Monatshefte für Chemie 111, 563—574 (1980)

Monatshefte für Chemie

Intramolecular Interactions I. The Use of Some *Mannich* Bases of Naphthols as Model Compounds for Intramolecular Hydrogen Bonding

Ernst Haslinger[a] and **Peter Wolschann**[b]

[a] Institut für Organische Chemie, Universität Wien, A-1090 Wien, Austria
[b] Institut für Theoretische Chemie und Strahlenchemie, Universität Wien, A-1090 Wien, Austria

(Received 31 October 1979. Accepted 11 January 1980)

Some model compounds for intramolecular hydrogen bonding are presented. The nmr, IR, UV and fluorescence spectra are shown to be suited for the study of such hydrogen bonds.

(Keywords: Hydrogen bond; Intramolecular proton transfer; Mannich bases)

Intramolekulare Wechselwirkungen, I. Einige Mannich-Basen von Naphtholen als Modellverbindungen für intramolekulare Wasserstoffbrückenverbindung

Eine Klasse von Verbindungen zur Untersuchung von intramolekularen Wasserstoffbrücken wird vorgestellt. NMR-, IR-, UV- und Fluoreszenzspektroskopie sind bestens geeignet, derartige Wasserstoffbrücken zu studieren.

Introduction

A hydrogen bond is an associative interaction between molecules containing a polar H—A-bond and an electron donor. Such molecular complexes are characterized by a unique geometry and by relative high energy of interaction; the energy varies from — 2 kJ/mol (e.g. $CHCl_3$-benzene) to — 160 kJ/mol (e.g. $F—H—F^-$). Symmetric and asymmetric hydrogen bonds are represented as $A\cdot\cdot H\cdot\cdot B$ or $A—H\cdot\cdot B$. A and B are atoms with greater electronegativity than hydrogen. If A and B belong to the same molecule intramolecular hydrogen bonding is possible if the spatial configuration is favorable. Hydrogen bonds determine the structure of molecules and molecular clusters in chemistry and biochemistry thus leading to a large number of publications dealing with thermodynamic and spectroscopic behavior of hydrogen bonding[1–4] as well as with the dynamics of the proton within the bridge eventually leading to proton transfer[5–7]. One of the most thoroughly investigated systems is the intermolecular association between phenols and aliphatic amines[8–15]. The thermodynamic and dynamic behavior of these complexes is sometimes difficult to study because of additional dissociation or association phenomena[16–18, 13]. An analogous system with intramolecular hydrogen bonds is represented by *Mannich* bases, which have been investigated recently[19–23].

Experimental evidences for hydrogen bonding is provided by the following:

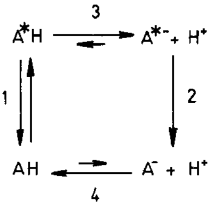
1. Atoms or molecules forming hydrogen bridges come closer together than the sum of their *van der Waals* radii would allow.

2. Hydrogen bonding increases the polarity of the molecules and decreases the electron density at the proton in the hydrogen bond. The former effect leads to a higher dipole moment than the vectorial addition of the isolated moments would suggest, especially if proton transfer along the hydrogen bond takes place. As a consequence of the latter effect the nmr chemical shifts appear at lower magnetic fields.

3. The H—A bond length is somewhat increased in the hydrogen bonded complex and consequently, the stretching vibrations in the IR spectra are shifted to smaller wavenumbers.

In aprotic solvents proton transfer in the excited state takes place only in hydrogen bonded complexes: Proton transfer on electronic excitation is a result of the difference in ionization constants of compounds like phenols, naphthols or aromatic amines[24–27] between the ground state and the excited state. Scheme 1 illustrates the proton transfer caused by light absorption:

Scheme 1



The excited molecule A^* can fluoresce or loose its energy by nonradiative conversion or it can dissociate into the excited anion A^{-*} and a proton. A^{-*} returns to the ground state by fluorescence or other processes and then it can accept a proton to reform A. Diffusion controlled dissociation of the proton (3) is fast enough only in strongly polar media, like water[28, 29]. In presence of proton acceptors forming hydrogen bonds to A, reaction step (3) is sufficiently fast again, so that excited state proton transfer occurs to a large extent[30,31].

