nucleus x, γ is the magnetic moment, and A and B are constants for a single series of atoms y.

The results of applying this correlation to the case of one-bond, carbon–metal coupling constants in the tetramethyl derivatives of group IV are given in Figure 1. Although the equation correlates geminal, metal–proton coupling constants quite well, the fit for one-bond, carbon–metal coupling constants is less satisfactory.

The main difference between eq 1 and 2 is in the choice of a form for the s orbital of the central atom. Both equations have arbitrary constants to absorb this unknown factor. Neither equation can predict the negative sign of the reduced carbon–fluorine coupling constant. For this, a more sophisticated treatment such as the molecular orbital theory of Pople and Santry is needed.[8]

The vicinal C–X–C–H coupling constants should be related to the H–X–C–H couplings in the trimethylmetal hydrides by the relationship $J_{\mathrm{CXCH}} = 0.3J_{\mathrm{HXCH}}$.[9] The results of this calculation are given in Table IV. As was the case for most of the carbon–proton vicinal coupling constants studied by Karabatsos, the observed values are more positive than those predicted. Though the magnitudes of the coupling constants are not predicted precisely, the trend toward smaller values with the heavier members of group IV is reproduced.

No discussion will be made of the variations in the ^{13}C spectra of the dimethyl derivatives of group IIb because of the limited amount of available data.

Since the completion of this work, several papers have appeared presenting the same or related data.[14] Thus, Dreeskamp and Stegmeir[15] have obtained carbon–metal and vicinal carbon–proton couplings in some of the same compounds by heteronuclear tickling techniques using ^{13}C-enriched samples. Litchman and Grant[16] have observed the carbon–carbon coupling in neopentane while McFarlane[17] has measured the tin–carbon coupling in tetramethyltin. Also, Dean and McFarlane[18] have reexamined the spectrum of dimethylmercury and determined the vicinal carbon–proton coupling by tickling techniques.

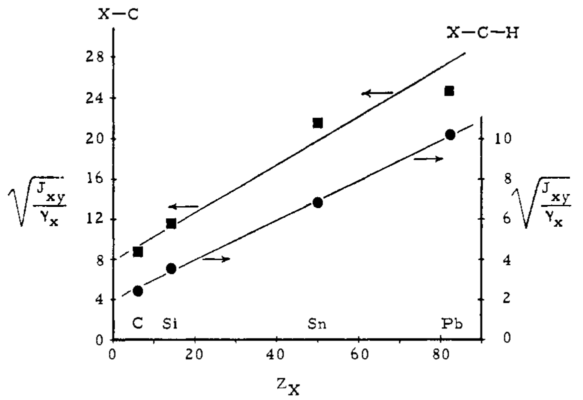

Figure 1. Reeves and Wells correlations of the C–X and X–C–H coupling constants in the tetramethyl derivatives of group IV: ●, X–C–H; ■, X–C.

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[14] This section added in proof.

[15] H. Dreeskamp and G. Stegmeir, *Z. Naturforsch.*, 22a, 1458 (1967).

[16] W. M. Litchman and D. M. Grant, *J. Am. Chem. Soc.*, 89, 6775 (1967).

[17] W. McFarlane, *J. Chem. Soc.*, *A*, 528 (1967).

[18] R. R. Dean and W. McFarlane, *Mol. Phys.*, 13, 343 (1967).

Equilibration Studies. The Energy Differences for Some Six-Membered Heterocyclic Methyl Amide–Imidate Isomer Pairs

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Contribution from the W. A. Noyes Chemical Laboratory, University of Illinois, Urbana, Illinois 61801. *Received August 31, 1967*

Abstract: The isomer pairs O-methylvalerolactim (**5**)–N-methylvalerolactam (**6**), 2-methoxypyridine (**7**)–N-methyl-2-pyridone (**8**), 4-methoxypyridine (**9**)–N-methyl-4-pyridone (**10**), and 2,6-diphenyl-4-methoxypyridine (**11**)–2,6-diphenyl-N-methyl-4-pyridone (**12**) have been equilibrated in the liquid phase by using the common alkylated derivatives as catalysts. Calorimetric determinations of the heats of isomerization at 130° for the first three cases, in conjunction with estimated differences in heats of vaporization, kinetic energies, and zero-point vibrational energies, allow estimates of the chemical binding energy differences for each isomer pair. In this sense, the amide is considerably more stable than the imidate for the pairs **5**–**6** and **7**–**8**; in contrast, the isomers **9**–**10** are of comparable stability. The present results indicate that environmental effects can contribute several kcalories/mole to the relative isomer stabilities in the condensed phase. The π-stabilization energy of **7** is estimated to be 6 ± 7 kcal/mol greater than that of **8**. A mechanism involving alkyl transfer from the catalyst to the imidate is suggested for the equilibration reaction and is supported by isotopic scrambling data.

Chemical, physical, and spectral investigations have established that an amide is generally more stable than its isomeric imidate.[2–6] Quantitative estimates of protomeric equilibria **1**–**2** are available for a large number of heteroaromatics[6] although contributions to

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[1] (a) Sun Oil Company Fellow, 1965–1966; (b) University of Illinois Fellow, 1966–1967.

[2] (a) F. Arndt and B. Eistert, *Ber.*, 71, 2040 (1938); (b) A. R. Katritzky and J. M. Lagowski, *Advan. Heterocyclic Chem.*, 1, 311 (1963).

[3] (a) H. Meislich, "Pyridine and Its Derivatives," Part III, E. Klingsberg, Ed., John Wiley and Sons, Inc., New York, N. Y., 1962, pp 619–631, 681; (b) J. W. Schulenberg and S. Archer, *Org. Reactions*, 14, 24 (1965).

[4] (a) C. A. Grob and B. Fischer, *Helv. Chim. Acta*, 38, 1794 (1955). (b) B. Pullman and A. Pullman, "Quantum Biochemistry," Interscience

the energy difference between the isomers from intermolecular association,[7,8] kinetic energies, and zero-point

$$-\overset{\overset{\displaystyle OR}{|}}{C}{=}N- \rightleftharpoons -\overset{\overset{\displaystyle O}{\|}}{C}-\overset{\overset{\displaystyle R}{|}}{N}-$$

1, R = H　　**2**, R = H
3, R = CH_3　　**4**, R = CH_3

energies present potential complications to generalizations about these systems.

The greater stability of the amide has been rationalized in different ways for different systems. Grob and Fischer favored assignment of a dominant π-stabilization energy for the acyclic amides they studied.[4a] The sum of the evidence[4,9–12] for such a π stabilization is convincing although the magnitude of the stabilization is somewhat subjective.[13–16] Pullman and Pullman suggested that the amide is favored in heteroaromatic molecules because of greater σ-framework stabilization energy.[4b] A discretional assignment of localized σ-bond energies is clearly critical to both arguments.

In this paper we report a study of the equilibration of some six-membered heterocyclic methyl amides **3** and imidates **4** by the catalytic function of the common alkylated derivative.[17,18] In principle this reaction is applicable to any isomers which have a common alkylated derivative. The present results, in conjunction with

$$R{-}A{-}B{=}C \xrightleftharpoons{RA{\cdots}B{\cdots}CR} A{=}B{-}C{-}R$$

evaluations of differences in heats of vaporization and zero-point vibrational and kinetic energies, allow estimates of the relative chemical binding energies for each isomer pair. These values, themselves of intrinsic thermodynamic interest, allow a comparison of the stabilization energies of **7** and **8**. The relationship of these results to previous investigations of similar, potentially protomeric systems is considered.

Results and Discussion

Liquid-Phase Equilibrations. The isomer pairs O-methylvalerolactim (**5**)–N-methylvalerolactam (**6**), 2-methoxypyridine (**7**)–N-methyl-2-pyridone (**8**), and 4-methoxypyridine (**9**)–N-methyl-4-pyridone (**10**) were equilibrated at 130° in 1–4 hr by the agency of the appropriate common alkylated derivative. Reaction was observed only in experiments starting with imidates **5**, **7**, and **9**, since equilibrium lies far on the side of amides **6**, **8**, and **10**. No imidates were detectable under conditions where control experiments showed that **5**, **7**, and **9** could easily be detected. Accordingly the equilibrium constants are greater than 2×10^3 for **5–6**, 10^5 for **7–8**, and 10^4 for **9–10** in favor of the amides. These values may be used to calculate limiting values for $\Delta G°$ under these conditions[19] (Table I).

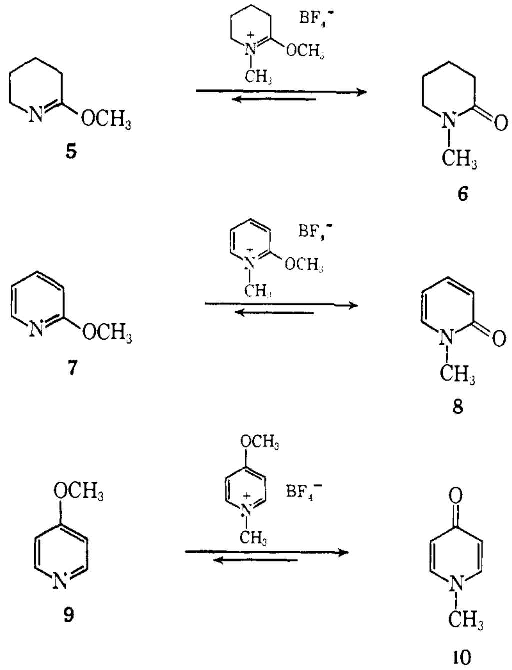

Table I. Standard Free Energies and Standard Enthalpies for Imidate–Amide Equilibrations at 130° (kcal/mol)

Reaction	$\Delta G_1°$	$\Delta H_1°$, kcal/mol	$\Delta G_g°$ [a]	$\Delta H_g°$ [a]
5 → **6**	>-5.6	-17.4 ± 0.5	>-3.5	-14.1 ± 2.0
7 → **8**	>-9.3	-12.4 ± 0.8	>-6.6	-8.0 ± 2.3
9 → **10**	>-7.4	-8.8 ± 0.5	>-3.0	-0.2 ± 2.0

[a] At 760 mm.

The reactions proceeded in high yield, and competing processes could not be detected by infrared, ultraviolet, or nmr spectroscopy, or by glpc. The pure components were stable under the conditions employed.

Quantitative data on the relative enthalpies of the isomers were obtained by measuring heats of reaction

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Publishers, Inc., New York, N. Y., 1963, pp 120–201, 206–208, and references cited therein. (c) The amide also appears to be favored in potentially tautomeric vinylogous systems: C. A. Grob and H. J. Wilkens, *Helv. Chim. Acta*, 50, 725 (1967); G. O. Dudek and R. H. Holm, *J. Am. Chem. Soc.*, 84, 2691 (1962).

(5) A. R. Katritzky, B. Wallis, R. T. C. Brownlee, and R. D. Topsom (*Tetrahedron*, 21, 1681 (1965)) have noted that, in molecules which have a nitrogen atom bonded to an electronegative atom bearing a lone electron pair, the imidate may be favored at equilibrium.

(6) A. R. Katritzky and J. M. Lagowski, *Advan. Heterocyclic Chem.*, 1, 347, 359, 363 (1963); 2, 11, 18, 36 (1964).

(7) This includes solvent effects. For an example, see A. R. Katritzky, F. W. Maine, and S. Golding, *Tetrahedron*, 21, 1693 (1965).

(8) Hydrogen bonding is likely to be important. For example, 2-pyridone is strongly intermolecularly associated by hydrogen bonding in nonpolar solvents: M. H. Krackov, C. M. Lee, and H. G. Mauther, *J. Am. Chem. Soc* , **87**, 892 (1965); G. G. Hammes and H. O. Spivey, *ibid.*, **88**, 1621 (1966).

(9) R. Huisgen, I. Ugi, H. Brade, and E. Rauenbusch, *Ann.*, **586**, 30 (1954); H. Pracejus, M. Kehlen, H. Kehlen, and H. Matschiner, *Tetrahedron*, 21, 2257 (1965), and references cited therein.

(10) H. S. Gutowsky, J. Jonas, and T. H. Siddall, *J. Am. Chem. Soc.*, 89, 4300 (1967), and references cited therein.

(11) P. Haake, W. B. Miller, and D. A. Tyssee, *ibid.*, 86, 3577 (1964); R. M. Moriarty and J. M. Kleigman, *J. Org. Chem.*, **31**, 3007 (1966), and references cited therein.

(12) S. Nagakura, *Bull. Soc. Chem. Japan*, **25**, 164 (1952).

(13) The most frequently cited value of the π-stabilization energy of 21 kcal/mol is due to Pauling, who also discusses this stabilization in terms of a 40% contribution of the usual dipolar structure to the amide resonance hybrid.[14–16]

(14) L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1960, pp 281–282.

(15) A similar estimate is made by Penfold for 2-pyridone on the basis of bond lengths from an X-ray analysis: B. R. Penfold, *Acta Cryst.*, 6, 591 (1953).

(16) A π-stabilization energy estimate of 24.0–26.6 kcal/mol has been made for N-methylvaleroactam by P. S. Ugryumov, *Zh. Obshch. Khim.*, 13, 222 (1943).

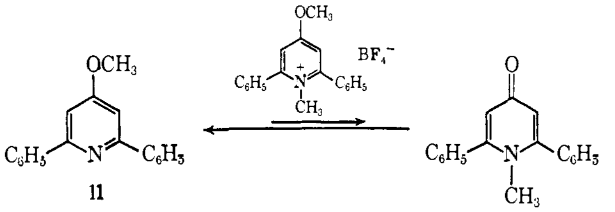
(17) A preliminary report of a portion of this work has appeared: P. Beak and J. Bonham, *Chem. Commun.*, 631 (1966).

