6.9 cps) at $\tau$ 8.85 (6 H, *gem*-Me), a septet ($J$ = 6.9 cps) at 6.57 (1 H, *t*-CH), a singlet at 6.18 (3 H, $OCH_3$), and two multiplets in the regions 2.0–2.3 (2 H, aromatic CH) and 3.0–3.3 (2 H, aromatic CH).

*Anal.* Calcd for $C_{11}H_{14}O_2$: C, 74.1; H, 7.9. Found: C, 74.2; H, 7.7.

The 2,4-dinitrophenylhydrazone, mp 122–123° (from ethanol), was obtained.

*Anal.* Calcd for $C_{17}H_{18}N_4O_5$: N, 15.6. Found: N, 15.7.

**p-Nitroisobutyrophenone**, mp 51.8–52.3° (from dilute ethanol), had a nmr doublet ($J$ = *ca.* 7 cps) at $\tau$ 8.76 (6 H, *gem*-Me), a septet ($J$ = 6.9 cps) at 6.43 (1 H, *t*-CH), and a complex multiplet in the region 1.6–2.1 (4 H, aromatic CH). The doublet had a symmetrically spaced further pair of peaklets inside.

*Anal.* Calcd for $C_{10}H_{11}NO_3$: C, 62.2; H, 5.7; N, 7.3. Found: C, 62.2; H, 6.2; N, 7.1.

The 2,4-dinitrophenylhydrazone melted at 147–149° (from ethanol–benzene).

*Anal.* Calcd for $C_{16}H_{13}N_5O_6$: N, 18.8. Found: N, 18.7.

**Reaction of 1-N-Morpholinobutene (IX) with Benzoyl Chloride.**—A solution of 14.1 g (0.1 mole) of benzoyl chloride in 50 ml of *p*-dioxane was added dropwise in 45 min to a stirred solution of 14.0 g (0.1 mole) of the enamine IX and 11 g (0.11 mole) of triethylamine in 50 ml of *p*-dioxane on an iced water bath. The mixture was allowed to stand overnight at room temperature. Triethylammonium chloride (14 g) was filtered and the filtrate was stirred with 10 ml of concentrated hydrochloric acid overnight at room temperature. Crude α-benzoyl-*n*-butyraldehyde, 9.5 g (54% yield), bp 110–130° (4 mm), was obtained by usual work-up. Analytical sample was obtained by repeated recrystallization from ether, mp 109–112°.[23]

*Anal.* Calcd for $C_{11}H_{12}O_2$: C, 75.0; H, 6.9. Found: C, 75.5; H, 6.9.

1-(2,4-Dinitrophenyl)-4-ethyl-5-phenylpyrazole, mp 130–131° (from ethanol), was prepared.

*Anal.* Calcd for $C_{17}H_{14}N_4O_4$: N, 16.6. Found: N, 16.3.

The copper chelate compound (green needles) melted at 172–175° (from ethanol). From the ethereal mother liquor of recrystallization of α-benzoyl-*n*-butyraldehyde was obtained 1.0 g of *n*-butyrophenone, bp 62–64° (0.5 mm); the 2,4-dinitrophenylhydrazone had mp and mmp 188–190° (from ethanol–benzene) (lit.[25] mp 187–189°).

**α-Benzoyl-*n*-butyraldehyde by Formylation of *n*-Butyrophenone.**—The formylation was carried out by the procedure of Claisen and Meyerowitz.[12a] The product was recrystallized from ether, mp 107–110°.[23] The infrared absorption spectrum was identical with that of α-benzoyl-*n*-butyrophenone prepared by the enamine method, and the 2,4-dinitrophenylhydrazine derivative showed no melting point depression on admixture with 1-(2,4-dinitrophenyl)-4-ethyl-5-phenylpyrazole described above.