In the present paper we want to introduce a model system for hydrogen bonding, which may be used for an extensive spectroscopic study of the thermodynamic and dynamic behaviour of intramolecular hydrogen bonds, in particular it seems to be suitable for fluorescence spectroscopy.

Scheme 2

II

R	R_2
$(CH_2)_5$	H
$(CH_2)_4$	Br
$(CH_2)_2O(CH_2)_2$	

I

R	R_1
$(CH_2)_5$	OCH_3
$(CH_2)_4$	H
$(CH_2)_2O(CH_2)_2$	Br
	NO_2

Results and Discussion

NMR Spectra of Compounds of Type I and II

The determination of the chemical shift of the proton in the hydrogen bridge is a quite sensitive experimental method for detection of hydrogen bonding. Figure 1 shows the nmr spectrum of a compound of type I. The signal of the bridge proton is found at very low field strength for all compounds of type I and II (between 9.8 and 14.0 ppm), typical for strong hydrogen bonding[32–36]. The value of δ_{O-H-X} depends on the substituents of the aromatic ring and on the nature of the nitrogen base, in particular on the strength of the hydrogen bond. In addition, the absorption of the bridge proton is highly sensitive to relatively small amounts of water and to temperature changes. Precise analyses of the chemical shifts of the hydrogen bonded proton and the line shape of the signal, as well as of the ^{13}C nmr spectra will be given elsewhere[37,38].

IR Spectra of Compounds of Type I and II

The stretching vibrations of the A—H or B—H bonds are very sensitive to hydrogen bonding[3,22,39,40]. The characteristic part of a typical IR spectrum of a compound of type II is shown in Figure 2. Even in a relatively polar solvent, like perdeuterated acetonitrile, there

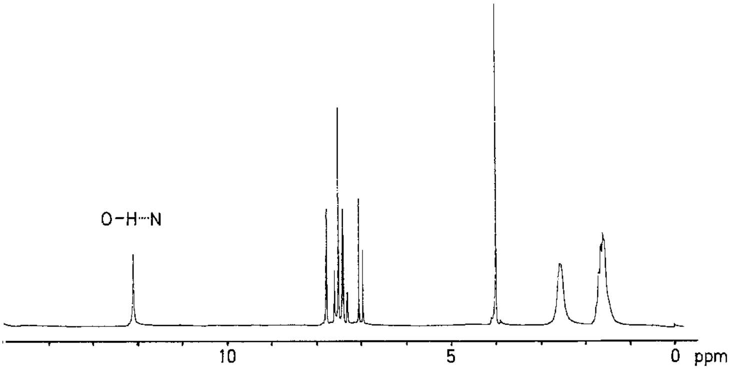


Fig. 1. ^{1}H-nmr (100 MHz) of 6-bromo-1-piperidinomethylene-2-naphthol in CDCl$_3$, *TMS* as internal standard. $T = 33\,°C$

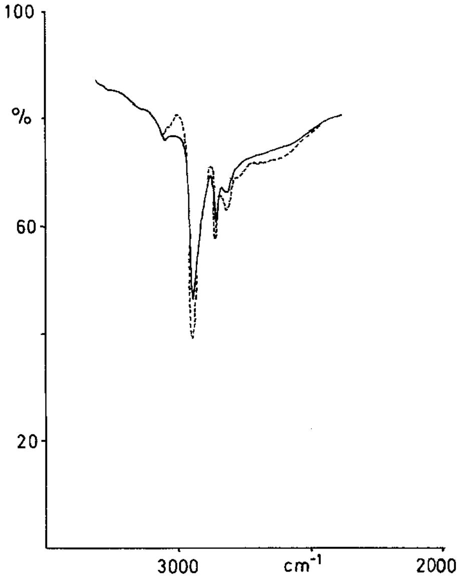


Fig. 2. IR of 6-bromo-1-piperidinomethylene-2-naphthol in CD$_3$CN. *A* $c = 0.1\%$; *B* $c = 0.01\%$

is no absorption corresponding to a free O—H bond ($\sim 3{,}500\,\mathrm{cm}^{-1}$). The broad signal between $2{,}500\,\mathrm{cm}^{-1}$ and $3{,}200\,\mathrm{cm}^{-1}$ indicates strong hydrogen bonding. Dilution (1:10) changes the IR spectra only sligthly. This is a strong argument in favour of an intramolecular hydrogen bond.