(18) P. Beak, *Tetrahedron Letters*, 863 (1963).

(19) Although the measurement was made at constant volume, the difference between the Gibbs and Helmholtz free energies for the liquid phase is negligible: F. D. Rossini, "Experimental Thermochemistry," Interscience Publishers, Inc., New York, N. Y., 1956, p 5; G. N. Lewis and M. Randall, "Thermodynamics," McGraw-Hill Book Co., Inc., New York, N. Y., 1923, p 158.

in a calorimeter of the type designed by Arnett, Bentrude, Burke, and Duggleby[20] but operated in an oven at 130°. The calorimeter was calibrated electrically for the reaction enthalpy measurements and, in separate experiments at 25°, gave correct values for the known heat of neutralization of aqueous sodium hydroxide. The resistance of the calibration heater was the same at 25 and 130°. The heat of stirring and heats of solution of the catalysts in the amides were not detectable under the experimental conditions. The measured heats of reaction correspond to the differences in enthalpy for the pure liquid isomers (ΔH_l°) under these conditions[19] and are presented in Table I.

Equilibration of 2,6-diphenyl-4-methoxypyridine (**11**) and 2,6-diphenyl-N-methyl-4-pyridone (**12**) *via* the catalytic action of the common alkylated derivative demonstrated that these isomers have similar liquid-phase energies. Calculated values of $\Delta H_l^\circ = 1.1 \pm 1.0$ kcal/mol and $\Delta S_l^\circ = 0.6 \pm 1.4$ Gibbs were obtained from equilibrium constants of 0.19 (130°), 0.23 (162°), 0.21 (200°), and 0.24 (250°).[21] Equilibrium was approached from both sides at 162 and 200°. The equilibrium constants were measured by nmr and the presence of both isomers at equilibrium was shown by infrared, nmr, and thin-layer chromatographic criteria. Isolation of the isomers from one run gave good agreement with the equilibrum constant determined by nmr spectroscopy. Qualitatively, it appears that the 1,2,6 steric interactions of **12** counterbalance the greater stability of the 4-pyridone (*vide supra*, **9**–**10**).



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12

The liquid-phase energy differences between the isomers **5**–**6**, **7**–**8**, and **9**–**10** include differences in intermolecular forces, kinetic energies, and zero-point vibrational energies, as well as differences in chemical binding energies.[22] The last term is the only one of importance to an understanding of differences in bonding energies, and the energy differences measured for the liquid state must be corrected for the first three terms.

$$\Delta E_l^\circ = \Delta E_{\text{intermolecular}} + \Delta E_{\text{kinetic}} + \Delta E_{\text{zero point}} + \Delta E_{\text{chemical binding}}$$

Conversion to the Gas Phase. The contributions resulting from intermolecular interactions may be eliminated by conversion of the observed energy differences to the gas-phase values at 130° (1 atm). The transformations involve a change in standard state and may be carried out by using the isothermal cycle shown in Figure 1 and assuming ideal gas behavior. The equations for the changes in enthalpy and free energy for these processes are listed below Figure 1. Isothermal conversion of ΔH_l° to ΔH_g° (1 atm) requires only the addition of the difference in the heats of vaporization of the isomers since no enthalpy change is associated with the isothermal compression of an ideal gas.[23] No free energy changes accompany the vaporization processes, and the isothermal expansion of an ideal gas from its vapor pressure to 1 atm accounts for the factor $RT \ln (760/p_x)$.

$$\begin{tikzcd}[row sep=large, column sep=huge]
I_g\,(1\text{ atm}) \arrow[r, shift left, "130^\circ"] \arrow[d, shift left] & A_g\,(1\text{ atm}) \arrow[l, shift left, "{\begin{array}{c}\Delta H_g^\circ\,(1\text{ atm})\\ \Delta G_g^\circ\,(1\text{ atm})\end{array}}"] \arrow[d, shift left, "b"] \\
I_g\,(p_I) \arrow[u, shift left, "b"] \arrow[d, shift left] & A_g\,(p_A) \arrow[u, shift left] \arrow[d, shift left, "a"] \\
I_l \arrow[u, shift left, "a"] \arrow[r, shift left, "130^\circ"] & A_l \arrow[l, shift left, "{\begin{array}{c}\Delta H_l^\circ\\ \Delta G_l^\circ\end{array}}"] \arrow[u, shift left]
\end{tikzcd}$$

a, p = vapor pressure at 130°
$H_g = H_l + \Delta H_{\text{vap}}$
$G_g = G_l$

b, $H_g\,(1\text{ atm}) = H_g\,(p_x)$
$G_g\,(1\text{ atm}) = G_g\,(p_x) - RT \ln (760/p_x)$

Figure 1. The isothermal transformations of enthalpies and free energies from the liquid to the gaseous state for a methyl imidate (I) and a methyl amide (A).

The heats of vaporization at 130° were estimated by empirical methods.[24] The Clausius–Clapeyron equation was solved for the heats of vaporization of **5**, **6**, **7**, **8**, **9**, and **10** at 130° (Table II) using nonreduced Cox–Antoine vapor pressure data.[25] The agreement among these estimates and those obtained by using the Othmer and Watson methods is good (Table X). The differences in the heats of vaporization for the isomer pairs were used to obtain the gas-phase standard enthalpy differ-

Table II. Estimated Heats of Vaporization for the Imidate–Amide Isomers at 130° (kcal/mol)

Compd	Estimated ΔH_{vap}[a]	$\Delta\Delta H_{\text{vap}}$, isomer pairs
5	9.7	3.3
6	13.0	
7	9.7	4.4
8	14.1	
9	11.4	
10	20.0	8.6

[a] The estimated error is ±0.75 kcal/mol.

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(20) E. M. Arnett, W. G. Bentrude, J. J. Burke, and P. M. Duggleby, *J. Am. Chem. Soc*., **87**, 1541 (1965)

(21) Catalyst decomposition occurred in some runs and the rearrangement at 250° was thermally induced.

(22) (a) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter 3; (b) G. J. Janz, "Estimation of Thermodynamic Properties," Academic Press, Inc., New York, N. Y., 1958, p 89; (c) K. B. Wiberg, "Physical Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1964, Chapter 2; (d) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, Chapters 1–3. In most discussions, the differences in zero-point and chemical binding energies are combined in the temperature-independent potential energy term.

(23) F. T. Wall, "Chemical Thermodynamics," W. H. Freeman and Co., San Francisco, Calif., 1958, p 115. Correction to zero vapor pressure would be desirable, but the independence of ΔH° on step b (Figure 1) and the limiting nature of the estimates of ΔG° suggest that, in this case, no significant error is introduced by the assignment of the gas at 1 atm as the standard state.

(24) (a) R. C. Reid and T. K. Sherwood, "The Properties of Gases and Liquids," 2nd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1966; (b) J. H. Perry, Ed., "Chemical Engineers' Handbook," 3rd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1950, p 301; (c) S. H. Fishtine, *Ind. Eng. Chem.*, **55**, (4) 20, (5) 49, (6) 47 (1963).

(25) The details of these calculations are given in the Experimental Section.

ences in Table I. The limiting values for the standard free energy differences shown in Table I were obtained using nonreduced Cox–Antoine vapor pressure data.

Differences in Kinetic and Zero-Point Energies. The lack of complete thermodynamic or spectral data for each compound precludes exact evaluation of the contributions of kinetic and zero-point energies to the energy differences between the isomers. However, reasonable estimates of these terms may be made.

The standard enthalpy, free energy, and entropy changes for a gas-phase isomerization, with the kinetic energy term expressed in terms of partition functions (Q) for an imidate (I)–amide (A) conversion, are[22]

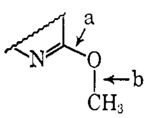
$$\Delta H^\circ = RT^2\frac{\partial \ln (Q_A/Q_I)}{\partial T} + \Delta E_{\text{zero-point}} + \Delta E_{\text{chemical binding}}$$

$$\Delta G^\circ = RT \ln (Q_A/Q_I) + \Delta E_{\text{zero-point}} + \Delta E_{\text{chemical binding}}$$

$$\Delta S^\circ = R \ln \frac{Q_A}{Q_I} + RT\frac{2 \ln (Q_A/Q_I)}{2T}$$

It is apparent that, if the ratio of partition functions is near unity, the standard enthalpy and free energy differences will be equivalent to the potential energy difference. Alternatively, this situation will be revealed by a small standard entropy term.

In principle, the ratios of partition functions for electronic, vibrational, and rotational excitation for each isomer pair at 130° are needed. The electronic term may be disregarded since only the ground electronic states should be occupied at 130°. The vibrational partition functions are sensitive mainly to low energy vibrations below *ca.* 600 cm^{-1}.[26] In the present cases, the number of significantly different vibrational modes in this region is probably small, and a large cumulation favoring either isomer is unlikely. Accordingly, the difference in vibrational partition functions at 130° is presumed to be negligible. Since **5**–**6** and **7**–**8** possess the same symmetry and nearly equivalent centers of mass, large differences in the molecular rotation partition functions would not be expected for either set. This assumption has been checked by calculation of the moments of inertia of **7** and **8**[27] and substitution of these values into standard equations.[22] The calculated ratio of partition functions is 1.01. Differences in internal rotations for **5**–**6** and **7**–**8** could be sources of appreciable standard entropy differences between the isomers. On the basis of the heavily favored *cis* orientation for the alkyl group and the carbonyl oxygen in methyl[28] and isopropyl formate,[29] it is assumed that rotamer i is preferred and that rotation about the ring carbon–oxygen bond (rotation a) can be ignored. The barrier about the methyl carbon–oxygen bond in i (rotation b) is assumed to be about 1200 cal/mol, analogous to that in methyl formate.[28] The methyl group rotational barrier in ii (rotation c) was estimated from this barrier, the barrier of 2720 cal/mol for dimethyl ether,[30] and the barrier of 3440 cal/mol for dimethylamine[31] to be 1500 cal/mol (1190/2720 × 3440). These estimated barriers were used to calculate entropies due to internal rotation of 3.2 and 3.1 cal/deg mol for i and ii, respectively.[32] The 0.1-Gibbs difference contributes 0.04 kcal/mol ($T\Delta S^\circ$ at 130°) to the difference between the standard enthalpies and free energies of these isomers. Moreover, these properties will differ from the potential energy by less than $T\Delta S^\circ$.[22] Even if the true value were an order of magnitude larger, the contribution from internal rotation differences would still be negligible. In summary, these estimations of partition function ratios and standard entropy differences suggest that kinetic energy contributions to the energy differences between O-methylvalerolactim (**5**)–N-methylvalerolactam (**6**) and 2-methoxypyridine (**7**)–N-methyl-2-pyridone (**8**) can be disregarded. Consequently, the enthalpy values for the gas phase at 130° may be considered equivalent to the potential energy differences between the isomers[33,34] (Table III). In this case, the standard enthalpy differences correspond to the standard free energy differences and equilibrium constants may be calculated. The values obtained are 10^8 for $\mathbf{5} \rightleftharpoons \mathbf{6}$, 10^5 for $\mathbf{7} \rightleftharpoons \mathbf{8}$, and 4 for $\mathbf{9} \rightleftharpoons \mathbf{10}$.



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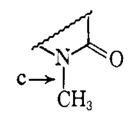

ii

The same approximations may be applied to the energy difference between 4-methoxypyridine (**9**) and N-methyl-4-pyridone (**10**) (Table III). In this case, however, the entropy difference between the isomers will be larger than in the above cases due to the twofold degeneracy of **10** relative to **9**. This gives an entropy difference of R ln 2 (1.4 Gibbs) in favor of **9**,[34,35] which amounts to an energy contribution of 0.56 kcal/mol at 130°. Encouragement for the assignment of small entropy differences in these cases may be found in the fact that the liquid-phase entropy difference between 2,6-diphenyl-4-methoxypyridine (**11**) and 2,6-diphenyl-N-methyl-4-pyridone (**12**) is 0.6 ± 1.4 Gibbs.[36]

The difference[22,37] in zero-point energies for each isomer pair could be exactly evaluated if all of the vibrational modes were assigned for each isomer. Unfortunately, complete assignments have not been made, and approximations must be used. For example, the sum of the differences in the ten absorptions assigned to ring stretching and hydrogen deformations for **7**[38] and **8**[39]

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(26) For discussion of a similar case, see ref 22d, pp 13–14.

(27) We are indebted to Dr. Virgil Weiss for these calculations. The moments obtained are (amu A^2): 7, I_a, 84.2, I_b, 284.6, and I_c, 368.3; 8, I_a, 139.5, I_b, 193.9, and I_c, 333.4.

(28) R. F. Curl, *J. Chem. Phys.*, 30, 1529 (1959).

(29) J. E. Piercy and S. V. Subrahmanyam, *ibid.*, 42, 1475 (1965).

(30) P. H. Kasai and R. J. Meyers, *ibid.*, 30, 1096 (1959).

(31) V. W. Laurie, quoted by D. R. Lide, Jr., *Ann. Rev. Phys. Chem.*, 14, 225 (1964).

(32) K. S. Pitzer, "Quantum Chemistry," Prentice Hall, Englewood Cliffs, N. J., 1953, pp 239, 494. A carbon–hydrogen bond distance of 1.086 Å and HCH bond angle of 110° were employed to calculate a distance of 0.96 Å between the H atom and the symmetry axis. The partition function (Q_f) for the methyl internal rotation was calculated to be 3.3 at 130°.

(33) Reference 22d, p 42.

(34) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 215.

(35) Reference 18c, p 262.

(36) This case may be more complicated than those of the other isomer pairs due to differences in the barriers to phenyl group rotations in 11 and 12.

(37) This is the difference in the sum of $^1/_2h\nu$ for all of the fundamental vibrational frequencies.

