0.83	$(pyr)_2CH^+$	2.82×10^4	SF
∟ ≫—Ph		$(thq)_2 CH^+$	$1.18 imes 10^4$	SF
∖ _{Bn} 1d		(ind) ₂ CH ⁺	4.31×10^{3}	SF
		(jul) ₂ CH ⁺	9.97×10^{2}	SF
_ N,	10.20, 0.71	(ani)(tol)CH ⁺	1.35×10^{8}	LFP
Me		(ani)(pop)CH ⁺	3.91×10^{7}	LFP
2		(ani) ₂ CH ⁺	2.03×10^{7}	LFP
		(ani)(fur)CH ⁺	7.47×10^{6}	LFP
		(pfa),CH ⁺	1.09×10^{5}	SF
		$(mfa)_2 CH^+$	$3.65 imes 10^4$	SF
		$(dpa)_2 CH^+$	5.99×10^{3}	SF
		(mor) ₂ CH ⁺	1.86×10^{3}	SF
-N.	9.81. 0.77	(ani)(pop)CH ⁺	6.16×10^{7}	LFP
Me	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	(ani) ₂ CH ⁺	3.44×10^{7}	LFP
3		(ani)(fur)CH ⁺	1.55×10^{7}	LFP
		(fur) ₂ CH ⁺	5.35×10^{6}	LFP
		(mfa) ₂ CH ⁺	3.86×10^4	SF
		$(dpa)_2 CH^+$	7.02×10^{3}	SF
		$(mor)_2 CH^+$	$1.70 imes 10^3$	SF
		(mpa) ₂ CH ⁺	$1.07 imes 10^3$	SF
∩ N	15.21, 0.69	(dma) ₂ CH ⁺	4.19×10^{5}	SF
└ _N └└ _{Me}		$(pyr)_2CH^+$	1.68×10^5	SF
H 4a		(thq) ₂ CH ⁺	$5.90 imes 10^4$	SF
		(ind) ₂ CH ⁺	2.82×10^{4}	SF
4a in CH ₃ CN	14.43, 0.79	$(pyr)_2CH^+$	2.30×10^{5}	SF
		$(thq)_2 CH^+$	$7.29 imes 10^4$	SF
		(ind) ₂ CH ⁺	2.89×10^4	SF
		(jul) ₂ CH ⁺	9.09×10^3	SF
4a in DMSO	14.58, 0.79	$(pyr)_2CH^+$	3.24×10^5	SF
		$(thq)_2 CH^+$	9.34×10^4	SF
		(ind) ₂ CH ⁺	3.29×10^4	SF
		(jul) ₂ CH ⁺	1.31×10^4	SF
Ň	14.62, 0.72	$(dma)_2CH^+$	2.75×10^{5}	SF
└ _N └ Ph		(pyr) ₂ CH ⁺	9.61×10^4	SF
H 4b		$(thq)_2 CH^+$	3.79×10^4	SF
		$(ind)_2 CH^+$	1.58×10^4	SF
	13.12, 0.69	$(mpa)_2 CH^+$	9.53×10^4	SF
		$(dma)_2CH^+$	2.02×10^4	SF
5		(pyr) ₂ CH ⁺	5.57×10^3	SF
		$(thq)_2 CH^+$	2.37×10^3	SF

[a] Nucleophilicity parameters N and s_N derived from Equation (1). [b] For abbreviations, see Table 1. [c] SF = stopped-flow. LFP = laser-flash photolysis.



Figure 3. Plots of $\log k$ for the reactions of the N-heterocyclic compounds **1a**–**d** and **4a**,**b** with benzhydrylium ions versus their electrophilicity parameters *E* in CH₂Cl₂ at 20 °C.



Figure 4. Plots of $\log k$ for the reactions of **2** with benzhydrylium ions versus their electrophilicity parameters *E* in CH₂Cl₂ at 20 °C.