Electronic Absorption Spectra of I and II

Generally, hydrogen bonding causes a bathochromic shift for chromophores acting as proton donors[3,40]. A comparison between the electronic absorption spectrum of 4-methoxy-1-naphthol and its reaction product with piperidine and formaldehyde (4-methoxy-2-piperidinomethylene-1-naphthol) shows a red shift of the absorption maxima, as demonstrated by the spectra in Fig. 3. In case of electron attracting groups bound to the proton donor group of the molecule, proton transfer may occur within the hydrogen bond.

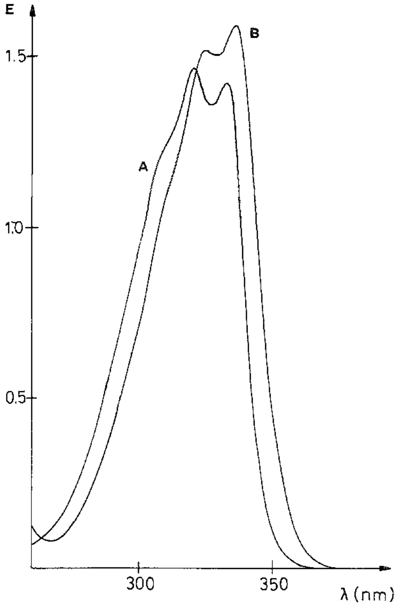


Fig. 3. UV spectra of 4-methoxy-1-naphthol (*A*) and 4-methoxy-2-piperidinomethylene-1-naphthol (*B*) in acetonitrile (*A*: $c = 2{,}5 \cdot 10^{-4}$ mol/l; *B*: $c = 2{,}5 \cdot 10^{-4}$ mol/l)

$$\mathrm{A{-}H \cdots B \rightleftarrows A^{-} \cdots H{-}B^{+}}$$

Such tautomeric equilibria are characterized by the appearence of a new band at higher wavelengths. Intermolecular proton transfer reactions in phenol-amine systems have been widely investigated using UV and visible spectroscopy[2,13,17,21,40,41]. The broad band at lower frequency corresponds to the absorption of the nonionized naphtholic group of the molecule (Fig. 3), the more intense absorption at higher wavelengths is caused by the naphtholate chromophor, which results from proton transfer from the oxygen to the nitrogen atom. Fig. 4 shows two examples of spectra of compounds in which the prototropic equilibria are shifted more towards the proton transfer complex. The amount of proton transfer, as expressed by the equilibrium constant K_{PT} is highly sensitive to the pK values of the proton acceptor and the proton donor groups. In compounds of type I and II there is no evidence of proton transfer if $R_3 = \mathrm{CH_3O}$— or H— (Fig. 3), there is some proton transfer if $R_3 = \mathrm{Br}$, and if $R_3 = \mathrm{NO_2}$ there exists strong tendency for proton transfer within the hydrogen bond.