(38) A. R. Katritzky and R. A. Jones, *J. Chem. Soc.*, 2947 (1960); A. R. Katritzky, *Quart. Rev.* (London), 13, 353 (1959). The absorptions assigned are at 1610, 1590, 1578, 1483, and 1420 cm^{-1} (ring stretching) and 1270, 1141, 1097, 1045, and 987 cm^{-1} (hydrogen deformations).

is 12 cm^{-1} or 0.02 kcal/mol. Another approach for evaluation of this difference involves the use of the sum of the differences in functional group stretching frequencies. By using one C=N (1578 cm^{-1}) and two C—O (1284 and 1032 cm^{-1}) bonds for **7**,[38] as compared to one C=O (1660 cm^{-1}) and two C—N (1389 and 1134 cm^{-1}) bonds for **8**,[39] a difference of 289 cm^{-1}, corresponding to 0.86 kcal/mol, is obtained. This use of an unrealistic group frequency model probably exaggerates the difference between the isomers. The structural similarities of the isomer pairs **5–6**, **7–8**, and **9–10** suggest that large, cumulative frequency shifts favoring one isomer are not likely, and the zero-point energy difference between the two isomers should be no greater than ± 1.5 kcal/mol.

Differences in Chemical Binding Energies. The differences in chemical binding energies for each of the imidate–amide isomer pairs as obtained from the preceding analysis are listed in Table III.[40]

Table III. Differences in Potential Energies, Zero-Point Vibrational Energies, and Chemical Binding Energies for the Imidate–Amide Isomers (kcal/mol)

Isomers	Potential energy difference	Zero-point vibrational energy difference	Chemical binding energy difference
5–6	14.1 ± 2.0	±1.5	14.1 ± 3.5
7–8	8.0 ± 2.0	±1.5	8.0 ± 3.5
9–10	0.2 ± 2.0	±1.5	0.2 ± 3.5

The importance of evaluating intermolecular interactions is illustrated by the differences in the gas-phase and liquid-phase enthalpies, $\Delta\Delta H_{\text{vap}}$, of 3.3 (**5–6**), 4.4 (**7–8**), and 8.6 (**9–10**) kcal/mol (Table II). In general, extrapolations from the results of liquid-phase determinations of thermodynamic stabilities to isolated molecules could be seriously in error if this correction were not made.[41] The preceding evaluations of the kinetic and zero-point energy differences for the isomers suggest that rationales of stability or reactivity differences of a few kilocalories/mole could be misleading[42] unless all of these effects are explicitly[43] considered or implicitly corrected by structural similarity.[22]

Despite the uncertainties introduced by the approximations, the accuracy of the chemical binding energy differences is better than the accuracy of present predictive methods. These uncertainties could be eliminated by complete spectral and thermochemical data for each isomer or by more accurate methods of calculation.

Amide–Imidate Stabilities. Since the amides N-methylvalerolactam (**6**) and N-methyl-2-pyridone (**8**) are of considerably lower energy than the corresponding isomeric imidates O-methylvalerolactim (**5**) and 2-methoxypyridine (**7**), this order may be expected for most related, six-membered, heterocyclic isomers. The equilibrium can, of course, be shifted by steric and electronic[5] effects. A case in which both effects might be operative may be seen in the comparison of the equilibria of **11–12** and **9–10**.

The extent to which the greater stability of the amides can be attributed to differences in σ and π energies depends wholly on the choice of σ energies from a wide range of possibilities. The difference in σ-bond energy of the amide relative to the imidate can be calculated using different sets of recommended values to be −4.7,[44] 3.8,[45] 4.4,[46] 7.7,[47] or 14.8[48] kcal/mol. If the 14.1 ± 3.5 kcal/mol energy difference between **5** and **6** is taken to be typical for amide–imidate equilibria, there is little difference between this value and the upper end of the range. This would suggest little difference in π energies of the amide and imidate; this result is not consistent with intuitive application of the resonance theory.[4a] If the lower end of the calculated σ-bond energy range is used, the amide may be considered to have 5–15 kcal/mol more π-stabilization energy than the imidate. This result is roughly consistent with previous estimates[4a,13] for amide–imidate isomers and simple molecular orbital calculations, which predict that the amide will be favored by a delocalization energy of 0.13β (Table IV). Although a σ-bond energy which provides a fit to expectation could be chosen, this choice would be arbitrary. An unambiguous method for meaningful separation of σ and π energies in these systems does not appear at this time.

The problem of selecting suitable models is central to our understanding of chemical bonding. This is especially evident in estimates of resonance energies in aromatic systems, where ambiguity is introduced by comparisons of measured properties of real molecules with assumed properties of nonexistent molecules.[49–52] The property which seems most generally used as characteristic of an aromatic system is that of an appreciable stabilization energy. Although the magnitude of this energy is highly dependent on the model choice, the usefulness of a semiquantitative model has been amply demonstrated.[51,53]

The present results can be used to estimate the relative stabilization energies of the heteroaromatic[51,54]

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(39) A. R. Katritzky and A. R. Hands, *J. Chem. Soc.*, 2202 (1958); D. Cook, *Can. J. Chem.*, **43**, 741 (1965). The absorptions assigned are at 1645, 1590, 1529, 1455, and 1389 cm^{-1} (ring stretching) and 1318, 1240, 1151, 1050, and 842 cm^{-1} (hydrogen deformations).

(40) The small difference between these values and those reported previously[17] is the result of using different methods to estimate the heats of vaporization at 130°.

(41) In most cases, this correction would be the difference in solvation energies for a common solvent.

(42) Uncorrected data may be useful in cases of large energy differences. T. L. Cottrell, "The Strengths of Chemical Bonds," Academic Press Inc., New York, N. Y., 1954, p 104, has pointed out that calculated zero-point and kinetic energies have low accuracy.

(43) See, for example, S. W. Staley, *J. Am. Chem. Soc.*, **89**, 1532 (1967).

(44) J. D. Cox, *Tetrahedron*, 19, 1175 (1963).

(45) G. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1955, pp 88–89.

(46) Reference 22, p 63; A. F. Bedford, A. E. Beezer, and C. T. Mortimer, *J. Chem. Soc.*, 2039 (1963).

(47) The method of Van Krevelen and Chermin was used: G. J. Janz, "Estimation of Thermodynamic Properties of Organic Molecules," Academic Press Inc , New York, N. Y., 1958, pp 66–68.

(48) T. L. Cottrell, "The Strengths of Chemical Bonds," 2nd ed, Butterworth & Co. (Publishers) Ltd., London, 1958, Chapter 10.

(49) This was clearly recognized by the early proponents of the resonance theory; see ref 14, p 215, and ref 40, pp 95, 604.

(50) H. Preuss, *Angew. Chem. Intern. Ed. Engl.*, **4**, 660 (1965).

(51) For discussions of aromatic character, see K. Hafner, *ibid.*, 3, 165 (1964); A. T. Balaban and Z. Simon, *Tetrahedron*, 18, 315 (1962); R. Breslow and E. Mohacsi, *J. Am. Chem. Soc.*, **85**, 431 (1963); M. E. Volpin, *Usp. Khim.*, **29**, 298 (1960); D. D. Craig, "Non-Benzenoid Aromatic Compounds," D. Ginsburg, Ed., Interscience Publishers, Inc., New York, N. Y., 1950.

(52) For example, estimates of the vertical resonance energy of benzene vary with the models chosen from 13 to 112 kcal/mol: (a) A. Streitwieser, Jr., "Molecular Orbital Theory," John Wiley and Sons, Inc., New York, N. Y., 1961, p 246; (b) M. J. S. Dewar and H. N. Schmeising, *Tetrahedron*, 11, 96 (1960).

(53) "Theoretical Organic Chemistry, Kekule Symposium," Butterworth & Co. (Publishers) Ltd., London, 1959.

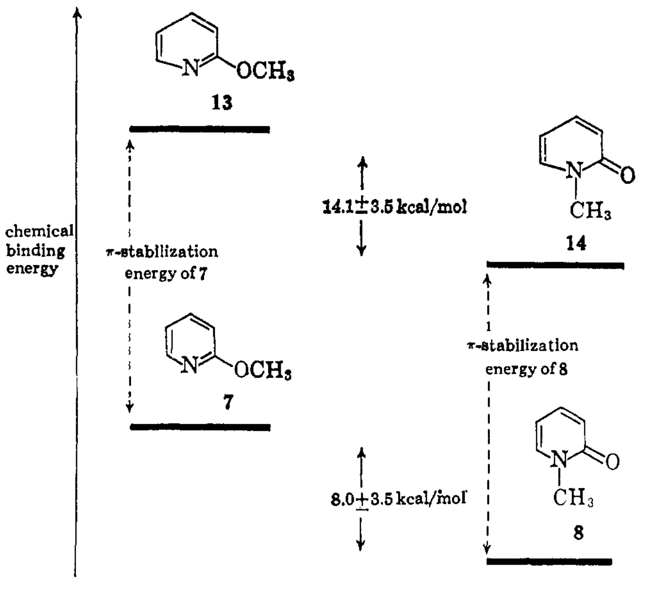

Figure 2. Estimate of the differences in stabilization energy for 2-methoxypyridine (**7**) and N-methyl-2-pyridone (**8**).

compounds 2-methoxypyridine (**7**) and N-methyl-2-pyridone (**8**). These stabilization energies do not include the stabilization energies of the isolated amide and imidate funtionalities. The localized bonding models are two double bonds and methyl imidate **13** for **7** and two double bonds and methyl amide **14** for **8** (Figure 2). If the localized double bonds are presumed to have the same energy in each model, the difference in the chemical binding energies of models **13** and **14** may be estimated to be the same as that for O-methylvalerolactim (**5**) and N-methylvalerolactam (**6**), 14.1 ± 3.5 kcal/mol. This use of an experimentally based value removes the ambiguity which would arise in calculations of the differences in σ- and π-bond energies for hypothetical molecules **13** and **14**. On the basis of these models and the difference in chemical binding energy between **7** and **8** (Table III), we may calculate a difference in chemical binding stabilization energies of 6.1 ± 7.3[55] (14.1–8.0 ± 3.5 + 3.8) kcal/mol in favor of **7** (Figure 2). This small difference in stabilization energies between **5**–**6** and **7**–**8** implies no great change in chemical binding energy due to possible participation of π bonding in the aromatic system. Although this might suggest that the contribution of π-delocalization energy to ground-state stability is not very great, the possibility of a comparably large contribution from delocalization in both **7** and **8** cannot be discounted.

Table IV. Calculated Delocalization Energies

Molecule	No.	Total E_π	Model E_π	Delocalization energy, β
$-\mathrm{N}{=}\overset{\vert}{\mathrm{C}}{-}\ddot{\mathrm{O}}-$	**5**	$4\alpha + 6.84\beta$	$4\alpha + 6.56\beta$	0.28
$>\ddot{\mathrm{N}}{-}\overset{\vert}{\mathrm{C}}{=}\mathrm{O}$	**6**	$4\alpha + 6.65\beta$	$4\alpha + 6.24\beta$	0.41
2-Methoxypyridine	**7**	$8\alpha + 12.77\beta$	$8\alpha + 10.56\beta^a$ $8\alpha + 10.84\beta^b$	2.21
N-Methyl-2-pyridine	**8**	$8\alpha + 12.10\beta$	$8\alpha + 10.24\beta^c$ $8\alpha + 10.65\beta^d$	1.86 1.45
4-Methoxypyridine	**9**	$8\alpha + 12.76\beta$	$8\alpha + 10.56\beta^a$	2.20
N-Methyl-4-pyridone	**10**	$8\alpha + 12.06$	$8\alpha + 10.24\beta^c$	1.82

[a] The model is 2 C=C, 1 C=N, and 1 $\ddot{\mathrm{O}}$. [b] The model is 2 C=C and 1 $\ddot{\mathrm{O}}$—C=N. [c] The model is 2 C=C, 1 C=O, and 1 N. [d] The model is 2 C—C and 1 N—C—O. These calculations were carried out using parameters recommended by Streitwieser, ref 52a, p 135.

The π-delocalization energies calculated for **5**, **6**, **7**, **8**, **9**, and **10** by the Hückel method are listed in Table IV. On this basis, the pyridines **7** and **9** possess greater delocalization energy than the pyridones **8** and **10**, with an insignificant difference in delocalization energy between the pairs **7** and **9** and **8** and **10**. The difference in delocalization energy between **7** and **8** on the basis of the following models (Figure 2) is 0.76β. If it is assumed that the method[56] is valid for these comparisons and that a parallel exists between calculated delocalization energies and stabilization energies,[57] there is then qualitative agreement between these calculations and our results.

Elvidge and Jackman[58,59] have suggested that the ring-current model, originally used by Pople[51,60–62] to rationalize nmr chemical shifts in aromatic systems, may be used to provide a quantitative measure of aromaticity and have estimated on this basis that N-methyl-2-pyridone (**8**) has 35 ± 5% the "aromaticity" of benzene, or a stabilization of 12–15 kcal/mol.

Abraham and Thomas[63] have provided cogent criticisms of this proposal. Questions of model choice and an evaluation of other contributions to the chemical shift led these authors[63] to conclude that the effect is qualitatively, but not quantitatively, useful as an indication of aromatic character. Musher[64] has suggested that the ring-current model is not theoretically justified and has no relation to aromatic character.

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(54) H. Meislich, "Pyridine and Its Derivatives," Part III, E. Klingsberg, Ed., John Wiley and Sons, Inc., New York, N. Y., 1962, p 623.

(55) The range resulting from the error estimates is probably too wide. It seems likely that the errors in the estimated heats of vaporization and zero-point vibrational energies for the pairs **5**–**6** and **7**–**8** would cancel substantially in subtraction.

