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Acid Catalysis of Nitronic Acid Formation from Nitroalkane Precursors

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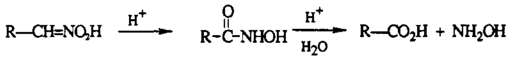
It is well known that isomerization of aldehydes and ketones to their enol isomers is catalyzed by both acids and bases. Despite claims to the contrary,[1] the same is not true for nitroalkane–nitronic acid prototropy. Such claims can be rationalized simply by proton transfer from nitroalkane to solvent (water).[2] In fact, this transformation (eq 1) is actually retarded in moderately concentrated aqueous acid, presumably because of the decline in the activity of water.[3] Edward and Tremaine have shown convincingly that other reactions of nitroalkanes which occur in acid media, e.g., the Nef and Victor Meyer reactions (eqs 2 and 3) owe their catalysis to events succeeding nitronic acid formation.[3,4]

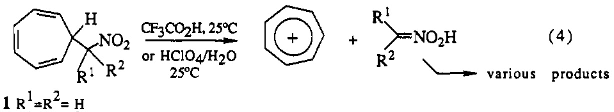
$$R{-}CH_2{-}NO_2 + H_2O \underset{slow}{\overset{slow}{\rightleftharpoons}} R{-}CH{=}NO_2^- + H_3O^+ \underset{fast}{\overset{fast}{\rightleftharpoons}} R{-}CH{=}NO_2H + H_2O \quad (1)$$

$$R{-}CH{=}NO_2H \xrightarrow{H^+} R{-}CH{=}O + \text{"HNO"} \quad (2)$$



$$R{-}CH{=}NO_2H \xrightarrow{H^+} R{-}\overset{O}{\overset{\|}{C}}{-}NHOH \xrightarrow[H_2O]{H^+} R{-}CO_2H + NH_2OH \quad (3)$$

We report here a reaction in which nitroalkanes lose an electrofuge, promoted by acid, to yield nitronic acids (eq 4).[5] In our case the electrofuge is tropylium ion (Tr^+) rather than a proton.



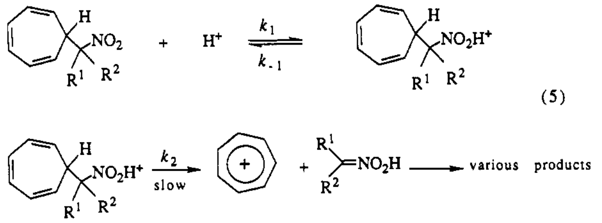
(4)

1 $R^1 = R^2 = H$
2 $R^1 = H$, $R^2 = CH_3$
3 $R^1 = R^2 = CH_3$

Evidence from ^1H NMR (CF_3CO_2H and CF_3CO_2D) and UV spectrophotometry (CF_3CO_2H and $HClO_4/H_2O$) shows that tropylium ion is formed quantitatively. Products derived from the exocyclic moiety were examined by ^1H NMR spectroscopy of reacting solutions in CF_3CO_2H. Compound **1** produced ca. 40% of formohydroxamic acid (Victor Meyer product) plus unidentified material. Compound **2** gave ca. 25% of acetohydroxamic acid plus other products. From **3** came ca. 20% of acetone (Nef product) as well as unidentified materials. Attempts to simulate development of nitronic acids in CF_3CO_2H were only partly successful in terms of eq 4. Addition of sodium nitronate salts $Na^+R^1R^2C{=}NO_2^-$ to CF_3CO_2H gave only nitromethane from $Na^+CH_2{=}NO_2^-$ and some nitroethane from $Na^+CH_3CH{=}NO_2^-$ along with the same products observed by cleavage of **2** and, from $Na^+(CH_3)_2C{=}NO_2^-$, the same products as were obtained by cleavage of **3**.[6]