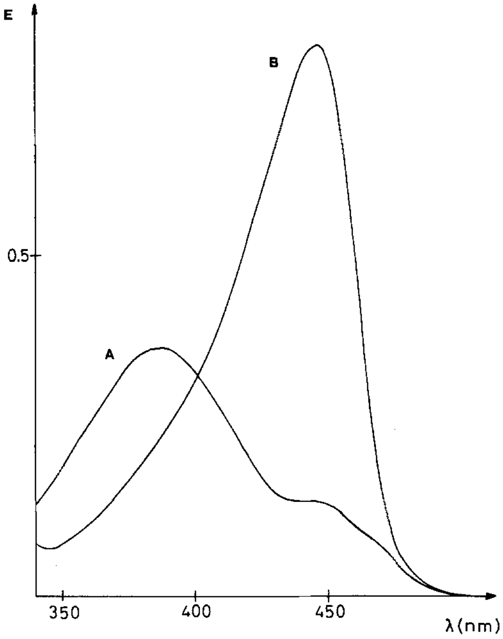


Fig. 4. UV spectra of 4-nitro-2-morpholinomethylene-1-naphthol (*A*) ($c = 4{,}5 \cdot 10^{-5}$ mol/l), and 4-nitro-2-piperidinomethylene-1-naphthol (*B*) ($c = 4{,}5 \cdot 10^{-5}$ mol/l) in acetonitrile

Fig. 4 shows the influence of the nitrogen base on K_{PT}: A comparison of the electronic absorption spectra of 4-nitro-2-morpholinomethylene-1-naphthol and 4-nitro-2-piperidinomethylene-1-naphthol clearly shows that the proton transfer equilibrium is shifted much further towards the zwitterionic form in the latter compound. K_{PT} is not only influenced by the acidity constants of the proton donor and the acceptor, there is also a drastic influence of the solvent on the average position of the proton in the hydrogen bridge[21,45,46]. An increase in dielectric permitivity leads to a stabilization of the strong polar proton transfer complex. Such a solvation effect is demonstrated by the spectra of 4-nitro-2-morpholinomethylene-1-naphthol in solvents of different polarity (Fig. 5). In benzene solution the proton transfer is very weak; in acetonitrile both forms of the proton transfer equilibrium are present, and in ethanolic solution the zwitterionic complex dominates. The zwitterionic form has the larger dipole moment and is strongly solvated by the polar solvent. Consequently it is stabilized relative to the less polar association complex.

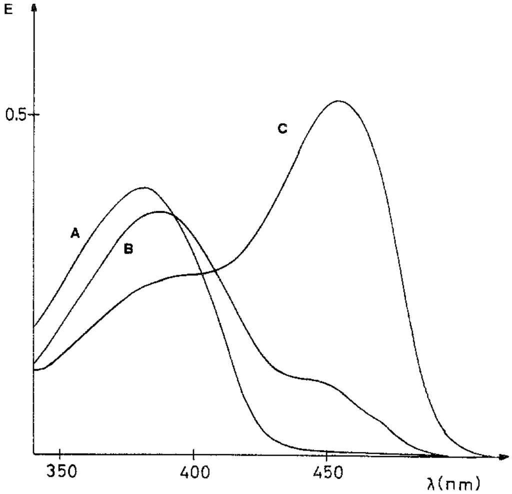


Fig. 5. UV spectra of 4-nitro-2-morpholinomethylene-1-naphthol in benzene (*A*), acetonitrile (*B*) and ethanol (*C*) ($c = 4{,}5 \cdot 10^{-5}$ mol/l)

Steady-State Fluorescence Spectra of I and II

Typical fluorescence spectra of compounds of type I and II are shown in Fig. 6. The band at 365 nm corresponds to the fluorescence of naphthol, the band at 420 nm can be explained by proton transfer in the excited state according to reaction step (3) in Scheme 1. The fluorescence spectra of 2-naphthol or 6-bromo-2-piperidinomethylene-2-naphthol in alkaline alcoholic solution show a similar peak at 420 nm. In contrast to the behaviour of 2-naphthol in acetonitrile, where no proton transfer has been observed in the excited state, the amount of proton transfer in the excited states I and II is extremely high; in the latter the proton is able to change its position rapidly because of the presence of a strong hydrogen bond. A similar effect has been observed in the case of intermolecular hydrogen bonded complexes[32, 47].