(56) (a) J. A. Berson, E. M. Evleth, Jr., and S. L. Manatt, *J. Am. Chem. Soc.*, **87**, 2901 (1965), have reported a modified Hückel method which correlates the dipole moments of the pyridones and their derivatives; (b) M. J. S. Dewar and G. J. Gleicher, *J. Chem. Phys.*, **44**, 759 (1966), have suggested that the Hückel method is valid only for alternate aromatic carbocycles and have proposed a semiempirical SCF method for calculation of ground-state properties.

(57) Reference 52a, Chapter 9.

(58) J. A. Elvidge and L. M. Jackman, *J. Chem. Soc.*, 859 (1961).

(59) For extensions and justifications of this proposal see: G. G. Hall, A. Hardisson, and L. M. Jackman, *Tetrahedron Suppl.*, **2**, 101 (1964); H. A. P. DeJongh and H. Wynberg, *ibid.*, **21**, 515 (1965); L. M. Jackman, Q. N. Porter, and G. R. Underwood, *Australian J. Chem.*, 18, 1221 (1965); J. A. Elvidge, *Chem. Commun.*, 160 (1965); D. W. Davies, *ibid.*, 258 (1965).

(60) J. A. Pople, *J. Chem. Phys.*, 24, 1111 (1956); J. A. Pople, W. G. Schneider, and J. H. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, pp 180–183, 247–265.

(61) For recent modifications see: B. P. Dailey, *J. Chem. Phys.*, **41**, 2304 (1964); A. F. Ferguson and J. A. Pople, *ibid.*, **42**, 1560 (1966), and references cited therein.

(62) The ring-current model has been generally used to justify the use of chemical shifts as a qualitative criterion of aromatic character: F. Sondheimer, *Pure Appl. Chem.*, 7, 363 (1963); L. M. Jackman, F. Sondheimer, Y. Amiel, D. A. Ben E-Frain, Y. Gaṇoi, R. Wolovsky, and A. A. Bothner-By, *J. Am. Chem. Soc.*, 84, 4307 (1962); E. Vogel and H. D. Roth, *Angew. Chem.*, 76, 145 (1964); G. M. Badger, J. A. Elix, and G. E. Lewis, *Australian J. Chem.*, 19, 1221 (1966); V. Boekelheide and J. B. Phillips, *J. Am. Chem. Soc.*, **89**, 1695 (1967)

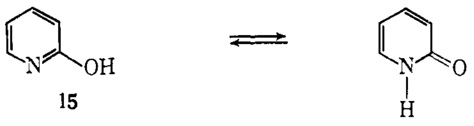
(63) R. J. Abraham and W. A. Thomas, *J. Chem. Soc., Sect. B*, 127 (1966).

(64) J. I. Musher, *J. Chem. Phys.*, **43**, 4081 (1965); see also J. M. Gadis and R. West, *ibid.*, **46**, 1218 (1967); J. I. Musher, *ibid.*, **46**, 1219 (1967).

An empirical test of the quantitative proposal of Elvidge and Jackman[58] may be made with the present data. If the stabilization energy of 2-methoxypyridine (**7**) is considered to be 38–40 kcal/mol, the same as that assigned to benzene[58] and pyridine, then the stabilization energy of N-methyl-2-pyridone (**8**) may be calculated from the previous difference in stabilization energies of **7** and **8** to be 32.9 ± 8.3 (39.6–6.1 ± 7.3 + 1) kcal/mol.[65] In this comparison the difference in stabilization energies of the imidate and amide functionalities is accounted for by the use of **5** and **6** as models. Therefore the estimated stabilization energy of **8** is not influenced by an arbitrary choice of relative stabilization energies for these functional groups. Furthermore, this stabilization energy for **8** includes no contribution from resonance stabilization of the isolated amide. This result is clearly not consistent with the estimate of 12–15 kcal/mol of Elvidge and Jackman[58] for the same compound and suggests that generally applicable quantitative assignments of "aromaticity" should not be made on the basis of nmr chemical shifts.[63,64] Obviously, a change in model could bring into agreement our results and those of Jackman and Elvidge, as well as those obtained through the use of any other model-dependent arguments. However, the many different criteria and discretionary choice of models for aromatic character suggest that a search for a generally acceptable and applicable quantitative criterion for this property is not likely to be profitable. Although the qualitative and empirical use of most criteria for aromatic character has been uniquely useful in providing insight and direction to theory and experiment,[51,53] aromaticity might best be considered a qualitative concept with some useful semiquantitative aspects.

Relation to Protomeric Systems. The relationship of the relative stabilities of N-methylvalerolactam (**6**) and O-methylvalerolactim (**5**) to the general problem of the relative chemical binding energies of potentially protomeric amides and imidic acids (**1–2**)[4,66,67] is not clear. Even a qualitative extrapolation from the results for the equilibration of **5** and **6** to the corresponding protomeric isomers would require accurate and presently unknown differences in the formally localized C–N, C–O, H–N, and H–O bonds of these molecules.

In the cases of the heteroaromatic isomers, the protomeric equilibrium has been extensively studied and found to favor the amide in solution.[68] Quantitative estimates of the equilibria **15** ⇄ **16** and **17** ⇄ **18** have been made in the classic works of Albert and Phillips[69] and Mason[70] using basicities and **7**, **8**, **9**, and **10** as model compounds. In aqueous solutions at 20°, **16** and **18** are favored by free energies of 4.1 and 4.5 kcal/mol, respectively.[70] In view of the previous discussion establishing large effects due to intermolecular association for the isomer pairs **5–6**, **7–8**, and **9–10** (*vide supra*), it appears that the differences in free energies of **15–16** and **17–18** could be dominated by contributions from these effects. Consequently, analysis of the protomer stabilities in terms of relative chemical binding energies is risky.[71] In fact, Levin and Rodionova[67a] recently reported an equilibrium constant of *ca.* 1 for the equilibration of **15–16** in the vapor phase at 300–614°. This disparity in the gas-phase and solution free energy data indicates that the latter do not provide a basis for accurate estimation of the potential energy difference between **15** and **16**.[72] It appears that data based on the equilibration of alkylated isomers should prove more useful for discussions of relative chemical binding energies than information obtained from studies of protomeric equilibria in solution.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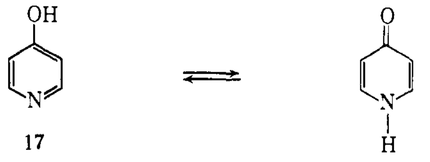
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Mechanism of the Catalytic Function. The equilibration of alkyltropic[73] isomers by the agency of the common alkylated derivative was conceived for the equilibration of 2- and 4-pyrone isomers *via* a pyrylium salt.[18] That the reaction was conceptually general and potentially applicable to any alkylated isomers having a common alkylated derivative was noted in the first report.

Analogous conversions of imidates to amides have been known for some time. Fry and Kendall were apparently the first workers to use a common alkylated derivative for this conversion.[74] In 1951, they reported the conversion of 2-methylthiobenzthiazole (**19**) to 2,3-dihydro-3-methylthiobenzthiazole-2-thione (**20**) upon

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(65) Similar stabilization energies for pyridine and benzene are implicit in the models and conclusions of Elvidge and Jackman. A resonance energy of 38–40 kcal/mol is used for benzene, and presumably the same value applies to pyridine for these authors state, "There is little doubt that pyridine is fully as aromatic as benzene."[58]

(66) L. Skulski, G. C. Palmer, and M. Calvin, *Tetrahedron Letters*, 1773 (1963).

(67) (a) E. S. Levin and G. N. Rodionova, *Dokl. Akad. Nauk SSSR*, **164**, 584 (1965), report that valerolactam is the only detectable tautomer in the gas phase; (b) E. Levin and G. N. Rodionova, *ibid.*, 172, 607 (1967).

(68) For reviews see: (a) ref 1b, pp 347–352; (b) A. Albert, "Physical Methods in Heterocyclic Chemistry," Vol. 1, A. R. Katritzky, Ed., Academic Press Inc., New York, N. Y., 1963, pp 36–40; (c) ref 49, p 621; (d) H. S. Mosher, "Heterocyclic Compounds," R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1950, pp 435–443.

(69) A. Albert and J. N. Phillips, *J. Chem. Soc.*, 1294 (1956).

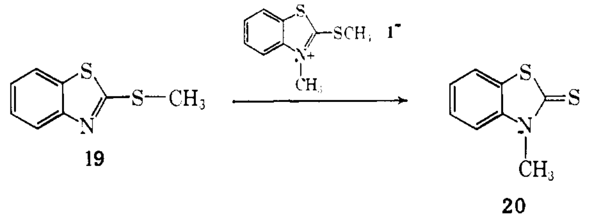
(70) S. F. Mason, *ibid.*, 674 (1958).

(71) The risk may be considerably reduced in rationales of equilibria for a series of structurally similar species since the nonbonding effects may cancel; see ref 70 and S. F. Mason, *Progr. Org. Chem.*, 6, 214 (1964).

(72) (a) A large difference in solvation energies might be expected for 15 and 16 on the basis of the strong self-association of 15 in nonhydrogen-bonding solvents.[8] Specific and strong hydrogen bonding may contribute significantly to the differences in solvation energies for protomeric systems. (b) If it is assumed that the gas-phase[67] energy difference approximates the potential energy difference between 15 and 16, then comparison of this small energy difference with the difference in chemical binding energy for 7 and 8 (Table III) would suggest that, in the methyl amide 3–methyl imidate 4, the amide is favored by *ca.* 7 kcal/mol more than for the corresponding protomers 1–2. Given this assumption and the difference in chemical binding energy for 5 and 6 (Table III), it can be suggested that the binding energy difference between valerolactim and valerolactam will be 5–10 kcal/mol in favor of the amide.

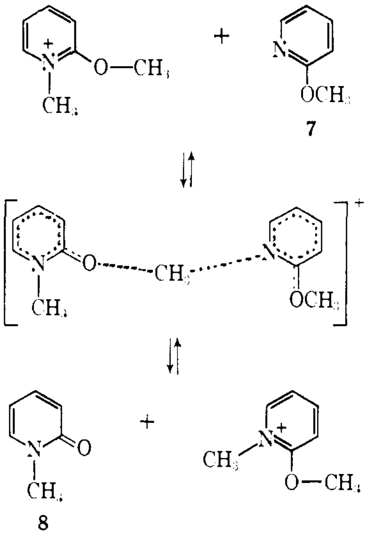
(73) This term is applied to isomers which differ in the position of an alkyl group. It follows directly from the generally used term prototropic, which describes isomers differing in the position of a proton.

(74) D. J. Fry and J. D. Kendall, *J. Chem. Soc.*, 1716 (1951); for recent, pertinent work on similar systems see J. J. D'Amico, S. T. Webster, R. H. Campbell, and C. E. Twine, *J. Org. Chem.*, 30, 3628 (1965); B. H. Klandermann, *ibid.*, 30, 2469 (1965).

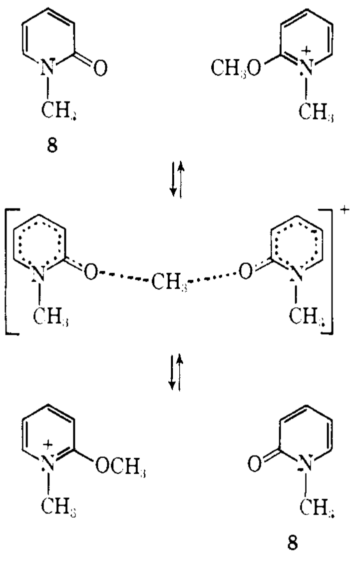


heating with the methiodide salt. The conversion of alkyl imidates to alkyl amides by the intermolecular action of an alkylating agent, the Lander rearrangement,[75] has been used extensively for the conversion of methoxypyridines to N-methylpyridones.[76] In 1897, Knorr and Rabbe, with remarkable insight, postulated the intermediacy of an N-alkylquinolinium iodide in the conversion of 2-methoxyquinoline or 2-ethoxyquinoline to N-methyl-2-quinolone with excess methyl iodide.[77] Analogous intermediates have since been proposed and studied by many others.[75,78] The principle difference between the Lander rearrangement, its variants, and the present equilibrations is the absence, in the latter, of a nucleophilic anion. In the earlier cases, such an ion could have acted as the alkyl transfer agent in a nitrogen-alkylation–oxygen-dealkylation sequence *via* pathways established for ambident amidinium species.[79–81] The thermal rearrangement of alkyl imidates to alkyl amides has also been used extensively for the conversion of methoxypyridines to N-methylpyridones.[82,83] Wiberg, Shryne, and Kintner have proposed[84] that this reaction is a radical process although the possibilities of ionic processes,[85] perhaps with trace catalysis,[86] or concerted rearrangements[87] have also been suggested for similar cases.

A reasonable formulation for the action of the catalyst in the conversion of 2-methoxypyridine (**7**) to N-methyl-2-pyridone (**8**) is the transfer of a methyl group from the catalyst oxygen atom to the nitrogen atom of the pyridine. The fact that the equilibrium lies far on the side



of the pyridone establishes that the reverse reaction, nitrogen-to-oxygen methyl transfer, will not be observed.[88] A possible identity process which may compete with oxygen-to-nitrogen methyl transfer is an oxygen-to-oxygen transfer involving the pyridone **8** and the catalyst.



If these pathways are followed, a reaction in which an isotopically labeled catalyst is used should give scrambling of the label in the products. This has been tested by use of labeled catalysts **21**[89] and **22**. The results of the reactions carried out with these catalysts are shown in Table V. The first entry, A, clearly demonstrates the operation of an oxygen-to-nitrogen rearrangement involving the catalyst in the formation of N-methyl-2-

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(75) J. W. Schulenberg and S. Archer, *Org. Reactions*, **14**, 24 (1965). The reaction may also be catalyzed by Lewis acids.

