# Flash Photolytic Decarbonylation and Ring-Opening of 2-(*N*-(Pentafluorophenyl)amino)-3-phenylcyclopropenone. Isomerization of the Resulting Ynamine to a Ketenimine, Hydration of the Ketenimine, and Hydrolysis of the Enamine Produced by Ring-Opening

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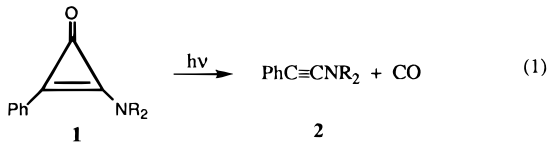
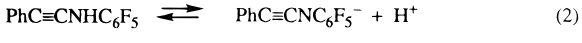
Flash photolysis of 2-(*N*-(pentafluorophenyl)amino)-3-phenylcyclopropenone, **4**, in aqueous solution was found to produce *N*-(pentafluorophenyl)phenylethynamine, **3**, by the expected photodecarbonylation reaction and also 2-phenyl-3-(*N*-(pentafluorophenyl)amino)acrylic acid, **5**, by an apparently unprecedented photochemical ring-opening process. The ynamine underwent rapid isomerization to *N*-(pentafluorophenyl)phenylketenimine, **9**, by an acid-catalyzed route that involves rate-determining proton transfer to the $\beta$-carbon atom of the ynamine and also by a base-catalyzed route involving equilibrium ionization of the N−H bond of the ynamine to give an ynamide ion followed by rate-determining $\beta$-carbon protonation of this ion. Saturation of the base catalysis allowed determination of the acidity constant of the ynamine; the result, $pQ_a = 10.23$, makes this amine a remarkably strong nitrogen acid. Hydration of the ketenimine **9** gave *N*-(pentafluorophenyl)phenylacetamide, **6**, as the ultimate product produced by this reaction route, and hydrolysis of the aminoacrylic acid **5** gave pentafluoroaniline, **7**, and 2-phenylformylacetic acid, **10**, which underwent decarboxylation to phenylacetaldehyde, **8**, as the ultimate products of this route.

We recently discovered that phenylaminocyclopropenones, **1**, undergo photolytic decarbonylation to acetylenic amines, **2**, commonly called ynamines, eq 1, and that the




**1** **2** (1)

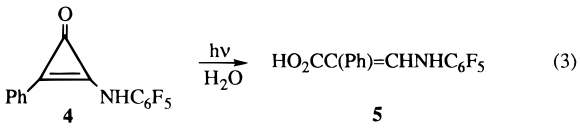
chemistry of these substances in aqueous solution, where they are very short-lived, can be examined using flash photolytic techniques.[1] Our studies have shown that the phenylethynyl group has a powerful weakening effect on the basicity of ynamines. This base-weakening influence is the counterpart of a very strong acid-strengthening effect that the phenylethynyl group has on the ionization of acetylenic alcohols (ynols),[2] and, in keeping with that, this group confers acidic properties on ynamines as well. We report here that introduction of yet another acidifying group, the pentafluorophenyl moiety, has the remarkable effect of producing an ynamine, **3**, that ionizes as an acid in dilute aqueous solution, eq 2.[3,4]




**3** (2)

We have also found that photodecarbonylation of the cyclopropenone precursor, **4**, used to generate this ynamine is accompanied by yet another photochemical process which produces the enamine **5**, eq 3. A similar ring-opening is a well known thermal reaction of cyclopropenones,[5] but the photochemical process that we have found appears to be unprecedented.

Part of this work has been published in preliminary form.[6]




**4** **5** (3)

## Experimental Section

**Materials. 2-(*N*-(Pentafluorophenyl)amino)-3-phenylcyclopropenone, 4**, was a sample that had been prepared before.[1b] ***N*-(Pentafluorophenyl)phenylacetamide**, **6**, was synthesized by treating phenylacetyl chloride with pentafluoroaniline, and **methyl 2-phenyl-3-(*N*-(pentafluorophenyl)amino)acrylate**, **11**, was obtained by allowing a solution of 2-(*N*-(pentafluorophenyl)amino)-3-phenylcyclopropenone in 5:1 methanol:acetone to stand at room temperature overnight.[7] These substances were characterized by their mass and NMR spectra; details are given in Table S1.[8] All other materials were best available commercial grades.

**Kinetics.** Flash photolytic rate measurements were made using conventional flash-lamp and eximer-laser systems that have already been described.[9] Excitation in the conventional system[9a] was provided by a pair of xenon lamps that produced

[⊗] Abstract published in *Advance ACS Abstracts,* July 1, 1997.

(1) (a) Chiang, Y.; Grant, A. S.; Kresge, A. J.; Pruszynski, P.; Schepp, N. P.; Wirz, *J. Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1346−1358. (b) Chiang, Y.; Grant, A. S.; Kresge, A. J.; Paine, S. W. *J. Am. Chem. Soc.* **1996**, *118*, 4366−4372. (c) Kresge, A. J.; Paine, S. W. *Can. J. Chem.* **1996**, *74*, 1373−1376.

(2) Chiang, Y.; Kresge, A. J.; Hochstrasser, R.; Wirz, J. *J. Am. Chem. Soc.* **1989**, *111*, 2355−2357. Chiang, Y.; Kresge, A. J.; Popik, V. V. *J. Am. Chem. Soc.* **1995**, *117*, 9165−9171.

(3) For theoretical analyses of these base-weakening and acid-strengthening effects see Smith, B. J.; Radom, 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) A brief review of ynol and ynamine chemistry appears in Chiang, Y.; Kresge, A. J.; Paine, S. W.; Popik, V. V. *J. Phys. Org. Chem.* **1996**, *9*, 361−370.

(5) Potts, K. T.; Baum, J. S. *Chem. Rev.* **1974**, *74*, 189−213.