The dependence of the excited state proton transfer on the substituent of the naphthol ring, or on the nature of the nitrogen base, as well as on the solvent is shown in Table 1. Even in 4-methoxy-2-morpholinomethylene-1-naphthol (a molecule with no proton transfer in the ground state) we found more or less complete proton transfer in the excited state in acetonitrile and ethanol. Unfortunately no fluorescence can be observed for compounds with nitro groups. Generally, in relatively polar solvents (acetonitrile, ethanol), proton transfer in the excited state occurs to a large extent. Cyclohexane, an apolar solvent, does not favor proton transfer. Only in some cases the fluorescence of the naphtholate anion can be observed; the differences in ionization constants between the ground state and the excited state are not so large here.

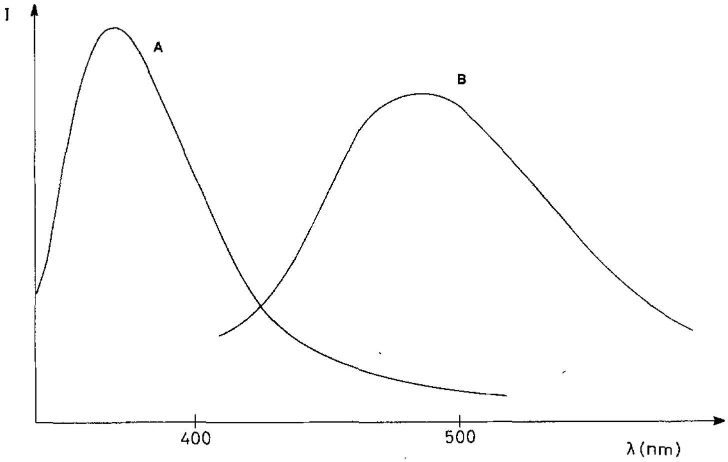


Fig. 6. Emission spectra of 4-methoxy-2-morpholinomethylene-1-naphthol in cyclohexane (*A*) and in acetonitrile (*B*) ($\lambda_{ex} = 335$ nm)

Finally, we can conclude that compounds of type I and II contain intramolecular hydrogen bonds and they seem to be convenient systems to study the behaviour of such intramolecular bonds by nmr-, IR-, electron absorption and fluorescence spectroscopy. Relatively easy synthetic access to compounds with different substituents on the

Table 1. *Maxima of fluorescence bands of compounds of type I and II* (λ *in nm*)

Naphtholic component	base	$\lambda_{\text{cyclohexane}}$	λ_{ethanol}	$\lambda_{\text{acetonitrile}}$
1-naphthol	piperidine	420	420	430
4-bromo-1-naphthol	piperidine	405	450	455
4-methoxy-1-naphthol	piperidine	375	480	490
4-methoxy-1-naphthol	morpholine	370	480	485
2-naphthol	piperidine	370	420	430
2-naphtholate	piperidine		430	
2-naphthol	morpholine	360	418	428
2-naphthol	pyrrolidine	367	420	434
6-bromo-2-naphthol	piperidine	415	435	445
6-bromo-2-naphthol	morpholine	365	440	443

aromatic ring or different nitrogen bases allows to vary the donor and acceptor properties of the atoms belonging to the hydrogen bridge, over a wide range. This enables us, to study the properties of hydrogen bonds with largely variable average positions of the central proton.

Acknowledgements

The authors wish to thank Prof. *P. Schuster* and Doz. *Jakubetz* for discussions, Mrs. *H. Martinek* and Mrs. *E. Silberbauer* for technical assistance, and the Fonds zur Förderung der wissenschaftlichen Forschung in Österreich for financial support (Projects 1217 and 3388).

Experimental

Substances of type I and II have been synthesized in analogy to procedures in literature[48, 49]:

0.1 mol of the amine was dissolved in 50 ml ethanol and cooled with ice. 10 ml aqueous formaldehyde solution (~ 37%) was added dropwise with stirring. After a few minutes a solution of 0.1 mol of the naphtholic compound in 30 ml ethanol was added and the reaction mixture was stirred for 30 min. The resulting precipitate was filtered and recrystallized twice in ethanol or aceton under argon atmosphere. In some cases it was necessary to warm up the reaction solution to about 50 °C to complete the reaction. Table 2 gives a survey of the synthesized compounds and their melting points.