(76) (a) N. V. Sidgwick, "The Organic Chemistry of Nitrogen," J. A. Taylor and W. A. Baker, Ed., Clarendon Press, Oxford, England, 1937, p 531; (b) ref 39, p 681; (c) E. Spath and G. Koller, *Ber.*, **56**, 2454 (1923); (d) L. A. Paquette and N. A. Nelson, *J. Org. Chem.*, **27**, 1085 (1962), and references cited therein.

(77) L. Knorr and P. Rabbe, *Ber.*, 30, 927 (1897).

(78) H. L. Wheeler, *Am. Chem. J.*, 23, 136 (1900); R. E. Benson and T. L. Cairns, *J. Am. Chem. Soc.*, 70, 2115 (1948); A. E. Arbuzov and V. E. Shishkin, *J. Gen. Chem. USSR*, **34**, 3628 (1964); L. A. Paquette, *J. Am. Chem. Soc.*, **87**, 5186 (1965); D. J. Brown and T. Teitei, *Australian J. Chem.*, **18**, 199 (1965); R. M. Bowman and M. F. Grundon, *J. Chem. Soc., Sect. C*, 1504 (1966); J. Pliml and M. Prystas, *Advan. Heterocyclic Chem.*, **8**, 115 (1967).

(79) S. Hünig, *Angew. Chem. Intern. Ed. Engl.*, **3**, 548 (1964); A. F. Vompe, N. V. Munich, N. F. Turitgyna, and L. V. Ivanova, *Dokl. Akad. Nauk SSSR*, **114**, 641 (1957); M. Vogel and J. D. Roberts, *J. Am. Chem. Soc.*, **88**, 2262 (1966); N. Kornblum and G. P. Coffey, *J. Org. Chem.*, **31**, 3447 (1966).

(80) H. Büchi, K. Steen, and A. Eschenmoser, *Angew. Chem. Intern. Ed. Engl.*, 3, 62 (1964), and references cited therein.

(81) Another analogy is the Michaeles–Arbusov rearrangement: G. Higetag and H. Teichmann, *Angew. Chem.*, **4**, 914 (1965); R. G. Harvey and E. R. De Sombre, "Topics in Phosphorus Chemistry," Vol. 1, M. Grayson and E. J. Griffith, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p 57. H. J. Teague and W. P. Tucker (*J. Org. Chem.*, 32, 3144 (1967)) have recently reported a related case in which a nucleophilic anion is required.

(82) L. Haitinger and A. Lieben, *Monatsh. Chem.*, 320 (1885); ref 54, p 681; for the migration of aryl groups, the reaction is the Chapman rearrangement (ref 75, p 1).

(83) Many recent examples involve Claisen-type rearrangements: R. B. Moffett, *J. Org. Chem.*, **28**, 2885 (1963); F. J. Dinan and H. Tieckelmann, *ibid.*, 29, 892 (1964); Y. Makisumi, *ibid.*, 30, 1986 (1965).

(84) K. B. Wiberg, T. M. Shryne, and R. R. Kintner, *J. Am. Chem. Soc.*, 79, 3160 (1957).

(85) D. J. Brown and R. V. Foster, *J. Chem. Soc.*, 4911 (1965); T. Taguchi, Y. Kawazoe, Y. Yoshihira, H. Kawayama, M. Mori, K. Tabata, and K. Harano, *Tetrahedron Letters*, 2717 (1965).

(86) J. W. Ralls and C. A. Elliger, *Chem. Ind.* (London), 20 (1961).

(87) L. A. Cohen and B. Witkop, "Molecular Rearrangements," Vol. 2, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p 981.

(88) If a free energy difference of 13 kcal/mol is used for the liquid-phase isomerization, nitrogen-to-oxygen transfer would be slower than oxygen-to-nitrogen transfer by a factor of *ca.* 10^{12} at 130°.

(89) The salt 21 was prepared by base-catalyzed deuterium exchange of 8 to give 6-*d*-N-methyl-2-pyridone,[90] followed by alkylation. The exchange is accompanied by 8% dideuteration. The second deuterium atom was shown to be at the 3 or 5 position by its disappearance upon formation of the 3,5-dibromo derivative.

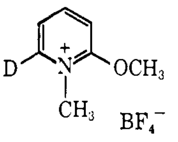
(90) P. Beak and J. Bonham, *J. Am. Chem. Soc.*, 87, 3365 (1965).

Table V. Deuterium Scrambling in the Reactions of Pyridines **7** and **9** and Pyridones **8** and **10** with the Labeled Catalysts **21**, **22**, **23**, and **24** at 130°

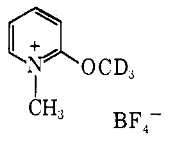
Reaction	Reactants	Time, hr	Deuterium content by nmr[a] Calcd, %	Pyridone obsd, %	Catalyst obsd, %	Molecular ion by mass spectrometry[b] m/e	Pyridone Calcd, %	Pyridone Obsd, %
A	**7** (0.98), **21** (0.30)	1.0	24	25	26	109	77	77
						110	21	21
						111	2	2
B	**8** (1.04), **21** (0.30)	1.0	22	24	25	109	78	78
						110	20	20
						111	2	2
C	**7** (0.936), **22** (0.296)	1.6	19	23	16[c]	109	81	77
						112	19	23
D	**8** (1.01), **22** (0.30)	120			Less than 5% scrambling observed			
E	**9** (1.03), **23** (0.31)	1.0	23	23	17	109	77	74
						110	1	1
						111	22	25
						112	1	0.1
F	**10** (1.16), **23** (0.31)	3.0	21	24	23	109	78	77
						110	1	2
						111	20	21
						112	1	1
G	**9** (0.964), **24** (0.295)	1.5	19	18	21	109	81	78
						112	19	22
H	**10** (0.964), **24** (0.290)	120			Less than 5% scrambling observed			

[a] Error is ±5%. The values are not corrected for small amounts of overlabeled catalyst. [b] Error is ±2%. The values are corrected to the isotopic composition of the catalyst. The spectra were determined at low ionizing voltage. [c] Equilibrium has probably not been achieved in this reaction. An oxygen-to-nitrogen transfer followed by an oxygen-to-oxygen or oxygen-to-nitrogen transfer is required.

pyridone from 2-methoxypyridine. The statistical distribution of the label in the catalyst further suggests a scrambling process other than oxygen-to-nitrogen rearrangement.[91] That this rearrangement is oxygen

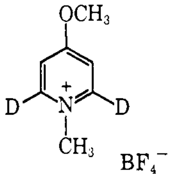


21

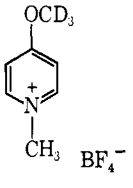


22

to oxygen is demonstrated by entry B (Table V), which shows that the label is scrambled into the pyridone and catalyst starting with the pyridone and labeled catalyst. Entry C confirms these conclusions since the observed scrambling requires both processes. The expected failure to observe nitrogen-to-oxygen transfer[88] is confirmed by entry D. Analogous conclusions may be drawn for the conversion of 4-methoxypyridine (**9**) to N-methyl-4-pyridone (**10**). In this case catalysts **23** and **24** were used, and the results are summarized in entries E–H in Table V.



23



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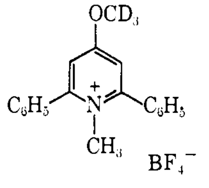

25

Similar isotope scrambling was observed when a mixture of 2,6-diphenyl-4-methoxypyridine (**11**) and 2,6-diphenyl-N-methyl-4-pyridone (**12**), with the catalyst **25**, was heated at 130° for 348 hr. Because of the complexity of the competing processes, the observed formation of 2,6-diphenyl-4-methoxy-d_3-pyridine could be explained by nitrogen-to-nitrogen and/or nitrogen-to-oxygen alkyl transfer. In this case, both oxygen-to-nitrogen and nitrogen-to-oxygen transfers may proceed at comparable rates.

Since the conversion of 2-methoxypyridine (**7**) to N-methyl-2-pyridone (**8**), catalyzed by 2-methoxy-N-methylpyridinium fluoroborate, does not appear to be inhibited by diphenylpicrylhydrazyl, radical processes such as those proposed for the thermal rearrangement[84] can probably be ruled out.[92]

Summary

Estimates of the relative chemical binding energies for the isomer pairs O-methylvalerolactim (**5**)–N-methylvalerolactam (**6**) and 2-methoxypyridine (**7**)–N-methyl-2-pyridone (**8**) show that the amide is more stable than the imidate in both cases, but by a smaller amount in the heteroaromatic pair. For the vinylogous amide–imidate pair, 4-methoxypyridine (**9**)–N-methyl-4-pyridone (**10**), the difference in chemical binding energy is small.

Experimental Section[93]

O-Methylvalerolactim (5) was prepared in 10% yield by the method of Ralls[94] or by base treatment of 2-methoxy-3,4,5,6-

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[91] If only nitrogen-to-oxygen rearrangement occurred, a statistical distribution in both the catalyst and the pyridone would not be expected.

[92] Quantitative comparisons with control reactions are difficult because the reaction mixture is initially heterogeneous.

[93] The melting points were determined with a Thomas-Hoover capillary apparatus and are corrected. The boiling points are uncorrected. The infrared spectra were determined on a Perkin-Elmer Model 521 infrared spectrometer. The ultraviolet spectra were measured on a Cary Model 14M spectrophotometer and a Perkin-Elmer Model 202 ultraviolet–visible spectrophotometer using methanol solutions. The proton magnetic resonance spectra were obtained on Varian Associates A-60, A-60A, and A-56/60 spectrometers using 10–30% chloroform-*d* solutions, unless otherwise noted. Chemical shifts are reported in δ, ppm relative to the internal standard tetramethylsilane. The molecular weight mass spectra were determined by Mr. J. Wrona on an Atlas CH4 mass spectrometer using, in most cases, an ionizing potential of *ca.* 15 eV. Preparative gas phase chromatography was performed using an Aerograph Model A-90P instrument. The microanalyses were performed by Mr. Joseph Nemeth and associates. The deuterium oxide (Columbia Organic Chemicals) and methyl-d_3 iodide (Merck Sharp and Dohme) were at least 99.5% pure.

[94] J. W. Ralls, *J. Org. Chem.*, 26, 66 (1961).

tetrahydropyridinium *p*-toluenesulfonate, prepared from valerolactam and methyl *p*-toluenesulfonate; bp 48° (15 mm) [lit.[94] 50–52° (17 mm)]. The infrared spectrum (neat) showed strong absorptions at 2940, 2860, 1670, 1430, 1360, 1220, 1020, and 960 cm^{-1}. The nmr spectrum exhibited resonances at δ 3.66 (3 H, singlet, OCH_3), 3.53 (2 H, complex multiplet, CH_2CO), 2.20 (2 H, complex multiplet, CH_2N), and 1.70 ppm (4 H, complex multiplet, $-CH_2CH_2-$).

N-Methylvalerolactam (6) was prepared in 46% yield according to the method of Leonard and Barthel,[95] bp 50° (0.6 mm) [lit.[95] 102–106° (15 mm)]. The infrared spectrum (neat) included strong absorptions at 2940, 2860, 1640, 1510, 1360, 1250, 1180, 1050, and 975 cm^{-1}. The nmr spectrum showed resonances at δ 3.32 (2 H, complex multiplet, CH_2N), 2.97 (3 H, singlet, NCH_3), 2.35 (2 H, complex multiplet, CH_2CO), and 1.81 ppm (4 H, complex multiplet, $-CH_2CH_2-$).

2-Methoxypyridine (7) was purchased from the Aldrich Chemical Company and purified by preparative glpc (6 ft × 0.25 in. o.d. 20% Carbowax 20M on Chromosorb W at 120°) and distillation through a 24-in. spinning-band column; bp 141–143° (lit.[96] 142–144°); nmr (CCl_4) δ 3.88 (3 H, singlet, OCH_3), 6.71 (2 H, multiplet, *H*-3 and *H*-5), 7.47 (1 H, multiplet, *H*-4), and 8.11 ppm (1 H, multiplet, *H*-6). The infrared and ultraviolet spectra were consistent with the established structure.

N-Methyl-2-pyridone (8) was prepared in 80–90% yield by the rearrangement of 2-methoxypyridine with a catalytic amount of methyl iodide. The material was freshly purified prior to use by distillation through a 24-in., spinning-band column, bp 80–82° (0.6 mm) [lit. 122–124° (11 mm)[97] and 82° (0.3 mm)[58]]. The nmr[58] (CCl_4), infrared,[98] and ultraviolet spectra[99] were consistent with the established structure.

4-Methoxypyridine (9) was prepared by the procedure of Haitinger and Lieben[82] from 4-chloropyridinium hydrochloride (Aldrich Chemical Company) and excess sodium methoxide in methanol (74% yield); bp 80–82° (15–20 mm) [lit.[82] 190° (738 mm)]. The nmr,[100] ultraviolet,[98,101] and infrared spectra were consistent with the established structure.