(23) The melting point of α-benzoyl-*n*-butyraldehyde has been reported to be 86–87°,[12a,24] but this melting point was not realized in our experiment. The enolizable 1,3-dicarbonyl compound may have a tendency to form polymorphs; see B. Eistert, F. Weygand and E. Csendes, *Chem. Ber.*, **84**, 745 (1951).

(24) S. Takagi and H. Yasuda, *Yakugaku Zasshi*, **79**, 467 (1959).

(25) M. S. Newman and A. Kutner, *J. Am. Chem. Soc.*, **73**, 4199 (1951).

# Hydrogen Bonding of Methanol with Pyridine Derivatives[1]

TEIJIRO KITAO[2] AND CHARLES H. JARBOE[3]

*Department of Pharmacology, School of Medicine, University of Louisville, Louisville, Kentucky*

*Received May 27, 1966*

Infrared spectroscopic studies in the 3000–4000-$cm^{-1}$ region were carried out in $CCl_4$ solution of nine hydrogen-bonding systems, in which methanol was a common proton donor. The proton acceptors were pyridine, 2-picoline, 2-ethylpyridine, 2-isopropylpyridine, 2-*t*-butylpyridine, 2,6-lutidine, 2-ethyl-6-methylpyridine, 2,6-diethylpyridine, and 2,6-diisopropylpyridine. Equilibrium constants for the formation of 1:1 complexes were determined. The enthalpies of complex formation were calculated from the temperature dependence of the spectra and are approximately 4 kcal/mole. The values of $\Delta\nu$, the difference in frequency for methanol monomer and the complex, were found to be temperature dependent. A linear relationship was found to exist between $\Delta\nu$ and pyridine base strength. The presence of bulky substituents at positions 2 or 2,6 was noted to impede the hydrogen-bonding reaction.

Interest in hydrogen bonding as an important parameter in drug pharmacodynamics originates in its participation in the complex events collectively termed "biological activity." Of particular concern to us have been the effects of steric hindrance on the thermodynamic properties of various simple hydrogen-bonding systems which may relate to the vastly more complicated chemistry of biophase reactions. To that end we have found pyridine to be a good proton acceptor model. Existing data on the thermodynamic properties of hydrogen-bonding reactions between pyridine derivatives and proton donors, especially alcohols, are scant.[4] Especially lacking have been studies on the way substituent groups adjacent to the heterocyclic nitrogen atom can alter its reactivity.

To further the development of a better understanding of hydrogen-bonding stereochemistry and to assist in the development of a working hypothesis on the mode of action of some drugs, it was desirable to determine the thermodynamic constants for several alcohol–pyridine systems. It was thought that the restricted access of a proton donor to a hindered pyridine could limit the degree of complexion in a manner similar to the steric inhibition of salt formation[5] and cause the equilibrium constants for complex formation to exhibit a dependence upon the size of pyridine substituent groups. Such a dependence has been inferred from nmr studies of hydrogen bonding in hindered phenols.[6]

This report concerns infrared spectroscopic studies carried out in the region of the fundamental OH stretching vibration. It covers reactions of pyridine, 2-picoline, 2-ethylpyridine, 2-isopropylpyridine, 2-*t*-butylpyridine, 2,6-lutidine, 2-ethyl-6-methylpyridine, 2,6-diisopropylpyridine, and 2,6-diethylpyridine with methanol at 18, 30, and 40°. The work was carried out at concentrations where only a 1:1 alcohol–base complex would be expected and methanol self-association would be prohibited. The equilibrium constants were determined by neglecting the contribution of

(1) These studies were supported by National Science Foundation Grant GB-2044, National Institutes of Health Grant GM 10363, and by a supporting grant from the Upjohn Co.

(2) Permanent address, Department of Chemistry, Radiation Center of Osaka Prefecture, Shinki-Cho, Sakai, Osaka, Japan.

(3) To whom inquiries should be directed.

(4) G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman, San Francisco, Calif., 1960.

(5) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 65.

