with a high degree of retention of configuration.[33]

Our observations on the steric course of hydroxylation at the methyl termini of *n*-octane can be accommodated by either of the discussed mechanisms, each with its own restrictions. The Groves et al.[29,30] mechanism should involve a normal hydrogen isotope effect.[28] Assuming that k_{rot} of the hypothetical trigonal 1-octanyl radical is not greater than k_{comb} with the hydroxyl radical, hydroxylation will proceed with retention as required by our results. Alternatively, simple insertion (Figure 2) or concerted attachment–rearrangement (Figure 3) would require that substitution of an oxenoid species for a hydrogen atom proceed with a primary kinetic isotope effect.

Acknowledgment. The support of this work by grants from the National Institutes of Health (AM 12156 and GM 19882) is gratefully acknowledged.

Registry No. 2, 81133-14-4; **3**, 81133-15-5; **4**, 62012-45-7; (1*R*)-[1-^3H,^2H,^1H]octane, 81133-16-6; (1*S*)-[1-^3H,^2H,^1H]octane, 81133-17-7; (1*RS*)-[1-^3H,^1H]octanol, 80446-73-7; (1*S*)-[1-^3H,^1H]octanol, 62012-44-6; (1*R*)-[1-^3H,^2H]octanol, 81133-18-8; [1-^{14}C]octane, 81133-19-9.

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[33] Lorland, J. P. *J. Am. Chem. Soc.* **1974**, *96*, 2867.

Communications to the Editor

Chemistry of Higher Order Mixed Organocuprates. 2.[1] Reactions of Epoxides[†]

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Received January 6, 1982

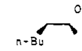
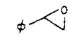
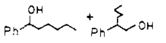
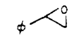
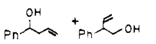
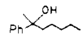
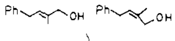
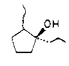
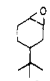
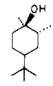
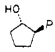
The formation of carbon–carbon bonds via substitution reactions is one of the characteristic modes in which organocopper reagents continue to play an important role in organic synthesis.[3] We have recently described the first general procedure, to our knowledge, for effecting such a process at a secondary, unactivated center. This occurs without significant competition from reduction and/or elimination, through the agency of higher order mixed organocuprates of the general formula $R_2Cu(CN)Li_2$, **1**.[1] As epoxide

$$\mathrm{CuCN} + 2\mathrm{RLi} \longrightarrow \underset{\mathbf{1}}{\mathrm{R_2Cu(CN)Li_2}}$$

cleavage is formally a substitution process,[3a] we were interested in evaluating the reactivity and efficacy of these newer species (i.e., **1**) for effecting ring opening. We now report our preliminary results which indicate that intermediates **1** are perhaps among the mildest and most efficient means available for generating carbon–carbon bonds by way of oxirane cleavage by using organocopper chemistry.

Literature reports of earlier efforts clearly demonstrate that, in general, reactions of homocuprates (i.e., R_2CuLi) with disubstituted epoxides oftentimes lead to mixtures of products resulting from rearrangement or elimination in addition to substitution.[4] Thus, while the efficiency of reactions in monosubstituted systems is high, 1,2-disubstituted cases afford product(s) in low to moderate yields. Two equivalents or more of cuprate are necessary, and reaction temperatures of 0 °C and higher are typical. Mixed Gilman reagents, RCu(CN)Li, are reported[5] to give good reactions with monosubstituted epoxides by using stoichiometric amounts of reagent, and yet in 1,2-disubstituted cases the efficiency drops considerably. Trisubstituted oxiranes, likewise, afford moderate yields of product(s) under these conditions.

Table I. Reactions of Epoxides with $R_2Cu(CN)Li_2$

Entry	Epoxide	RLi	Product(s)[a]	Ratio	Yield, %[b]
1		n-BuLi[c]			95[d]
2		n-BuLi[e]		85 8[f]	93
3		 Li[g]		57 35[f]	92
4		n-BuLi[h]			96
5		PhLi[i]		77 19[n]	96
6		n-PrLi[j]			86[d]
7		EtLi[k]			98
8		PhLi[l]	[m]		98

