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Electrophilicity parameters for σ-complexation by uncharged electron-deficient aromatic and heteroaromatic structures

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Using appropriate sets of reference nucleophiles, the reactivity of neutral electrophiles of widely different reactivity and structure has been ranked on the comprehensive electrophilicity scale of Mayr (*Acc. Chem. Res.*, 2003, 36, 66), holding promise of a general rationalization of σ-complexation processes and related S_NAr substitutions.

In the last three decades the field of anionic σ-complexation has received a great deal of attention, covering a wide variety of reaction types involving both aromatic and heteroaromatic electron-deficient molecules as well as neutral and anionic nucleophilic reagents. The subject has been summarized in a number of reviews as well as monographs.[1–3] In addition to information derived from structure–reactivity relationships, there is an important synthetic potential to these reactions, leading to functionalization of aromatic and heteroaromatic rings.[1–5] However, further advances in the development of this field require continuing revision of reactivity correlations in order that the potential of this area reach fruition.

One such correlation that we have emphasized through works in our laboratories is the gradation of electrophilic reactivity from the traditional nitroaromatic electrophiles such as 1,3,5-trinitrobenzene (TNB) to much more highly reactive electrophiles, the most remarkable example being the 4,6-dinitrobenzofuroxan (DNBF) structure.[6] As a revealing illustration of the leap in reactivity induced by this structural change, one can cite the thermodynamics of H_2O addition to DNBF which is 10^{10} more favorable compared to TNB.[1,7]

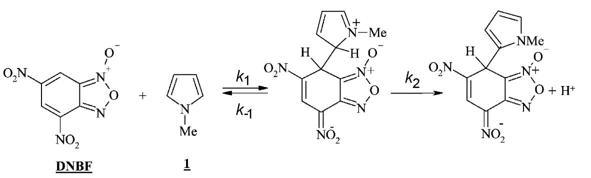
An important step in the understanding of nucleophilicity and electrophilicity has derived recently from the work of Mayr and co-workers.[8,9] Using a series of diarylcarbenium ions and various π-excessive systems as reference sets for electrophiles and nucleophiles, respectively, these authors have shown that it is possible to describe the rates of a large variety of electrophile–nucleophile combinations by the three-parameter equation:

$$\log k(20\ ^\circ\mathrm{C}) = s(N + E) \qquad (1)$$

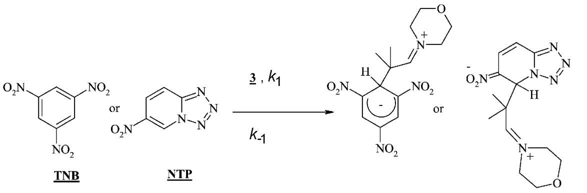
The E parameter is a measure of the strength of the electrophile while the N and s parameters characterize the reactivity of the nucleophile. Within that equation, shown to hold for reagents associated with E or N values covering many orders of magnitude, the feasibility and rate of many interactions have been predicted, the limiting condition being $E + N \geqslant -5$. In developing the relationship of eqn. (1), Mayr has essentially modulated the strength of the electrophilic partner through structural variations of benzhydrylium, tritylium, tropylium or benzenediazonium-type cations. So far, the description of the reactivity of uncharged electrophiles has been restricted to the behaviour of a few Michael acceptors and quinone methides.[10]

In this communication, we report for the first time that σ-complexation reactions involving neutral electrophiles of widely differing reactivity and structure, namely DNBF, 6-nitrotetrazolopyridine (NTP) and TNB, can also be classified under the rubric of the Mayr relationship (eqn. (1)). This finding holds promise for expanding greatly the range of coupling reactions which can be envisioned with these neutral electrophiles. Moreover, the expansion of the applicability of eqn. (1) to these types of processes further demonstrates the generality of this relationship.

Using sets of reference nucleophiles consisting (Fig. 1) of: *N*-methylpyrrole **1**, *N*-methylindole **2** and enamines **3–5** for DNBF, enamines **3–6** for NTP, and enamines **3**, **5** and **6** for TNB,[11] the E values for these three electrophiles could be derived from a kinetic study of the corresponding C–C bond forming reactions in acetonitrile solution. These are exemplified for DNBF in eqn. (2) and for NTP and TNB in eqn. (3).