Scheme 5. Relative nucleophilic reactivities of the nucleophiles 1a-d and 4a,b towards (pyr)₂CH⁺ in CH₂Cl₂. [a] *k* for the reaction of 1c with (pyr)₂CH⁺ was calculated by using Equation (1), the *N* and s_N values from Table 2, and the electrophilicity *E* from Table 1.

Scheme 5 shows that the tetrahydropyrimidine derivatives **4a** and **4b** are 16 and 30 times more nucleophilic than the imidazolines **1a** and **1b**, respectively. This ring size effect

parallels the previously observed reactivities of cyclic guanidines^[10g] and isothioureas,^[10f] that is, amidines in six-membered rings are generally one order of magnitude more nucleophilic than the corresponding amidines in five-membered rings.^[10e-10g]

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Replacement of the 2-methyl group in 1a or 4a by the phenyl group in 1b or 4b reduces the reactivity by a factor of 3 and 1.7, respectively. Although the replacement of the NH proton of 1a by the electron-withdrawing acetyl group $(1a \rightarrow 1c)$ decreases the reactivity by a factor of 183, the replacement of the NH proton of 1b by the electron-donating benzyl group $(1b \rightarrow 1d)$ increases the reactivity by a factor of 8.7.

Scheme 6 illustrates the effect of heteroatoms at the 3position of 2-methylpyrroline (5). The replacement of "CH₂" by "O" ($5 \rightarrow 3$) reduces the reactivity by a factor of 102. Because electrophilic attack takes place at the sp² lone pair of nitrogen, which resides in the plane of the ring, the reduction of nucleophilicity can be explained by the inductive effect of "O", which overcompensates the mesomeric effect. The replacement of "O" by "S" ($3 \rightarrow 2$) does not have a significant influence on the nucleophilic reactivities of the N-heterocycles. The lower electronegativity and weaker +M effect of "S" relative to "O" clearly compensate each other. Compensation of the opposing inductive and resonance effects also explains why the introduction of the "NH" group in place of "CH₂" ($5 \rightarrow 1a$) causes only a marginal increase in the nucleophilicity.



Scheme 6. Relative nucleophilic reactivities of the nucleophiles 1a, 2, 3, and 5 towards $(mor)_2CH^+$ in CH₂Cl₂. [a] *k* was calculated by using Equation (1), the *N* and s_N values are from Table 2, and the electrophilicity *E* from Table 1.

Reactions with Michael Acceptors

To examine the applicability of the nucleophilicity parameters N and s_N in Table 2 to the reactions with other types of electrophiles, we studied the rates of the reactions of the cyclic amidines **1a**,**d** and **4a** with the Michael acceptors **12a**–**d**, the electrophilicity parameters of which have previously been determined.^[13]

The rates of the reactions of **1a**,**d** and **4a** with **12a**–**d** were measured by the same photometric method as described above for their reactions with benzhydrylium ions, that is, by following the decay of the absorbances of **12a**–**d** at or close to their absorption maxima at 20 °C in CH₂Cl₂. The resulting second-order rate constants are listed in Table 3. Although **1d** is 2.7 times more nucleophilic than **1a**, it does not react with any of the Michael acceptors studied because of the high reversibility of these reactions.

Table 3. Comparison of the calculated and experimental secondorder rate constants $k [\text{M}^{-1}\text{s}^{-1}]$ for the reactions of the nucleophiles **1a,d** and **4** with the Michael acceptors **12a–d** in dichloromethane at 20 °C.

Electrophile	E ^[a]	Nucleophile	k ^{exp}	k ^{calc [b]}
	-9.15	1 a	7.37×10^3	8.00×10^2
		1d	h.r. ^[c]	1.94×10^3
0200 12a		4 a	7.38×10^4	$1.52 imes 10^4$
	-10.11	1 a	h.r. ^[c]	1.46×10^2
		1d	h.r. ^[c]	3.09×10^2
12b		4 a	2.73×10^2	3.30×10^3
0 II	-10.28	1 a	8.16×10^2	$1.08 imes 10^2$
		1d	h.r. ^[c]	2.23×10^2
MeO 0 0 0 12c		4 a	$1.00 imes 10^4$	2.52×10^3
0	-10.37	1 a	$4.76 imes 10^2$	9.19×10^{1}
NMe		1d	h.r. ^[c]	1.88×10^2
MeO O NO 12d Me		4 a	$6.15 imes 10^3$	2.19×10^3

[a] Electrophilicity parameters *E* are taken from ref.^[13] [b] Calculated by using Equation (1), the *N* and s_N values are from Table 2, and the *E* values from Table 3. [c] Highly reversible.

