A remarkable mechanistic dichotomy in the acid-catalysed decomposition of the N- and C-adducts of indolide anions with 1,3,5-trinitrobenzene

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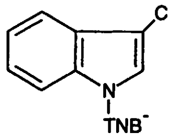
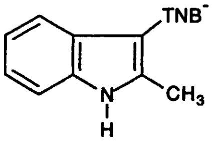
Decomposition of the N- and C-adducts of indolide anions with 1,3,5-trinitrobenzene is subject to specific acid-catalysis in the former case and general-acid-catalysis in the latter through an S_EAr process.

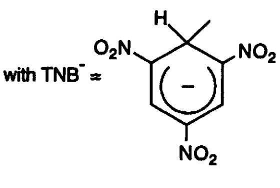
The interaction of potentially ambident nucleophiles with electron-deficient nitroaromatic compounds has revealed some unusual instances of kinetic and thermodynamic control, as well as being of synthetic utility in the new types of covalently bonded structures that are afforded between the donor and acceptor.[1–5] We have previously shown that in the interaction of indolide anion with nitroaromatics σ-adduct formation can occur either at the C or N centres, *i.e.* indole can act as both a carbon and nitrogen nucleophile, and that the N-adduct is formed through kinetic control while the C-adduct forms as a result of thermodynamic control.[6] In this communication we report the unexpected finding that the acid-induced decomposition of the TNB–indolide N-adducts occurs by a different mechanism from that of the C-adducts. We also show that the mechanism of decomposition of the C-adducts, to indoles and TNB, follows that of typical electrophilic aromatic substitutions (S_EAr).[7]



N-1



C-2



The N-adduct N-1 and the C-adduct C-2 have been employed (in the form of alkali salts) as prototype indole complexes in our kinetic studies for the following reasons: (*i*) the isolation of N-1 as a crystalline potassium or sodium salt is made possible by the fact that substitution of the 3-position of the indole ring by the methyl group prevents the formation of the isomeric C-adduct;[6] (*ii*) C-2 is isolated as the thermodynamically stable product of the reaction of 2-methylindolide anion with TNB.[6] In this instance, the isomeric N-adduct is formed initially, but it cannot be isolated as a pure crystalline salt because of its subsequent decomposition to C-2.

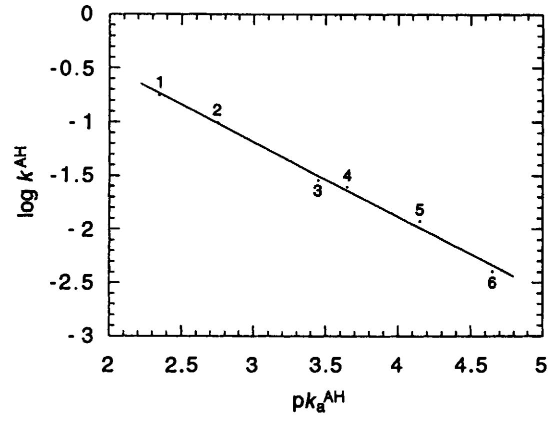


Fig. 1 Brønsted plot for catalysis of the decomposition of the C-adduct **C-2** by carboxylic acids in aqueous solution: (1) cyanoacetic acid; (2) chloroacetic acid: (3) methoxyacetic acid; (4) formic acid; (5) γ-aminobutanoic acid; (6) acetic acid

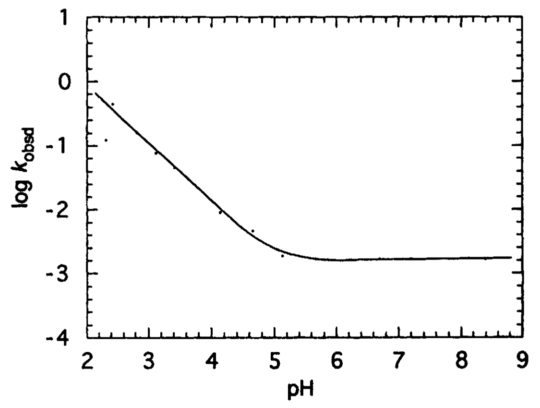


Fig. 2 pH dependence of the observed rate constant (k_{obsd}/s^{-1}) for decomposition of the N-adduct **N-1** in aqueous solution

The decomposition of both **N-1** and **C-2** was studied under pseudo-first-order conditions with a large excess of the acid or buffer reagents over the adduct concentration (~ 3 × 10^{-5} mol dm^{-3}) in aqueous solution at 25 °C. Dilute HCl solutions (5 × 10^{-4}–0.01 mol dm^{-3}) and a number of carboxylic acid buffers whose total buffer concentration was typically 0.06–0.2 mol dm^{-3} were used for this purpose. The ionic strength was kept constant at I = 0.2 mol dm^{-3} (KCl). The reactions were followed spectrophotometrically by monitoring the disappearance of the adducts at their λ_{max}(430 nm for **N-1**; 470 nm for **C-2**) or the appearance of products. In agreement with the low pK_a values (~ − 1) previously reported for protonation of the *p*-nitro group of TNB σ-adducts in aqueous solution,[8,9] no evidence for the transient formation of nitronic acids in the decomposition of **N-1** and **C-2** was obtained under the