(2)



(3)

In all systems, only one relaxation process corresponding to the formation of the expected σ-adducts was observed, allowing a facile determination of the second order rate constants k_1 for the nucleophilic addition step (Table 1).[12,14] In accord with eqn. (1), plots of ($\log k_1$)/s *versus* the N values for the various nucleophiles employed were linear (Fig. 1), affording E values of −5.1, −8.9 and −13.1 for DNBF, NTP and TNB, respectively.[15]

It is interesting that within the E scale developed by Mayr, covering a range from +6 to −13, DNBF has an E value which is essentially the same as that for 4-nitrobenzenediazonium cation ($E = -5.1$), approaching that of the tropylium cation family as well as a number of metal-coordinated carbenium ions.[8] While this ranking rationalizes our previous finding that DNBF is capable to undergo C–C coupling with such weak carbon nucleophiles as pyrroles or indoles,[6,13] it also suggests that the rich chemistry established for tropylium and benzenediazonium systems could find analogy with DNBF.[8,16,17]

On the other hand, the E value of −13.1 for TNB ($\mathrm{p}K_a^{H_2O} = 13.43$) corresponds to the bottom of the E scale for electron deficient substrates, being in the same range as the E values recently reported for a few uncharged Michael acceptors.[10b] With an E value of −8.9, NTP represents an intermediate heteroaromatic electrophile ($\mathrm{p}K_a^{H_2O} = 7.55$). Interestingly, plotting the

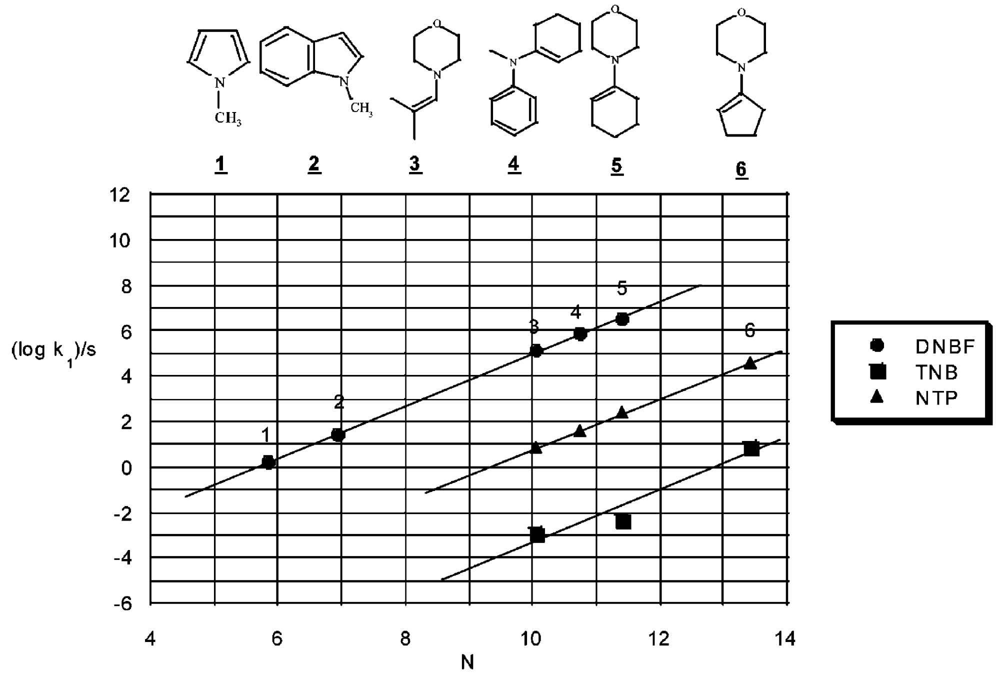


Fig. 1 Plots of (log k_1)/s for DNBF, NTP and TNB *versus* the N parameters for the reference nucleophiles **1–6** at 20 °C in acetonitrile.

Table 1 Rate constants k_1 ($dm^3\ mol^{-1}\ s^{-1}$) for the C–C coupling of DNBF, NTP and TNB with nucleophiles **1–6** in acetonitrile[a]

Nuc[b]	**1**	**2**	**3**	**4**	**5**	**6**
N	5.85	6.93	10.04	10.73	11.4	13.41
s	1.03	0.8	0.82	0.81	0.83	0.82
DNBF	1.81	13.4	1.6×10^4	5.8×10^4	2.6×10^5	—
NTP	—	—	5	19.24	99	5140
TNB	—	—	3.8×10^{-3}	—	1.14×10^{-2}	5

[a] T = 20 °C; experimental error in the rate constants ±3%; [b] s and N values taken from ref. 11.

above E values *versus* the $pK_a^{H_2O}$ values for covalent H_2O addition to DNBF ($pK_a^{H_2O} = 3.75$), NTP and TNB gives a good three point linear plot (not shown). Should this linearity be substantiated for other electron-deficient aromatics, this could be indicative of a general relationship, requiring only $pK_a^{H_2O}$ values for the obtention of E. A correlation of this type has actually been found by Mayr in a study of water addition to carbocations.[17] Further studies are anticipated towards ranking of selected aromatic and heteroaromatic structures which are representative of σ-complexation processes. In turn this will enable one to predict the feasibility of effecting S_NAr-type substitutions through subsequent rearomatization of the σ-complexes.[1–4]

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