[a] All compounds gave satisfactory IR, NMR, and mass spectral data. [b] Isolated yields unless noted otherwise. [c] Reaction run at −20 °C for 2 h with 1.1 equiv of reagent. [d] By quantitative VPC using a 6 ft × 1/8 in. column (20% SE-30 on Chromosorb W). [e] Reaction was conducted at −40 °C over 2 h with 1.3 equiv of reagent. [f] Determined by isolation. [g] Product formed over 2.5 h at −10 °C using 2.3 equiv of reagent. [h] Starting material consumed in 2 h at −20 °C using 1.3 equiv of reagent. [i] A total of 1.1 equiv of reagent was sufficient at −45 °C over 1.5 h. [j] Run at 0 °C over 8 h with 2 equiv of cuprate. [k] Carried out at 0 °C for 6 h with 2 equiv of reagent. [l] Required room temperature overnight (10 h) with 2 equiv of reagent. [m] No cyclopentanone was detected by VPC. [n] Determined by NMR analysis.

In contrast to reactions of RR′CuLi (R = alkyl, R′ = alkyl, CN), mono-, di-, and trisubstituted epoxides reacted with **1** to afford excellent yields of products(s) in all examples investigated. The results are summarized in Table I. Several noteworthy features of this method deserve comment. As is the case with RCu(CN)Li, ca. 1.1–1.3 equiv of reagent is sufficient for complete consumption of starting material (entries 1, 2, 4). Not surprisingly, the less reactive reagent derived from vinyllithium (i.e., **1**, R = vinyl) required 2.3 equiv, while the fused-ring systems (entries 6–8) gave good reactions with 2 equiv of the corresponding mixed

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[†] Dedicated to Professor H. H. Wasserman on the occasion of his 60th birthday.

[1] Lipshutz, B. H.; Wilhelm, R. S. *J. Am. Chem. Soc.* **1981**, *103*, 7672.

[2] Recipient of American Cancer Society Junior Faculty Research Award, 1981–1983.

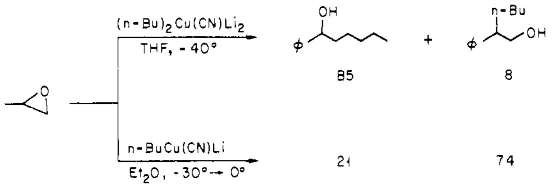
[3] (a) Posner, G. H. *Org. React.* **1975**, *22*, 353. (b) Normant, J. F. *Pure Appl. Chem.* **1978**, *50*, 709. (c) Jukes, A. E. *Adv. Organomet. Chem.* **1974**, *12*, 215. (d) Smith, R. A.; Hannah, D. J. *Tetrahedron* **1979**, *35*, 1183.

[4] (a) Herr, R. W.; Wieland, D. M.; Johnson, C. R. *J. Am. Chem. Soc.* **1970**, *92*, 3813. (b) Hartman, B. C.; Livinghouse, T.; Rickborn, B. *J. Org. Chem.* **1973**, *38*, 4346. (c) Johnson, C. R.; Herr, R. W.; Wieland, D. M. *Ibid.* **1973**, *38*, 4263.

[5] (a) Acker, R. D. *Tetrahedron Lett.* **1977**, 3407. (b) Acker, R. D. *Ibid.* **1978**, 2399.

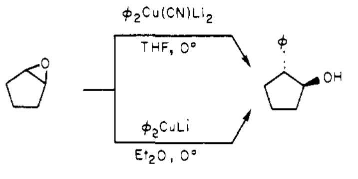
higher order cuprate. As expected,[6] an allylic epoxide (entry 5) reacted rapidly at low temperature (−45 °C) to afford a ca. 4:1 ratio of E/Z allylic alcohols. Interestingly, **1**, R = phenyl, was found to participate in the coupling sequence with either activated (entry 5) or unactivated (entry 8) substrates. This is contrary to previous observations[1] involving secondary halides where phenyl ligands on copper gave reduction as the major pathway with very little product of substitution.

The examples in Table I also serve to illustrate the regiochemical aspects of epoxide opening with reagents **1**. Styrene oxide reacted with **1** (R = *n*-Bu) to give an 85:8 ratio of secondary to primary alcohols (eq 1) indicating a strong preference for attack by **1** at the less hindered rather than more electrophilic site. It is worthy of note that this is a complete reversal from that which has been realized by using RCu(CN)Li.[5a] Whether this is due to a solvent effect or, more likely, a change in the nature of the copper complex involved[1] (i.e., dimeric[7] vs. monomeric[8]) is not clear at this time. The more sluggish transfer of a vinyl group (entry 3) leads to an increased population of product derived from attack at the benzylic position. This may be a function of relative size of the two reagents (i.e., **1**, R = *n*-Bu vs. vinyl).[9] Placement of a methyl group in the α position (entry 4) serves to direct addition exclusively to the β site.