(6) B. G. Somers and H. S. Gutowsky, *J. Am. Chem. Soc.*, **85**, 3065 (1963).

methanol monomer to the OH stretching vibration of complexes. The thermodynamic properties $-\Delta F$, $-\Delta H$, and $-\Delta S$ were calculated from the temperature dependence of the spectra and the usual thermodynamic relations.

## Experimental Section

All spectral measurements were made on a Perkin-Elmer Model 137G grating-type infrared spectrophotometer. The machine used in this work recorded frequency linearly. Accuracy of the measurements is estimated to be $\pm 2$ cm$^{-1}$. The scan speed was 24 min/drum revolution and the spectrophotometer was connected to a Sargent No. S-72180-20 auxiliary recorder through a pen position readout accessory. This arrangement permitted a precision of approximately $\pm 0.5\%$ in reading percentage transmittance in the 30–50% range on the recorder. The 0 and 100% lines were adjusted just prior to each measurement. The spectral slit width was programmed to vary from 10 cm$^{-1}$ at 4081 cm$^{-1}$ to 5 cm$^{-1}$ at 3333 cm$^{-1}$. The spectrophotometer, including the sample chamber, was purged with dry nitrogen. The sample chamber was isolated from the atmosphere by a polyethylene cover to prevent cell window sweating at low temperatures and energy loss due to atmospheric water.

The cells were 2.499 × 1.9 cm Pyrex cylinders equipped with 10/13 ⅎ joints at the middle and sodium chloride end windows. These were surrounded with a close-fitting hollow brass shell, threaded on each end and fitted with open-window brass screw caps to secure the components. Teflon gaskets prevented the caps from damaging the salt windows. The brass outer shells were provided with tubular inlets and outlets placed at opposite ends and at 180° to one another. The sample and reference cells were thermostated by series connection with a Haake Series F circulator–heater which was coupled to a Brinkman Thermo-Cool heat pump. This regulator system controlled intracell temperature to $\pm 0.1°$. The experiments were arranged so that all temperature changes were positive. Under these conditions a 15-min equilibration was sufficient to attain a uniform temperature throughout the cell system.

Carbon tetrachloride was the solvent used in these studies. The ordinary spectroscopic grade contains too much water for use with long path cells. To prevent loss of energy in the critical spectral region and to eliminate any possible error due to hydrogen bonding between water and either the base or the alcohol, the carbon tetrachloride was totally dehydrated (no absorbance above base line in the 4000- to 3000-cm$^{-1}$ range). To desiccate the solvent it was shaken with phosphorus pentoxide for at least 24 hr. It was then distilled from fresh phosphorus pentoxide, using an all-glass apparatus, into an actinic glass erlenmeyer flask containing a layer of Woelm neutral alumina. The resultant absolute carbon tetrachloride was stored in a phosphorus pentoxide desiccated drybox and used within 24 hr.

Reagent grade absolute methanol contains spectroscopically demonstrable quantities of water which also represent a potential source of error. Water-free methanol was prepared by standard procedures[7] and stored over Woelm neutral aluminum oxide. When treated in this way there is no water side band on the methanol hydroxyl peak at 3643 cm$^{-1}$. The pyridine, 2-picoline, 2-ethylpyridine, and 2,6-lutidine were reagent grade and dried over potassium hydroxide, fractionated using a spinning-band column and shown by gas chromatography to contain only one component. The remaining five compounds were synthesized by a modification of the Brown and Murphy[8] procedure, which uses methyl iodide as an alkylating agent in liquid ammonia and sodium amide mixture. 2-Isopropylpyridine, bp 158–160° (lit.[8] bp 159.8°), mp (picrate) 117–118° (lit.[8] mp 118.1°), was prepared from 2-ethylpyridine. 2-Ethyl-6-methylpyridine, bp 160–162° (lit.[9] bp 160–161.5°), mp (picrate) 127–129° (lit.[9] mp 127–130°), and 2,6-diethylpyridine, bp 170–173° [lit.[9] bp 91° (40 mm)], mp (picrate) 114–15.5° (lit.[3] mp 115–117°), were prepared from 2,6-lutidine. 2-*t*-Butylpyridine, bp 167–169° [lit.[8] bp 169° (743 mm)], mp (picrate) 103–105° (lit.[8] mp 104–105.2°), and 2,6-diisopropylpyridine, bp 191–194° (lit.[10] bp 194.1–194.5°), were prepared from 2-isopropylpyridine and 2,6-diethylpyridine by using potassium amide instead of sodium amide. Each compound was checked for purity by standard gas chromatographic procedures subsequent to spinning-band fractionation.

