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Ambident Reactivity of Enolate Ions toward 1,3,5-Trinitrobenzene. The First Observation of an Oxygen-Bonded Enolate Meisenheimer Complex

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Electron-deficient polynitroaromatics such as 1,3-dinitrobenzene (DNB) or 1,3,5-trinitrobenzene (TNB, **1**) have hitherto been observed to react with aldehydes or ketones that contain α hydrogens to yield only the carbon-bonded Meisenheimer-type anionic σ-complexes; the oxygen-centered adducts have, surprisingly, never been detected.[2] Indeed, the Janovsky reaction,[3] involving formation of deep red-colored solutions from the interaction of DNB or TNB with α-H-containing carbonyl compounds (in basic media), forms the basis of a variety of pharmaceutical tests.[4] The favorable thermodynamics associated with C-adduct formation between enolate ions and nitroaromatics is well documented.[5] A wealth of interesting chemistry has emerged from investigations of Meisenheimer C-adducts, including the 1,3-diadducts formed as a result of intramolecular cyclization involving another methylene functionality α to the carbonyl group.[6]

Lack of observation of O-bonded enolate adducts of TNB *under any conditions* has, nevertheless, been puzzling. One explanation that has been advanced is that C-attack is favored for **1**, as a prototypical "soft" electrophile with a low-lying LUMO.[7] However, calculations by Houk and Paddon-Row[8] show that enolate O-attack should be favored regardless of the hardness or softness of the electrophile; the activation energy for O-attack is lower than that for C-attack, even though the latter is favored thermodynamically. Other calculations suggest that the ratio of C- to O-attack may be related to the keto−enol energy differences (ΔH_{k-e}) for the neutral parent carbonyl compounds.[9] Further, Zhong and Brauman correlated the gas phase O versus C reactivity of a series of enolates, including acetophenone enolate, with ΔH_{k-e}.[10]

In our work on ambident reactivity in σ-complex formation,[11] we have focused on the C- and O-reactivity of phenoxide ion toward TNB[11a,b,e] and the C- and N-reactivity of aniline, as well as the ambident reactivity of phenoxide toward super-electrophiles, such as 4,6-dinitrobenzofuroxan (DNBF).[11a,d] Current work complements our recent examination of regioselectivity[12] in Meisenheimer complex formation.[12a] This communication reports the first unambiguous observation of enolate O-adduct formation with TNB, which can occur under suitable conditions in addition to C-adduct formation.

We have used the acetophenone enolate anion in the current work because it is representative of simple enolates and since it can only undergo mono-addition, in contrast to acetone which partakes in 1,3-diadduct formation with TNB.[6] Our study was carried out in acetonitrile−dimethoxyethane (MeCN−DME) which is amenable to examination at relatively low temperatures, in contrast to the common usage of dimethyl sulfoxide as solvent in Meisenheimer complex studies which, consequently, are limited to temperatures close to ambient.[11b,e]

In a typical experiment acetophenone enolate, as the potassium salt,[13] was reacted in the presence of 18-crown-6 with **1** at −50 °C in acetonitrile−dimethoxyethane (MeCN-d_3:DME-d_{10}, 1:1, v/v; reactant concentrations: 0.06 M, 18-C-6: 0.1 M); the reaction was monitored by 400 MHz ^{1}H NMR spectroscopy while the temperature was increased in 5 °C increments after 30 min periods, at which point spectra were recorded. The ^{1}H NMR spectrum of the deep red solution, recorded after 1 h at −40 °C, contained dominant[14] signals characteristic of the O-bonded $TNB\cdot OC(CH_2)Ph^-$ enolate adduct, **2**, as follows (δ ppm, J Hz): H_1, 6.93 (t, 1H, $J = 1.3$); $H_{3,5}$, 8.37 (d, 2H, $J = 1.3$); H_v, 4.41, 3.96 (br s, 2H); aryl-H 7.38−7.94 (m, 5H). On raising the temperature to −35 °C the signals of **3** began to decline in tandem with growth in the signals assignable to the $TNB\cdot CH_2COPh^-$ C-adduct, **3.** The aryl-H resonances of **3** could not be discerned at this stage because of overlap with those of **2**; later in the experiment the following appropriate assignment could be made: H_1, 5.22 (tt, 1H, $J = 0.8$, 6.0), $H_{3,5}$, 8.29 (d, 2H, $J = 0.8$); H_α, 3.05 (d, 2H, $J = 6.0$, α-CH_2); H_o, 7.99 (apparent d,[15] 2H); H_p, 7.57 (apparent t,[15] 1H); H_m, 7.48 (apparent t,[15] 2H). Continued increase in temperature led to further development in the spectrum due to **3** while at the same time resonances of the $TNB\cdot OH^-$ adduct, **4**,[11b] appear. Formation of **4** can be ascribed to solvolytic processes involving adventitious water in the solvent.[11b,e] Upon further increase in the temperature to 20 °C the signals of **2** had completely

