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The pK_a of an Acetylenic Amine, N-(Pentafluorophenyl)-2-phenylethynamine, Ionizing as an Acid in Aqueous Solution

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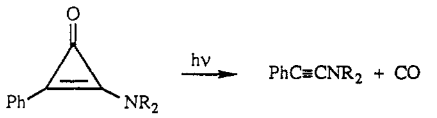
We recently discovered that photodecarbonylation of phenylaminocyclopropenones, **1**, in aqueous solution produces ynamines, **2**, as short-lived transient species, eq 1.[1] Our work showed ynamines to be remarkably weak bases



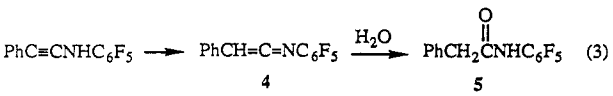
1 2 (1)

and, provided they had an ionizable N–H bond, *i.e.*, were either primary or secondary amines, to be correspondingly strong acids as well. In this respect, ynamines resemble their oxygen analogs, ynols, where the acetylenic group also exerts a very strong acid-strengthening effect.[2,3] In these initial studies we did not determine the pK_a's of any of the ynols or ynamines we examined, and we consequently could only set lower limits on the acid-strengthening effect. We wish to report that we have now found that N-(pentafluorophenyl)-2-phenylethynamine, **3**, undergoes acid dissociation in aqueous solution, eq 2, with pK_a = 10.28, and that this has allowed

$$\underset{\mathbf{3}}{\mathrm{PhC{\equiv}CNHC_6F_5}} + \mathrm{H_2O} \rightleftharpoons \mathrm{PhC{\equiv}CNC_6F_5^-} + \mathrm{H_3O^+} \qquad (2)$$

us to fix the acidifying effect in this case at 10 pK units or 14 kcal mol^{-1}.

We generated this ynamine as before[1] by flash photolysis of the corresponding aminocyclopropenone[4] and found that its rapid hydration to N-(pentafluorophenyl)phenylacetamide, **5**, occurs through prior isomerization to a ketenimine, **4**, eq 3, as is the case with other secondary ynamines.[1] This reaction of



$$\mathrm{PhC{\equiv}CNHC_6F_5} \longrightarrow \underset{\mathbf{4}}{\mathrm{PhCH{=}C{=}NC_6F_5}} \xrightarrow{\mathrm{H_2O}} \underset{\mathbf{5}}{\mathrm{PhCH_2\overset{O}{\overset{\|}{C}}NHC_6F_5}} \qquad (3)$$

the ynamine to the ketenimine is catalyzed by both acids and bases, and rate measurements made at 25.0 ± 0.1 °C in $HClO_4$ and NaOH solutions as well as HCO_2H, CH_3CO_2H, $H_2PO_4^-$, NH_4^+, and HCO_3^- buffers produced the rate profile shown in Figure 1.[6]

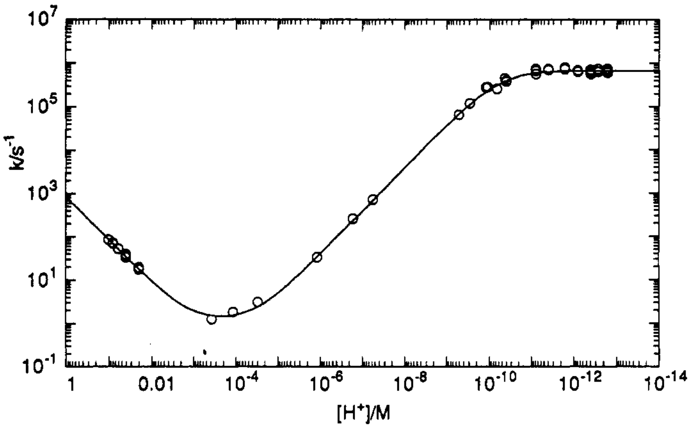


Figure 1. Rate profile for isomerization of N-(pentafluorophenyl)-2-phenylethynamine to the corresponding ketenimine in aqueous solution at 25 °C.