Other qualitative observations include the following. (1) Compound **1**, our slowest-cleaving substrate, undergoes no isotopic hydrogen exchange in CF_3CO_2D under conditions where **1**–**3** leads to tropylium ion. This result excludes mechanisms in which ring carbons are reversibly protonated or in which the α-CH bond is reversibly cleaved. (2) The proton-decoupled ^{13}C NMR spectrum of the tropylium ion formed from compound **1** shows a single spike, with no satellites, at δ 156.05 whether the reaction is conducted in CF_3CO_2H or in CF_3CO_2D. No $C_7H_6D^+$ is formed in CF_3CO_2D. Thus irreversible protonation of a ring carbon followed by C–C cleavage may be ruled out. (3) Nitromethane, nitroethane, 2-nitropropane, and phenylnitromethane also show no hydrogen exchange, demonstrating again that nitroalkanes do not lose an α-proton under these conditions. (4) Similarly, we see no Nef or Victor Meyer products derived from **1**–**3**, that is, no TrCHO, $TrCOCH_3$, or TrCONHOH, products which would be expected from α-proton loss. (5) The 3° nitroalkane, $(CH_3)_3CNO_2$, undergoes no change whatsoever in CF_3CO_2H after 100 h. Thus, acid-catalyzed C–N cleavage does not occur under these reaction conditions.

These results support eq 4 as the reaction under study and allow us to postulate eq 5, an A-1 cleavage, as the mechanism for nitronic acid production. C–C cleavage concerted with proton transfer is not ruled out by our results.[7] We believe this to be *the first example of acid-catalyzed nitronic acid production from a nitroalkane precursor.*



(5)

Pseudo-first-order rate constants for acid-catalyzed cleavage of **1**–**3** were measured in CF_3CO_2H and in $HClO_4/H_2O$ solutions; these are listed in Table I. Rate constants in $HClO_4/H_2O$ were linearly correlated by the Cox–Yates excess acidity function, X_o,[8,9] and the resulting parameters are also found in the table.

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† On leave from Shanghai University of Science and Technology.

[1] (a) Feuer, H.; Nielsen, A. T. *Tetrahedron* **1963**, *19*, Suppl. 1, 65. A possible case of acid-catalyzed tautomerization is reported by these authors. 2,5-Dinitro-1,6-hexandiols are epimerized in 1 MHCl at 60–100 °C. Epimerization did not occur in the absence of acid. The corresponding dimethyl ethers do not epimerize under these conditions. The authors argue that intramolecular hydrogen-bonding to the developing nitronic acid moiety stabilizes the transition state. (b) Cundall, R. B.; Locke, A. W. *J. Chem. Soc. (B)* **1968**, 98. (c) Coombes, R. B. In *Comprehensive Organic Chemistry*; Sutherland, I. O., Ed.; Pergamon Press: Oxford, 1979; Vol. 2, p 335.

[2] (a) Bell, R. P. *Acid-Base Catalysis*; Oxford University Press: London, 1941; pp 71–72. (b) Lewis, E. S. In *The Chemistry of Amino, Nitroso, and Nitro Compounds and Their Derivatives*; Patai, S., Ed.; Wiley: Chicester, 1982; Part 2, pp 720–721. (c) Junell, R. *Z. Phys.Chem.* **1929**, *A141*, 71 (quoted by Bell in ref 2a). (d) Pedersen, K. J. *Kgl. Danske Vid. Selskab Math.-Fys. Medd.* **1932**, *12*, 1 (quoted by Bell and Lewis in refs 2a and 2b, respectively).

[3] Edward, J. T.; Tremaine, P. H. *Can. J. Chem.* **1971**, *49*, 3483, 3493.

[4] Edward, J. T.; Tremaine, P. H. *Can. J. Chem.* **1971**, *49*, 3489.

[5] Compounds **1**–**3** were synthesized according to the method of Reingold et al.: Reingold, I.D.; Trujillo, H. A.; Kahr, B. E. *J. Org. Chem.* **1986**, *51*, 1627.

