Acknowledgment. Financial support by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung, Bern, is gratefully acknowledged (Grant 2.885-0.80). Special thanks go to Professor R. Huisgen, München, for stimulating discussions and valuable comments while he stayed as a guest of honor at the University of Lausanne. This communication is dedicated to Professor G. Wittig, Heidelberg, who celebrated his 85th anniversary on 16 June 1982.

Registry No. (*Z*)-2-Nonene, 6434-77-1; (*E*)-2-nonene, 6434-78-2; (*Z*)-4,4-dimethyl-2-pentene, 762-63-0; (*E*)-4,4-dimethyl-2-pentene, 690-08-4; (*Z*)-1-phenyl-1-propene, 766-90-5; (*E*)-1-phenyl-1-propene, 873-66-5; (*Z*)-1-(*p*-chlorophenyl)-1-propene, 1879-52-3; (*E*)-1-(*p*-chlorophenyl)-1-propene, 1879-53-4; heptanal, 111-71-7; 2,2-dimethylpropanal, 630-19-3; benzaldehyde, 100-52-7; *p*-chlorobenzaldehyde, 104-88-1; triphenylethylidenephosphorane, 1754-88-7; triethylethylidenephosphorane, 17847-85-7.

An Inverse Reactivity–Selectivity Relationship. Kinetic Nitrogen Isotope Effects on Methyl Transfer to Pyridines

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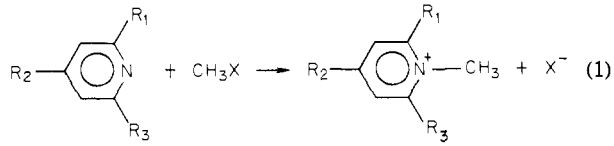
Received May 28, 1982

We report that values of the $^{14}N/^{15}N$ rate constant ratio for methyl transfer to alkyl-substituted pyridines (eq 1: R_1, R_2, R_3 = H, H, H; H, CH_3, H; CH_3, H, CH_3) decrease (become more



inverse) as CH_3X becomes more reactive and may also decrease as the pyridine becomes more reactive. Numerical values are given in Table I.

These changes in k_{14}/k_{15} demonstrate increasing selectivity for ^{15}N in preference to ^{14}N as reactivity increases and thus are in violation of the reactivity–selectivity principle.[1] They also are in violation of commonly accepted rules concerning the effects of substituents on transition-state structures; those rules predict that increases in reactivity that result from changes in the leaving group (or, with less certainty, in the nucleophile) will decrease the N–CH_3 bond order in the transition state.[2] Such a decrease in N–CH_3 bonding would make k_{14}/k_{15} *less* inverse.

However, these observed changes in k_{14}/k_{15} are consistent with a very recent prediction by Pross and Shaik[3] that such "anti-Hammond" effects should result from changes in quantum mechanical mixing of configurations in the transition state and should, when comparisons are made within a limited family of reactions, dominate the more familiar effects of structural perturbations of the free energy surface.

The reactions were run in aqueous acetonitrile (10% acetonitrile, 0.96 mol fraction of water). The nucleophile was in excess, and the reactions were run to completion; thus the fraction of reaction for the nitrogen is given by the initial CH_3X/nucleophile ratio.[4]

Table I. Values of k_{14}/k_{15} at 25 °C[a]

	CH_3X[c]		
nucleophile[b]	CH_3I	CH_3OTs	CH_3OTf
2,6-Me_2py	1.004 ± 0.002[d]	1.000 ± 0.002[e]	0.986 ± 0.002[f]
py	1.001 ± 0.001[d]	1.001 ± 0.002[e]	0.976 ± 0.001[f,h]
			0.976 ± 0.001[g,h]
4-Me(py)	1.001 ± 0.001[d]	0.993 ± 0.002[e]	0.972 ± 0.005[f]