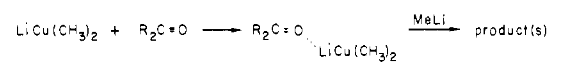
(1)

The stereochemical consequences of the coupling reaction can be seen from entries 1 and 6–8. Epoxides are well-known to give products from reactions with traditional cuprates reflecting inversion at the reacting center.[3a] The same stereochemical observation has been made from studies employing reagents **1**. Treatment of cyclopentane oxide with Ph$_2$CuLi gave **2** (eq 2), identical (TLC, VPC, IR, NMR, mass spectrometry) with the material obtained using **1**, R = Ph (entry 8).



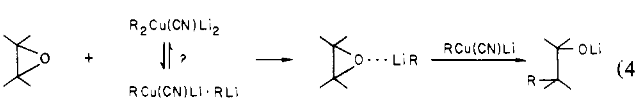
(2)

The possibility that the reactive species in these reactions may actually be RCu(CN)Li·RLi, as opposed to the discreet reagents **1** was next investigated. We were very much aware of Ashby's contributions which had shown that addition of Me$_3$CuLi$_2$ to ketones was a result of initial complexation of Me$_2$CuLi with the carbonyl group, followed by rapid attack of MeLi (eq 3).[11]



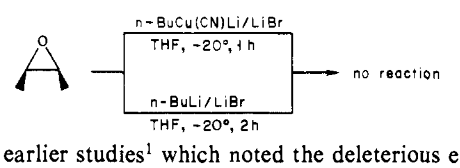
$$\mathrm{LiCu(CH_3)_2 + R_2C{=}O \longrightarrow R_2C{=}O\cdots LiCu(CH_3)_2 \xrightarrow{MeLi} product(s)} \qquad (3)$$

Furthermore, the higher order homocuprate Me$_3$CuLi$_2$ exists in equilibrium with Me$_2$CuLi + MeLi.[12] This phenomenon, with respect to epoxides, may provide the necessary ingredients for electrophilic attack (eq 4) similar to that found with ketones.[11]



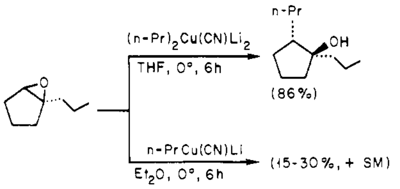
(4)

That R$_2$Cu(CN)Li$_2$ contains an equilibrium percentage of RCu(CN)Li·RLi, however, remains to be established. As the reactions were all conducted in THF, the likelihood is slim that complexation is occurring. That is, Et$_2$O is usually the solvent of choice for epoxide opening with R$_2$CuLi (R = Me, Ph), as THF is reported to retard reactions of this type.[4a] This is presumably due to the ability of THF to effectively compete with the substrate for association with a Lewis acid (Li$^+$).[10] Further support can be garnered from the experimental finding that the reaction of *cis*-2-butene oxide with either *n*-BuCu(CN)Li or *n*-BuLi in the presence of 1 equiv of dry LiBr[11a] afforded none of the anticipated product (eq 5). The inhibitory properties of LiBr are consistent with our earlier studies[1] which noted the deleterious effects of additives in the reactions of **1** (with halides). Hence, it would appear that the reactive species in this procedure may well be "R$_2$Cu(CN)Li$_2$".



(5)

In conclusion, the use of higher order mixed cuprates for the "nucleophilic" opening of oxiranes has several advantages over the more conventional copper reagents. Reaction conditions surrounding the use of **1** are considerably milder (i.e., fewer equivalents of reagent, lower temperatures) while yields of product(s) are superior to those found by using their Gilman-type counterparts. For example, the cyclopentene oxide shown in eq 6, under similar conditions,[13] afforded a significantly better result (86% vs. ~23%) by using **1**, R = *n*-Pr. Epoxides undergo cleavage at the less sterically encumbered position with a net inversion of configuration. These generalizations impart considerable regio- and stereochemical predictability to this methodology.[14] Further



(6)