(6) Andraos, J.; Chiang, Y.; Grant, A. S.; Guo, H.-X.; Kresge, A. J. *J. Am. Chem. Soc.* **1994**, *116*, 7411−7412.

(7) Farnum, D. G.; Chickos, J.; Thurston, P. E. *J. Am. Chem. Soc.* **1966**, *88*, 3075−3081.

(8) Supporting information; see paragraph at the end of this paper regarding availability.

(9) (a) Chiang, Y.; Hojatti, M.; Keeffe, J. R.; Kresge, A. J.; Schepp, N. P.; Wirz, J. *J. Am. Chem. Soc.* **1987**, *109*, 4000−4009. (b) Andraos, J.; Chiang, Y.; Huang, C.-G.; Kresge, A. J.; Scaiano, J. C. *J. Am. Chem. Soc.* **1993**, *115*, 10605−10610.

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light over the entire spectral region from the ultraviolet through the visible; the laser system[9b] operated at $\lambda = 248$ nm.

Some reactions were too slow to allow accurate monitoring by flash photolysis, and these were therefore followed using a Cary 2200 spectrometer. The reactions were first initiated by a single flash from the conventional system, and the reacting solutions were then quickly transferred to the Cary instrument.

The temperature of all reaction solutions was controlled at 25.0 ± 0.05 °C, and observed rate constants were calculated by least-squares fitting of exponential functions.

**Acidity Constant Determinations.** Acid dissociation constants were determined spectrophotometrically, by monitoring the changes in UV absorbance that the substrates underwent upon ionization. Absorbance measurements were made with a Cary 2200 spectrometer whose cell compartment was thermostated at 25.0 ± 0.05 °C; solutions containing a constant stoichiometric concentration of substrate were employed. The data so obtained were analyzed by least squares fitting of eq 4, in which $A_A$ and $A_B$ are the absorbances of the

$$A_{obs} = \frac{A_A[H^+] + A_B Q_a}{Q_a + [H^+]} \quad (4)$$

acidic and basic forms of the substrate, respectively, and $Q_a$ is its acidity constant.

## Results

**Reaction Identification.** Flash photolysis of 2-(*N*-(pentafluorophenyl)amino)-3-phenylcyclopropenone in aqueous solution produces several different reaction products. Using HPLC analysis with authentic-sample spiking, we have identified three of these products as *N*-(pentafluorophenyl)phenylacetamide, **6**, pentafluoroaniline, **7**, and phenylacetaldehyde, **8**. The first of these products is formed immediately, whereas the second and

$PhCH_2CONHC_6F_5$ (**6**) $C_6F_5NH_2$ (**7**) $PhCH_2CHO$ (**8**)

third take some tens of minutes to appear.

This product complexity has its counterpart in the UV spectral changes that occur following flash photolysis. There is at first a rapid rise in absorbance in the region $\lambda = 260-265$ nm, and that is then followed by a considerably slower decay. This is similar to the changes observed before in the flash photolysis of other secondary aminocyclopropenones,[1a,b] where the rise was identified as formation of a phenylketenimine by isomerization of a phenylethynamine, itself formed by the still more rapid decarbonylation reaction of eq 1, and the decay was identified as hydration of the ketenimine to a phenylacetamide. An analogous assignment may be made in the present case, with the absorbance rise corresponding to isomerization of *N*-(pentafluorophenyl)phenylethynamine, **3**, to *N*-(pentafluorophenyl)phenylketenimine, **9**, as shown in eq 5. However, as Figure 1 illustrates, the absorbance decay in the present case is biphasic, with the data

$$PhC{\equiv}CNHC_6F_5\ (\mathbf{3}) \rightarrow PhCH{=}C{=}NC_6F_5\ (\mathbf{9}) \quad (5)$$

conforming well to a double exponential rate law for two concurrent first-order reactions. This raises the question as to which component of this biphasic decay represents the hydration of *N*-(pentafluorophenyl)phenylketenimine to *N*-(pentafluorophenyl)phenylacetamide, **6**, eq 6, and which corresponds to some other reaction.

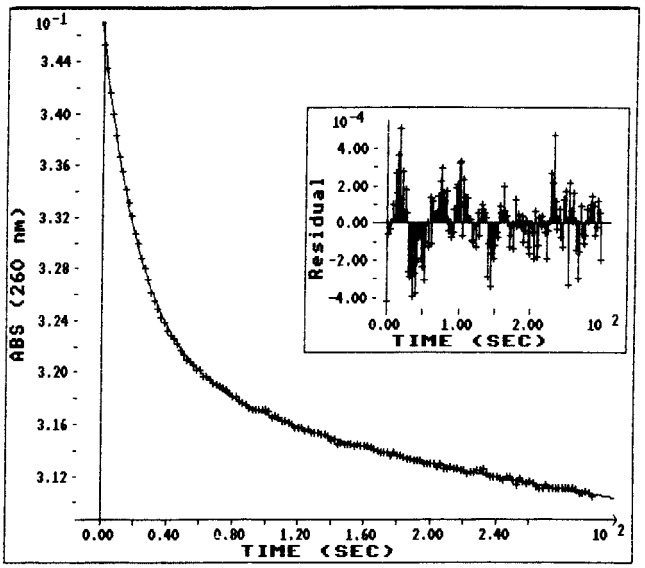



**Figure 1.** Biphasic absorbance decay following a faster absorbance rise produced by flash photolysis of 2-(*N*-(pentafluorophenyl)amino)-3-phenylcyclopropenone in aqueous 0.04 M acetic acid buffer solution, buffer ratio = 1; the inset shows deviations from least squares fit of a double exponential rate law.

$$PhCH{=}C{=}NC_6H_5\ (\mathbf{9}) \xrightarrow{H_2O} PhCH_2CONHC_6F_5\ (\mathbf{6}) \quad (6)$$