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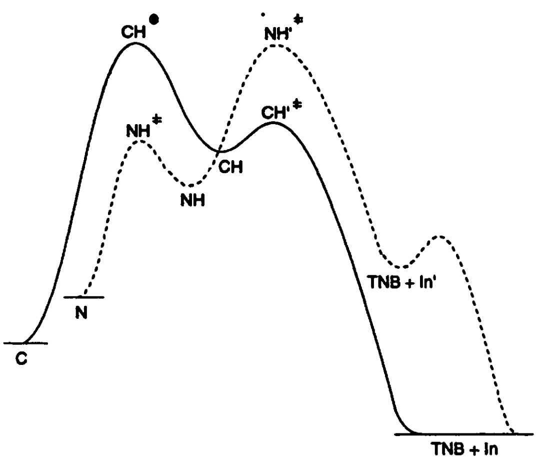
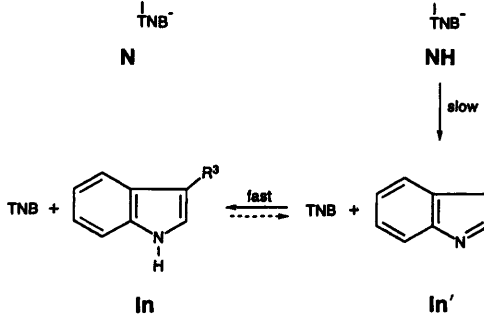


Fig. 3 Energy profiles for the acid catalysed decomposition of N-bonded and C-bonded indolide adducts of TNB

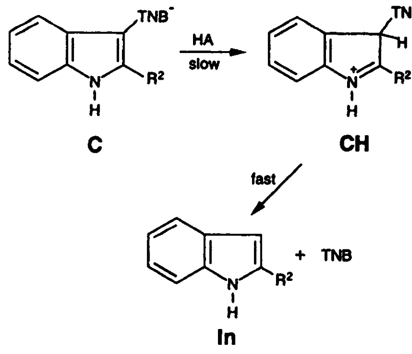
experimental conditions chosen. The results are illustrated in Figs. 1 and 2. In the case of **C-2**, a direct dependence of the observed rate constant [eqn. (1)] upon the concentration of the various acid catalysts was observed and the results for the series of carboxylic acids used describe a satisfactory Brønsted relationship (Fig. 1; $a_{\text{AH}} = 0.69$). In contrast, a pH–rate profile typical for specific acid catalysis at low pH was observed for **N-1** (Fig. 2). In accord with the much lower thermodynamic stability of **N-1**, the derived k^{H^+} as well as k_o values are much higher for **N-1** than for **C-2**; $k^{\text{H}^+} = 90\ \text{dm}^3\ \text{mol}^{-1}\ \text{s}^{-1}$; $k_o = 1.69 \times 10^{-3}\ \text{s}^{-1}$ for **N-1**; $k^{\text{H}^+} = 5.4\ \text{dm}^3\ \text{mol}^{-1}\ \text{s}^{-1}$ for **C-2**. For this latter adduct, the k_o value referring to the solvent-assisted or spontaneous decomposition was actually too low to be measured.

$$k_{\text{obsd}} = k_0 + k^{\text{H}^+}[\text{H}^+] + k^{\text{RCOOH}}[\text{RCOOH}] \qquad (1)$$

From the observation of general acid catalysis in the case of the C-adduct and of specific hydrogen ion catalysis for the N-adduct one can construct the energy profiles in Fig. 3, in which there are two salient points that differentiate the two mechanistic pathways. First, protonation of the N-adduct (**N**) to give **NH** occurs as a fast pre-equilibrium and bond cleavage to TNB is rate-determining, while in the case of the C-adduct it is the protonation to **CH** that is rate-determining and departure of TNB is fast. Secondly, while decomposition of the protonated C-adduct, **CH**, to TNB and indole occurs in one step, the decomposition of the protonated N-adduct, **NH**, requires two steps, since departure of TNB leaves an isomer of indole (**In'**), which then tautomerises rapidly to indole itself (**In**). The two pathways are illustrated in Schemes 1 and 2.



Scheme 1



Scheme 2

In constructing the energy profiles in Fig. 3 we have been guided by the following considerations. (*i*) The C-adduct (**C**) must be at a lower energy level than the N-adduct (**N**) since the former is obtained under thermodynamic control. (*ii*) Of the two protonated adducts, **CH** is of higher energy compared to **NH** since the pK_a for protonation at C3 will be lower for **C** than for **N**. This follows since the trinitrocyclohexadienyl moiety (TNB^-) is known to exert an appreciable electron-withdrawing effect[10–12] and for protonation at C3 this effect will be felt more strongly when TNB is attached to C3 than when it is attached to the nitrogen centre. (*iii*) The decomposition of **CH** to indole and TNB is energetically highly favourable since this gives rise to two fully aromatic molecules in one step and proceeds with an early transition state and a low energy barrier (Hammond). On the other hand the decomposition of the protonated N-adduct will be characterized by a high energy barrier. Here bond cleavage occurs between the positive nitrogen centre and the sp^3 carbon centre of the TNB moiety which also carries partial positive charge[10,12] and this mutual repulsion leads to bond cleavage, akin to the situation in the benzidine rearrangement.[13,14] Finally, the tautomerization of **In'** to **In** must be a fast process.

The conclusion that may be drawn from this work is that the decomposition of the C-adduct is essentially an electrophilic aromatic substitution ($\text{S}_\text{E}\text{Ar}$) in which the TNB moiety at C3 of the indole ring is displaced by H^+. Confirmation of this is provided by the finding of a significant isotope effect, $k^{\text{H}^+}/k^{\text{D}^+} = 3.6$, when the decomposition is carried out in HCl–DCl media, which is comparable to the values observed in other rate-determining C-protonation processes.[15–18] Moreover the Brønsted a value for the acid decomposition of the C-complex, 0.69, is also in the range of established $\text{AS}_\text{E}2$ processes, including $\text{S}_\text{E}\text{Ar}$ processes.[7,18,19]

In future work it will be important to determine whether the dichotomy of mechanisms observed in the present study is general for C- and N-adducts, or whether one can modulate this through changing electron demand/supply by means of structural changes.

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