The pKₐ 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
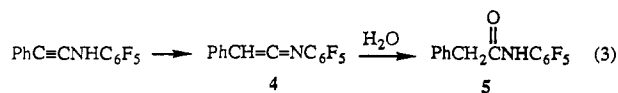
$$PhC{\equiv}CNR_2 + CO \qquad (1)$$
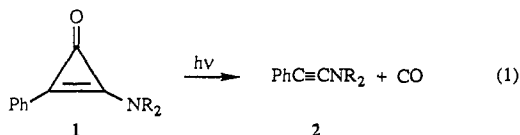
and, provided they had an ionizable N–H bond, *i.e.*, were either primary or secondary amines, to be correspondingly strong acids as well. In this respect, ynamines resemble their oxygen analogs, ynols, where the acetylenic group also exerts a very strong acid-strengthening effect.[2,3] In these initial studies we did not determine the pKₐ'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 pKₐ = 10.28, and that this has allowed

$$PhC{\equiv}CNHC_6F_5 + H_2O \rightleftharpoons PhC{\equiv}CNC_6F_5^- + H_3O^+$$
$$\mathbf{3} \qquad\qquad\qquad\qquad\qquad (2)$$
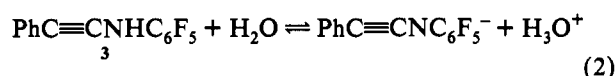
us to fix the acidifying effect in this case at 10 pK units or 14 kcal mol⁻¹.

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

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

the ynamine to the ketenimine is catalyzed by both acids and bases, and rate measurements made at 25.0 ± 0.1 °C in HClO₄ and NaOH solutions as well as HCO₂H, CH₃CO₂H, H₂PO₄⁻, NH₄⁺, and HCO₃⁻ buffers produced the rate profile shown in Figure 1.[6]

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 $k_{H^+}/k_{D^+} = 3.27 \pm 0.09$; this step is then followed by rapid

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

proton loss from nitrogen, eq 4. The basic leg derives from a process in which hydroxide

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

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.

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

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 $k_{HO^-}/k_{DO^-} = 4.1 \pm 0.2$ for the hydroxide-ion catalyzed process to $k_{H_2O}/k_{D_2O} = 7.9 \pm 0.4$ 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 $K_a = (5.29 \pm 0.01) \times 10^{-11}$ M, $pK_a = 10.28 \pm 0.01$.[7] Measurements made in D₂O solution lead to the isotope effect on this acidity constant $K_a^{H_2O}/K_a^{D_2O} = 3.77 \pm 0.28$, 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**, pKₐ = 20, based upon pKₐ = 23.1 determined in DMSO solution[9] and the change-of-solvent increment $\delta\,pK_a = -2.9$, obtained from the values for aniline itself in DMSO, pKₐ = 30.6,[10] and in H₂O, pKₐ = 27.7.[11] That puts the acid-strengthening effect of the phenylethynyl group in

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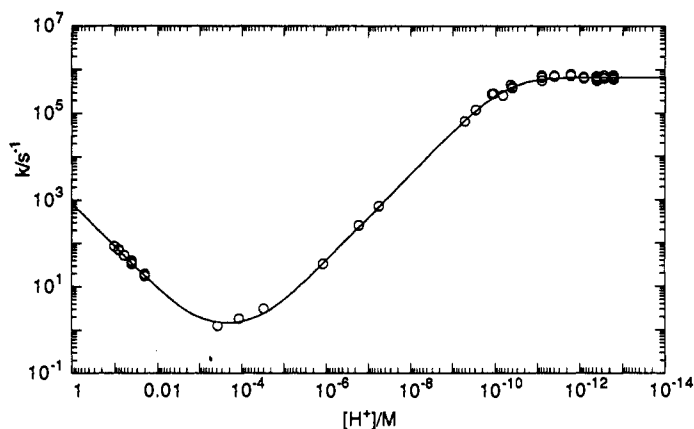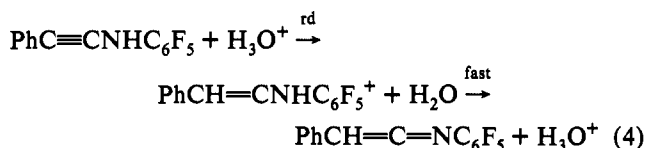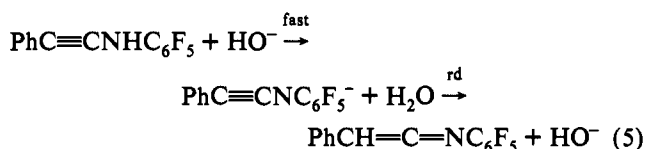
(7) This is a *concentration* dissociation constant applicable at the ionic strength of the kinetic measurements, μ = 0.10 M.

(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.

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

$$C_6F_5NH_2 \qquad\qquad PhC{\equiv}CNH_2 \qquad\qquad NH_3$$

$$\mathbf{7} \qquad\qquad\qquad \mathbf{8} \qquad\qquad\qquad \mathbf{9}$$
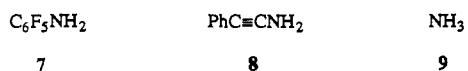
phenylethynylamine, **8**, with ammonia, **9**, but the reduction can be attributed to partial saturation of the phenylethynyl group

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

effect in the present case by the already strongly acidifying pentafluorophenyl substituent.

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