and contained a Ag|AgCl reference electrode separated from the solution by an asbestos fiber junction placed as close as possible to the working electrode, a working electrode consisting of a smooth platinum disk (Beckman No. 39273), and a platinum wire auxiliary electrode separated from the solution by a medium porosity sintered glass frit which was placed just opposite the reference electrode. In addition, the cell was flushed through a port with inert gas. The reference electrodes were calibrated by periodic checks against the known reduction potentials of naphthoquinone, and appropriate corrections for iR drop were also made. The cell itself was immersed in a temperature-controlled bath. Additional details of the apparatus and techniques used are reported elsewhere.[39]

Acknowledgment. Support of this work by the National Institutes of Health is gratefully acknowledged.

A Study of Substituent Effects on Nuclear Magnetic Resonance Spectral Parameters of N-Substituted Methylamines[1]

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Contribution from the Department of Chemistry, University of Detroit, Detroit, Michigan 48221. *Received May 21, 1973*

Abstract: A method is presented that allows primary and secondary amines to be dried sufficiently for the observation of H–N–C–H pmr spin–spin coupling. By means of this method the values of J_{HNCH} were examined for a series of N-substituted methylamines and were found to be quite dependent on the N substituent. A correlation is presented between the value of J_{HNCH} and the chemical shift of the *N*-methyl group extrapolated to infinite dilution in carbon tetrachloride. Large solvent shifts are shown to occur for the *N*-methyl group in aromatic methylamines but not for aliphatic systems. One possible explanation for this is presented.

Small traces of water or acid catalyze hydrogen exchange in relatively basic primary and secondary amines such that H–N–C–H spin–spin coupling is normally not observed. This hydrogen exchange is thought to occur through the following equilibrium[2]

$$R_2NH + H_2O \rightleftharpoons R_2NH_2^+ + OH^-$$

In recent years several reports of H–N–C–H coupling have appeared, but in almost all cases the conditions were such that slow hydrogen exchange would be expected either because of substituents present on the nitrogen which reduce its basicity or because the nitrogen site is blocked by coordination to a Lewis acid. Indeed, Rae has reported that the ability to observe coupling in ring-substituted *N*-methylanilines is dependent on the base strength of the amine,[3] with coupling being easily observed for weakly basic systems. Coupling was also reported for methylaminobis(trifluoromethyl)phosphine.[4]

The possibility of cross nitrogen–proton coupling was alluded to by Meek and Springer in the case of complexes in which the fourth coordination site of the nitrogen atom was occupied by a boron derivative.[5] Similar phenomena have been observed for boron complexes of other strong bases, *e.g.*, $BF_3 \cdot NH_2CH_3$, $BF_3 \cdot NH(CH_3)_2$,[6] and $B(CH_3)_3 \cdot NH_2NHCH_3$.[7] It is of interest to note here that in the last case, a solution of the uncomplexed methylhydrazine exhibited no pmr coupling even though the substance was dried over anhydrous barium hydroxide and carefully distilled under vacuum.

Most attempts to observe H–N–C–H coupling in strongly basic amines have been futile with typical examples being the study of neat monomethylamine in the condensed phase[8] and work with substituted hydrazines in solution.[9]

Bichlmeir and West observed coupling in the spectra of *N,N*-bis(trimethylsilyl)methylhydrazine and *N,N*-bis(ethyldimethylsilyl)methylhydrazine[10] because, they postulated, the method used in the preparation of compounds rigorously excluded all traces of moisture.

Because of the limited number of systems studied, little work has been done on the correlation of the magnitude of J_{HNCH} with the nature of nitrogen substituents. Rae has studied the magnitude of J_{HNCH} as a function of substitution in a series of N-substituted benzylamines[11] and he found that the magnitude of J decreased with an increase in the electronegativity of the N-substituent, but only a small range of electronegativities was examined. Because of the previously mentioned limitation on base strengths, only strongly electron withdrawing groups could be used as substituents.