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[6] (a) Wender, P. A.; Erhardt, J. M.; Letendre, L. J. *J. Am. Chem. Soc.* **1981**, *103*, 2114. (b) Staroscik, J.; Rickborn, B. *Ibid.* **1971**, *93*, 3046. (c) Herr, R. W.; Johnson, C. R. *Ibid.* **1970**, *92*, 4979. (d) Anderson, R. J. *Ibid.* **1970**, *92*, 4978. (e) Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1979**, 675. (f) Marino, J. P.; Hiroyuki, A. *J. Am. Chem. Soc.* **1981**, *103*, 2907. (g) Marino, J. P.; Hatanaka, N. *J. Org. Chem.* **1979**, *44*, 4467. (h) Marino, J. P.; Hiroyuki, A. *Synthesis* **1980**, *11*, 872. (i) Ziegler, F. E.; Cady, M. A. *J. Org. Chem.* **1981**, *46*, 122.

[7] Pearson, R. G., Gregory, C. D. *J. Am. Chem. Soc.* **1976**, *98*, 4098 and references therein.

[8] Ashby, E. C.; Watkins, J. J. *J. Am. Chem. Soc.* **1977**, *99*, 5312.

[9] That is, if lithium chelation activates the epoxide toward nucleophilic attack,[10] (*n*-Bu)$_2$Cu(CN)Li$_2$ would be expected to be more discriminating based on steric factors.

[10] Wieland, D. M.; Johnson, C. R. *J. Am. Chem. Soc.* **1971**, *93*, 3047.

[11] (a) Ashby, E. C.; Noding, S. A. *J. Org. Chem.* **1979**, *44*, 4371. (b) Ashby, E. C.; Lin, J. J.; Watkins, J. J. *Tetrahedron Lett.* **1977**, 1709. (c) Ashby, E. C.; Watkins, J. J. *Chem. Commun.* **1976**, 784.

[12] Ashby, E. C.; Watkins, J. J. *J. Am. Chem. Soc.* **1977**, *99*, 5312.

[13] Et$_2$O is the preferred solvent for reactions of R$_2$CuLi and RCu(CN)Li with epoxides.[4,5] We have not as yet examined the effect of modifying the reaction solvent. These studies will be included in a full account of this work to be reported shortly.

[14] A typical experimental procedure for the preparation of 2-phenylheptan-2-ol (Table I, entry 4) is as follows: Copper cyanide[15] (0.10 g, 1.1 mmol) was placed in a two-neck 25-mL round-bottom flask equipped with a magnetic stir bar. The salt was azeotropically dried with toluene (2 × 2.0 mL) with successive purging with argon. Dry THF (2.0 mL) was added and the slurry cooled to −78 °C. *n*-Butyllithium (0.98 mL, 2.0 mmol, 2.17 M) was added dropwise producing a tannish yellow solution, which was warmed to −20 °C. α-Methylstyrene oxide (0.10 g, 0.75 mmol, freshly distilled) was dissolved in 1.0 mL of THF, cooled to −20 °C, and transferred to the cuprate via cannula with a subsequent wash with 0.5 mL of cold (−20 °C) THF. The reaction was stirred at this temperature for 2 h and then quenched with 5 mL of a 90% NnH$_4$Cl/10% NH$_4$OH solution. After stirring at room temperature for ca. 30 min, the solution was transferred to a separatory funnel, and 5 mL of a saturated aqueous NaCl solution was added. This was then extracted with ether (3 × 7 mL), and the extracts were dried over K$_2$CO$_3$. Following filtration, the ether was removed in vacuo, yielding a light yellow oil that was chromatographed on silica gel (30% Et$_2$O/pentane) to afford 0.134 g (96%) of a clear oil: TLC (SiO$_2$, 1:1 Et$_2$O/pentane) R_f 0.50; IR (neat) 3410, 1600, 1490, 1025, 760, 700 cm^{-1} NMR (CDCl$_3$)δ 7.48–7.08 (5 H, m), 1.81 (1 H, s, OH), 1.98–1.60 (2 H, m), 1.54 (3 H, s), 1.32–1.04 (6 H, m), 0.94–0.69 (3 H, unresolved t); mass spectrum (*m/e*, relative %), 192 (M$^+$, 0.76), 175 (57), 83 (100), 71 (44). High-resolution mass spectrum: calcd for C$_{13}$H$_{20}$O, 192.1514; found; 192.1500.

