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THE THERMODYNAMICS OF THE FORMATION OF PYRIDINIUM YLIDES FROM CARBENES

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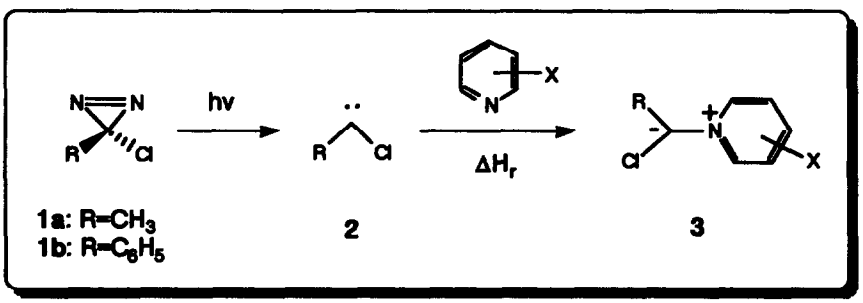
Summary: *The enthalpies of reaction for complexation of methyl- and phenylchlorocarbene with substituted pyridines are determined by photoacoustic calorimetry. The enthalpies are similar for the two carbenes and can be related to the pK_a's of the pyridines. Steric interactions between the carbenes and several substituted pyridines result in an apparent decrease in the reaction enthalpy from that predicted by the pyridine pK_a's.*

Electrophilic carbenes can react as Lewis acids and form ylides with compounds containing non-bonding electrons pairs, such as carbonyls, nitriles, ethers and alcohols.[1] The reaction with pyridine to form pyridinium ylides has been extensively used in several recent laser flash photolysis studies to study the kinetics of "invisible" carbene reactions.[2] For example, the substituted carbenes, 2a,b, photogenerated from diazirine precursors, 1a,b, form pyridinium ylides, 3a,b, whose kinetics are monitored by transient absorption spectroscopy.



Although the kinetics for formation of these ylides are known (X=H),[2] no thermodynamic data are currently available. In this regard, we wish to now report on the thermodynamics of ylide formation between substituted pyridines and methyl- and phenylchlorocarbene by photoacoustic calorimetry (PAC).[3,4] These studies examine both electronic and steric effects on the thermodynamics of ylide formation, and comment on the generality of the pyridinium probe technique for the study of carbene kinetics.

The heats of reaction for ylide formation between carbenes 2a,b and substituted pyridines are determined by photoacoustic calorimetry (PAC).[5] Irradiation of 1a,b in heptane results in a single heat deposition, reflecting formation of the carbene 2a,b, $\Delta H(1\rightarrow2)$. Irradiation of 1a,b in heptane with added pyridine (0.1 M) also results in a single heat deposition, reflecting initial carbene formation, 2a,b, and subsequent ylide formation, 3a,b, $\Delta H(1\rightarrow3)$. The difference in these values, ΔH_r, yields the heat of reaction for ylide formation, $\Delta H(2\rightarrow3)$.[6] Alternatively, the two heat depositions, $\Delta H(1\rightarrow2)$ and $\Delta H(2\rightarrow3)$, can be time-resolved separately at lower pyridine concentrations.[3] The bimolecular rate constants for the formation of pyridinium ylides 3a,b (X=H),[7] as determined by PAC, are in good

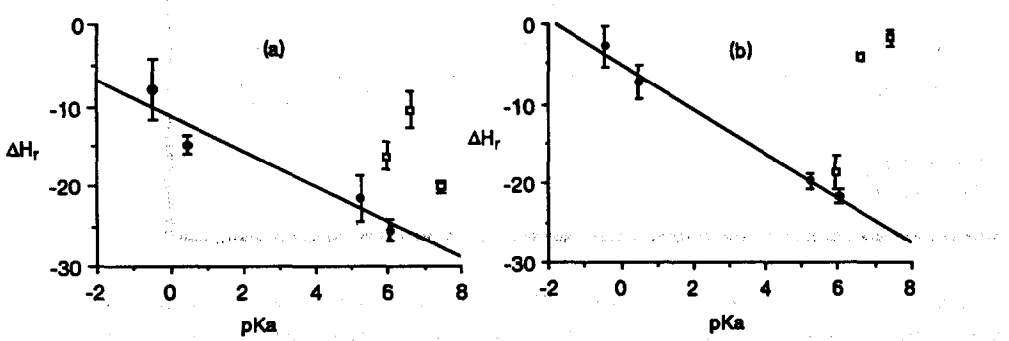
agreement with those measured for ylide formation by nanosecond flash photolysis.[2] The ΔH_f values obtained by PAC are given in Table 1, in addition to the pyridines' pK_a and gas-phase proton (PA) affinity values. Plots of ΔH_f versus the pK_a of the substituted pyridines are given in Figure 1.

Table 1. Experimental Heats of Reaction for Ylide Formation Between Substituted Pyridines and 2a,b[a,b]

Pyridine	pK_a[c]	PA[d]	ΔH_f(2a)[e-g]	ΔH_f(2b)
2-F	-0.44	211.8	-7.9 [3.7]	-2.8 [2.6]
2-Cl	0.49	214.8	-14.7 [1.1]	-7.3 [2.1]
H	5.25	220.4	-21.1 [2.9]	-19.6 [1.0]
2-CH_3	5.94	223.7	-16.0 [1.8]	-18.6 [2.0]
4-CH_3	6.03	223.7	-25.1 [1.4]	-21.6 [1.0]
2,6-CH_3	6.60	227.1	-10.3 [2.3]	-4.1 [0.2]

[a] In heptane, 295 K, see ref. 5. [b] Average of at least 5 measurements. [c] Values in water, ref. 9. [d] Ref. 11 [e] In kcal/mol. [f] Errors in parentheses are ±1σ. [g] Values corrected for quantum yield for formation of 2a , Φ = 0.67, see ref. 6.