[a] Solvent is 10% (v/v) CH_3CN in H_2O. Temperature uncertainty is ca. ±0.1 °C for reactions of CH_3I and CH_3OTs, ca. ±1 °C for reactions of CH_3OTf. Uncertainties are standard deviations of the listed means of ratios from two or more separate experiments. [b] 2,6-Me_2py is 2,6-dimethylpyridine; py is pyridine; 4-Me(py) is 4-methylpyridine. [c] CH_3OTs is methyl *p*-toluenesulfonate, CH_3OTf is methyl trifluoromethanesulfonate. [d] $[Nucleophile]_0 = 0.50$ M; $[CH_3I]_0 = 0.010$ M. [e] $[Nucleophile]_0 = 0.25$ M; $[CH_3OTs]_0 = 0.0050$ M. [f] $[Nucleophile]_0 = 0.010$ M; $[CH_3OTf]_0 = 0.0010$ M. [g] $[py]_0 = 0.0016$ M; $[CH_3OTf]_0 = 0.00040$ M. [h] The observation that k_{14}/k_{15} is independent of $[py]_0$ for py + CH_3OTf verifies that our mixing time was short in comparison to the half-time for this reaction; for all runs using CH_3OTf, a solution of CH_3OTf in CH_3CN was injected into a rapidly stirred solution of the nucleophile.

The $^{15}N/^{14}N$ ratio in the *product* was measured by an adaption of a known procedure:[5] The methylpyridinium ion was isolated as the tetraphenylborate salt and purified by recrystallization, and its nitrogen was converted to N_2.[6] The $^{15}N/^{14}N$ ratio in the N_2 was then measured by using a Micromass 602E isotope-ratio mass spectrometer. The $^{15}N/^{14}N$ ratio in the *reactant* was determined by a parallel procedure in which the pyridine first was converted quantitatively into the methylpyridinium ion by reaction with excess CH_3X. The k_{14}/k_{15} isotopic rate constant ratio was calculated as described by Melander and Saunders[7] from these two $^{15}N/^{14}N$ ratios and the fraction of reaction.

Values of "bond-formation" kinetic isotope effects such as these are products of two factors: a "*normal*" (tending to make $k_{14} > k_{15}$) factor, which is equal to the isotopic ratio of imaginary frequencies for motion along the reaction coordinate, and an "*inverse*" (tending to make $k_{14} < k_{15}$) factor, which arises from bond formation to the isotopic atom.[8] This inverse factor directly measures the selectivity for ^{15}N in preference to ^{14}N and should become more inverse as the N–CH_3 bond order in the transition state increases. The normal (frequency ratio) factor can be shown to decrease toward unity as that N–CH_3 bond order increases.[9,10] Thus both factors which contribute to the observed k_{14}/k_{15} isotopic selectivity ratio should be simply related to the N–CH_3 bond order in the transition state: A sufficiently low N–CH_3 bond order should give $k_{14}/k_{15} > 1$, a sufficiently high N–CH_3 bond order should give $k_{14}/k_{15} < 1$, and decreasing values of k_{14}/k_{15} (observed here as reactivity increases) should accompany increasing N–CH_3 bonding in the transition state.

The order of increasing reactivity of CH_3X is $CH_3I < CH_3OSO_2C_6H_4CH_3 \ll CH_3OSO_2CF_3$.[11] Table I shows that selectivity

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(1) For reviews of the reactivity–selectivity principle, see: (a) Pross, A. *Adv. Phys. Org. Chem.* **1977**, *14*, 69–126. (b) Johnson, C. D. *Chem. Rev.* **1975**, *75*, 755–765.

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(4) Corrections of this fraction for the effect of the competing reaction of CH_3X with water were required only for the reactions of CH_3OTf. Uncertainties in these corrections are too small to affect the observed ordering of the k_{14}/k_{15} values.

(5) Shearer, G. B.; Kohl, D. H.; Commoner, B. *Soil Sci.* **1974**, *118*, 308–316.

(6) The Kjeldahl digestion in ref 5 was modified as described by Fish and Collier (Fish, U. B.; Collier, P. R. *Anal. Chem.* **1958**, *30*, 151–152) in order to achieve quantitative conversion of the pyridinium nitrogen.

(7) Melander, L.; Saunders, W. H., Jr. "Reaction Rates of Isotopic Molecules"; Wiley-Interscience: New York, 1980; p 100.