The more rapid component of this biphasic decay is complete within a few seconds, which gives it the same time scale as formation of *N*-(pentafluorophenyl)phenylacetamide, observed as an immediately generated reaction product. That suggests that this more rapid absorbance decay represents the ketenimine hydration reaction of eq 6. This assignment is supported by the fact that the reactivity and form of acid−base catalysis shown by this absorbance decay are consistent with expectation based upon an earlier study of ketenimine hydration using authentic ketenimine substrates (*vide infra*).[10]

The slower component of the biphasic absorbance decay occurs on a time scale consistent with the generation of pentafluoroaniline and phenylacetaldehyde, which were observed as reaction products requiring some tens of minutes to appear, and that suggests that the slower decay is associated with the formation of these substances. A common reaction of cyclopropenones is nucleophile-assisted ring opening,[5] which in the present case would generate the enamine 2-phenyl-3-(*N*-(pentafluorophenyl)amino)acrylic acid, **5**, as shown in eq 3. Hydrolysis of this enamine would then produce pentafluoroaniline, **7**, and 2-phenylformylacetic acid, **10**, eq 7, which is known to decarboxylate readily giving phenylacetaldehyde, **8**, eq 8.[11]

$$HO_2CC(Ph){=}CHNHC_6F_5\ (\mathbf{5}) \xrightarrow{H_2O} C_6H_5NH_2\ (\mathbf{7}) + HO_2CCH(Ph)CHO\ (\mathbf{10}) \quad (7)$$

$$HO_2CCH(Ph)CHO\ (\mathbf{10}) \longrightarrow PhCH_2CHO\ (\mathbf{8}) + CO_2 \quad (8)$$

This assignment receives support from a comparison of rates of reaction based upon this slower absorbance

(10) McCarthy, D. G.; Hegarty, A. F. *J. Chem. Soc., Perkin Trans. 2* **1980**, 579−591.
(11) Strukov, I. T. *J. Gen. Chem. USSR* **1952**, *22*, 1077−1084.

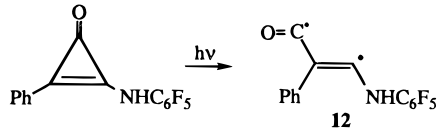
decay with rates of hydrolysis of the methyl ester of the enamine-acid, methyl 2-phenyl-3-(*N*-(pentafluorophenyl)-amino)acrylate, **11**, eq 9, to whose hydrolysis this absor-

$$\underset{\mathbf{11}}{MeO_2CC(Ph)=CHNHC_6H_5} \xrightarrow{H_2O} C_6F_5NH_2 + MeO_2CCH(Ph)CHO \quad (9)$$

bance decay is being attributed. These rates of reaction were measured in aqueous perchloric acid solution over a range of acid concentrations at a constant ionic strength (0.10 M). The data are summarized in Tables S2 and S3.[8] In both cases, observed first-order rate constants were accurately proportional to acid concentration; least squares analysis gave $k_{obs} = (4.83 \pm 2.15) \times 10^{-5} + (1.25 \pm 0.03) \times 10^{-2}[HClO_4]$ for the absorbance decay and $k_{obs} = (4.69 \pm 3.79) \times 10^{-5} + (1.06 \pm 0.06) \times 10^{-2}[HClO_4]$ for hydrolysis of the enamine-ester. The close correspondence of these two rate laws suggests that similar processes are being monitored in the two cases, *i.e.*, that both reactions are enamine hydrolyses.

Further evidence that this assignment is correct comes from the solvent isotope effect on the slower component of the biphasic absorbance decay. This isotope effect was determined by measuring rates in $D_2O$ solutions of perchloric acid, again over a range of acid concentrations. Least squares analysis of the data, summarized in Table S2,[8] gave $k_{obs} = -(0.37 \pm 1.95) \times 10^{-5} + (4.14 \pm 0.30) \times 10^{-3}[DClO_4]$, which, together with the $H_2O$ result provides the isotope effect $k_H^+/k_D^+ = 3.02 \pm 0.24$. The hydrolysis of deactivated enamines such as this is known to occur by rate-determining hydron transfer to $\beta$-carbon to give isotope effects in the normal direction,[12] like the present result.

Although the ring-opening reaction generating an enamine found here provides products similar to those expected from the well-known thermal ring-opening of cyclopropenones,[5] the present process cannot be a thermal reaction. The cyclopropenone precursor is stable in the solutions used for flash photolysis; no products are formed until the system is irradiated, and the reaction must consequently be a photochemical process. It seems unlikely, moreover, that this photochemical reaction occurs by a mechanism similar to the thermal process, which is believed to be initiated by nucleophilic attack at the carbonyl carbon atom of the cyclopropenone,[5] for it is not clear that photoexcitation would increase the susceptibility of this carbon atom to nucleophilic attack. Carbonyl group photochemistry is dominated instead by radical reactions, and a plausible primary process in the present case woud be α-cleavage, as shown in eq 10. The ensuing biradical, **12**, is a resonance hybrid of several structures, including the ketene-carbene, **13**, and addi-




(10)

tion of water to that would give the postulated product, 2-phenyl-3-(*N*-(pentafluorophenyl)amino)acrylic acid, **5**. α-Cleavage is a well known photochemical primary process, but its occurrence in cyclopropenone chemistry appears to be unprecedented.

(12) Keeffe, J. R.; Kresge, A. J. In *The Chemistry of Enamines*; Rappoport, Z., Ed.; John Wiley and Sons: New York, 1994; pp 1049–1109.