The spectra have been recorded on a Varian XL 100-15 nmr spectrometer, a Perkin-Elmer 225 IR-spectrometer, a Perkin-Elmer 575 UV and visible spectrophotometer and a Spex Fluorolog fluorescence spectrophotometer.

Table 2. *Synthesized compounds of type I and II*

	m. p. (°C)
2-piperidinomethylene-1-naphthol	112
4-bromo-2-piperidinomethylene-1-naphthol	95
4-nitro-2-piperdinomethylene-1-naphthol	189 (Z)
4-nitro-2-morpholinomethylene-1-naphthol	144—146
4-nitro-2-pyrrolidonomethylene-1-naphthol	169—171
4-methoxy-2-piperidinomethylene-1-naphthol	91—92
4-methoxy-2-morpholinomethylene-1-naphthol	134—136
1-piperidinomethylene-2-naphthol	111—112
1-morpholinomethylene-2-naphthol	114
1-pyrrolidinomethylene-2-naphthol	86—88
6-bromo-1-piperidinomethylene-2-naphthol	110—111
6-bromo-1-morpholinomethylene-2-naphthol	99—101

References

[1] *G. C. Pimentel* and *A. L. McClellan*, The Hydrogen Bond. San Francisco: Freeman. 1960.

[2] *S. N. Vinogradov* and *R. H. Linnell*, Hydrogen Bonding. New York: Van Nostrand Reinhold. 1971.

[3] *M. D. Joesten* and *L. J. Schaad*, Hydrogen Bonding. New York: Marcel Dekker. 1974.

[4] *P. Schuster*, *G. Zundel*, and *C. Sandorfy*, The Hydrogen Bond. Recent Developments in Theory and Experiments I-III. Amsterdam: North Holland. 1976.

[5] *E. Caldin* and *V. Gold*, Proton Transfer Reactions. London: Chapman and Hall. 1975.

[6] *C. H. Bamford* and *C. F. H. Tipper*, Comprehensive Chemical Kinetics, Vol. 8: Proton Transfer. Amsterdam: Elsevier. 1977.

[7] *P. Schuster*, *P. Wolschann*, and *K. Tortschanoff*. Dynamics of Proton Transfer in Solution in: Molecular Biology, Biochemistry and Biophysics (*I. Pecht* and *R. Rigler*, eds.), Vol. 24. Berlin-Heidelberg-New York: Springer. 1977.

[8] *H. Ratajczak* and *L. Sobczyk*, J. Chem. Phys. **50**, 556 (1969).

[9] *J. Jadzyn* and *J. Malecki*, Acta Physica Polonica **A 41**, 599 (1972).

[10] *J. Malecki*, J. Chem. Soc. Faraday Trans. II **72**, 1214 (1976).

[11] *L. Sobczyk*, Pure & Appl. Chem. **51**, 1659 (1979).

[12] *M. DeMaeyer*, *P. Wolschann*, and *L. Hellemans*, in: Techniques and Applications of Fast Reactions in Solution (*W. J. Gettins* and *E. Wyn-Jones*, eds.), p. 501. D. Reidel Publ. Comp. 1979.

[13] *H. Romanoski* and *L. Sobczyk*, J. Phys. Chem. **79**, 2535 (1975).

[14] *E. L. Simmons*, Progr. Reaction Kinetics **8**, 161 (1977).

[15] *G. D. Burfoot* and *E. F. Caldin*, J. Chem. Soc. Faraday Trans. I **72**, 963 (1976).

[16] *G. Beier* and *P. Schuster*, in preparation.

[17] *R. A. Hudson*, *R. M. Scott*, and *S. N. Vinogradov*, J. Phys. Chem. **76**, 1989 (1972).

[18] *Z. Dega-Szafran* and *M. Szafran*, J. Mol. Struct. **45**, 33 (1978).

[19] *G. Beier*, Doctoral Thesis, University of Vienna 1975.

[20] *A. Sucharda-Sobczyk* and *S. Ritter*, Polish J. of Chemistry **52**, 1555 (1978).