Solutions were gravimetrically prepared by the use of sealed, methanol-containing capillaries which were crushed in volumetric flasks of appropriate size and containing a small quantity of carbon tetrachloride. The experimental solutions were prepared by successive dilution. All solutions and dilutions were made just prior to use in order to minimize evaporative loss of the alcohol. All operations, including the filling of cells, were conducted in a desiccated drybox. The experimental solutions were normally made to contain approximately 0.005 mole/l. of methanol and approximately 0.05, 0.10, 0.5 or 0.20 mole/l. of base. The measurements were made at 18, 30, and 40°.

## Results and Discussion

It is well known that equilibrium constants describing the formation of hydrogen-bonded complexes can be obtained *via* infrared spectroscopy. Usually the conditions of measurement are adjusted to promote formation of a 1:1 complex and to inhibit self-association of the alcohol. For the system methanol–pyridine, the equilibrium reaction may be written as

$$CH_3OH + NC_5H_5 \rightleftharpoons CH_3OH \cdots NC_5H_5 \qquad (1)$$

If $C_c$, $C_m$, and $C_b$ are equilibrium concentrations of complex, methanol, and base, respectively, and $C_m^0$ and $C_b^0$ are the concentrations of methanol and base in the absence of complex formation, then the equilibrium constant $K_c$ (activity coefficients set at unity) is given by

$$K_c = C_c/C_mC_b = C_c/(C_m^0 - C_c)(C_b^0 - C_c) \qquad (2)$$

In this work, concentrations of methanol and base were selected to ensure that $C_b^0 >> C_m^0$ and $C_m$. Then

$$K_cC_b^0 = \alpha_c/(1 - \alpha_c)(1 - x\alpha_c) \qquad (3)$$

where $C_c/C_m^0 = \alpha_c$, $C_m/C_m^0 = \alpha_m$, $C_m^0/C_b^0 = x$, and $\alpha_c + \alpha_m = 1$. Thus, when $x = 0$

$$\lim_{x \to 0} (\alpha_c) = 1/(1 + 1/K_cC_b^0) \qquad (4)$$

If the apparent absorption coefficient ($E$) represents not only methanol absorption, $\epsilon_m\alpha_m$, but also absorption by the complex, $\epsilon_c\alpha_c$, then

$$E = \epsilon_m \alpha_m + \epsilon_c \alpha_c = \epsilon_m + (\epsilon_c - \epsilon_m)\alpha_c \qquad (5)$$

where $\epsilon_m$ and $\epsilon_c$ are the molar absorption coefficients of methanol and complex.

On substituting eq 4 into eq 5, we obtain

$$\lim_{x \to 0} (E) = \epsilon_m + (\epsilon_c - \epsilon_m)K_cC_b^0/(1 + K_cC_b^0) = \epsilon \qquad (6)$$

If the contribution of complex to the OH stretching vibration of methanol monomer is neglected, then

$$(\epsilon_m - \epsilon)/C_b^0 = \epsilon K_c \qquad (7)$$

It is seen that, if $(\epsilon_m - \epsilon)/C_b^0$ is plotted against $\epsilon$, the slope of the line will give $K_c$. If complex is the only contributor to the observed OH stretching vibration of the complex then

$$\epsilon/K_cC_b^0 = \epsilon_c + (-\epsilon) \qquad (8)$$

From eq 8 it is seen that the reciprocal equilibrium constant, $1/K_c$, can be calculated from the slope of the $(-\epsilon)$ *vs.* $\epsilon/C_b^0$ curve. The values of $K_c$ obtained from eq 8 should agree with those from eq 7. We obtained reasonable agreement using either method but chose to use the values derived from eq 8 because of their over-all