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(13) Potassium acetophenone enolate was prepared in THF and precipitated with dry hexane (Brown, C. A. *J. Am. Chem. Soc.* **1973**, *95*, 982); the isolated potassium salt redissolved in DME-d_{10} was added to the TNB solution (in MeCN-d_3) to initiate the reaction. The potassium enolate likely exists in solution as "loose" ion pairs (Buncel, E.; Menon, B. C. *J. Org. Chem.* **1979**, *44*, 317; *J. Am. Chem. Soc.* **1980**, *102*, 3499). The potassium enolate and TNB were present in equimolar initial concentrations (0.06 M).

(14) Initial spectra also contain small extraneous peaks including signals due to the C- adduct, **3**, albeit in low concentration (**3** $\leq$ 8% of **2**), as well as peaks of residual acetophenone. In some runs, small signals are also found for the hydride adduct of TNB (H_1 3.88; $H_{3,5}$ 8.26 (Taylor, R. P. *Chem. Commun.* **1970**, 1463)).

(15) The aryl-H signals are *apparent* triplets or doublets with unresolved coupling.

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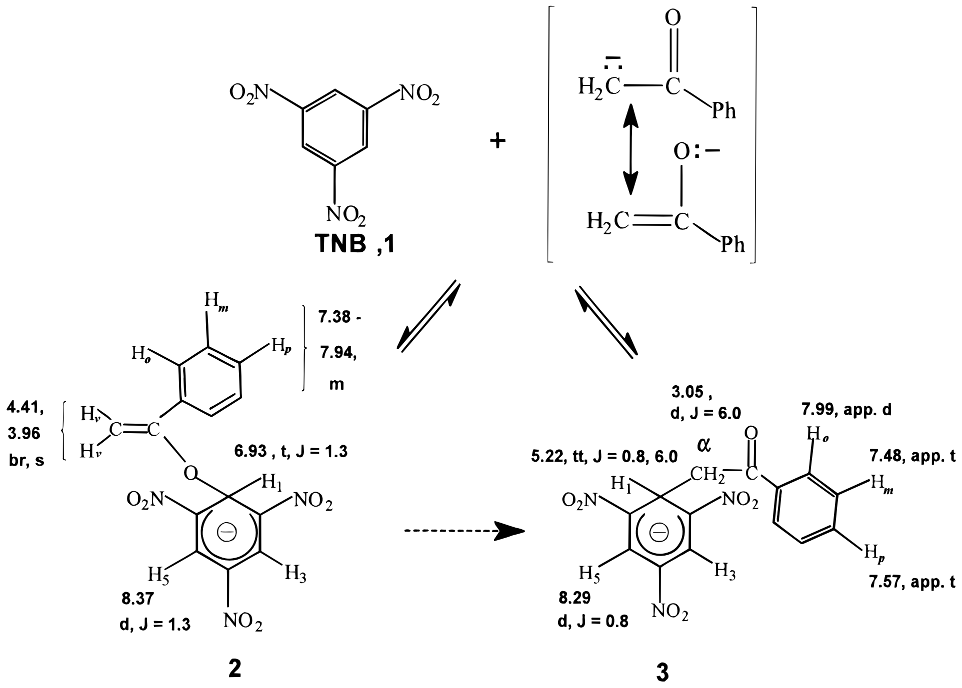
Scheme 1



disappeared in favor of **3** and **4** (ratio of 2:1) and then remained stable in solution for several days.[16]