[21] *V. M. Schreiber*, *A. Koll*, and *L. Sobczyk*, Bull de L'Academie Pol. des Sciences **26**, 651 (1978).

[22] *A. Sucharda-Sobczyk* and *L. Sobczyk*, Bull. de L'Academic Pol. des Sciences **26**, 549 (1978).

[23] *A. Koll*, *M. Rospenk*, and *L. Sobczyk*, in press.

[24] *A. Weller*, Prog. React. Kinet. **1**, 187 (1961).

[25] *M. Ofran* and *J. Feitelson*, Chem. Phys. Letters **19**, 427 (1973).

[26] *Z. R. Grabowski* and *W. Rubaszewska*, J. Chem. Soc. Faraday Trans. I **73**, 11 (1977).

[27] *W. R. Laws* and *L. Brand*, J. Phys. Chem. **83**, 795 (1979).

[28] *Th. Förster*, Zeitschr. f. Elektrochemie **54**, 531 (1950).

[29] *N. M. Trieff* and *B. R. Sundheim*, J. Phys. Chem. **69**, 2044 (1965).

[30] *A. Matsuyama* and *H. Baba*, Bull. Chem. Soc. Japan **44**, 1162 (1971).

[31] *A. Matsuzaki*, *S. Nagakura*, and *K. Yoshihara*, Bull. Chem. Soc. Japan **47**, 1151 (1974).

[32] *M. Ilcyscin*, *L. le Van*, and *H. Ratajczak*, in: Protons and Ions Involved in Fast Dynamic Phenomena (*P. Laszlo*, ed.). Amsterdam: Elsevier. 1976.

[33] *Th. Duda* and *M. Szafran*, Bull. de L'Academie Pol. des Sciences **26**, 207 (1978). a) *B. Brycki*, *Z. Dega-Szafran*, and *M. Szafran*, Adv. in Mol. Rel. and Int. Proc. **15**, 71 (1979).

[34] *G. S. Denisov*, *N. S. Golubev*, and *A. I. Koltsov*, Adv. in Mol. Rel. and Int. Proc. **11**, 283 (1977).

[35] *B. Brzezinski*, Org. Magn. Res. **12**, 432 (1979).

[36] *B. Brzezinski*, Org. Magn. Res. **8**, 283 (1976).

[37] *A. Koll*, *M. Rospenk*, and *L. Sobczyk*, in preparation.

[38] *E. Haslinger*, in preparation.

[39] *Th. Zeegers-Huyskens*, Spektrochim. Acta **21**, 221 (1965).

[40] *Th. Zeegers-Huyskens* and *P. Huyskens*, in: Molecular Interactions (*W. J. Orville-Thomas* and *H. Ratajczak*, eds.). London: Wiley. 1979.

[41] *G. Zundell* and *A. Nagyrevi*, J. Phys. Chem. **82**, 685 (1978).

[42] *J. Kraft*, *S. Walker*, and *M. D. Magee*, J. Phys. Chem. **79**, 881 (1975).

[43] *A. Wojtowicz* and *J. Malecki*, Bull. de L'Academie Pol. des Sciences **25**, 385 (1977).

[44] *H. Baba*, *A. Matsuyama*, and *H. Kokubun*, Spectrochim. Acta **25 A**, 1709 (1969).

[45] *Z. Pawelka* and *L. Sobczyk*, Roz. Chemii Ann. Soc. Chim. Pol. **49**, 1383 (1975).

[46] *A. Wojtowicz* and *J. Malecki*, Roz. Chemii Ann. Soc. Chim. Pol. **50**, 2121 (1976).

[47] *N. Mataga* and *Y. Kaifu*, Mol. Phys. **7**, 137 (1963).

[48] *F. F. Blicke*, Mannich Reactions in Organic Reactions, Vol. 1, p. 303. New York: Wiley. 1947.

[49] *W. E. Hahn* and *J. Weglewski*, Lodz. Tow. Nauk. Wydz. III, Acta Chim. **11**, 67 (1966).