N-Methyl-4-pyridone (10) was prepared as previously described.[90]

N-Methyl-2-methoxy-3,4,5,6-tetrahydropyridinium Fluoroborate. A solution of silver fluoroborate, 13.7 g (0.07 mol), N-methylvalerolactam, 7.9 g (0.07 mol), and methyl iodide, 22.8 g (0.16 mol), in 60 ml of 1,2-dichloroethane was stirred for 24 hr. Silver iodide was removed by filtration and washed with 60 ml of chloroform. The filtrate and washings were combined, dried with anhydrous magnesium sulfate, and concentrated at reduced pressure to a syrup which crystallized upon addition of cold ethyl ether. The yield of N-methyl-2-methoxy-3,4,5,6-tetrahydropyridinium fluoroborate was 12.5 g (83%). The infrared spectrum (chloroform) showed absorptions at 3020, 2950, 1665, 1480, !398. 1365 1335, 1305, 1275, 1040–1100 (broad), 960, and 845 cm^{-1}. The nmr spectrum (acetone-d_6) showed resonances at δ 4.31 (3 H, singlet, OCH_3), 3.77 (2 H, complex multiplet, CH_2N), 3.30 (3 H, singlet, NCH_3), 3.03 (2 H, complex multiplet, CH_2CO), and 2.00 ppm (4 H, complex multiplet, $-CH_2CH_2-$). An analytical sample of this hygroscopic salt. mp 141–143° (sealed tube), was obtained by recrystallization from ethanol–ethyl acetate.

Anal. Calcd for $C_7H_{14}NOBF_4$: C, 39.07; H, 6.51; N, 6.51. Found: C, 39.03; H, 6.57; N, 6.22.

The same compound was prepared in 25% yield by a similar methylation of O-methylvalerolactim. Identity was established by mixture melting point (137–141°) and infrared and nmr spectral criteria.

2-Methoxy-N-methylpyridinium fluoroborate (26) was prepared from N-methyl-2-pyridone (**8**) and 2-methoxypyridine (**7**) by the procedure previously described for 4-methoxy-N-methylpyridinium fluoroborate.[90] Recrystallization from absolute ethanol–ethyl ether gave the fluoroborate salt (30–50%), mp 81–83°; ultraviolet (methylene chloride) λ_{max} 282 mμ (ϵ 7600); infrared (Nujol) absorptions at 1638 1589, 1515, 1310 (broad), 1050 (broad). and 780 cm^{-1}; nmr (acetone-d_6), δ 4.20 (3 H, singlet, NCH_3), 4.44 (3 H, singlet, OCH_3), 7.80 (2 H, multiplet, *H*-3 and *H*-5), and 8.69 ppm (2 H, multiplet, *H*-4 and *H*-6). The assignment of the NCH_3 and OCH_3 resonances at δ 4.20 and 4.44. respectively, was based on chemical shift comparisons with the OCD_3 derivative (*vide infra*). The products from the reaction of the pyridine or pyridone were identical as shown by melting point and infrared criteria.

Anal. Calcd for $C_7H_{10}NOBF_4$: C. 39.86; H, 4.74; N, 6.65. Found: C, 39.67; H. 4.82; N 6.53.

4-Methoxy-N-methylpyridinium fluoroborate was prepared as previously described.[88]

Deuteration of N-Methyl-2-pyridone. A solution of 2.41 g of N-methyl-2-pyridone (**8**) in 25 ml of 1.5 *M* sodium deuterioxide was heated at reflux for 1–2 weeks. After saturation with sodium chloride, the reaction mixture was extracted with methylene chloride. The extracts were dried over magnesium sulfate, concentrated, and distilled to give 1.61 g (67%) of deuterated N-methyl-2-pyridone, bp 80° (0.4 mm); infrared (neat) absorptions at 1649, 1570, 1530, 1400, 1160, and 1138 cm^{-1}. A molecular weight mass spectrum indicated 1.6 ± 1% C_6H_7NO, 90 ± 1% C_6H_6DNO, and 8.4 ± 1% $C_6H_5D_2NO$. The nmr spectrum (neat) consisted of a singlet at δ 3.62 (3 H, NCH_3) and multiplets. approximated as an AMX pattern. at 6.25 (1 H, *H*-5, $J_{45} = 6.5$ Hz, $J_{35} = 1.5$ Hz), 6.57 (1 H, *H*-3, $J_{34} = 9$ Hz). and 7.50 ppm (1 H *H*-4).[102] Integration of the expanded ring proton region indicated less than 5% protium in the 6 position. The position of the second deuterium could not be determined from the spectrum.

Anal. Calcd for C_6H_6DNO: C 64.98; H, 6.36; N. 12.72. Found: C. 65.23; H, 6.48; N. 12.50.

Bromination of 0.210 g of the dideuterated pyridone in glacial acetic acid gave a 23% yield of 3,5-dibromo-N-methyl-4-pyridone-6-*d*, mp 181–183° (lit.[103] melting point of undeuterated, 181–183°); infrared ($CHCl_3$) absorptions at 1649, 1570, 1530, 1435, 1400, 1160, and 1138 cm^{-1}; nmr, δ 3.60 (3 H, singlet, NCH_3) and 7.78 ppm (1 H, singlet, *H*-4). A molecular weight mass spectrum indicated the presence of 4 ± 1% $C_6H_5Br_2NO$ and 96 ± 1% $C_6H_4DBr_2NO$. This result establishes that the second deuterium atom must have been at C-3 or C-5.

2-Methoxy-N-methylpyridinium-6-*d* Fluoroborate (21) (90%) and 2-Methoxy-N-methylpyridinium-3(5)-6-d_2 Fluoroborate (8%). This mixture was prepared from the mixture of deuterated N-methyl-2-pyridones, described above, in a manner similar to the preparation of **26**; mp 81–83°; infrared (Nujol) absorptions at 1629, 1580, 1500, 1292. 1050 (broad), and 820 cm^{-1}; nmr (acetone-d_6), two singlets at δ 4.15 (3 H, NCH_3) and 4.37 (3 H, OCH_3) and three multiplets, approximated as an AMX pattern, at δ 7.59 (1 H, *H*-5, $J_{45} = 7.5$ Hz, $J_{35} = <2$ Hz), 7.79 (1 H, *H*-3, $J_{34} = 9$ Hz), and 8.54 ppm (1 H, *H*-4).

Anal. Calcd for $C_7H_9DNOBF_4$: C. 39.67; H, 4.72; N, 6.61. Found: C, 39.55; H, 4.78; N, 6.71.

2-Methoxy-d_3-N-methylpyridinium fluoroborate (22) was prepared in 76% yield in a manner similar to the preparation of **26** using N-methyl-2-pyridone (1.90 mmol) and 99.5% methyl-d_3 iodide (2.7 mmol), mp 80–82°; nmr (acetone-d_6), δ 4.25 (3 H, singlet, NCH_3), 7.84 (2 H, multiplet, *H*-3 and *H*-5), and 8.75 ppm (2 H, multiplet. *H*-4 and *H*-6).

Anal. Calcd for $C_7H_7D_3NOBF_4$: C, 39.28; H, 4.72; N, 6.65. Found: C, 39.44; H, 4.97; N. 6.42.

Deuteration of N-Methyl-4-pyridone. The reaction, carried out as previously reported[90] except that a reaction time of 12 days was used, provided primarily N-methyl-4-pyridone-2,6-d_2 which was 96 ± 5% deuterated as shown by nmr criteria. A molecular weight mass spectrum indicated 6 ± 1% C_6H_6DNO, 89.9 ± 2% $C_6H_5D_2NO$, and 4.0 ± 2% $C_6H_4D_3NO$. The third deuterium atom was shown to occupy the 3 position by preparation of the 3,5-dibromo derivative from this sample. Mass spectral analysis indicated 6.5 ± 1% $C_6H_4DBr_2NO$ and 93.5 ± 1% $C_6H_3D_2Br_2NO$.

4-Methoxy-N-methylpyridinium-2,6-d_2 (23) (90%), 4-Methoxy-N-methylpyridinium-2-*d* (60%), and 4-Methoxy-N-methylpyridinium-2,3,6-d_3 Fluoroborates (4%). Alkylations of the deuterated pyridones by the procedure reported for **26** gave fluoroborate salts, mp 55–57°; infrared (Nujol) absorptions at 1620, 1560, 1320, 1285, 1050 (broad). 760, and 710 cm^{-1}; nmr (acetone-d_6), δ 4.20 (singlet, OCH_3). 4.37 (singlet, NCH_3), and 7.63 ppm (singlet, *H*-3 and *H*-5).

4-Methoxy-d_3-N-methylpyridinium fluoroborate (24) was prepared in 76% yield in a manner similar to the preparation of **26** using

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(101) S. F. Mason, *J. Chem. Soc.*, 1253 (1949).

(102) For comparison, see C. L. Bell, R. S. Egan, and L. Bauer, *J. Heterocyclic Chem.*, 2, 420 (1965).

(103) M. L. Miles, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, 30, 1007 (1965).

N-methyl-4-pyridone (1.9 mmol) and 99.5% methyl-d_3 iodide (2.7 mmol), mp 52–55°; infrared (Nujol) absorptions at 1575, 1520, 1050 (broad), 845, and 715 cm^{-1}; nmr (acetone-d_6), δ 4.32 (3 H, singlet, NC*H*$_3$), 7.52 (2 H, AA′BB′ multiplet, *H*-3 and *H*-5), and 8.67 ppm (2 H, AA′BB′ multiplet, *H*-4 and *H*-6).

Anal. Calcd for $C_6H_7D_3NOBF_4$: C, 39.28; H, 4.72; N, 6.55. Found: C, 39.49; H, 5.06; N, 6.41.

2,6-Diphenyl-4-pyridone was prepared by the procedure of Hauser and coworkers[104] from 1,5-diphenyl-1,3,5-pentanetrione and ammonia, mp 177–180° (lit.[101,104] 175–179°). The nmr and infrared spectra were consistent with the established structure.

2,6-Diphenyl-4-chloropyridine was prepared by the reaction of 2,6-diphenyl-4-pyridone with phosphorus pentachloride and phosphorus oxychloride according to the procedure of Petrenko-Kritschenko and Schottle,[105] mp 75–78° (lit.[105] 72°). The nmr spectrum was consistent with the established structure.

2,6-Diphenyl-4-methoxypyridine (11). A solution containing 7.0 g of 2,6-diphenyl-4-chloropyridine and 14 g of sodium methoxide in 150 ml of absolute methanol was heated at reflux for 240 hr. The mixture was then poured into ice water and the aqueous solution extracted several times with ethyl ether. The extracts were combined, dried, and concentrated to give 6.4 g of impure **11**. Several recrystallizations from absolute methanol and 95% ethanol gave 3.2 g (44%) of 2,6-diphenyl-4-methoxypyridine (**11**), mp 79–81°; ultraviolet λ_{max} 248 mμ (ε 30,900), shoulder at 282 mμ (ε 10,290); infrared absorptions ($CHCl_3$) at 1595, 1580, 1565, 1498, 1466, 1425, 1405, 1362, 1080, 1070, 1045, 1028, 895, and 692 cm^{-1}; nmr, δ 3.85 (3 H, singlet, OC*H*$_3$), 7.14 (2 H, singlet, *H*-3 and *H*-5), 7.38 (6 H, multiplet, Ar*H*), and 8.04 ppm (4 H, multiplet, Ar*H*).

Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.59; H, 5.88; N, 5.34.

2,6-Diphenyl-N-methyl-4-pyridone (12) was prepared by a modification of earlier procedures[100,101] by heating 2,6-diphenyl-4-pyrone in 40% aqueous methylamine solution for 72 hr at reflux. The orange solid collected upon concentration was recrystallized once from benzene–hexane, chromatographed on alumina with methylene chloride elution, and recrystallized three times from benzene–hexane to give **12** (34%); mp 188–190° (lit.[100,101] 185–188°); nmr, δ 3.17[106] (singlet, NC*H*$_3$), 6.40 (singlet, *H*-3 and *H*-5), and 7.49 ppm (singlet, Ar*H*). The ultraviolet and infrared spectra were consistent with the established structures.

Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.52; H, 5.75; N, 5.25.

2,6-Diphenyl-4-methoxy-N-methylpyridinium Fluoroborate. This compound was prepared from 2,6-diphenyl-N-methyl-4-pyridone by methods used for **26**. The white solid was recrystallized twice from ethyl acetate–ethyl ether to give a 40–60% yield of the fluoroborate salt, mp 115–117°; ultraviolet (methanol, λ_{max} 240 mμ (ε 2180) and 282 mμ (ε 954); infrared ($CHCl_3$) absorptions at 1629, 1575, 1483, 1417, and 1050 cm^{-1} (BF_4^-, broad); nmr, δ 3.67 (3 H, NC*H*$_3$), 4.09 (3 H, OC*H*$_3$), 7.21 (2 H, *H*-3 and *H*-5), and 7.65 ppm (10 H, Ar*H*).

After heating at 130° for 144 hr in a sealed tube, a white crystalline material, mp 155–156°, was quantitatively recovered. The nmr and infrared spectra of this compound were identical with those of the lower melting material. Recrystallization from ethyl acetate–methylene chloride–ethyl ether gave no change in the melting point. Seeding a solution of the lower melting form with the higher melting form gave the compound which melted at 155–156°.

Anal. Calcd for $C_{19}H_{18}NOBF_4$: C, 62.83; H, 4.99; N, 3.86. Found: C, 62.83; H, 5.09; N, 3.62.

Attempted preparation of 2,6-diphenyl-4-methoxy-N-methylpyridinium fluoroborate from 2,6-diphenyl-4-methoxypyridine by these procedures gave only 2,6-diphenyl-4-methoxypyridinium fluoroborate.

4-Methoxy-*d*$_3$-2,6-diphenyl-N-methylpyridinium fluoroborate (25) was prepared in 90% yield from 0.321 g (1.22 mmol) of 2,6-diphenyl-N-methyl-4-pyridone, 0.287 g (1.48 mmol) of silver fluoroborate, and 0.15–0.25 ml of methyl-d_3 iodide, mp 142–147°; infrared ($CHCl_3$) absorptions at 1629, 1603, 1579, 1499, 1471, 1445, 1430, 1366, and 1050 cm^{-1}; nmr, δ 3.70 (3 H, NC*H*$_3$), 7.25 (2 H, *H*-3 and *H*-5), and 7.70 (10 H, ArH). Recrystallization of 0.038 g from ethyl acetate–ethanol–ethyl ether gave 0.029 g of the analytical sample, mp 150–152°.