Comparison of the experimental rate constants k^{exp} with the rate constants k^{calc} calculated by using Equation (1) and the *N* and s_N parameters in Table 2 and the *E* values from ref.^[13] shows agreement within factors of 3 to 11. In view of the simplicity of the three-parameter Equation (1), we consider these deviations acceptable because the electrophilicities of the Michael acceptors **12** were determined from their reactions with carbanions in DMSO and the nucleophilicity parameters of **1** and **4** are derived from their reactions with benzhydrylium ions in CH₂Cl₂ (Table 2). We therefore conclude that the rates of the reactions of the nucleophiles **1** and **4** with electrophiles with known electrophilicity parameters *E* can be predicted by using Equation (1) and the *N* and s_N parameters reported in Table 2.

Equilibrium Constants and Intrinsic Barriers

As the reactions of the nucleophiles 1–5 with the colored benzhydrylium ions give colorless products, equilibrium constants for these reactions were also measured photometrically. Because of the proportionality between the concentrations and absorbances of the colored benzhydrylium

$$Ar_{2}CH^{+} + Nu \xrightarrow{K} Ar_{2}CH - Nu^{+}$$
(3)

$$\kappa = \frac{\left[\operatorname{Ar}_{2}\operatorname{CH}-\operatorname{Nu}^{+}\right]}{\left[\operatorname{Ar}_{2}\operatorname{CH}^{+}\right]\left[\operatorname{Nu}\right]} = \frac{A_{0} - A}{A\left[\operatorname{Nu}\right]}$$
(4)

where $[Nu] = [Nu]_0 - [(A_0 - A)/\varepsilon d]$ ε = molar absorption coefficient d = path length FULL PAPER

CH₂Cl₂ at 20 °C.

Table 4. Equilibrium constants *K*, reaction free energies ΔG° , activation free energies ΔG^{\neq} , and intrinsic barriers ΔG_0^{\neq} for the reactions of nucleophiles **1–3** with benzhydrylium ions Ar₂CH⁺ in

Nucleophile	Ar_2CH^+	K [M^{-1}]	$\Delta G^{0 [a]}$ [kJ mol ⁻¹]	$\Delta G^{\neq [b]}$ [kJ mol ⁻¹]	$\Delta G_0^{\neq [c]}$ [kJ mol ⁻¹]
Me	$(mor)_2 CH^+$	3.10×10^4	-25.2	52.9	64.9
Ac 1c	(111)2011	5.51 ~ 10	-19.9	54.0	05.0
CN→Ph	(ind) ₂ CH ⁺ (iul) ₂ CH ⁺	2.67×10^{3} 7.00×10^{3}	-30.5 -21.6	51.4 54.9	65.8 65.3
Bn 1d	$(lil)_2CH^+$	8.10×10^{3}	-21.9	57.5 ^[d]	68.0
∑Me	$(mfa)_2 CH^+$	2.27×10^4 7.20 × 10 ³	-24.4	46.2	57.8
3 2	$(\text{upa})_2 \text{CH}^+$ $(\text{mor})_2 \text{CH}^+$	6.38×10^2	-15.7	53.4	61.0
Me	$(mor)_2 CH^+$	4.07×10^{3}	-20.2	53.6	63.3
<u> </u>	(mpa) ₂ CH ⁺	6.57×10^{2}	-15.8	54.8	62.5

[a] Calculated by using the equilibrium constants K in this table $(\Delta G^{\circ} = -RT \ln K)$. [b] Calculated by using the rate constants in Table 2, determined by using the Eyring equation. [c] Calculated by using Equation (5). [d] Calculated by using Equation (1), N and $s_{\rm N}$ values from Table 2 and E values from Table 1.

ions, the equilibrium constants K for the reaction in Equation (3), which are listed in Table 4, were calculated by using Equation (4), in which A_0 and A are the absorbances of Ar_2CH^+ before and after the addition of nucleophiles, respectively.