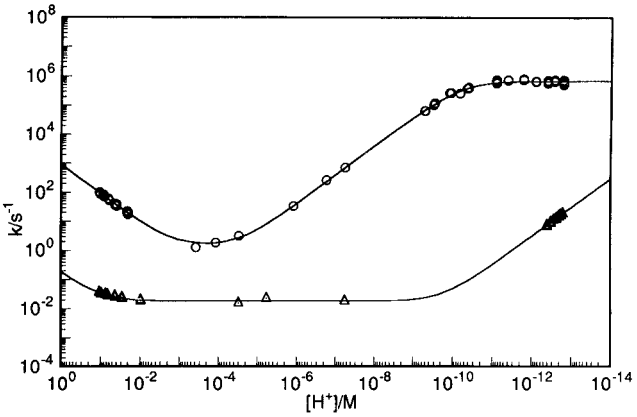
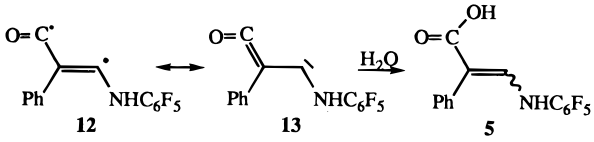



**Figure 2.** Rate profiles for the isomerization of *N*-(pentafluorophenyl)phenylethynamine to *N*-(pentafluorophenyl)phenylketenimine (○) and hydration of the ketenimine (△) in aqueous solution at 25 °C, ionic strength = 0.10 M.




(11)

**Phenylethynamine Isomerization.** The rise in absorbance at $\lambda = 260-265$ nm observed upon flash photolysis of 2-(*N*-(pentafluorophenyl)amino)-3-phenylcyclopropenone, attributed to isomerization of *N*-(pentafluorophenyl)phenylethynamine to *N*-(pentafluorophenyl)ketenimine, eq 5, conformed well to a single exponential rate law. Observed first-order rate constants obtained by least-squares fitting of such an expression were determined in aqueous perchloric acid and sodium hydroxide solutions as well as in formic acid, acetic acid, biphosphate ion, ammonium ion, and bicarbonate ion buffers. All measurements were made at constant ionic strength (0.10 M). The data so obtained are summarized in Tables S4–S6.[8]

The rate measurements in buffers were made in series of solutions of constant buffer ratio and constant ionic strength (0.10 M) but varying buffer concentration; this served to hold hydronium ion concentrations constant along a given buffer series. Buffer catalysis was found, with observed first-order rate constants conforming to the expected linear rate law of eq 12; the data were consequently analyzed by least squares fitting of this expres-

$$k_{obs} = k_o + k_{cat}[buffer] \quad (12)$$

sion. The zero-buffer-concentration intercepts, $k_o$, together with observed rate constants measured in perchloric acid and sodium hydroxide solutions, are displayed as the upper rate profile of Figure 2. Hydrogen ion concentrations of the buffers needed for this purpose were obtained by calculation, using literature values of the buffer acid ionization constants and activity coefficients recommended by Bates.[13]

Buffer catalysis was strong in the more acidic buffers ($HCO_2H$, $CH_3CO_2H$, and $H_2PO_4^-$), but it became progressively weaker as the acid strength of the buffer acid decreased and was practically nonexistant in $NH_4^+$ and $HCO_3^-$ buffers. The form of the buffer catalysis was

(13) Bates, R. G. *Determination of pH Theory and Practise*; Wiley: New York, 1973; p 49.

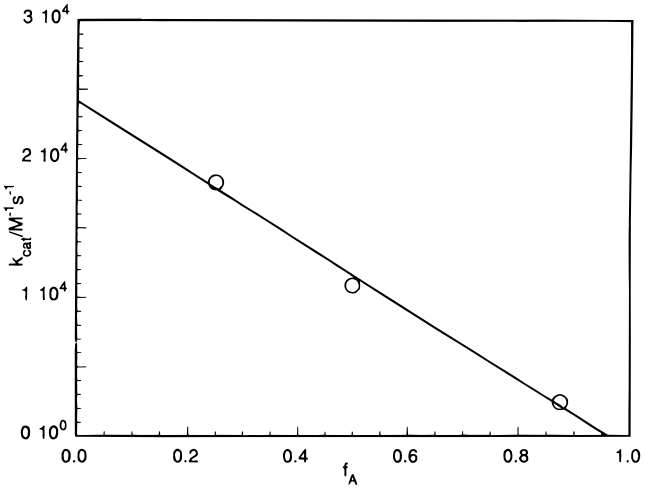



**Figure 3.** Rate data for the isomerization of 2-(*N*-(pentafluorophenyl)phenylethynamine to *N*-(pentafluorophenyl)phenylketenimine in aqueous $H_2PO^-/HPO_4^{2-}$ buffer solutions plotted according to eq 13.

determined with the aid of eq 13, in which $k_B$ and $k_{HA}$ are general base and general acid catalytic coefficients,

$$k_{cat} = k_B + (k_{HA} - k_B)f_A \qquad (13)$$

respectively, and $f_A$ is the fraction of buffer present as acid. The data for $H_2PO_4^-$ buffers plotted according to this equation are displayed in Figure 3; it may be seen that they conform to this relationship well. Least squares analysis gave $k_{HA} = -(0.98 \pm 1.07) \times 10^3$ $M^{-1}$ $s^{-1}$ and $k_B = (2.42 \pm 0.12) \times 10^4$ $M^{-1}$ $s^{-1}$ for these buffers, and the data for acetic acid buffers provided $k_{HA} = (1.02 \pm 2.57)$ $M^{-1}$ $s^{-1}$ and $k_B = (3.47 \pm 0.09) \times 10^2$ $M^{-1}$ $s^{-1}$. These results show that buffer catalysis is wholly of the general base type.

Some rate measurements were also made in $D_2O$ solutions of hydrochloric acid, sodium hydroxide, and biphosphate ion buffers. These data are summarized in Tables S4−S6[8] as well.

The measurements in $D_2O$ solutions of hydrochloric acid were made over a range of acid concentration where, as in the case of $H_2O$ solutions of perchloric acid, observed rate constants increased linearly with acid concentration. Linear least squares analysis gave the second-order rate constant $k_{D^+} = (2.71 \pm 0.06) \times 10^2$ $M^{-1}$ $s^{-1}$, which, when combined with its $H_2O$ counterpart, provides the isotope effect $k_{H^+}/k_{D^+} = 3.26 \pm 0.10$.