[6] Nitronate anions are protonated on carbon at rates in the order $CH_2{=}NO_2^- > CH_3CH{=}NO_2^- > (CH_3)_2C{=}NO_2^-$ (see Table II). It is possible that in our simulation, local high [nitronate$^-$] allows O-protonation to be reversible, thereby enabling C-protonation to occur for $CH_2{=}NO_2^-$ and $CH_3CH{=}NO_2^-$. In reaction 4, nitronic acids are generated in the absence of nitronate neighbors.

[7] From the medium-independent rate constant for acid-catalyzed fragmentation of compound **3**, our fastest substrate, we can calculate $\Delta G^{\neq} = 24.7$ kcal/mol. Modeling the aqueous solution basicity of **1**–**3** after that of nitromethane ($pK_a \approx -12$, see: Arnett, E. M. In *Progress in Physical Organic Chemistry*; Cohen, S. G., Streitweiser, A., Taft, R. N., Eds.; Wiley-Interscience: New York, 1963; Vol. 1, p 223) gives $\Delta G°$ for protonation as approximately 16 kcal/mol. Hence, a two-step mechanism is not only possible but likely.

[8] Cox, R. A.; Yates, K. *Can. J. Chem.* **1979**, *57*, 2944. The excess acidity concept is a second-generation treatment of the acidity of nondilute aqueous mineral acids. It rests on a linear free energy assumption concerning the activity coefficient behavior of structurally different bases and their conjugate acids (see: Bunnett, J. F.; Olsen, F. P. *Can. J. Chem.* **1966**, *44*, 1899). Extrapolation of a Cox–Yates plot to $X_o = 0$ gives the medium-independent, second-order rate constant for the hypothetical standard state: $[H_3O^+] = 1.00M$, all activity coefficients = 1.00.

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Table I. Rate Constants (25 °C) for Acid-Catalyzed Cleavage of (7-Cycloheptatrienyl)nitroalkanes **1–3**[a]

compound	$k/10^{-5}$ (s^{-1}) CF_3CO_2H	k_0 (M^{-1} s^{-1}) $HClO_4/H_2O$[b]	slope ($m^{*}m^{\ddagger}$) of Cox–Yates X_0 plot (r^2)[b]
$TrCH_2NO_2$ (**1**)	3.35	7.52×10^{-10}	1.34 ± 0.08 (0.990)
$TrCH(CH_3)NO_2$ (**2**)	59.0	3.04×10^{-7}	0.94 ± 0.07 (0.982)
$TrC(CH_3)_2NO_2$ (**3**)	1180	4.72×10^{-6}	1.05 ± 0.07 (0.990)

[a] Determined by UV spectrophotometric observation of tropylium ion at 272 (CF_3CO_2H) or 274 nm ($HClO_4/H_2O$). [b] The medium-independent, second-order rate constant, k_0, is the value of k_{exp} (s^{-1}) for $X_0 = 0$ (ref 8): $\log k(s^{-1})/[H^+] = m^{*}m^{\ddagger}X_0 + \log k_0$.

Table II. Rate Constants, pK_a Values, and Tautomerization Equilibrium Constants for Simple Nitroalkanes (H_2O, 25 °C)

compound	pK_a	k_{H_2O} (s^{-1})[a]	k_{OH^-} (M^{-1} s^{-1})[a]	$k_{H_3O^+}$ (M^{-1} s^{-1})[b]	K_{taut}[c]
CH_3NO_2	10.22[d]	4.3×10^{-8} [e,f]	27.6[g]	715	1.1×10^{-7} [e,h]
$CH_3CH_2NO_2$	8.60[d]	3.7×10^{-8} [i]	5.19[g]	15	8.9×10^{-5} [e]
$(CH_3)_2CHNO_2$	7.74[e]	4×10^{-9} [g]	0.355[j]	0.22	2.8×10^{-3} [e]