(7) J. A. Reddick and E. E. Toops, "Organic Solvents," Vol. 7, A. A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1955.
(8) H. C. Brown and W. A. Murphy, *J. Am. Chem. Soc.*, **73**, 3308 (1951).
(9) H. L. Lochte and I. H. Cheavens, *ibid.*, **79**, 1667 (1957).
(10) H. C. Brown and B. Kanner, U. S. Patent 2,780,626 (1957).

TABLE I

SPECTRAL AND THERMODYNAMIC PROPERTIES OF HYDROGEN-BOND FORMATION IN METHANOL–PYRIDINE SYSTEMS

| No. | Pyridine | $-\Delta H$, kcal/mole | $-\Delta F$,[a] kcal/mole | | $-\Delta S$,[a] eu | | $K_c$,[a] l./mole | $\Delta\nu$,[a] cm$^{-1}$ | p$K_a$[e] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Pyridine | 4.4 | 1.9[b] | 0.51[c] | 7.2[b,d] | 11.7[c,d] | 2.31[d] | 287 | 4.38 |
| 2 | 2-Picoline | 4.0 | 2.0 | 0.66 | 6.6[b] | 11.2[c] | 3.05 | 317 | 5.05 |
| 3 | 2-Ethylpyridine | 4.3 | 1.9 | 0.57 | 6.9[b,d] | 11.5[c,d] | 2.63[d] | 315 | ... |
| 4 | 2-Isopropylpyridine | 4.2 | 1.7 | 0.32 | 7.8[b,d] | 12.3[c,d] | 1.73[d] | 311 | 4.82 |
| 5 | 2-*t*-Butylpyridine | 4.0 | 1.6 | 0.22 | 8.1[b] | 12.7[c] | 1.45 | 295 | 4.68 |
| 6 | 2,6-Lutidine | 4.0 | 2.2 | 0.88 | 5.9[b] | 10.5[c] | 4.42 | 338 | 5.77 |
| 7 | 2-Ethyl-6-methylpyridine | 4.0 | 2.2 | 0.84 | 6.0[b] | 10.6[c] | 4.14 | 339 | ... |
| 8 | 2,6-Diethylpyridine | 3.9 | 2.0 | 0.64 | 6.7[b,d] | 11.3[c,d] | 2.96[d] | 339 | ... |
| 9 | 2,6-Diisopropylpyridine | 3.8 | 1.2 | −0.17 | 9.4[b,d] | 14.0[c,d] | 0.756[d] | 329 | 5.34 |

[a] Interpolated value at 25°. [b] All values based on $K_x$ in units of mole fraction. [c] All values based on $K_c$ in units of liter per mole. [d] Corrected value for 4 kcal/mole of $-\Delta H$. [e] Values of p$K_a$ in 50% aqueous ethanol for pyridines; see ref 11.

better consistency. This choice was somewhat arbitrary and based on personal preference.

In his investigation of hydrogen bonding in alcohol–base systems Becker[11] found it necessary to correct calculated equilibrium constants for alcohol self-association and for overlapping of complex and monomer peaks. The values of $\Delta\nu$, the difference in frequency between monomer and complex bands maxima, for the systems we have studied are recorded in Table I. It is notable that the shifts are larger than those recorded for O–H···O complexes.[11] Graphical resolution of the spectra support the premise that contribution of alcohol monomer to the OH stretch of the complexes can be neglected when making equilibrium constant determinations. Thus, by the use of eq 8 we determined $K_c$ values for each system at 18, 30, and 40°. The resultant constants (Table I) are in, mole concentration (liters per mole) units and are converted into mole fraction (mf$^{-1}$) units, $K_x$, by the expression