(8) Fry, A. In "Isotope Effects in Chemical Reaction"; Collins, C. J., Bowman, N. S., Eds.; Van Nostrand-Reinhold: Princeton, 1970; Chapter 6.

(9) Bigeleisen, J.; Wolfsberg, M. *J. Chem. Phys.* **1954**, *22*, 1264; Figure 1, Curve 7.

(10) Reference 7, pp 315–318.

(11) The relative reactivities are $CH_3I:CH_3OTs:CH_3OTf = 1:10:\sim10^5$. This $CH_3I:CH_3OTs$ ratio is from conductimetric rate measurements in dilute aqueous solution which gave 10.3 and 9.5 for pyridine and 4-picoline, respectively.[12] This $CH_3OTs:CH_3OTf$ ratio is estimated from the corresponding hydrolysis rates in aqueous solution.[13,14]

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for ^{15}N increases in that *same* order for the two sulfonate X's and may also in the iodide/tosylate comparisons. This is contrary to the reactivity–selectivity principle, which states that increasing reactivity should be accompanied by *decreasing* selectivity. Similarly the implied increase in the N–CH_3 transition state bond order as CH_3X bbecomes more reactive is contrary to expectations based on the usual free energy surface models.[2] Those models assume that the barrier is "symmetric" in the sense that in the neighborhood of the transition state the barrier is an even function of the reaction coordinate about its maximum; it is that symmetry which is responsible for predictions that, as CH_3X becomes more reactive, both its selectivity and the N–CH_3 transition-state bond order should decrease.[15] Whether the variations in N–CH_3 transition state bonding reported here arise from an unsymmetric barrier, the Pross–Shaik effect,[3] or the asynchronous changes in solvation and bonding that have been proposed[16,17] to explain anomalous observations for other methyl transfers presently remains an open question.

These entering-group isotope effects confirm other evidence that the reactivity–selectivity principle and predictions based on symmetric free energy surface models are not always obeyed by nucleophilic displacements. Examples of the breakdown of the expected relationship between selectivity and reactivity in S_N2 reactions have been reviewed by Pross.[18] Arnett and Reich[17] have shown that rate ratios (nonisotopic) for quaternizations of 3- and 4-substituted pyridines are independent of the reactivity of the alkylating agent. Pross and Shaik[3] review some leaving-group isotope effects and nonisotopic substituent effects on benzyl transfers that suggest that changes in leaving groups which increase the rate also increase the nucleophile–carbon bond order in the transition state. A complementary example of the apparent effect on carbon-leaving-group bond order of changing the nucleophile is provided by Grimsrud and Taylor,[19] who observed that k_{35}/k_{37} chlorine-leaving-group isotope effects are larger for anionic sulfur nucleophiles than for the less reactive anionic oxygen nucleophiles.

For the effect on transition-state structure of changing the *leaving* group, as Pross and Shaik emphasize,[20] information concerning variation in the *nucleophile*–carbon bond order is required to distinguish between their prediction and possible predictions based on symmetric free energy surface models. *Entering*-group *isotope* effects such as those presented here provide the most direct information on that bond order. In contrast, conclusions based on the effects of nonisotopic structural changes can be challenged,[21,22] and the complementary use of leaving-group isotope effects to distinguish between predictions concerning the effect of changing the nucleophile on carbon-leaving-group bonding are more subject to ambiguities that arise from the changing desolvation free energy of the nucleophile.[19,23] Clearly, further measurements of entering-group isotope effects on these and related reactions are required in order to explore the generality of our conclusions. Such experiments are in progress.

Acknowledgment. We thank D. H. Kohl and Georgia Schearer for their help and instruction concerning the measurement of the $^{15}N/^{14}N$ ratios. The Micromass 602E isotope ratio spectrometer was purchased with the assistance of a grant from the National Science Foundation (PCM 7823276).

Registry No. 2,6-Me_2(py), 108-48-5; py, 110-86-1; 4-Me(py), 108-89-4; CH_3I, 74-88-4; CH_3OTs, 80-48-8; CH_3OTf, 333-27-7; ^{15}N, 14390-96-6.