One of us recently reported[12] a method of drying samples sufficiently to allow for the observation of H–N–C–H coupling in strongly basic systems. This method involved the exhaustive drying of the amine samples by refluxing the commercially available amines over sodium–potassium alloy (NaK) for several days in a vessel attached to a high vacuum system. (Caution, hydrogen gas is produced in this process and care

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(1) Presented in part at the American Chemical Society 5th Central Regional Meeting, Cleveland, Ohio, 1973.

(2) C. S. Springer, Jr., and D. W. Meek, *J. Phys. Chem.*, **70**, 481 (1966).

(3) I. D. Rae, *Aust. J. Chem.*, **19**, 409 (1966).

(4) A. H. Cowley, M. J. S. Dewar, W. R. Jackson, and W. B. Jennings, *J. Amer. Chem. Soc.*, **92**, 1085 (1970).

(5) D. W. Meek and C. S. Springer, Jr., *Inorg. Chem.*, **5**, 445 (1966).

(6) A. Derek, H. Clague, and A. Danti, *Spectrochim. Acta, Part A*, **23**, 2359 (1967).

(7) L. K. Peterson and G. L. Wilson, *Can. J. Chem.*, **49**, 3171 (1971).

(8) L. Paolillo and E. D. Becker, *J. Magn. Resonance*, **3**, 200 (1970).

(9) J. R. Crook and K. Schug, *J. Amer. Chem. Soc.*, **86**, 4271 (1964).

(10) B. Bichlmeir and R. West, *J. Organometal. Chem.*, **32**, 35 (1971).

(11) I. D. Rae, *Aust. J. Chem.*, **19**, 1983 (1966).

(12) K. L. Henold, *Chem. Commun.*, 1340 (1970).

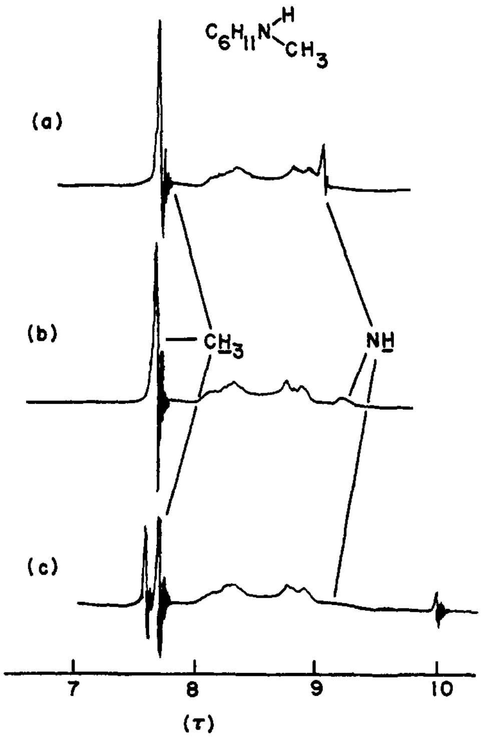


Figure 1. Pmr spectra of *N*-methylcyclohexylamine: (a) fresh reagent grade; (b) dried over NaK alloy; and (c) with $Zn(CH_3)_2$ added.

should be taken to avoid a buildup of pressure.) The sample was subsequently distilled under vacuum into an nmr sample tube.

We would now like to report a much more convenient method of drying amine samples for pmr studies along with H–N–C–H coupling constants for a number of N-substituted methylamines. Because of the larger number of compounds studied, we are able to make some comments on the dependence of J_{HNCH} on the nature of the nitrogen substituent.

Results

As mentioned earlier, a method has been developed to dry commercially available amines for pmr spectral measurements.[12] Unfortunately this method suffers from three severe limitations. (1) The method is time consuming, often requiring several days. (2) Even after exhaustive drying, hydrogen exchange still occurs in more basic amines because of moisture adsorbed on the glass of the vacuum line and sample tube. This problem can be avoided if the entire vacuum line is well flamed before the amine is condensed into the sample tube (this is found to be necessary even when a McLeod gauge registers a vacuum of 10^{-6} Torr). (3) Primary and secondary amines are attacked by active metals to form the corresponding metal amide salts and hydrogen gas, making this a rather destructive method.