Table 4 shows that the 2-methylimidazoline derivative 1c is a 50 times stronger Lewis base than 2-methylthiazoline [2, reference $(mor)_2CH^+$] and an eight times stronger Lewis base than 2-methyloxazoline [3, reference $(mor)_2CH^+$]. Although a direct comparison of the equilibrium constants is not possible, the data in Table 4 demonstrate that *N*-benzylated 2-methylimidazoline (1d) is a much stronger Lewis base than 1c, 2, and 3 because it gives adducts even with the weakly Lewis acidic benzhydrylium ions (lil)₂CH⁺, (jul)₂CH⁺, and (ind)₂CH⁺.

Comparison of the rate and equilibrium constants for the reactions of benzhydrylium ions with the imidazoline derivative **1d** and other commonly used nucleophilic organocatalysts (Scheme 7) illustrates that **1d** reacts with electrophiles at a rate similar to PPh₃, but 10 and 2.5×10^3 times more slowly than 4-(dimethylamino)pyridine (DMAP) and 1,4-diazabicyclo[2.2.2]octane (DABCO), respectively. However, **1d** is a 200–300 times stronger Lewis base than PPh₃ and DABCO, comparable to the Lewis basicity of DMAP.^[10] This breakdown of the rate–equilibrium relationship indicates that these reactions have different Marcus intrinsic barriers ΔG_0^{\neq} , the barriers of the corresponding reactions without any thermodynamic driving force ($\Delta G^{\circ} =$ 0).^[14]

Substitution of the activation free energies ΔG^{\neq} (derived from the rate constants in Table 2 by using the Eyring equation) and Gibbs free energies ΔG° (= $-RT \ln K$) into the



Scheme 7. Comparison of the rate and equilibrium constants for the reactions of $(ind)_2CH^+$ with **1d**, DABCO, DMAP, and PPh₃ in CH₂Cl₂. [a] In CH₃CN from ref.^[10h] [b] From ref.^[10a,d]

Marcus Equation (5)^[14] yields the intrinsic barriers ΔG_0^{\neq} for these reactions, which are listed in Table 4.

$$\Delta G^{\neq} = \Delta G_0^{\neq} + 0.5\Delta G^{\circ} + \left[(\Delta G^{\circ})^2 / 16\Delta G_0^{\neq} \right]$$
⁽⁵⁾

Table 4 shows that the intrinsic barrier ΔG_0^{\neq} for the reaction of the benzhydrylium ion $(\text{mor})_2\text{CH}^+$ with **2** is 2 kJ mol⁻¹ smaller than that for the reaction with **3**, and 4 kJ mol⁻¹ smaller than that for the reaction with **1c**. From the data for the series S < O < NAc, one can conclude that the product stabilizing mesomeric effect of O and, even more so, of NAc is only partially developed in the transition states of the reactions with benzhydrylium ions.^[15]

According to Scheme 7, the reaction of $(ind)_2CH^+$ with the imidazoline derivative **1d** has a much higher intrinsic barrier ($\Delta\Delta G_0^{\neq} = 6 \text{ kJ mol}^{-1}$) than the corresponding reactions with DMAP and PPh₃. Although **1d** is a 10² times stronger Lewis base than PPh₃, both **1d** and PPh₃ attack electrophiles with similar rates. On the other hand, despite the similar Lewis basicities of **1d** and DMAP, imidazole **1d** reacts 10 times more slowly than DMAP because of the higher reorganization energy needed for the formation of a resonance stabilized amidinium ion from **1d**. In comparison with **1d**, the higher nucleophilicity (>10³ times) of the weaker Lewis base DABCO (>10² times) can analogously be explained by the lower intrinsic barriers ($\Delta\Delta G_0^{\neq} =$ 20 kJ mol⁻¹) of its reactions with electrophiles.