J. Am. Chem. Soc. **1982**, *104*, 2307–2308

accounts of the reactions and applications of these highly reactive yet relatively stable organocopper species will be reported in due course.

Acknowledgment. Financial assistance from the National Institutes of Health (GM 28128), the American Cancer Society (JFRA No. 37 to B.H.L.), and the Committee on Research (UCSB) is gratefully acknowledged. We also thank Professors Bruce Rickborn and Ralph Pearson and Dr. David M. Floyd (FMC Corp.) for helpful discussions.

Registry No. 1 (R = *n*-Bu), 80473-69-4; **1** (R = CH=CH$_2$), 80473-65-0; **1** (R = Ph), 80473-66-1; **1** (R = *n*-Pr), 80473-72-9; **1** (R = Et), 80473-71-8; *erythro*-3-methylheptan-2-ol, 81120-76-5; 1-phenylhexan-1-ol, 4471-05-0; 2-phenylhexan-1-ol, 25755-73-1; 1-phenyl-3-buten-1-ol, 936-58-3; 2-phenyl-3-buten-1-ol, 6052-63-7; 2-phenylheptan-2-ol, 4436-90-2; (*E*)-2-methyl-4-phenyl-2-buten-1-ol, 52497-56-0; (*Z*)-2-methyl-4-phenyl-2-buten-1-ol, 58732-17-5; *trans*-1,2-dipropylcyclopentanol, 38338-76-0; 4-*tert*-butyl-2-ethyl-1-methylcyclohexanol, 81120-77-6; *trans*-2-phenylcyclopentanol, 42086-64-6; *cis*-2-butene oxide, 1758-33-4; styrene oxide, 96-09-3; 2-methylstyrene oxide, 2085-88-3; 2-methyl-2-vinyloxirane, 1838-94-4; 1-propylcyclopentene oxide, 30762-73-3; 4-*tert*-butyl-1-methylcyclohexene oxide, 81176-58-1; cyclopentene oxide, 285-67-6.

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(15) CuCN was purchased from both MCB (tan powder) and Fluka (green crystals). Both were used directly out of the bottle as received without any purification whatsoever.

Ion–Molecule Complexes in Decompositions of Gaseous Cations: 130-nm Photolysis of 4-Pyridyl Ethers

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Riverside, California 92521

Received November 2, 1981

The intermediacy of ion–molecule complexes in unimolecular[1-4] and bimolecular[5,6] gas-phase reactions has been a subject of substantial recent interest. We have lately demonstrated the importance of reaction 1 in unimolecular fragmentations of molecular ions derived from aryl alkyl ethers.[2,3] The species shown in brackets represents an ion–molecule complex that results from breaking the weakest covalent bond of the parent ion. The charged and the neutral fragments formed have insufficient kinetic energy to overcome their mutual charge–dipole attraction and must stay within several angstroms of each other until they react with one another via an exothermic ion–molecule reaction.

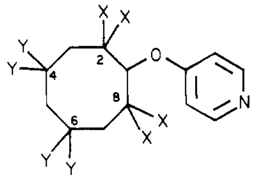
$$\mathrm{ROAr}^{+\cdot} \rightarrow \underbrace{[\mathrm{R}^+ \quad \mathrm{ArO}\cdot]}_{\text{ion–molecule complex}} \rightarrow \text{decomposition products} \qquad (1)$$

In previously reported cases,[1-6] ion–molecule complexes decompose via proton-transfer reactions (sometimes reversible) from the charged to the neutral moiety. In the case of reaction 1 where Ar = phenyl, the decomposition products are phenol molecular ions and neutral olefins, whose structures reveal rearrangements of R$^+$ within the complex.

Table I. Distribution of Label in Principal Fragment Ions from 130-nm Photolysis of Specifically Deuterated Cyclooctyl 4-Pyridyl Ethers at 10^{-7} torr[a]

position of substitution	% of Σ[b]			corrected isotope ratio[c]	
	m/z 96	*m/z* 97	*m/z* 98	$C_5H_5DNO^+$	$C_5H_4D_2NO^+$
d_0 (1)	44.1	2.6	0.2	0[d]	0[d]
2,2,8,8-d_4 (2)	41.0	16.6	6.0	0.354[e]	0.124[e]
4,4,6,6-d_4 (3)	36.5	12.6	4.0	0.297[e]	0.104[e]
5,5-d_2	51.6	7.6	1.0	0.082[d]	0.004[d]
1-d_1	44.5	4.3	0.3	0.037[d]	0.001[d]