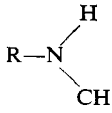
We felt that all of these problems could be alleviated if a method could be found to get rid of small traces of water after the amine is introduced into the sample tube. To this end a small amount of a reactive organometallic substance, dimethylzinc, was added to about 0.5 ml of the amine in the sample tube. Samples which had been only cursorily dried over sodium and had shown no evidence of H–N–C–H coupling before addition of the organometallic substance did so immediately upon addition. An example of the effect of drying can be seen in Figure 1. A reaction of the type

$$(CH_3)_2Zn + H_2O \longrightarrow CH_3ZnOH + CH_4$$

is very likely responsible for the ability of dimethylzinc to dry the amine. Because of the very small quantities involved, however, the presence of methane could not be verified in the pmr spectrum.

It appears that the only function of the dimethylzinc is desiccation and that its ability to act as a Lewis acid is relatively unimportant because of the small quantities present. This was verified by adding comparable amounts of boron trifluoride in place of dimethylzinc. The pmr spectra of these samples showed no H–N–C–H coupling. The use of dimethylzinc is found to be relatively convenient because of its high volatility making it easy to handle in a vacuum system. It should be noted that it is quite air and water sensitive and must be handled with great care, with a vacuum line being essential.

In order to establish substituent effects on H–N–C–H spin–spin coupling constants, a number of N-substituted methylamines have been studied. While no work has been done by us to establish the sign of the coupling constants for these compounds, the sign J_{HNCH} is generally regarded as positive[13] and we will do so here. The first-order coupling constants in I have been determined by the separation in the doublet of the methyl resonance for all compounds studied. The N–H resonance is of little utility because it is severely broadened by quadrupolar interactions with the nitrogen nucleus (see Figure 1c). Values of J_{HNCH} (first order) for various methylamines are tabulated in Table I. Also included are the chemical shifts of the methyl resonance in neat solution and those extrapolated to infinite dilution in carbon tetrachloride.



I

Discussion

It is now apparent that H–N–C–H spin–spin coupling in relatively basic primary and secondary amines can be observed if the samples are sufficiently dried. The method reported here of preliminary drying of the amines over Na or NaK alloy for short periods of time followed with a small quantity of dimethylzinc has worked effectively for all amines studied in this laboratory. This is a much less destructive method than that reported earlier[12] because the time that the amine is in contact with the active metal is drastically reduced.

The range of values of the first-order coupling constants J_{HNCH} reported here for a series of N-substituted methylamines is 4.8–6.5 Hz depending on the nitrogen substituent. In view of Rae's findings that a rough correlation exists between the magnitude of the chemical shift and J_{HNCH} in a limited series of benzylamines,[11] we have attempted a similar correlation using the data

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(13) L. M. Jackman and S. Sternhell, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Pergamon Press, New York, N. Y., 1969.

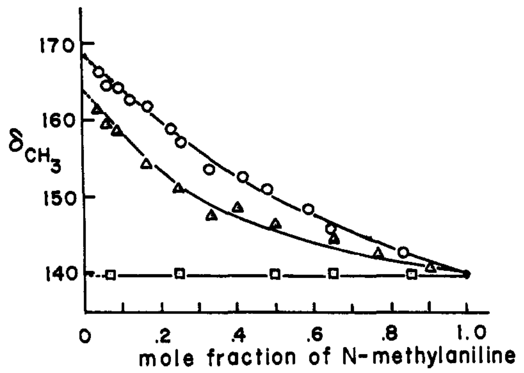
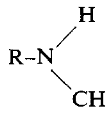
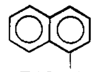


Figure 2. The *N*-methyl chemical shift for *N*-methylaniline as a function of mole fraction in carbon tetrachloride (○), cyclohexane (△), and benzene (□).