Nucleofugalities

Equation (6), which is formally analogous to Equation (1), has recently been suggested as a basis for a nucleofugality scale, allowing calculation of the rate constants of heterolytic cleavage k_{\leftarrow} (at 25 °C) from the electrofugality parameters $E_{\rm f}$ of the electrofuges, the nucleofugality parameters $N_{\rm f}$, and the nucleofuge-specific sensitivity parameters $s_{\rm fc}^{[16]}$

$$\log k_{\leftarrow}(25 \text{ °C}) = s_{\rm f}(E_{\rm f} + N_{\rm f}) \tag{6}$$

In analogy to the procedure used to determine the nucleophile-specific parameters N and s_N , the N_f and s_f parameters were obtained from linear plots of $\log k_{\leftarrow}(25 \text{ °C})$ versus the electrofugality parameters (E_f) of the benzhydrylium ions reported in ref.^[16] However, as the number



of k_{\leftarrow} values in Table 5 that are available for each of the nucleofuges is not sufficient to derive reliable values for $s_{\rm f}$, we followed the previously recommended procedure^[10f,16] and assumed $s_{\rm f} = 1.0$ to calculate the nucleofugality parameters of the N-heterocycles in Table 5, which are compared with the previously characterized nucleofuges in Figure 5.

Table 5. Reverse rate constants k_{\leftarrow} for the reactions of nucleophiles 1–3 with benzhydrylium ions (Ar₂CH⁺) in CH₂Cl₂ at 20 °C.

Nucleophile	$\mathrm{Ar}_{2}\mathrm{CH}^{+}$	$E_{\rm f}$	$k_{\leftarrow}^{[a]} [s^{-1}]$	$N_{\rm f}$ ^[b]
N Me	$(mor)_2 CH^+$	3.03	$7.26 imes 10^{-2}$	-4.0
	$(mpa)_2 CH^+$	3.46	4.22×10^{-1}	
N Ph	$(ind)_2 CH^+$	4.83	$1.61 imes 10^{-2}$	-6.5
N Ad	$(lil)_2 CH^+$	5.05	$4.36\times 10^{\text{-2}\text{[c]}}$	
Bn	$(jul)_2 CH^+$	5.61	1.42×10^{-1}	
	$(dpa)_2 CH^+$	1.78	8.32×10^{1}	-2.5
S	$(mor)_2 CH^+$	3.03	2.92	
2	$(mfa)_2 CH^+$	3.13	1.61	
	$(mor)_2 CH^+$	3.03	4.18×10^{-1}	-3.3
	$(mpa)_2 CH^+$	3.46	1.63	

[a] $k_{-} = k/K$. [b] Calculated by using Equation (6) and neglecting the small difference in temperature. [c] Calculated by using Equation (1) to calculate k.



Figure 5. Comparison of the nucleofugalities $N_{\rm f}$ of the heterocycles 1–3 with those of other organocatalysts (solvent is CH₂Cl₂ unless otherwise stated, $N_{\rm f}$ from Table 5 and refs.^[10f,16]).

Conclusions

We have found that the rate constants for the reactions of the N-heterocyclic compounds 1-5 with benzhydrylium

ions follow the linear free-energy relationship (1), which allowed us to determine the nucleophilicity parameters N and s_N for 1–5 and to compare them with those of commonly used nucleophilic organocatalysts (Figure 6). The N values in Figure 6 show that the imidazoline derivatives 1 are moderately reactive N-nucleophiles. Although they are 10 to 10^3 times less nucleophilic than DHPB, DBU, DBN, or DMAP, the imidazolines 1 are 10 to 10^2 times more nucleophilic than imidazoles and benzimidazoles. On the other hand, the tetrahydropyrimidine derivatives 4 have nucleophilicities similar to THTP, DBU, and DBN.