The rate measurements in $D_2O$ solutions of sodium hydroxide solutions were made at a single hydroxide ion concentration (0.10 M) in the region of the high basicity plateau where observed rate constants were independent of acid or base concentration (see Figure 2). Replicate measurements gave the averge value $k_{D_2O} = (7.43 \pm 0.23) \times 10^4$ $s^{-1}$, which, when combined with the average rate constants determined in $H_2O$ solutions of sodium hydroxide at the same concentration, gave the isotope effect $k_{H_2O}/k_{D_2O} = 8.50 \pm 0.41$.

The measurements in $D_2O$ solutions of biphosphate buffers were done at a single buffer ratio, exactly the same as that for one of the sets of solutions of this buffer in $H_2O$. Once again, observed rate constants increased linearly with increasing buffer concentration and application of eq 12 gave a catalytic coefficient and zero-concentration intercept, which, when combined with their $H_2O$ counterparts, provided the isotope effects $(k_{cat})_{H_2O}/(k_{cat})_{D_2O} = 3.22 \pm 0.20$ and $(k_o)_{H_2O}/(k_o)_{D_2O} = 29.8 \pm 1.6$. The latter value is a comparison at equal hydrogen ion concentrations, *i.e.* $[H^+] = [D^+]$ $(= 5.53 \times 10^{-8}$ M); the isotope effect on the ionization of biphosphate ion needed to make such a comparison was taken from the literature.[14]

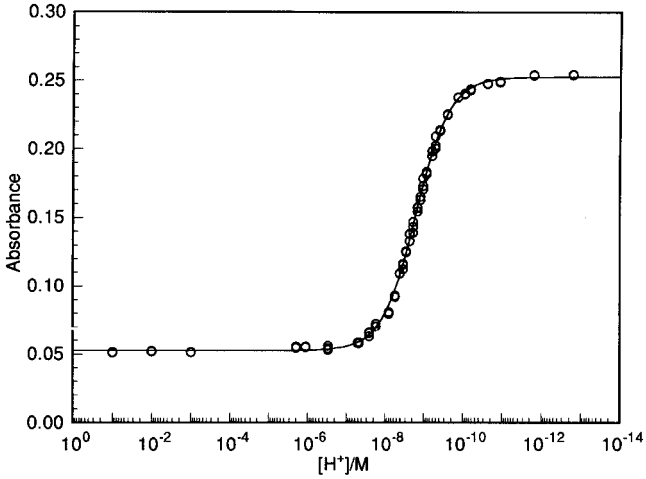



**Figure 4.** Sigmoid titration curve for the ionization of 2-(*N*-(pentafluorophenyl)amino)-3-phenylcyclopropenone as a nitrogen acid in aqueous solution at 25 °C.

**Hydration of Phenylketenimine.** Rates of reaction based upon the faster component of the biphasic decay in absorbance at $\lambda = 260-265$ nm observed upon flash photolysis of 2-(*N*-(pentafluorophenyl)amino)-3-phenylcyclopropenone in aqueous solution, and attributed to hydration of *N*-(pentafluorophenyl)phenylketenimine, were determined in perchloric acid and sodium hydroxide solutions as well as in acetic acid and biphosphate ion buffers. All measurements were made at constant ionic strength (0.10 M). The data so obtained are summarized in Tables S7−S9.[8]

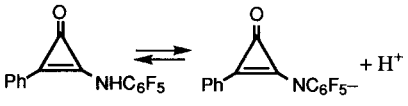
Rates of reaction in series of buffer solutions at constant buffer ratio increased with increasing buffer concentration, with observed first-order rate constants conforming to the linear rate law of eq 12. Least squares analysis gave zero-buffer-concentration intercepts, which, together with the rate constants measured in perchloric acid and sodium hydroxide solution, are displayed as the lower rate profile of Figure 2. The form of buffer catalysis was again evaluated using the relationship of eq 13; the data for acetic acid buffers gave $k_{HA} = -(0.10 \pm 1.28) \times 10^{-1}$ $M^{-1}$ $s^{-1}$ and $k_B = (7.10 \pm 0.93) \times 10^{-1}$ $M^{-1}$ $s^{-1}$, which shows that the catalysis was again wholly of the general base type.

**Acidity Constants.** The acidity constants of two substances, 2-(*N*-(pentafluorophenyl)amino)-3-phenylcyclopropenone and *N*-(pentafluorophenyl)benzamide, ionizing as nitrogen acids, were determined by monitoring the UV absorbance changes that these substances underwent, at $\lambda = 310$ and 280 nm respectively, as the acidity of their solutions was varied. Measurements were made at constant ionic strength (0.10 M) in aqueous solutions of hydrochloric acid, sodium hydroxide, and biphosphate ion, monohydrogen *t*−butylphosphonate ion, ammonium ion, and bicarbonate ion buffers. The data so obtained are summarized in Tables S10 and S11.[8]

As Figure 4 illustrates, the results conformed well to the expected sigmoid relationship of eq 4. Least squares

(14) Gary, R.; Bates, R. G.; Robinson, R. A. *J. Phys. Chem.* **1964**, *68*, 3806−3809.