Table I. First-Order H-N-C-H Coupling Constants[a] and Chemical Shifts[b] for Compounds of the Type



R	$J_{H-N-C-H}$, Hz	δ_{CH_3}, ppm	
		Neat	CCl_4 solution[c]
$-C_6H_{11}$	6.47	2.33	2.33
$-C_4H_9$	6.45	2.35	2.34
$-CH_2C_6H_5$	6.24	2.23	2.39
$-NH_2$	6.15	2.43	2.50
$-CH_3$	6.11		
$-N[Si(CH_3)_3]_2$	5.6[d]		
o-$C_6H_5CH_3$	5.20	2.49	2.87
$-C_6H_5$	5.17	2.31	2.82
p-$C_6H_5CH_3$	5.17	2.44	2.79
o-$C_6H_5NO_2$	5.14 5.4[e]	2.93	3.03
	5.06	2.18	2.97
$-P(CF_3)_2$	4.9[f]		
p-$C_6H_5NO_2$	4.8[e]		

[a] Values of J_{HNCH} are for neat solutions unless otherwise noted. [b] TMS is used as an internal standard. [c] Extrapolated to infinite dilution. [d] Reference 10, solution in chlorobenzene. [e] Reference 3, solution in pyridine. [f] Reference 4, solution in $CHFCl_2$.

in Table I. A least-squares treatment of the data shows it to obey the equation

$$J_{HNCH}\,(\text{Hz}) = 12.02 - 0.04\delta_{CH_3}\,(\text{Hz})$$

The standard deviation of J is 0.11 Hz and the correlation coefficient is -0.986. The largest deviations from linearity appear to be for compounds which have aromatic groups attached directly to the nitrogen atom. This is somewhat to be expected since weak interactions are known to exist between carbon tetrachloride as a solvent and aromatic solutes.[14]

The linearity of this relationship strongly suggests that the magnitude of J_{HNCH} is related to the electron-withdrawing ability of the nitrogen substituent in such a way that as the ability of that group to withdraw electron density from the H-N-C-H framework increases, the coupling constant decreases and at the same time the *N*-methyl resonance moves downfield from TMS.

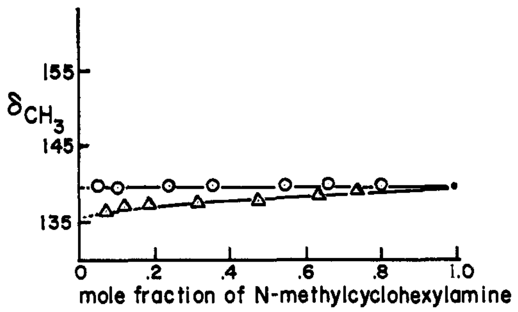


Figure 3. The *N*-methyl chemical shift for *N*-methylcyclohexylamine as a function of mole fraction in carbon tetrachloride (○) and benzene (△).

Of some interest is the case of *N*-methylhydrazine (I, R = NH_2). The chemical shift of the methyl group and J_{HNCH} correspond quite closely to those found for alkyl-substituted methylamines. This indicates that the amino group is not acting as an electron-withdrawing group but instead as a weakly electron-donating group in *N*-methylhydrazine.

Finally, the large downfield shifts which occur for the *N*-methyl group in aromatic-substituted methylamines on going from the neat amine to infinite dilution in carbon tetrachloride (Table I) should be noted. Figure 2 shows that diluting *N*-methylaniline (I, R = C_6H_5) with carbon tetrachloride or cyclohexane causes a drastic downfield shift in the *N*-methyl resonance. Figure 3 reveals, however, that no shift at all occurs upon dilution of *N*-methylcyclohexylamine (I, R = C_6H_{11}) in carbon tetrachloride. Apparently the high field chemical shifts of the *N*-methyl group in neat aromatic derivatives are derived from an intermolecular interaction between the methyl group of one molecule with the aromatic ring of another. It is well known[15] that molecular association is not necessary to cause such shifts. The fact that this anisotropic shielding also occurs when the aromatic amines are dissolved in benzene (*cf.* Figure 2) argues for a solute–solvent interaction and against any requirement for intermolecular association through hydrogen bonding to orient the aromatic rings with respect to the methyl groups.