In other experiments the acid lability of the σ-adducts was tested. It was found that **2** and **4** were instantly decomposed on addition of trifluoroacetic acid (TFA) while those of **3** decomposed only slowly in the acidic solution, as expected.[5,6,11]

The experimental evidence that we have presented in support of the structure of **2** and **3**[17] is conclusive. Noteworthy is the characteristic downfield shift of the sensitive sp^3 C(1)−H signal in the O-adduct **2** relative to the C-adduct, **3**;[1] the H_1 chemical shift of **2** (δ 6.93) is particularly diagnostic of the O-adduct. Alkoxide O-adducts have H_1 signals located in the range of 6.0−6.4 ppm, phenoxide O-adducts (which are similar to enolate O-adducts in that the attached oxygen center is also adjacent to an sp^2-hybridized carbon site) have H_1 signals in the range of 6.7−7.0 ppm, and H_1 signals for C-adducts are typically found at 5.0−5.4 ppm in MeCN−DME media.[11b,e] Assignment of the O-adduct **2** is also supported by observation of the signals of the vinylic protons, which are located in the region of spectrum previously found for model vinyl ethers; the vinyl protons of α-methoxystyrene appear at δ 4.76 and 4.30, while those of ethyl vinyl ether are centered at 4.17 and 3.94 ppm. Finally, the facile acid lability of **2** (as compared to the C-adduct, **3**) clinches the assignment.

The fact that the dominant adduct at low temperature is **2** which gives way in time and as a function of increasing temperature to **3** is characteristic of kinetically controlled O-adduct formation while the C-adduct is the product of thermodynamic control (Scheme 1). Our results are consistent with the calculations of Houk and Paddon-Row,[8] as well as studies of Crampton and workers which show that intrinsic (Marcus)[10] kinetic barriers for O-nucleophilic attack on TNB are generally lower than those for C-attack.[18] A further implication of the results is that the lack of observation of O-bonded enolate adducts of polynitroaromatics is not attributable solely to the softness of the electrophiles. Finally, the mechanism of the transformation of **2** into **3** deserves comment. As shown in Scheme 1 (equilibria) the O-adduct may dissociate back to TNB and the enolate anion, followed by attack via the C-site of the enolate to give **3**.[2,11a] However, rearrangement (Scheme 1, dashed arrow) could occur by an internal [3,3] sigmatropic shift[19] of **2** akin to the Claisen rearrangement of allyl vinyl ethers.[20] Extension of the current work to other common enolates is underway and should lead to a quantitative understanding of the oxygen versus carbon reactivity of enolates toward electron deficient aromatics, including polynitroaromatics, as well as shed light on the pathways for rearrangement.

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[16] Other side reactions which could conceivably occur in this system include oxidation of the C-adduct to picryl acetophenone, in a formal hydride transfer. However, this process would be favored through using excess TNB, which could yield a variety of reduction products, whereas in the present study equimolar TNB and enolate were used. We thank a referee for bringing this to our attention.

[17] The spectroscopic characteristics of **3** are in good agreement with those reported for typical TNB C-adducts (ref 5b,6). It was not possible to obtain the ^{13}C NMR spectrum of **2**, due to its short lifetime even at low temperatures; the ^{13}C NMR parameters (MeCN-d_3:DME-d_{10}; ambient temperature; 100.1 MHz) for **3** (refer to Scheme 1, structure **3** for numbering) are as follows: 37.4 (C−1), 133.7 (C−2,6), 126.4 (C−3,5), 123.4 (C−4), 43.1 (C−α), 198.5 (carbonyl), 138.8, 129.9, 129.4, 134.0 (phenyl ring of acetophenone enolate moiety).

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