$$K_x = K_c/V_s \backsimeq 10K_c$$

where $V_s$, the solvent molar volume, is about 0.1 l. for $CCl_4$.[12] The enthalpy change of complex formation, $-\Delta H$, is calculated from the slope of the ($R$ ln $K_x$) *vs.* $1/T$ curve, according to the van't Hoff equation

$$4.5758\mathrm{d}\ (\log K_x)/\mathrm{d}(1/T) = -\Delta H$$

The free-energy change, $-\Delta F$, interpolated to 25° and the entropy change, $-\Delta S$, were calculated on the basis of the equilibrium constants for complex formation in both mole fraction units and liters per mole. The values are given in Table I.

The most interesting of the thermodynamic quantities is $-\Delta H$, a measure of hydrogen bond energy. It is estimated that the values of $-\Delta H$ are accurate to about ±0.4 kcal/mole. Considering the limitations in accuracy, we detect no significant trends in $-\Delta H$, but estimate its value to be approximately 4 kcal/mole in all the systems studied. Among the few comparisons that can be made with literature values of $-\Delta H$ for alcohol–pyridine systems, Tsuboi's value of 3 kcal/mole for methanol–pyridine[13] is considerably lower than our value, while Becker's value of 3.9 kcal/mole for the same system[11] is consistent with our value of 4 kcal/mole. Our values of $-\Delta S$ range from 10.5 to 14.0 entropy units (eu) (based on $K_c$ in liters per mole) and are in reasonable agreement with entropy

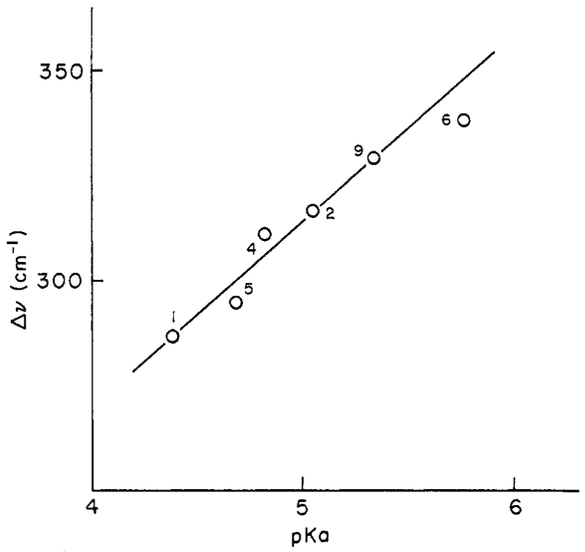


Figure 1.—Plot of p$K_a$ (in 50% aqueous ethanol) of pyridines *vs.* $\Delta\nu$ for methanol–pyridine complexes. Data taken from Table I.

of interaction changes of similar systems. Becker's value of 10.8 eu for methanol–pyridine[11] is reasonably close to our value of 11.7 eu for the same system.

The OH stretching mode and its harmonics are shifted to lower frequencies by hydrogen-bond formation. In many systems the shift is about 10% $\nu$.[1] Our data show a consistent and linear increase in $\Delta\nu$ with decreasing temperature. Similar behavior was reported previously for various alcohols with pyridine. The temperature variations range from 0.4 to 0.6 cm$^{-1}$/deg and are in reasonable agreement with the literature.[11] The data for $\Delta\nu$ furnish a test for the often-challenged linear relationship between $\Delta H$ and $\Delta\nu$ which was first suggested by Badger and Bauer[14] and later confirmed for various types of phenol donor complexes.[15,16] Our results contrast with this relation. However, the restricted range of $\Delta H$ values tends to minimize the disagreement. It will be noted that an apparent relationship seems to exist between base strength and $\Delta\nu$. This suggests that $\Delta\nu$ or $\nu$ for the complex may provide an index of reactivity. Support for this proposal was offered by Gordy and Stanford,[17] who showed a similar relation between $\Delta\nu$ and the basicity constants of a series of bases. It is seen from Figure 1 that a plot of the available pertinent p$K_a$