The acid-catalyzed limb of this profile represents rate-determining proton transfer from the hydronium ion to the β-carbon atom of the ynamine, as evidenced by the kinetic isotope effect k_{H^+}/k_{D^+} = 3.27 ± 0.09; this step is then followed by rapid proton loss from nitrogen, eq 4. The basic leg derives from a process in which hydroxide

$$\mathrm{PhC{\equiv}CNHC_6F_5} + \mathrm{H_3O^+} \xrightarrow{\mathrm{rd}} \mathrm{PhCH{=}CNHC_6F_5^+} + \mathrm{H_2O} \xrightarrow{\mathrm{fast}} \mathrm{PhCH{=}C{=}NC_6F_5} + \mathrm{H_3O^+} \qquad (4)$$

ion first removes the proton from nitrogen in a rapidly established preequilibrium, followed by rate-determining reprotonation on carbon by a water molecule, eq 5.

$$\mathrm{PhC{\equiv}CNHC_6F_5} + \mathrm{HO^-} \xrightarrow{\mathrm{fast}} \mathrm{PhC{\equiv}CNC_6F_5^-} + \mathrm{H_2O} \xrightarrow{\mathrm{rd}} \mathrm{PhCH{=}C{=}NC_6F_5} + \mathrm{HO^-} \qquad (5)$$

The break in the rate profile near pC_{H^+} = 10 represents a shift in the preequilibrium and a change from ynamine plus hydroxide ion to yniminium ion (**6**) plus water as the initial state of the reaction. This change in initial state is accompanied by the expected increase in solvent isotope effect from k_{HO^-}/k_{DO^-} = 4.1 ± 0.2 for the hydroxide-ion catalyzed process to k_{H_2O}/k_{D_2O} = 7.9 ± 0.4 for the "uncatalyzed" reaction.

It follows from this mechanistic assignment that the break in the basic portion of the rate profile corresponds to the acidity constant of N-(pentafluorophenyl)-2-phenylethynamine ionizing as an acid, eq 2. Least-squares analysis gives the result K_a = (5.29 ± 0.01) × 10^{-11} M, pK_a = 10.28 ± 0.01.[7] Measurements made in D_2O solution lead to the isotope effect on this acidity constant $K_a^{H_2O}/K_a^{D_2O}$ = 3.77 ± 0.28, which is a reasonable value for an acid of this strength.[8]

This is a remarkably large acidity constant for an amine ionizing as an acid in aqueous solution: most amines take on a proton rather than give one up in this medium. The present result may be compared with an estimate of the aqueous solution acidity constant for pentafluoroaniline, **7**, pK_a = 20, based upon pK_a = 23.1 determined in DMSO solution[9] and the change-of-solvent increment δ pK_a = −2.9, obtained from the values for aniline itself in DMSO, pK_a = 30.6,[10] and in H_2O, pK_a = 27.7.[11] That puts the acid-strengthening effect of the phenylethynyl group in

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(1) Chiang, Y.; Grant, A. S.; Kresge, A. J.; Pruszynski, P.; Schepp, N. P.; Wirz, J. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1356–1358.

(2) Chiang, Y.; Kresge, A. J.; Hochstrasser, R.; Wirz, J. *J. Am. Chem. Soc.* **1989**, *111*, 2355–2357.

(3) For a theoretical analysis of this acid-strengthening effect, see: Smith, B. J.; Random, L.; Kresge, A. J. *J. Am. Chem. Soc.* **1989**, *111*, 8297–8299. Smith, B. J.; Radom, L. *J. Am. Chem. Soc.* **1992**, *114*, 36–41.

(4) N-(Pentafluorophenyl)phenylaminocyclopropenone was prepared by treating phenylchlorocyclopropenone[5] with pentafluoroaniline; it was characterized by its NMR, IR, and mass spectra.

(5) Chicos, J. S.; Patton, E.; West, R. *J. Org. Chem.* **1974**, *39*, 1647–1650.

(6) The data obtained in buffer solutions were extrapolated to zero buffer concentration; all measurements were made at ionic strength = 0.10 M.

(7) This is a *concentration* dissociation constant applicable at the ionic strength of the kinetic measurements, μ = 0.10 M.

(8) Laughton, P. M.; Robertson, R. E. *Solute–Solvent Interactions*, Coetzee, J. F., Ritchie, C. D., Eds., M. Dekker: New York 1969; Chapter 7.

(9) Vlasov, V. M.; Terekhova, M. I.; Petrov, E. S.; Shatenshtein, A. I.; Yakobson, G. G. *Zhur. Org. Khimii* **1981**, *17*, 2025–2031.

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the present system at 20 − 10.28 = 10 p*K* units. This result is considerably less than the lower limit of 17 p*K* units we estimated before in a comparison of the parent

$C_6F_5NH_2$ **7** $PhC{\equiv}CNH_2$ **8** NH_3 **9**

phenylethynylamine, **8**, with ammonia, **9**, but the reduction can be attributed to partial saturation of the phenylethynyl group effect in the present case by the already strongly acidifying pentafluorophenyl substituent.

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(10) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463.

(11) Stewart, R. *The Proton: Applications to Organic Chemistry*; Academic Press: New York 1985; p 70.