**Table 1. Summary of Rate and Equilibrium Constants[a]**

| Process | Constant |
|---|---|
| $PhC{\equiv}CNHC_6F_5 \rightleftharpoons PhC{\equiv}CNC_6F_5^- + H^+$ | $Q_a = 5.86\times10^{-11}$ M; $pQ_a = 10.23$ $Q_H/Q_D = 3.50$ |
| $PhC{\equiv}CNHC_6F_5 \xrightarrow{H^+} PhCH{=}CNHC_6F_5^+$ | $k_{H^+} = 8.91\times10^{2}$ $M^{-1}$ $s^{-1}$; $k_H/k_D = 3.26$ |
| $PhC{\equiv}CNHC_6F_5 \xrightarrow[-HO^-]{H_2O} PhCH{=}CNHC_6F_5^+$ | $k_o = 1.08$ $s^{-1}$ |
| $PhC{\equiv}CNC_6F_5^- \xrightarrow[-HO^-]{H_2O} PhCH{=}C{=}NC_6F_5$ | $k_o' = 6.52\times10^{5}$ $s^{-1}$; $k_H/k_D = 8.50$ |
| $PhC{\equiv}CNC_6F_5^- \xrightarrow[-OAc^-]{HOAC} PhCH{=}C{=}NC_6F_5$ | $k'_{HA} = 1.61\times10^{8}$ $M^{-1}$ $s^{-1}$ |
| $PhC{\equiv}CNC_6F_5^- \xrightarrow[-HPO_4^=]{H_2PO_4^-} PhCH{=}C{=}NC_6F_5$ | $k'_{HA} = 6.84\times10^{7}$ $M^{-1}$ $s^{-1}$; $k_H/k_D = 3.22$ |
| $PhCH{=}C{=}NC_6F_5 \xrightarrow[H_2O,\,-H^+]{H^+} PhCH_2CONHC_6F_5$ | $k_{H^+} = 1.88\times10^{-1}$ $M^{-1}$ $s^{-1}$ |
| $PhCH{=}C{=}NC_6F_5 \xrightarrow{H_2O} PhCH_2CONHC_6F_5$ | $k_o = 2.00\times10^{-2}$ $s^{-1}$ |
| $PhCH{=}C{=}NC_6F_5 \xrightarrow[H_2O,\,-HO^-]{HO^-} PhCH_2CONC_6F_5$ | $k_{HO^-} = 2.05\times10^{2}$ $M^{-1}$ $s^{-1}$ |
|  | $Q_a = 1.57\times10^{-9}$ M; $pQ_a = 8.80$ |
| $PhCONHC_6F_5 \rightleftharpoons PhCONC_6F_5^- + H^+$ | $Q_a = 7.35\times10^{-11}$ M; $pQ_a = 10.13$ |

[a] Aqueous solution, 25 °C, ionic strength = 0.10 M

analysis gave $Q_a = (1.57 \pm 0.02) \times 10^{-9}$ M, $pQ_a = 8.803 \pm 0.005$ for 2-(*N*-(pentafluorophenyl)amino)-3-phenylcyclopropenone,[15] and $Q_a = (7.35 \pm 0.12) \times 10^{-11}$ M, $pQ_a = 10.134 \pm 0.007$, for *N*-(pentafluorophenyl)benzamide.[15]

## Discussion

**Phenylethynamine Isomerization.** Our previous studies[1] have shown that secondary phenylethynamines undergo isomerization to phenylketenimines by rate-determining protonation on $\beta$-carbon followed by rapid proton loss from nitrogen of the ensuing keteniminium ion, **14**, eq 14. As expected for such a reaction, the present ynamine isomerization shows acid catalysis,

$$PhC{\equiv}CNHR \xrightarrow[r.d.]{H^+} PhCH{=}CNHR^+ \xrightarrow[fast]{-H^+} PhCH{=}C{=}NR \quad (14)$$

**14**

evidenced by the diagonal segment at the high acidity end of the rate profile of Figure 2, and it also gives a hydrogen ion isotope effect in the normal direction, $k_{H^+}/k_{D^+} = 3.26$, also as expected for the process of eq 14. The hydrogen-ion catalytic coefficient for the present isomerization, moreover, conforms well to a correlation of catalytic coefficients for the rate-determining carbon protonation of other phenylethynamines.[1b] It would seem safe to conclude, therefore, that the presently observed process is an ynamine−ketenimine isomerization reaction that occurs by the mechanism of eq 14.

The rate profile of Figure 2, however, shows some additional features that indicate another reaction mechanism is operating as well. There is a region of base catalysis, indicated by the diagonal segment extending from $[H^+] = 10^{-4}$ to $10^{-10}$ M, which eventually becomes saturated producing a downward bend in the profile. Downward bends such as this are often caused by acid ionization of the substrate,[16] and this suggests that the base catalysis is due to equilibrium ionization of the ynamine to an ynamide ion, **15**, followed by rate-determining protonation of this ion on $\beta$-carbon by solvent water, eq 15. Since a proton is provided in the prior equilibrium but is not used up in the rate-determining step, the overall rate of reaction will be inversely proportional to hydrogen ion concentration, which is equivalent to being directly proportional to hydroxide ion

(15) This is a concentration dissociation constant, applicable at the ionic strength of the measurements (0.10 M).

(16) Loudon, G. M. *J. Chem. Ed.* **1991**, *68*, 973−984.

$$\mathrm{PhC{\equiv}CNHC_6F_5} \rightleftharpoons \mathrm{PhC{\equiv}CNC_6F_5^-} + \mathrm{H^+} \quad (15)$$
$$\mathbf{15} \downarrow \mathrm{H_2O}$$
$$\mathrm{PhCH{=}C{=}NC_6F_5}$$

concentration, as observed. The ynamide ion can be expected to be much more reactive to carbon protonation than is the neutral ynamine—enolate ions, for example, are many orders of magnitude more reactive than the corresponding enols[17]—and this mechanism would be the preferred route even when the equilibrium concentration of ynamide ion is very low. Eventually, however, at sufficiently low hydrogen ion concentrations, the equilibrium will shift from a preponderance of ynamine to a preponderance of ynamide ion, and the advantage of going from a less reactive to a more reactive species will be lost and base catalysis will become saturated, again as observed.