Figure 1. Heat of Reaction for Ylide Formation, ΔH_f, versus pK_a of Substituted Pyridines; (a) 2a, (b) 2b. Open squares represent 2-methyl- and 2,4-dimethylpyridine.



The data reveal several interesting trends. First, the above plots show reasonable linear correlations between the PAC ΔH_f values and the pK_a's of the pyridines (2a: c.c .= 0.94, 2b: c.c .= 0.99, excluding 2-methyl- and 2,6-dimethylpyridine). The ΔH_f values and the gas-phase proton affinities of the pyridines are also linearly correlated (2a: c.c .= 0.98, 2b: c.c .= 0.97, excluding 2-methyl- and 2,6-dimethylpyridine).[11] This suggests that the strength of the newly formed bond is directly related to the electron donating ability of the pyridine. The reversibility of ylide formation under the reaction conditions should in part be determined by the magnitude of ΔH_f.[12] For

example, the predicted "irreversible" formation of pyridinium ylides 3a,b (X=H) is supported by flash photolysis studies in which the ylides are found to be extremely long-lived (>100 μs for 3b) under conditions where the carbenes should not be.[2] However, the weakly coordinated pyridinium ylides, i.e. with electron withdrawing groups on the pyridine, may indeed be formed "reversibly". Product and flash photolysis studies are currently in progress to test this prediction.

Second, the reaction enthalpies for 2a are slightly greater than those for 2b, i.e. 2a is a stronger Lewis acid towards the pyridines than 2b. The small difference in the "stability" of carbenes 2a and 2b relative to their respective ylides 3a and 3b may potentially account for their different rates of complexation with the pyridines.[7,10] However, steric effects also need to be considered. Although ΔH_f for pyridinium ylide formation should decrease as the "stability" of the carbene increases, the results indicate that carbenes which are significantly more "stable" than 2b may also form pyridinium ylides.[13] Third, the changes in ΔH_f with varying pyridine pK_a for the two carbenes are similar (2a: slope = -2.3, 2b: slope = -2.8), i.e. the slope is independent of carbene substitution, R = CH_3 or C_6H_5. At present, it is unclear whether substitution on the carbene will greatly affect its sensitivity to the electronic effects of the pyridines.

Fourth, the ΔH_f values for carbene complexation with 2-methyl- and 2,6-dimethylpyridine are significantly less that those predicted from the pyridine pK_a values. The poor correlation indicates that the carbenes are more sensitive to steric interactions with the pyridines than is a proton.

The carbene acidities towards the substituted pyridines can be compared to other Lewis acids.[14] For example, the enthalpies of complexation of BH_3 and $B(CH_3)_3$ with pyridine, 17.9 and 21.3 kcal/mol, are quite similar to those of carbenes 2a and 2b.[15] In addition, the steric effects observed in the complexation of the *ortho* methylated pyridines with the carbenes 2a and 2b are also observed with the bulky $B(CH_3)_3$, but not with BH_3.

Future studies will investigate both the kinetics and thermodynamics of "electrophilic" carbenes with other neutral and ionic nucleophiles as a function of carbene substitution, solvent polarity, and temperature.

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(5) Excitation is by nitrogen laser (337 nm, 84.8 kcal/mol) and detection employs either a 2.25 or a ~ 0.5 MHz transducer. The results are unaffected by sample concentration (0.2-0.8 OD) or argon degassing. 2-Hydroxybenzophenone is used as the calibration compound. Compounds 1a,b were prepared by the Graham procedure.[16] The commercial pyridines were distilled before use.

(6) (a) The $\Delta H_r = (\alpha_1 - \alpha_2)E_{h\nu} / \Phi_c$ where α_1 and α_2 are the PAC determined fractions of the incident photon energy released as heat without and with added pyridine, respectively, $E_{h\nu}$ is the incident laser energy, and Φ_c is the quantum yield for formation of the carbene. For 1a: $\Phi_c = 0.67$[8] and 1b: $\Phi_c = 1.0$.[3a] (b) In the absence of the pyridines, carbene 2a undergoes a unimolecular 1,2 hydrogen shift to yield vinyl chloride with a rate constant of $1.4 \times 10^6\ s^{-1}$. However, in the presence of the pyridines (0.1M), this pathway should be minor and so should not affect the determined heats of complexation.

(7) The bimolecular rate constants for complexation of 2a and 2b with pyridine (0 - 0.066 M) are 1.2×10^{10} and $4.8 \times 10^8\ M^{-1}s^{-1}$, respectively.

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(10) In contrast, the difference in the heats of reaction of carbenes 2a and 2b with CH_3OH to form OH insertion products is somewhat greater, ~ 14 kcal/mol. The ΔH_r's of the carbenes 2a and 2b with CH_3OH are -64.2[8] and -50.9[3a] kcal/mol, respectively.

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(12) The reversibility of the reaction will depend on the reaction conditions, i.e. the reaction rates of the carbenes and ylides to give products.

(13) A comparison of the heats of reaction of methylene and substituted carbenes with CH_3OH can be used to evaluate carbene "stabilities". However, this comparison may not have much predictive value in that pyridine complexation and OH insertion are quite different reactions.

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