It is quite surprising to note, then, that this anisotropic shielding does not exist to anywhere near the same extent when aliphatic-substituted methylamines are dissolved in benzene. Figure 3 shows that the *N*-methyl group of methylcyclohexylamine shifts upfield only 3.5 Hz when extrapolated to infinite dilution in benzene, a minor shift when compared with that for aromatic amines. It appears that the solvent benzene molecules are unable to get near the *N*-methyl group in this compound. The most likely explanation for this is a steric one. When the substituent is a saturated group (I, R = alkyl), the tetrahedral orientation around the nitrogen along with a bulky substituent attached to it preclude the close approach by the solvent molecules. However, when the substituent R is an aromatic group, possible overlap of the nitrogen lone pair with the aromatic π system could cause the geometry about the nitrogen atom to be considerably more planar. This, along with a planar aromatic group as the substituent, should allow for much closer approach by the solvent.

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(14) G. Kotowycz and T. Schaefer, *Can. J. Chem.*, **46**, 3110 (1968).

(15) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, N. Y., 1959, Chapter 16.

Experimental Section

All of the amines used in these studies were commercially available from Eastman Kodak Co. and Aldrich Chemical Co. They were refluxed briefly over sodium metal (caution, hydrogen gas is generated in this step) and introduced into a high vacuum system[16] where they were condensed into a vessel containing liquid NaK alloy. It was necessary to leave the amines in these vessels from 1 to 3 days and it was found to be imperative that the hydrogen pressure be relieved periodically. Pmr samples were prepared by condensing the amine and internal standard into the sample tube. If dimethylzinc was added to the amine it was added at this point. The amount of dimethylzinc added to each sample was less than 10^{-5} mol as measured *via* a calibrated volume on the vacuum line. All pmr samples were sealed under vacuum to exclude the laboratory atmosphere.

Dimethylzinc was prepared by the method of Hota and Willis[17] using methyl iodide, zinc dust, and copper powder.

Pmr spectra were measured on a Varian A-60-A spectrometer. All pmr parameters were measured by linear interpolation between audiofrequency side bands of TMS and are accurate to ±0.05 Hz.

Acknowledgment. We would like to thank the Research Corporation for its gracious support of this work.

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[16] D. F. Shriver, "The Manipulation of Air-Sensitive Compounds," McGraw-Hill, New York, N. Y., 1969.

[17] N. K. Hota and C. J. Willis, *J. Organometal. Chem.*, **9**, 171 (1967).

Electron Spin Resonance Study of Cycl[3.3.3]azine[1] Radical Ions

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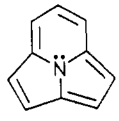
Contribution from Physikalisch-Chemisches Institut der Universität Basel, 4056 Basel, Switzerland, and the Department of Chemistry, University of Edinburgh, Edinburgh EH9 3JJ, Scotland. *Received April 27, 1973*

Abstract: Esr data (g values and proton, ^{14}N, and ^{13}C coupling constants) are reported for the radical cation and anion of cycl[3.3.3]azine (**4**). A simple model, which correlates the HOMO and LUMO of **4** with the degenerate nonbonding orbitals (ψ_S and ψ_A) of [12]annulene (**6**), accounts for the main features of the π-spin distribution in the radical ions $\mathbf{4}\cdot^{+}$ and $\mathbf{4}\cdot^{-}$. This model also predicts the almost identical π-spin populations observed for the cation $\mathbf{4}\cdot^{+}$ and the isoelectronic phenalenyl radical ($\mathbf{5}\cdot$). The central nitrogen atom in $\mathbf{4}\cdot^{+}$ and $\mathbf{4}\cdot^{-}$ is presumably coplanar with the 12-membered ring. Contrary to the neutral compound **4**, this ring has been considered not to exhibit bond alternation in $\mathbf{4}\cdot^{+}$ and $\mathbf{4}\cdot^{-}$. In addition to $\mathbf{4}\cdot^{+}$ and $\mathbf{4}\cdot^{-}$, radical ions of some substituted cycl[3.3.3]azines have been studied by esr spectroscopy. They include the 1,3-dicyano derivative (**4a**), the 1,3-di-*tert*-butyl ester (**4b**), and the corresponding monoester (**4c**), an intermediate in the thermal decarboxylation of **4b** to **4**. The effect of substitution on the π-spin distributions in the radical ions $\mathbf{4}\cdot^{+}$ and $\mathbf{4}\cdot^{-}$ is qualitatively discussed.