Support for this reaction mechanism comes from isotope effects. The solvent isotope effect on the reaction in the low-acidity plateau region, where base-catalysis has become saturated and the reaction consists of simple carbon protonation by water, is $k_{H_2O}/k_{D_2O} = 8.5$. This is a reasonable value for hydron transfer from a water molecule; it is large because the primary isotope effect produced by the hydron in transit is augmented by a secondary effect generated by solvation of the hydroxide ion being left behind.[18] The solvent isotope effect in the region of base catalysis, on the other hand, is much greater: $k_{H_2O}/k_{D_2O} = 29.8$. This is because the reaction now starts from unionized ynamine as its initial state, and the observed rate constant is consequently equal to the product of the rate constant for the rate-determining step, $k$, and the equilibrium constant for the prior step, $Q_a$:$k_{obs} = kQ_a$; the observed isotope effect is therefore the product of isotope effects on the two steps. Since the isotope effect on $k$ has been determined from rate measurements made in the region of base-catalysis saturation, that on $Q_a$ may be evaluated; the result is $(Q_a)_{H_2O}/(Q_a)_{D_2O} = 3.51 \pm 0.25$. This is a reasonable value for ionization of an acid of this strength ($pQ_a = 10.23$, *vide infra*); for example $(K_a)_{H_2O}/(K_a)_{D_2O} = 3.12$ has been reported for ammonium ion ($pK_a = 9.27$) and $(K_a)_{H_2O}/(K_a)_{D_2O} = 4.17$ for phenol ($pK_a = 10.00$).[19]

The reaction mechanism of eq 15 is also supported by the fact that isomerization is catalyzed by buffers and that the catalysis is wholly of the general base type in acetic acid and biphosphate ion buffers. The rate-determining step of this mechanism, proton transfer from an acid catalyst to the substrate, will be subject to general acid catalysis. However, in the region where undissociated ynamine is the initial state of the reaction, as is the case in acetic acid and biphosphate ion buffers, the prior equilibrium will add an inverse dependence on hydrogen ion concentration, and the net result will be general base catalysis, as observed.

The fact that buffer catalysis became progressively weaker and more difficult to detect as the acidity of the buffer acid decreased is also consistent with the mechanism of eq 15. The rate-determining step of this mechanism can be expected to be a very fast reaction, and in fact the very large general acid catalytic coefficients, $k_{HA} = 1.61 \times 10^8\ M^{-1}\ s^{-1}$ and $6.84 \times 10^7\ M^{-1}\ s^{-1}$ for acetic acid and biphosphate ion, respectively, can be calculated for this step from the observed general base catalytic coefficients and the acidity constant of the ynamine, $Q_a = 5.86 \times 10^{11}$ M (*vide infra*). Such very fast reactions will have reactant-like transition states and low values of the Bronsted exponent $\alpha$;[20] the two catalytic coefficients cited above do in fact give $\alpha = 0.27$. General acid catalysis becomes difficult to detect in systems with low Bronsted exponents because reaction through proton transfer from the solvent is dominant, and this dominance becomes stronger the weaker the general acid.[21] General acid catalysis of the rate-determining step in the present ynamine isomerization by such weak acids as ammonium and biphosphate ions will consequently be swamped by the water reaction, which, because of the prior substrate ionization equilibrium, will be translated into observed general base catalysis being overwhelmed by a hydroxide ion reaction. In the early stages of our investigation of this reaction, we in fact failed to detect general base catalysis and in a preliminary publication reported the process to be subject only to specifc hydroxide ion catalysis.[1a]

The isotope effect on general base catalysis in biphosphate ion buffers also supports the proposed reaction mechanism. The observed effect, $k_H/k_D = 3.22$, is the product of the isotope effect on the prior equilibrium deprotonation of the substrate, whose equilibrium constant is equal to the acidity constant of the substrate divided by that of the biphosphate ion, and the isotope effect on the rate-determining carbon-protonation step. Since the isotope effect on the acidity constant of the substrate has been determined here and that on the ionization of biphosphate ion is available from the literature,[14] the isotope effect on the rate-determining step can be evaluated. The result is $k_H/k_D = 3.15 \pm 0.30$. The normal direction ($k_H/k_D > 1$) of this isotope effect is as expected for rate-determing hydron transfer from biphosphate ion to carbon, and its modest magnitude is consistent with the great speed of this reaction ($k_H = 6.8 \times 10^7\ M^{-1}\ s^{-1}$) and its consequent reactant-like, unsymmetrical transition state.[22]

With this assignment of a mechanism to the base-catalyzed portion of the present ynamine isomerization reaction, a complete rate law interpreting the rate profile shown in Figure 2 may be written. This is shown in eq 16, where $k_H{}^+$ is the rate constant for carbon protonation

$$k_{obs} = k_H{}^+[H^+] + k_o + k'_oQ_a/(Q_a + [H^+]) \quad (16)$$

of the unionized substrate by hydrogen ion, $k'_o$ is the rate constant for carbon protonation of the ionized form by water, and $Q_a$ is the acidity constant of the ynamine. The rate constant $k_o$ represents the short, horizontal region of the profile at $[H^+] = 10^{-3}$–$10^{-4}$ M. The molecular

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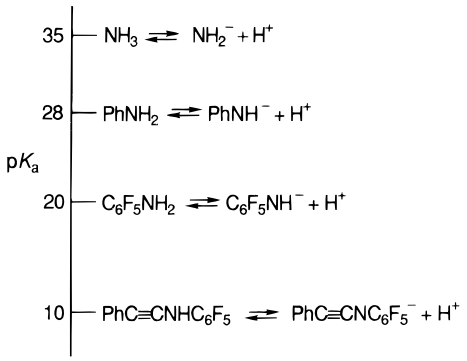



**Figure 5.** Acidity scale for some amines ionizing as acids in aqueous solution.

interpretation of this rate constant is ambiguous: it could represent carbon protonation of the unionized substrate by water, or carbon protonation of the ionized form by hydrogen ion. Least squares fitting of eq 16 gave $k_H^+ = (8.91 \pm 0.19) \times 10^2$ $M^{-1}$ $s^{-1}$, $k_o = 1.08 \pm 0.11$ $s^{-1}$, $k'_o = (6.52 \pm 0.12) \times 10^5$ $s^{-1}$, and $Q_a = (5.86 \pm 0.27) \times 10^{-11}$, $pQ_a = 10.232 \pm 0.020$.[15]