(11) E. D. Becker, *Spectrochim. Acta*, **17**, 436 (1961).
(12) U. Liddel and E. D. Becker, *ibid.*, **10**, 70 (1957).
(13) M. Tsuboi, *J. Chem. Soc. Japan, Pure Chem. Sect.*, **72**, 146 (1951).
(14) R. M. Badger and S. H. Bauer, *J. Chem. Phys.*, **5**, 839 (1937).
(15) M. D. Josten and R. S. Drago, *J. Am. Chem. Soc.*, **84**, 3817 (1962).
(16) R. West, D. L. Powell, M. K. T. Lee, and L. S. Whatley, *ibid.*, **86**, 3227 (1964).
(17) W. Gordy and S. C. Stanford, *ibid.*, **8**, 170 (1940).

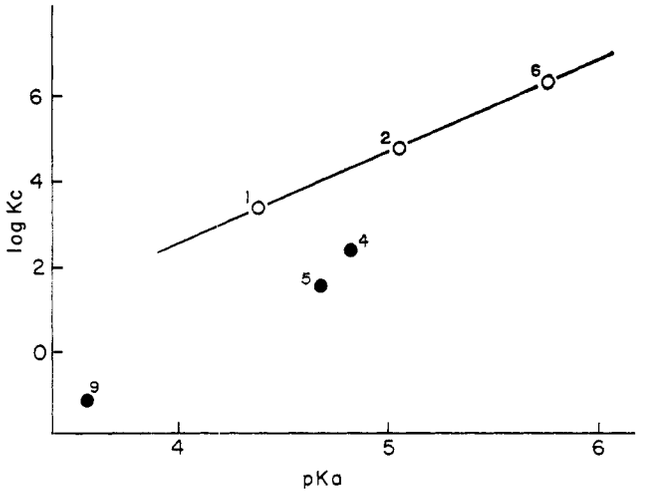


Figure 2.—Plot of $pK_a$ (in 50% aqueous ethanol) of pyridines *vs.* log $K$ for methanol–pyridine complexes. Based on data in Table I.

values[18] and the values of $\Delta\nu$ shows a reasonable linear correlation. In this sort of a relationship steric effects would not be expected except in exceptional circumstances, *e.g.*, the reaction between *t*-butyl alcohol and 2,6-di-*t*-butylpyridine. There is, however, definite evidence for steric effects in certain of these systems. We attribute the quantitative differences between 2,6-lutidine and 2,6-diisopropylpyridine to steric hindrance. It is suggested that the decreased $-\Delta S$ of complexion for the 2,6-lutidine system reflects an increased electron density at the nitrogen atom resulting from the (+I) inductive effect of the methyl groups and that the increased steric requirements of 2,6-diisopropylpyridine lead to steric strains in the complex and cause the $-\Delta S$ to be large. Observations with molecular models bear out this suggestion of strain. However, it is more profitable to compare the equilibrium constants at 25° in order to demonstrate trends in inductive and steric effects. From such a comparison it appears that hydrogen bonding ability is determined by a synthesis of the electronic and steric effects in a given system. In Figure 2, the values of log $K_c$ are plotted against $pK_a$ for the pyridines in 50% aqueous ethanol solution. The points for pyridine, 2-picoline and 2,6-lutidine describe a straight line. This is in agreement with the proposal[19] that the $pK_a$ of organic bases is correlatable with hydrogen-bonding ability when the bases are closely related in structure. The data indicate that the effects of methyl groups in the 2 and 2,6 positions on basicity and hydrogen bonding ability are largely electronic in nature. It is seen from Figure 2 that introduction of other alkyl groups at these same positions results in points which clearly depart from the relation and demonstrate that some other factor governs the degree of association in these cases. We suggest this to be steric hindrance.