Anal. Calcd for $C_{19}H_{15}D_3NOBF_4$: C, 62.31; H, 4.96; N, 3.83. Found: C, 62.22; H, 5.00; N, 3.67.

Equilibration of O-Methylvalerolactim (5) and N-Methylvalerolactam (6). The reactions were carried out in sealed tubes degassed by a freeze–pump–thaw technique. A sealed tube containing 0.138 g of O-methylvalerolactim (**5**) and 0.029 g of N-methyl-2-methoxy-3,4,5,6-tetrahydropyridinium fluoroborate was heated at 130° for 2 hr. The catalyst, 0.019 g (66%), was precipitated by addition of 8.0 ml of ethyl ether to a solution of the product mixture in 1.2 ml of methylene chloride. This material was identified as N-methyl-2-methoxy-3,4,5,6-tetrahydropyridinium fluoroborate by infrared and nmr criteria. In other runs using carbon disulfide in place of methylene chloride, the catalyst was recovered in 80–85% yields. Glpc analysis of the solution using phenyl ether as an internal standard indicated a 104 ± 5% yield of N-methylvalerolactam (**6**). This product was collected by preparative glpc and identified by infrared and nmr spectral analyses. In other experiments, the equilibration was followed by nmr spectroscopy and all resonances could be accounted for by the presence of only **5**, **6**, and catalyst. The reactants and products were shown to be stable, by themselves, under the reaction conditions.

Attempted Detection of 5 at Equilibrium by Glpc. Detection of the minor isomer **5** was attempted by glpc using an Aerograph Model A-600-B gas chromatograph equipped with a hydrogen flame ionization detector and a 2 ft × $^1/_8$ in. o.d. column of 20% Carbowax 20M on base-washed Chromosorb W at an oven temperature of 130°. Heating 0.087 g of **5** and 0.022 g of the catalyst for 3 hr at 130° gave a mixture which contained less than 5 × 10^{-4} parts of **5** relative to **6**.

Equilibration of 2-Methoxypyridine (7) and N-Methyl-2-pyridone (8). Equilibrations and controls were performed essentially as described above for **5**. A mixture of 0.230 g of **7** and 0.036 g of 2-methoxy-N-methylpyridinium fluoroborate, heated at 130° for 3.5 hr, gave 0.031 g (86%) of impure 2-methoxy-N-methylpyridinium fluoroborate, mp 54–64°, as shown by infrared and nmr criteria, and 0.219 g (95%) of **8**, as shown by infrared, ultraviolet, and nmr criteria. Similar results were obtained beginning with N-methyl-2-pyridone (92% yield) and the catalyst (93% yield). The reactants and products were stable, by themselves, under the reaction conditions. Degassed samples of 2-methoxypyridine were stable at 185 and 230° for 20 hr.

Attempted Detection of 7 at Equilibrium by Glpc. Detection of the minor isomer **7** was attempted as for **5**. Separate mixtures of 0.188 g of N-methyl-2-pyridone and 0.163 g of 2-methoxypyridine with 0.022 and 0.023 g of catalyst, respectively, were heated at 130° for 3 hr. No 2-methoxypyridine (**7**) was detected in the product and a detection limit for **7** of 1 × 10^{-5} relative to **8** was established by the use of standard solutions.

Equilibration of 4-Methoxypyridine (9) and N-Methyl-4-pyridone (10). In a manner analogous to the above equilibrations, 0.204 g of 4-methoxypyridine and 0.039 g of 4-methoxy-N-methylpyridinium fluoroborate were heated at 130° for 3.5 hr. Impure 4-methoxy-N-methylpyridinium fluoroborate, 0.037 g (97%), was isolated (semisolid) and identified by infrared and ultraviolet analyses. A deliquescent solid, mp 88–92°, identified as N-methyl-4-pyridone by infrared, ultraviolet, and nmr criteria, was isolated in 101 ± 5% yield (0.207 g). Similar results were obtained when N-methyl-4-pyridone (104% yield) was treated with the catalyst (80% isolated yield) under the same conditions.

4-Methoxypyridine was converted upon heating at 130° for 20 hr to a mixture containing 3% N-methyl-4-pyridone as shown by infrared and ultraviolet spectral analyses. The importance of using freshly purified material was illustrated by the fact that samples of **9**, which had been purified several months earlier, rearranged to mixtures containing 8 and 29% of the pyridone after heating at 130° for 5 and 24 hr, respectively. The catalyst and **10** were stable under reaction conditions.

Attempted Detection of 4-Methoxypyridine at Equilibrium by Glpc. When a 1.5 ft × $^1/_8$ in. o.d. 20% Carbowax 20M on Chromosorb W column was used, the smallest amount of **9** which could be detected was 1 × 10^{-4}, relative to **10**. Separate equilibration mixtures containing 200 mg of **9** and **10** with 32 mg of catalyst were heated at 130° for 18 hr and no 4-methoxypyridine was detected in either reaction mixture.

Equilibration of 2,6-Diphenyl-4-methoxypyridine (11) and 2,6-Diphenyl-N-methyl-4-pyridione (12). The reactants and catalyst, 2,6-diphenyl-4-methoxy-N-methylpyridinium fluoroborate, were sealed in a Pyrex tube under a nitrogen atmosphere and heated for

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(104) R. J. Light and C. R. Hauser, *J. Org. Cnem.*, 25, 538 (1960).

(105) P. Petrenko-Kritschenko and J. Schottle, *Ber.*, 42, 2020 (1909).

(106) The upfield shift of the N-methyl resonance relative to the corresponding signal in N-methyl-4-pyridone (δ 3.71) suggests that the favored conformation of the phenyl groups is perpendicular to the plane of the pyridone ring. See T. H. Regan and J. B. Miller, *J. Org. Chem.*, 32, 592 (1967), for discussion of a similar system.

the times indicated in Table VI. After reaction, the ratio of **12** to **11** was determined by nmr spectroscopy from integration areas of the N- and O-methyl proton signals on a 100-Hz scan of that region. In separate experiments at 162°, **11** and **12** were recovered unchanged after 138 hr, and the catalyst was isolated intact after 67 hr. Partial decomposition (*ca.* 25%) of the catalyst did occur at 162° in the equilibration mixtures. The catalyst was almost completely destroyed at 200° and none could be detected in the equilibration mixture at 250°. Although 2,6-diphenyl-4-methoxypyridine was stable at 200° for 192 hr, 2,6-diphenyl-N-methyl-4-pyridone isomerized slowly to an equilibrium mixture at 200°. The "thermal" rearranegment at 250°, beginning with pure **11**, gave a ratio of **12**:**11** of only 0.08 after heating for 72 hr, but a catalytic isomerization (with catalyst decomposition) gave a ratio of **12**:**11** of 0.24 after the same time. The thermal rearrangement of **12** gave equilibrium ratios of *ca.* 0.26 after 50 hr. The presence of each isomer in the equilibrium mixture was established by thin-layer chromatograms of the reaction products, which were identical with those of authentic mixtures. The nmr and infrared spectra of the product mixture showed signals for only **11**, **12**, and the catalyst.

Table VI. Equilibrium Constants at Various Temperatures for the Catalyzed Equilibrations of **11** and **12**

Temp, °C	Reactants, g **11**	 **12**	 2,6-Diphenyl-4-methoxypyridinium fluoroborate	Time, hr	K = **12/11**
130	0.111		0.026	360	0.19
	0.103		0.027	264	0.18
	0.192		0.053	360	0.19
				Av	0.19
162	0.101		0.024	66	0.22
	0.104		0.023	94	0.20
	0.119		0.022	138	0.22
	0.100	0.032	0.032	49	0.27[a]
	0.102	0.032	0.032	49	0.24[a]
				Av	0.23
200[a]	0.100		0.025	144	0.18
	0.130		0.028	144	0.24
	0.123		0.022	192	0.19
		0.138	0.031	144	0.21
		0.124	0.029	144	0.20
		0.123	0.030	192	0.22
				Av	0.21

[a] Catalyst partially or completely decomposed.

The results of the catalyzed isomerizations at 130 ± 1, 162 ± 1, and 200 ± 1° are shown in Table VI. A plot of ln K *vs.* $1/T$ gave $\Delta H_1°$, 1.1 ± 1 kcal/mol, and $\Delta S_1°$, 0.6 ± 1.4 Gibbs. The thermal rearrangement at 250° was included in this plot, and the errors were estimated from lines of maximum and minimum slope through the point from 130° and any other point. Larger errors would not be introduced by using other primary points, except for a line between the points at 162 and 200°, which would ignore the values at 130 and 250°.

Isolation of the Diphenyl Isomers from an Equilibration Mixture. A mixture of 0.111 g of **11** and 0.026 g of **12** was heated at 130° for 360 hr, and the subsequent nmr analysis showed a ratio of **12** to **11** of 0.19. The nmr sample was then concentrated to give 0.138 g of a viscous oil which, by tlc (9:1 acetone–methanol), showed the presence of **11**, **12**, and 2,6-diphenyl-4-methoxy-N-methylpyridinium fluoroborate. Leaching the oil with ethyl ether gave, upon evaporation of the solvent, 0.085 g of **11**, as shown by its melting point and infrared spectrum.

The ether-insoluble residue was chromatographed on 4 g of alumina and eluted with 100 ml of methylene chloride in 10-ml fractions. The first fraction gave another 0.010 g of **11**, mp 67–74°. The next four fractions gave 0.019 g of the catalyst, as shown by melting point (154–156°), mixture melting point (154–156°), and infrared criteria. Elution with 9:1 methylene chloride–methanol gave a mixture, in the first fractions, which was separated by extensive leaching with ethyl ether into another 0.006 g of **11** and 0.017 g of **12**, as shown by melting point (183–189°), mixture melting point (186–189°), and infrared and mass spectral criteria. A total of 0.095 g of **11**, 0.107 g of catalyst, and 0.025 g of **12** was isolated; these results were consistent with the equilibrium constant obtained by nmr.

Calorimetric Determination of Liquid-Phase Heats of Equilibration for the Imidate–Amide Pairs at 130°. A calorimeter of the type described by Arnett, Bentrude, Burke, and Duggleby[20] was modified for enthalpy measurements at 130°. The calorimeter chamber is a 300-ml dewar flask fitted with a Teflon head. The head is equipped with a heater, thermistor, stirrer, thermometer, and plunger. The reaction vessel consists of a 10-ml Pyrex bottle with a threaded neck. A threaded brass cap, which holds the plunger and contains a silicone rubber gasket, is used to tightly seal the reaction vessel. The plunger shaft is fitted with a rubber O-ring and projects upward through a brass insert in the Teflon head. The brass cap screws into the brass insert, forcing the O-ring to tighten firmly around the plunger shaft. The reaction vessel is suspended on the underside of the head for a run. The dimensions of the head and vessel are such that the vessel is immersed in the chamber fluid (Dow Corning "200 fluid," 50 cSt) when the head is in place. For operations at 130°, the calorimeter chamber, with the head in place, is installed in a large, insulated electric oven. The oven temperature is maintained at 130–132° during a measurement.

In the initial runs, the calibration heater power supply and the method of measuring the calibration current were those described by Arnett and coworkers,[20] except for the absence of a base-line compensator. A standard resistance of 5.92 ± 0.03 ohms and a heater resistance of 61.55 ± 0.05 ohms were used. In later runs, a stabilized dc power supply, equipped with a potentiometer and a four-lead heater (78.8 ± 0.05 ohms), was used for calibration.[107] The output of this dc supply was variable such that the potential drop across the heater resistance could be stepped in 10.0-mV increments to any value between 0.00 and 9.99 V. The accuracy of the potentiometer was established to be ±0.02 V by comparing potentiometer readings with those of a differential voltmeter (John Fluke Manufacturing Co., Inc., Model 830 B) in a testing configuration where these instruments, the dc supply output, and a dummy load (78 ohms) were elements in a parallel network. In the calorimetric experiments, the heat development rates and calibration intervals were chosen so that the calibration traces on the recorder chart corresponded in both duration and temperature increase with the reaction traces. The average deviation of calibrations before and after each reaction was less than 2%. The accuracy of each electrical calibration system was checked at 25° by measuring the heat of reaction, ΔH_{298}, for the process

$$\mathrm{NaOH \cdot 100H_2O + HCl \cdot 10H_2O = H_2O + NaCl \cdot 110H_2O}$$

which was calculated to be 14.8 kcal/mol.[108] The average result with the fixed voltage power supply was 15.0 ± 0.6 kcal/mol for three determinations. With the variable-voltage power supply, the average for three determinations was 14.8 ± 0.5 kcal/mol. For these experiments, *ca.* 0.55 ml of 5.1 N HCl was used to neutralize 5.00 ml of 0.500 N NaOH. It was established that the resistance of the calibration heater is the same at 25 and 130° in each case.

The following description outlines the general procedure used for determinations of heats of reaction at 130°. A weighed sample of imidate and a sealed glass bulb containing the catalyst were placed in the reaction vessel. The plunger was carefully positioned to hold the catalyst bulb upright and the vessel was sealed by firmly tightening the brass cap. The vessel was then suspended from the Teflon head, which was lowered into the chamber in the oven at 130°. The fluid in the chamber, which had been preheated to *ca.* 145°, cooled to 130–132° upon thermal equilibration of the entire system. Two to five electrical calibrations were performed over the temperature range anticipated for the isomerization. After cooling the chamber and its contents to the original temperature, the catalyst bulb was broken with the plunger and the reaction mixture stirred periodically. Control experiments indicated no measurable heat effect due to stirring. After *ca.* 1 hr, no further heat evolution was observed. The chamber and its contents were again recooled to the original temperature and the electrical calibrations repeated. The average of the calibrations was used to calculate $\Delta H_1°$ (130°). Nmr analysis of the product mixture showed complete conversion to the amide in all cases except one (Table IX).