**Phenylethynamine Acidity.** The acid dissociation constant determined here for *N*-(pentafluorophenyl)phenylethynamine, $pQ_a = 10.23$, shows this substance to have a remarkably strong acidity for an amine ionizing as a nitrogen acid in aqueous solution: most amines take on a proton rather than give one up in this medium. This ynamine, for example, is 23 pK units more acidic than ammonia, for which $pK_a = 35$ in aqueous solution has been estimated.[23]

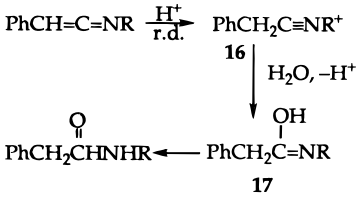
This striking increase in acidity may be divided into contributions from the phenylethynyl group and the pentafluorophenyl group by making comparisons with the acidity constant of pentafluoroaniline ionizing as an acid. A directly measured value of the latter is unfortunately not available for aqueous solution, but an estimate can be made using $pK_a = 23.1$ determined in DMSO[24] and the change of solvent increment $\Delta pK_a = -2.9$. This increment is based upon comparisons using two different nitrogen acids, each giving the same result: for aniline, $pK_a$(DMSO) = 30.6,[25] $pK_a(H_2O) = 27.7$,[26] and $\Delta pK_a = -2.9$; and for *N*-(pentafluorophenyl)benzamide, $pK_a$(DMSO) = 13.0,[24] $pK_a(H_2O) = 10.1$ (this work), and $\Delta pK_a = -2.9$. The resulting estimate, $pK_a = 20.2$ for pentafluoroaniline in aqueous solution, puts this substance 15 pK units below ammonia and 10 pK units above *N*-(pentafluorophenyl)phenylethynamine. Thus, 40% of the difference between this ynamine and ammonia may be assigned to the phenylethynyl group and 60% to the pentafluorophenyl group. These comparisons are presented in graphical form in Figure 5.

**Ketenimine Hydration.** The rate profile of Figure 2 for the hydration of *N*-(pentafluorophenyl)phenylketenemine to *N*-(pentafluorophenyl)phenylacetamide shows both acid and base catalysis as well as an uncatalyzed region. This is consistent with an earlier detailed study of ketenimine hydration in which acid and base catalysis and an uncatalyzed reaction were also found.[10] The rate law required by such a process is shown in eq 17, and least squares fitting of the present data using this expression gave $k_H^+ = (1.88 \pm 0.08) \times 10^{-1}$ $M^{-1}$ $s^{-1}$, $k_o =$

$$k_{obs} = k_H^+[H^+] + k_o + k_{HO^-}[HO^-] \qquad (17)$$

$(2.00 \pm 0.04) \times 10^{-2}$ $s^{-1}$, and $k_{HO^-} = (2.05 \pm 0.02) \times 10^2$ $M^{-1}$ $s^{-1}$.

The previous investigation of ketenimine hydration[10] established a mechanism for the acid-catalyzed reaction consisting of rate-determining protonation of the substrate on $\beta$-carbon followed by hydration of the ensuing nitrilium ion, **16**, giving an amidol intermediate, **17**, which rapidly tautomerized to an amide product, eq 18. Ketenimines with aliphatic substituents on nitrogen were




(18)

found to react more rapidly than the substrates with a phenyl group in this position, consistent with the greater ability of aliphatic groups over phenyl to stabilize the positive charge of the nitrilium ion by inductive electron release. The pentafluorophenyl group will be even poorer than phenyl at stabilizing this positive charge, and it is significant therefore that $k_H^+$ for *N*-(pentafluorophenyl)-phenylketenimine obtained here is 500 times less than that determined before for *N*-(phenyl)phenylketenimine. The previous data for the *N*-phenyl substrate and three ketenimines with aliphatic nitrogen substituents do in fact give a good Hammett correlation using $\sigma_I$ constants,[27] and extrapolation of this to *N*-pentafluorphenyl gives the prediction $k_H^+ = 0.62$ $M^{-1}$ $s^{-1}$, consistent with the measured value $k_H^+ = 0.19$ $M^{-1}$ $s^{-1}$.

Base catalysis of ketenimine hydration was investigated in the previous study for only one substrate, the *N*-phenyl derivative, and a quantitative prediction of the rate constant expected for the present *N*-pentafluorophenyl analog is therefore not possible. It is significant, however, that the *N*-pentafluorophenyl derivative is more reactive than the *N*-phenyl derivative, inasmuch as the base-catalyzed reaction can be expected to occur either by nucleophilic attack of hydroxide ion on the α-carbon atom of the ketenimine group or by general-base-assisted attack of a water molecule at this site; reaction through either one of these mechanisms will be promoted by the more strongly electron-withdrawing pentafluorophenyl group.

The general effect of the pentafluorophenyl group has been to suppress acid catalysis and promote base catalysis, as expected. This dominance of base catalysis extends even to the uncatalyzed region of the rate profile, where buffer catalysis was found to be of the general base type for the *N*-pentafluorophenyl derivative examined here, in contrast to the general acid buffer catalysis in this region found for the substrates with aliphatic *N*-substituents studied before.[10] In this respect, the hydration of *N*-(pentafluorophenyl)phenylketenimine resembles

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the hydration of ketenes themselves, where base catalysis is strong and acid catalysis is either weak or nonexistent.[28]

**Acknowledgment.** We are grateful to Dr. R.-Q. Xie for supplying spectral data characterizing *N*-(pentafluorophenyl)phenylacetamide and to the Natural Sciences and Engineering Research Council of Canada for financial support of this work.

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**Supporting Information Available:** Tables S1−S11 (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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