[a] Relative abundances of fragment ions do not change with variation of the nominal pressure from 4×10^{-8} to 2×10^{-7} torr. Conventional mass spectra were recorded at $\leq 10^{-6}$ Torr for 1 and 2 on an MS-902 using 12- and 70-eV electron impact ionization, and the same distribution of fragment ions was observed. Contributions from ion-molecule reactions can therefore be dismissed. [b] The quadrupole mass filter of the photoionization mass spectrometer gives wide variations from day to day in intensities of molecular ions relative to these fragment ions. Values of % Σ are reported for optimized instrument settings, but the variation among them is not significant. The *m/z* 96:97:98 ratio does not change substantially even when the molecular ion intensity fluctuates by an order of magnitude. [c] Relative to $C_5H_6NO^+ = 1$; corrected for ^{13}C natural abundance, but not for incomplete deuteration of starting material. [d] Standard deviation of the mean <0.002. [e] Mean of three independent series. Standard deviation of the mean is ≤ 0.007.



1, X = Y = H
2, X = D; Y = H
3, X = H; Y = D

We have previously described reaction 1 as a gas-phase analogue of solvolytic elimination.[2,3] This communication describes chemical consequences of the radical nature of the leaving group, ArO·. In the case of Ar = 4-pyridyl we find that first a proton and then a hydrogen atom are transferred from the alkyl to the aryloxy moiety. This reaction was anticipated on thermodynamic grounds. The 4-pyridyloxy radical was expected to be an excellent gas-phase base.[7] Its conjugate acid ought to have a hydrogen atom affinity ≥ 90 kcal/mol[8] and should therefore be able to abstract allylic hydrogens. We observe this reaction sequence from low-energy ionization of a variety of alkyl 4-pyridyl ethers and describe here our results from 130-nm photolysis of cyclooctyl 4-pyridyl ether, **1**.[9] The cyclooctyl ether was chosen for scrutiny because the cyclooctyl cation is known to have a bridged structure,[10] which leads to a characteristic interconversion of ring positions[11,12] that

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(1) Bowen, R. D.; Williams, D. H. *J. Chem. Soc., Chem. Commun.* **1981**, 836–838 and references contained therein.

(2) Morton, T. H. *J. Am. Chem. Soc.* **1980**, *102*, 1596–1602.

(3) Hall, D. G.; Morton, T. H. *J. Am. Chem. Soc.* **1980**, *102*, 5686–5688.

(4) Longevialle, P.; Botter, R. *J. Chem. Soc., Chem. Commun.* **1980**, 823–825.

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(7) Reported proton affinities of substituted pyridines lie in the range 209–236 kcal/mol as compared to the proton affinities of simple acyclic and ≥4-member-ring cyclic alkenes, which lie below 204 kcal/mol [Aue, D. H.; Bowers, M. T. In "Gas Phase Ion Chemistry"; Bowers, M. T., Ed.; Academic Press: New York, 1979; Vol. 2, pp 2–51]. We estimate the proton affinity of the 4-pyridyloxy radical to be ≥220 kcal/mol, based on the reported proton affinity of 4-methoxypyridine (226.6 kcal/mol) and the fact that the proton affinity of phenoxy radical is only 3 kcal/mol less than that of anisole.[2]

(8) If we take the adiabatic IP of 4-hydroxypyridine to be no lower than 15 kcal/mol below the reported first vertical ionization potential [Cook, M. J.; El Abbady, S.; Katritsky, A. R.; Guimon, C.; Pfister-Guillouzo, G. *J. Chem. Soc., Perkin Trans. II* **1977**, 1652–1656] and estimate its proton affinity to be at least 220 kcal/mol, the hydrogen atom affinity of the corresponding molecular ion is >105 kcal/mol. Other tautomers may have lower hydrogen atom affinities, but we surmise that a lower bound is given by the hydrogen atom affinity of the molecular ion of *N*-methyl-4-pyridone, which is >90 kcal/mol. This value is based on the experimental gas-phase basicity of the neutral molecule, 222.3 kcal/mol [Aue, D. H., personal communication], from which we infer a proton affinity of 229.6 kcal/mol, and the assumption that the adiabatic IP is no lower than 15 kcal/mol below the reported first vertical IP [Cook, et al.].

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