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(107) We are grateful to R. Anderson and associates for the design and assembly of this equipment.

(108) "Selected Values of Chemical Thermodynamic Properties," National Bureau of Standards Circular 500, U. S. Government Printing Office, Washington, D.C., 1952, pp 22–24, 448–451.

Side reactions involving the imidates, amides, or catalysts were not detected by ultraviolet, infrared, or nuclear magnetic resonance spectroscopy, by thin layer chromatography, or by glpc. An estimate of the sensitivity of the measured heat effects to possible side reactions may be made using the first entries in Tables VII, VIII, and IX and the material balances from the isolation experiments (*vide supra*). The amounts of catalysts unaccounted for after isolation from equilibrations of **5**–**6**, **7**–**8**, and **9**–**10** were, respectively, 20, 15, and 5%. If these amounts of catalysts were totally consumed in side reactions which produced 5% of the measured heat effect in each case, then these reactions would have involved enthalpy changes of respectively 88, 87, and 106 kcal/mol. The unrealistically large magnitude of these values and the satisfactory precision of the calorimetric measurements using varying catalyst levels suggest that side reactions of the catalysts do not contribute significantly to the measured enthalpy changes. The isolated yields of amides are high (100 ± 5%) and it seems reasonable that these yields should be less than actual reaction yields. In view of the lack of evidence for spurious reaction products in the equilibration experiments and the good material balances in these experiments, it is clear that systematic errors due to heat effects of side reactions will be less than the random errors in the calorimetric experiments.

Table VII. Calorimetrically Determined $\Delta H_{\mathrm{i}}^\circ$ between O-Methylvalerolactim (**5**) and N-Methylvalerolactam (**6**) at 130°

5	Initial moles × 10^2 of N-methyl-2-methoxy-3,4,5,6-tetrahydropyridinium fluoroborate	Q_e, cal/mm	Obsd defl, mm	$\Delta H_{\mathrm{i}}^\circ$, kcal/mol
0.798	0.038	4.26	31.5	−16.8
0.811	0.037	4.24	34.0	−17.8
0.865	0.045	4.03	36.5	17.0
			Av	−17.2

Table VIII. Calorimetrically Determined $\Delta H_{\mathrm{i}}^\circ$ between 2-Methoxypyridine (**7**) and N-Methyl-4-Pyridone (**8**) at 130°

7	**8**	Initial moles × 10^2 of 2-methoxy-N-methylpyridinium fluoroborate	Q_e, cal/mm	Obsd defl, mm	$\Delta H_{\mathrm{i}}^\circ$, kcal/mol
7.49		0.366	8.67	110	−12.7
7.68		0.405	7.88	105	−10.8
1.91		0.100	1.75	140	−12.8
1.90		0.096	4.38	55	−12.7
1.19		0.099	4.24	51	−11.8
1.98	2.06	0.190	4.25	65	−13.9
				Av	−12.4

Table IX. Calorimetrically Determined $\Delta H_{\mathrm{i}}^\circ$ between 4-Methoxypyridine (**9**) and N-Methyl-4-Pyridone (**10**) at 130°

9	**10**	Initial moles × 10^2 of 4-methoxy-N-methylpyridinium fluoroborate	Q_e, cal/mm	Obsd defl, mm	$\Delta H_{\mathrm{i}}^\circ$, kcal/mol
5.15		0.309	7.46	45.5	−8.7[a]
4.87		0.468	4.20	95	−8.2
2.86	0.99	0.388	4.05	68	−9.6
				Av	−8.8

[a] Corrected to include 0.016 mol of unreacted **9**.

Control experiments demonstrated that no leakage or isomerization of the imidates occurred while the calorimeter chamber was attaining thermal stability. No heats of solution of the catalysts in the amides were detected. The amounts of reactants, the recorder calibration, Q_e (cal/mm), the observed recorder pen deflection (mm) during the reaction, each calculated $\Delta H_{\mathrm{i}}^\circ$ (130°) (kcal/mol), and the average values of $\Delta H_{\mathrm{i}}^\circ$ (130°) are listed in Tables VII, VIII, and IX. The average deviations are *ca.* 6% and the estimated error is ±0.5 kcal/mol.

Isotope Scrambling in the Catalytic Isomerizations of 2-Methoxypyridine-N-methyl-2-pyridone and 4-Methoxypyridine-N-methyl-4-pyridone. A mixture containing *ca.* 1.0 mmol of methoxypyridine or methylpyridone and 0.3 mmol of the appropriate labeled catalyst was heated in a sealed tube for the time indicated and the products were isolated in 90–100% yields by the techniques described for the equilibrations of the unlabeled compounds. Table V shows the over-all deuterium content in the recovered pyridones and catalysts as determined by nmr, the deuterium incorporation in the recovered pyridones as determined by mass spectrometry, and the deuterium incorporation in the pyridones expected for complete scrambling. Both analytical methods gave results consistent with complete isotope scrambling.

Isotope Scrambling in the Catalyzed Equilibrations of 2,6-Diphenyl-4-methoxypyridine and 2,6-Diphenyl-N-methyl-4-pyridone. A mixture of 0.101 g (0.388 mmol) of **11**, 0.20 g (0.076 mmol) of **12**, and 0.056 g (0.154 mmol) of **25** was heated at 130° for 348 hr, and the products were analyzed by nmr. The resonances ascribed to the O- and N-methyl protons in the nmr spectrum of the catalyst exhibited equal areas. The values expected for total scrambling are 80% CH_3 and 20% CD_3 in each of these positions. The pyridine **11** and pyridone **12** were isolated and shown by mass spectrometry to contain 84 + 2% OCH_3 and 16 ± 2% OCD_3 and 80 ± 2% NCH_3 and 20 ± 2% NCD_3, respectively. These values were consistent with the predicted values.

Attempted Diphenylpicrylhydrazyl Inhibition of the Catalyzed Isomerization of 2-Methoxypyridine to N-Methyl-2-pyridone. A solution of 0.024 g (6.14 × 10^{-5} mol) of commercial diphenylpicrylhydrazyl (DPPH) in 1.009 g of 2-methoxypyridine was used in the following experiments. A sample of 0.166 g was diluted to 100 ml with absolute methanol. Visible spectral analysis of a 25-ml aliquot, which had been diluted to 50 ml, gave ϵ for DPPH 12,930 at 520 mμ. Analysis of a 0.200-g sample which had been heated for 12 min at 130° indicated no isomerization to **8** and that 83% of the initial DPPH was present. Two equilibration mixtures prepared from 204 mg and 0.181 g of the pyridine–DPPH solution and 0.0612 g of 2-methoxy-N-methoxy-N-methylpyridinium fluoroborate were heated at 130° for 12 min. The former sample contained 48% of the initial DPPH and substantial amounts of N-methyl-2-pyridone as determined by visible and ultraviolet spectral criteria, respectively. Glpc analysis of the other equilibration mixture indicated 80% conversion of **7** to **8**, which is consistent with the conversion expected using approximate rates for this isomerization.

Estimated Heats of Vaporization at 130°. The heats of vaporization of **5**, **6**, **7**, **8**, **9**, and **10** at 130° were estimated by three methods. The results are listed in Table X. The Clausius–Clapeyron

Table X. Estimated Heats of Vaporization at 130° (kcal/mol)

Compound	Clausius–Clapeyron calcn	Othmer plot	Watson correl
O-Methylvalerolactim (**5**)	9.7	9.7	9.3
N-Methylvalerolactam (**6**)	13.0	13.6	12.9
2-Methoxypyridine (**7**)	9.7	9.5	9.3
N-Methyl-2-pyridone (**8**)	14.1	14.5	13.8
4-Methoxypyridine (**9**)	11.4	12.0	11.2
N-Methyl-4-pyridone (**10**)	20.0	*a*	18.8

[a] See ref 16.

equation[109] was solved using nonreduced Cox-Antoine vapor pressure data[110] for each liquid at 129 and 131°. The Watson correlations[111] required the critical temperatures of the compounds and their heats of vaporization at the normal boiling points. The former were estimated by the Lydersen method,[112] and the latter calculated using the Fishtine-Kistiakowsky equation.[113] Othmer plots[114,115] for compounds **5**, **6**, **7**, **8**, and **9** were linear, and N-methylacetanilide was used as the reference liquid.[116] The vapor pressure data for the imidates and amides were obtained from a nomograph,[117] and published data were available for the reference liquid.[118] The heat of vaporization of N-methylacetanilide at 130° (14.2 kcal/mol) was calculated using the Clausius-Clapeyron equation as described above; a Watson correlation gave good agreement (14.3 kcal/mol).

The accuracy of the estimation methods in the present applications is unknown, but an uncertainty of ±0.75 kcal/mol for the values in Table X seems reasonable. The agreement among these three sets of values might be misleading because the methods are not strictly independent. The values from the Clausius-Clapeyron calculations were used in the solution of the isothermal energy cycles (Table I).

Acknowledgment. We are grateful to the U. S. Public Health Service (Grant GM-12595) for support of this work.

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(109) I. M. Klotz, "Chemical Thermodynamics," W. A. Benjamin, Inc., New York, N. Y., 1964, p 174.

(110) Reference 24a, pp 117-120; the vapor pressures of the liquids at 130°, required for calculation of the standard free energy term limits (Table I), were computed by this method.

(111) K. M. Watson, *Ind. Eng. Chem.*, **35**, 398 (1943).

(112) Reference 24a, pp 8-10.

(113) See ref 24c.

(114) D. F. Othmer, *Ind. Eng. Chem.*, **32**, 841 (1940).

(115) Reference 24b, pp 301, 341, and references cited therein.

(116) The lack of reliable vapor pressure data for 10 precluded the use of the Othmer method for this compound.

(117) S. B. Lippincott and M. M. Lyman, *Ind. Eng. Chem.*, **38**, 320 (1946).

(118) Reference 24b, p 160.

Stereochemistry of Reductive Elimination by Chromium(II) Complexes

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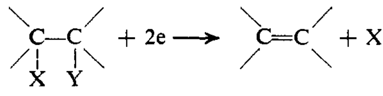
Abstract: The reductive elimination of *erythro*- and *threo*-2-bromo-3-butyl derivatives of hydroxide, acetate, *p*-tosylate, chloride, and bromide with Cr^{II} was carried out quantitatively under a variety of conditions. With the exception of vicinal dibromides, all of these derivatives gave the same mixture of *cis*- and *trans*-butene-2 from each epimeric pair. In the initial and rate-determining step, an equilibrated free radical is postulated as a common intermediate from each *erythro*- and *threo*-3-substituted butyl bromide by reaction with Cr^{II}. Stereospecificity in reductive elimination of *vicinal* dibromides is attributed to a bromine-bridged radical formed by neighboring group participation in the homolytic removal (ligand transfer) of bromine by Cr^{II}. This is in accord with previous measurements of enhanced rates of reduction of 1,2-dibromides by Cr^{II}. Stereospecific *trans* elimination of vicinal bromines by Cr^{II} can be induced by dimethyl sulfoxide or pyridine as solvent or by the use of excess ethylenediamine as ligand. The bromine-bridged radical is opened stereospecifically by a second Cr^{II} to yield a β-bromoalkylchromium intermediate. Factors which influence *trans* elimination from the latter are discussed. Epoxides also yield alkenes quantitatively with Cr^{II} but the reduction is not stereospecific. Episulfides showed partial stereoselectivity; a more labile sulfur-bridged radical is postulated as an intermediate.

A number of reducing agents are available for reductive elimination of vicinal dihalides to alkenes (eq 1a, X, Y = halogen). Most of these reagents, however,



(1a)

are ineffective or react only slowly with the analogous β-substituted alkyl halides (eq 1a, X = halogen; Y = HO, AcO, H_2N, etc.). Recently we found that ethylenediaminechrominum(II) reagent is an exceedingly efficient reducing agent, which is particularly effective with organic halides.[1] This versatile reagent will reduce a variety of vicinal dihalides, 2-substituted alkyl halides, and epoxides and episulfides to the corresponding alkene at room temperatures.[2] The reactions afford alkene in high yield and, therefore, offer a potentially useful reagent for organic synthesis. As usually conducted, the reaction is homogeneous, and, thus, has certain advantages over those reagents such as zinc in kinetic studies.

Zinc, however, is a useful reagent in dehalogenation of vicinal dibromides, particularly because of the stereospecific *trans* elimination of both bromines in selected cases,[3] especially those derived from simple alkenes.[4,5] In view of versatility of the Cr^{II}en reagent for reductive eliminations, it would be desirable to ascertain the factors which control the stereochemical course of the elimination. In previous studies, we have described our efforts (mostly kinetic) to elucidate the mechanism of

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(1) J. Kochi and P. Mocadlo, *J. Amer. Chem. Soc.*, **88**, 4094 (1966).

(2) J. Kochi, D. Singleton, and L. Andrews, *Tetrahedron*, in press.

(3) W. Young, Z. Jesaitis, and L. Levanas, *J. Amer. Chem. Soc.*, **59**, 404 (1937); W. Schubert, B. Rabinovitch, N. Carson, and V. Sims, *ibid.*, **74**, 4590 (1952).

(4) House and Ro have cited a number of examples in which debromination with zinc is not stereospecific (H. House and R. Ro, *ibid.*, **80**, 183 (1958).

(5) Recently C. Stevens and J. Valicenti, *ibid.*, **87**, 838 (1965), have demonstrated by use of radiobromine tracers that elimination of bromocyclohexane derivatives by zinc is not stereospecific.