[a] For deprotonation of the nitroalkane by the indicated base. [b] For protonation of the nitronate anion, calculated as $k_{H_3O^+} = k_{H_2O}/K_a$. [c] K_{taut} = [nitronic acid]/[nitroalkane]. [d] Pearson, R. G.; Dillon, R. L. *J. Am. Chem. Soc.* **1953**, *75*, 2439. [e] Turnbull, D.; Maron, S. H. *J. Am. Chem. Soc.* **1943**, *65*, 212. [f] Reference 2c. [g] Bell, R. P.; Goodall, D. M. *Proc. R. Soc. London A* **1966**, *294*, 273. [h] Wheland, G. W. *Advanced Organic Chemistry*, 3rd ed.; Wiley: New York, 1960; p 719. [i] Wheland, G. W.; Farr, J. *J. Am. Chem. Soc.* **1943**, *65*, 1433. [j] Kresge, A. J.; Drake, D. A.; Chiang, Y. *Can. J. Chem.* **1974**, *52*, 1889.

Two points are evident from these data: (1) the reactions are strongly acid-catalyzed; the slopes of the X_0 plots are around 1.0 or more, akin to those found for other A-1 reactions[8] and (2) the substrate reactivity order is **3** > **2** > **1**. This is of interest because the opposite order is obtained for the deprotonation of the corresponding simple nitroalkanes whether by H_2O or by OH^- (see Table II). The latter result, in which the rate of nitronate anion formation is *inversely* related to the acidity of the nitroalkane precursors, is part of what is known as "the nitroalkane anomaly".[10] In the present case (eq 4), the more stable the nitronic acid, the faster it is produced by acid-catalyzed C–C cleavage; the anomaly does not occur.

The anomalous rate–equilibrium relationships found for deprotonation of nitroalkanes are attributable to severe transition-state imbalance between the extent of C–H cleavage and relocation of the developing negative charge into the NO_2 function.[10,11] For the cleavages of **1–3**, we postulate that protonation of the nitro group causes sufficient electrostatic pull that the departure of the electrofuge and development of C=N double bond character at the transition state are more synchronous. The transition state, therefore, has enough nitronic acid character that the most stable nitronic acid forms fastest.

The lack of acid catalysis of nitroalkane–nitronic acid isomerization can be ascribed to the very weak basicity of nitroalkanes.[12] It is doubtful that compounds **1–3** are significantly more basic than simple nitroalkanes; hence, it is step 2, the cleavage step of eq 5, which is responsible for the success of the reactions.[13] Evidently, tropylium ion is a superior electrofuge. Not only is it a weaker acid than the solvated proton,[14] but its departure is unimolecular, not requiring the covalent participation of the weak bases present in our reaction media.[15]

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(12) Nitromethane is not measurably protonated in 99–100% H_2SO_4 by cryoscopy: Hantzsch, A. *Z. Phys.Chem.* **1907**, *61*, 257. Hammett, L. P. *Physical Organic Chemistry;* McGraw-Hill: New York, 1940; p 47. Conductivity measurements in H_2SO_4 give $K_b \cong 2.5 \times 10^{-3}$ M: Gillespie, R. J.; Solomons, C. *J. Chem. Soc.* **1957**, 1796. It is largely or completely protonated in various superacid media: Deno, N. C.; Gaugler, R. W.; Schultze, T. *J. Org. Chem.* **1966**, *31*, 1968. Hogeveen, H. *Recl. Trav. Chim. Pays-Bas* **1968**, *89*, 1320. Olah G.; Kiovsky, T. E. *J. Am. Chem. Soc.* **1968**, *90*, 6461.

(13) Semiempirical MO calculations (AM1 and MNDO) indicate the gas-phase proton affinities of **1** and 3-nitromethyl-1,4-cycloheptadiene to be within 0.1 kcal/mol of one another. We thank Dr. Scott Gronert, SFSU, for these calculations.

(14) K_{eq} for the reaction $Tr^+ + H_2O \rightarrow TrOH + H^+$ is $10^{-4.7}$: Doering, W. v. E.; Knox, L. H. *J. Am. Chem. Soc.* **1954**, *76*, 3203.

(15) For other C–C cleavages involving electrofugic Tr^+, see: Conrow, K. *J. Am. Chem. Soc.* **1959**, *81*, 5461.