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(14) Lee, J. Ph.D. Thesis, Washington University, St. Louis, MO, 1981.
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(18) Reference 1a, pp 106, 107.
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(20) Reference 3, p 3706.
(21) Reference 17, p 5902.
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New Heterocuprates with Greatly Improved Thermal Stability[1]

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Received June 25, 1982

Organocopper reagents have become indispensable for organic synthesis[2] in spite of three serious shortcomings: (1) homocuprates, R_2CuLi, waste one R group in most applications; (2) heterocuprates, RCuXLi (X = ligand bonded to Cu via a heteroatom), are thermally unstable and must be used at low temperatures;[3] (3) acetylenic mixed cuprates, RCuR'Li (R' = 1-alkynyl ligand), are much less reactive than the corresponding homocuprates.[4] House and DuBose[5] summarize the synthetic chemist's predicament most succinctly: "Thus, the reaction temperatures required to form and use $(R_2CuLi)_n$ reagents are often approximately the same as the temperatures where thermal decomposition becomes a serious competing reaction." We have invented two new classes of heterocuprates based upon phosphido and amido ligands that exhibit a remarkable degree of thermal stability and also have good reactivity in typical organocuprate reactions, thus overcoming the above problems.

Cuprates based upon diphenylphosphidocopper(I),[6] **1**, can be prepared by adding 1 equiv of Li reagent or Grignard reagent to **1** at −20 to 0 °C (method A), or by adding 1 equiv of $LiPPh_2$ to an organocopper(I) reagent (RCu) at −50 °C (method B). Exposure of **1** to O_2 yields a new complex, **2**.[7] Cuprates can also be prepared from **2** by addition of RLi at 0 °C (method C).[7] All three methods are convenient to run as one- or two-flask procedures.[8] The basic structural feature of these diphenylphosphido cuprates is suggested to be a dimeric unit consisting of two Cu atoms connected by bridging diphenylphosphides, as was revealed by X-ray crystallography in the benzene complex of diphenyl-

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(6) Issleib, K.; Fröhlich, H.-O. *Chem. Ber.* **1962**, *95*, 375. Method IIb was used starting from Ph_2PLi and $CuBr{\cdot}SMe_2$ without the aqueous workup (see ref 8). The product of method IIa (aqueous workup) is not useful for preparing cuprates.
(7) The empirical formula of **2** (determined by complete microanalysis) corresponds to $Cu(PPh_2)(O_2)$. Whitesides, G. M.; San Filippo, J., Jr.; Casey, C. P.; Panek, E. J. *J. Am. Chem. Soc.* **1967**, *89*, 5302. Treatment of cuprates with O_2 decomposes them with coupling of the organic residue, therefore the oxygen in **2** must be very tightly bound.
(8) A solution of $LiPPh_2$ in ether or THF is prepared by adding 1.0 equiv of RLi to $HPPh_2$ (Orgmet) at −50 °C and allowing the mixture to warm to room temperature. Standard syringe techniques are used with a nitrogen atmosphere. The yellow (ether)/orange (THF) solution is transferred to 1.0 equiv of $CuBr{\cdot}SMe_2$ (Aldrich) at 0 °C, and the resulting suspension is allowed to stir at room temperature for 1 h to afford **1** as a brick-red solid, which can be washed free of LiBr with fresh solvent. Removal of the supernatant and injection of 1.0 equiv (22.4 mL/mmol) of O_2 produces **2**. Unreacted O_2 is flushed out with Ar, and fresh solvent is introduced. For formation of the cuprates, 1.0 equiv of RLi or RMgBr is added to **1** at 0 °C or −20 °C, respectively, and the reaction mixture is stirred for 15 min before being cooled to −50 °C where the substrate (1.0 equiv, dissolved in solvent, also containing internal standard if desired) is added. The course of the reactions may be followed by GLC on 10 ft × 1/8 in. OV101 or Carbowax 20M (both 5% on Chromosorb W-HP) columns by using temperature programming (45–225 °C at 20 °C/min or 45–155 °C at 10 °C/min).

0002-7863/82/1504-5824$01.25/0