The cyclazines are a class of compounds consisting of a cyclic π-electron system (π perimeter) bridged by a central sp^2-hybridized nitrogen atom.[3,4] Its first representative, the cycl[3.2.2]azine (**1**),[1] synthesized by Windgassen, *et al.*,[3] can be regarded either as an isoelectronic aza analog of the aceindylenyl anion ($\mathbf{2}^-$) or as a bridged [10]annulene (**3**). In fact, some of the properties of **1** can be rationalized in terms of $\mathbf{2}^-$, whereas others are more satisfactorily accommodated by **3**.[5,6]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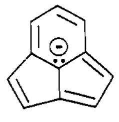
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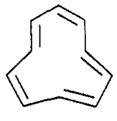
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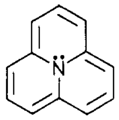
Recently, further compounds in the cyclazine series have become available through the work of Leaver, *et al.*,[7,8] who synthesized two novel systems, cycl[3.3.3]azine (**4**) and cyclopenta[*h*]cycl[4.2.2]azine (**7**).[1] The highly symmetrical compound **4** is of special interest,[9] being structurally related to the isoelectronic phenalenyl anion ($\mathbf{5}^-$) and the [12]annulene (**6**).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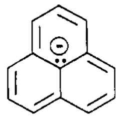
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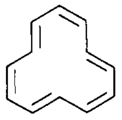
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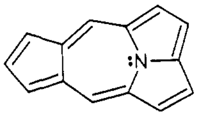
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The radical anion $\mathbf{1}\cdot^{-}$ of cycl[3.2.2]azine has been extensively studied by esr spectroscopy.[6] Furthermore, esr spectra have been recently reported[10] for the radical anions of **7** and some derivatives of **1**. Attempts to prepare the radical cations of **1** and **7** were unsuccessful.[11]

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[1] According to IUPAC nomenclature, cycl[3.3.3]azine (**4**) must be denoted pyrido[2,1,6-*de*]quinolizine. Analogously, cycl[3.2.2]azine (**1**) and cyclopenta[*h*]cycl[4.2.2]azine (**7**) should be pyrido[2,1,6-*cd*]pyrrolizine and cyclopenta[4,5]azepino[2,1,7-*cd*]pyrrolizine, respectively. For the sake of simplicity and because of the popularity of the cyclazine notation, we have used it throughout the paper.

[2] (a) Universität Basel; (b) University of Edinburgh.

[3] R. J. Windgassen, Jr., W. H. Saunders, Jr., and V. Boekelheide, *J. Amer. Chem. Soc.*, **81**, 1459 (1959).

[4] R. D. Brown and B. A. Coller, *Mol. Phys.*, **2**, 158 (1959).

[5] F. Gerson, E. Heilbronner, N. Joop, and M. Zimmermann, *Helv. Chim. Acta*, **46**, 1940 (1963); V. Boekelheide, F. Gerson, E. Heilbronner, and D. Meuche, *ibid.*, **46**, 1951 (1963).

[6] N. M. Atherton, F. Gerson, and J. N. Murrell, *Mol. Phys.*, **6**, 265 (1963); F. Gerson and J. D. W. van Voorst, *Helv. Chim. Acta*, **46**, 2257 (1963); see also F. Gerson and J. H. Hammons in "Nonbenzenoid Aromatics," J. P. Snyder, Ed., Academic Press, New York, N. Y., 1971, pp 137–140.

[7] D. Farquhar and D. Leaver, *Chem. Commun.*, 24 (1969).

[8] M. A. Jessep and D. Leaver, *ibid.*, 790 (1970)

[9] M. J. S. Dewar and N. Trinajstic, *J. Chem. Soc. A*, 1754 (1969).

[10] F. Gerson, J. Jachimowicz, B. Kowert, and D. Leaver, *Helv. Chim. Acta*, **56**, 258 (1973).

[11] F. Gerson and J. Jachimowicz, unpublished work.