**Acknowledgment.**—It is a pleasure to acknowledge Dr. Reisuke Soda and Miss Charlotte M. Schmidt for their help and valuable discussions.

(18) H. C. Brown and B. Kanner, *J. Am. Chem. Soc.*, **75**, 3865 (1953).

(19) (a) M. Tamres, S. Searles, E. M. Leighly, and D. M. Mohrman, *ibid.*, **76**, 3983 (1954); (b) A. Halleux, *Bull. Soc. Chim. Belges*, **63**, 381 (1959).

# Preferential Methyl Eliminations in Camphor and Isoborneol on Electron Impact[1]

DONALD R. DIMMEL[2] AND JOSEPH WOLINSKY

*Department of Chemistry, Purdue University, Lafayette, Indiana*

*Received August 26, 1966*

The mass spectra of isoborneol and camphor were studied by the deuterium-labeling technique. The base peak in these compounds (*m/e* 95) corresponds to a dimethylcyclopentenyl ion (**5**) and arises from loss of carbon atoms 2 and 3, together with a selective loss of the C-9 and C-10 methyl groups. The mechanism of this fragmentation is discussed in terms of a preferred *trans*-methyl migration to an adjacent, electron-deficient carbon atom. The C-8 and C-9 methyl groups are lost more frequently than the C-10 methyl group when isoborneol fragments to *m/e* 139 and 121 ions. The origin of the other principal fission products is also discussed.

Until recently very little has been published on the mass spectra of bicyclic terpenes. In most cases the spectra have been presented with little or no discussion of the origin of the major peaks.[3-6] The reason for this is the unusually complicated fragmentation reactions that occur upon electron impact of these molecules which are so prone to undergo carbonium ion or free-radical rearrangements. The single attempt[7] to explain the breakdown of camphor upon electron impact could not be substantiated by deuterium-labeling experiments.[8] Our need for a method to help elucidate the structures of bicyclic terpenes related to and derived from the camphene sultones[9] led us to undertake a detailed mass spectral analysis of camphor (**1**) and isoborneol (**31**). The results reported herein further point out[8] the importance of employing extensive deuterium labeling in gaining an understanding of the fission reactions of these compounds.

**Camphor.**—Weinberg and Djerassi[8] have reported the mass spectra of camphor and its 3,3-$d_2$ and 10-$d_1$ analogs. Their conclusions regarding the fragmentation reactions of camphor are reproduced in Scheme I. They have also shown that the *m/e* 110, 109, 108, 95, 83, and 81 peaks are composed of hydrocarbon ions.

(1) Abstracted from part of the thesis submitted by D. R. D. in partial fulfillment of the requirements for the Ph.D. degree from Purdue University, Aug 1966.

(2) National Institutes of Health Predoctoral Fellow, 1964–1966.

(3) A. F. Thomas and B. Willhalm, *Helv. Chim. Acta*, **47**, 475 (1964).

(4) R. Ryhage and E. von Sydow, *Acta Chem. Scand.*, **17**, 2025 (1963).

(5) (a) E. von Sydow, *ibid.*, **17**, 2504 (1963); (b) *ibid.*, **18**, 1099 (1964); (c) *ibid.*, **18**, 1791 (1964).

(6) B. Willhalm, A. F. Thomas, and M. Stoll, *ibid.*, **18**, 1573 (1964).

(7) (a) R. I. Reed, "Ion Production by Electron Impact," Academic Press Inc., New York, N. Y., 1962, pp 204–206; (b) R. I. Reed, "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press Inc., New York, N. Y., 1963, Chapter 13.

(8) D. S. Weinberg and C. Djerassi, *J. Org. Chem.*, **31**, 115 (1966).

(9) J. Wolinsky, D. R. Dimmel, and T. W. Gibson, "The Chemistry of Camphene Sultones," to be published.