Figure 6. Comparison of the nucleophilicities N of the nucleophiles 1–5 with those of other nucleophilic organocatalysts (solvent is CH₂Cl₂ unless otherwise stated, N from Table 2 and ref.^[9h]).

Because the electrophiles attack the lone pair in the plane of the N-heterocycles, the nucleophilic reactivity order $3\approx 2 < 1a\approx 5$ can be rationalized by the interplay of inductive and mesomeric effects of the heteroatoms at the 3-position of the ring.

Substitution of the rate and equilibrium constants into the Marcus Equation (5) yielded the intrinsic barriers ΔG_0^{\neq} , which show that the reactions of electrophiles with the imidazoline **1d** require more reorganization energy than the corresponding reactions with PPh₃, DMAP, or DABCO. As a result, **1d** is a weaker nucleophile than DMAP, which has a similar Lewis basicity.

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Experimental Section

General: CH₂Cl₂ was freshly distilled from CaH₂ prior to use. Commercially available acetonitrile (VWR, Prolabo, HPLC-gradient grade) and DMSO (Acros, 99.9%, Extra Dry, AcroSeal) were used as received. Compounds **1a** (ABCR), **1b** (Aldrich), **2** (Aldrich), and **3** (ABCR) were purchased and used without further purification. Compound **5** was purchased (Aldrich) and distilled prior to use. Compounds **1c**,^[17a] **1d**,^[17b] **4a**,^[17c] and **4b**^[17c] were synthesized according to the procedures in the quoted references. Benzhydrylium tetrafluoroborates,^[9b] phosphonium salts,^[12c] and Michael acceptors^[13] were prepared as described previously.

Kinetics: The reactions of the nucleophiles 1–5 with the benzhydrylium ions Ar₂CH⁺ and Michael acceptors 12 were followed photometrically at or close to the absorption maxima of Ar₂CH⁺ and 12 by stopped-flow UV/Vis spectroscopy or laser flash photolysis. The pseudo-first-order rate constants k_{obs} (s⁻¹) were obtained by least-squares fitting of the absorbances to the monoexponential function $A_t = A_0 \exp(-k_{obs}t) + C$. The second-order rate constants k($M^{-1}s^{-1}$) were obtained from the slopes of the linear plots of k_{obs} against the nucleophile concentrations. For details, see the Supporting Information.

Equilibrium Constants: Equilibrium constants were determined by UV/Vis spectroscopy. Small amounts of stock solutions of the nucleophiles **1**, **3**, and **4** were added to solutions of $Ar_2CH^+BF_4^-$ and **12** in CH_2Cl_2 and the absorbances of electrophiles were monitored at their corresponding λ_{max} before (A_0) and immediately after (A) the addition of nucleophiles. This procedure was carried out with different concentrations of the nucleophiles **1**, **3**, and **4**. The temperature was kept constant at 20.0 ± 0.1 °C by using a circulating bath thermostat. For details, see the Supporting Information.

Reactions of the Nucleophiles 1–4 with Benzhydrylium Ions: A detailed description of the preparation and characterization of the reaction products 7–11 is given in the Supporting Information.

Supporting Information (see footnote on the first page of this article): Preparation and characterization of the products, details of the individual runs of the kinetic experiments, determination of the equilibrium constants, and NMR spectra.

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Nucleophilicity Parameters

Me ON	Me S N	MeN [《] N	Me HN_N	Me HN∕_N	Me BnN∕√N	S N N N		NMe ₂ NH NNN
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10		11	12		13	14	15	16 N

Rate and equilibrium constants for the reactions of 2-imidazolines and related Nheterocyclic compounds with diarylcarbenium ions have been measured in CH₂Cl₂ at

20 °C. These data were employed to determine their nucleophilicities and Lewis basicities, which were compared with other nucleophilic organocatalysts.

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Nucleophilic Reactivities and Lewis Basicities of 2-Imidazolines and Related N-Heterocyclic Compounds

Keywords: Kinetics / Structure-reactivity relationships / Lewis basicities / Thermodynamics / Nucleophilic addition / Organocatalysis