

**152. n- $\pi$ -Interaction in Enamines and Enaminoketones. A  $^{15}\text{N}$ -NMR. Study<sup>1)</sup>**

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*Summary*

$^{15}\text{N}$ -Chemical shifts of 32 enamines, 11 enaminoketones and 28 closely related amines have been determined with the isotope in natural abundance. In order to eliminate substituent effects, differential chemical shifts  $\Delta\delta(\text{N})$  are defined as  $\delta_{\text{N}}(\text{amine}) - \delta_{\text{N}}(\text{enamine})$ . This parameter is shown to correlate well with the free enthalpy of activation  $\Delta G^\ddagger$  for restricted rotation about the N-C( $\alpha$ ) bond in enamines with extended conjugation.  $\Delta\delta(\text{N})$  values of substituted anilino-styrenes correlate also with  $^{13}\text{C}$ -chemical shifts of the  $\beta$ -carbon in the enamine system and with *Hammett*  $\sigma$ -constants of the aniline substituents. The experimental results suggest that differential  $^{15}\text{N}$  shifts are a useful probe to study n, $\pi$ -interaction in enamines.

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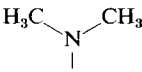

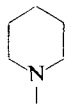
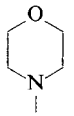
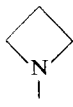
**1. Introduction.** – Enamines are very reactive compounds, easily accessible and of great importance in synthetic chemistry. They have also attracted the attention of structural chemists and spectroscopists because of the variable extent of interaction between the nitrogen lone pair and the  $\pi$ -electrons of the carbon-carbon double bond. This interaction is largely responsible for the specific physical and chemical properties of enamines. Spectroscopic studies of resonance effects in enamines and enaminoketones (vinylogous amides) have included UV. [2], IR. [3] and in recent years,  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR. spectroscopy [2] [4–7]. Magnetic resonance methods have also been utilized to investigate stereoisomerism, in particular conformational effects [7]. Chemical shifts depend among other factors upon electron density at the nucleus under investigation. Whereas several attempts have been made to interpret proton [3] [6] and carbon chemical shifts [3] [7] in terms of electron delocalization in enamines, no such study has been undertaken using nitrogen magnetic resonance and, in particular,  $^{15}\text{N}$ -NMR. spectroscopy. A preliminary study of  $^{14}\text{N}$  shifts of enaminoketones [8] was handicapped by the inaccuracy of the chemical shifts (very broad signals). Improved instrumentation now permits the investigation of  $^{15}\text{N}$  chemical shifts in enamines and the corresponding amines with natural isotope abundance. The  $^{15}\text{N}$  nucleus yields precise chemical shift data suitable for a study of substituent effects in enamines. We report the first results of our investigations.

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<sup>1)</sup>  $^{15}\text{N}$ -NMR. Spectroscopy, Part III; Part II [1].

**2. Chemical shifts of enamines.** – We have divided the  $^{15}\text{N}$  chemical shift data into three groups: data of typical enamines (cyclic and open-chain), of enamines with extended conjugation and of enaminketones. The chemical shifts of the first class, with the typical variation of the amine component, *i.e.*, dimethylamino, pyrrolidino, piperidino and morpholino, are summarized in *Table 1*. The chemical shift range extends from  $-348$  to  $-303$  ppm<sup>2)</sup>. The data of the secondary and tertiary amines corresponding to the series of bases given above are also included in this table. The chemical shifts of the latter are in the range of  $-369$  to  $-312$  ppm. There is considerable overlap of the chemical shift ranges in the two classes of compounds. However, the enamine nitrogen is always less shielded than the nitrogen of a closely related amine.  $^{15}\text{N}$  shifts of aliphatic amines have been shown to lie, generally, between  $-360$  and  $-315$  ppm [9] [10]. Thus, enamine chemical shifts extend beyond this range towards lower shielding constants.

Table 1.  $^{15}\text{N}$ -Chemical shifts [ $\delta$ , ppm] of typical enamines  $R-X$  and closely related amines  $R-X$

R	X				
					
cyclohex-1-enyl	-330.1 <b>1</b>	-303.0 <b>2</b>	-303.6 <b>3</b>	-308.4 <b>4</b>	-314.2 <b>5</b>
cyclopent-1-enyl	-331.4 <b>6</b>	-306.7 <b>7</b>	-307.2 <b>8</b>	-311.6 <b>9</b>	-
$(\text{CH}_3)_2\text{C}=\text{CH}-$	-347.5 <b>10</b>	-318.5 <b>11</b>	-321.9 <b>12</b>	-326.4 <b>13</b>	-
H-	-368.5 <sup>a)</sup> <b>36</b>	-339.8 <b>37</b>	-339.5 <b>38</b>	-346.4 <b>39</b>	-
$\text{CH}_3-$	-362.8 <sup>b)</sup> <b>40</b>	-335.8 <b>41</b>	-339.8 <b>42</b>	-344.0 <b>43</b>	-
$\text{CH}_3\text{CH}_2\text{CH}_2-$	-354.5 <b>44</b>	-325.4 <b>45</b>	-329.7 <b>46</b>	-333.8 <b>47</b>	-
cyclohexyl	-348.4 <b>48</b>	-314.9 <b>49</b>	-323.4 <b>50</b>	-326.5 <b>51</b>	-
cyclopentyl	-342.1 <sup>c)</sup> <b>52</b>	-312.2 <b>53</b>	-317.2 <b>54</b>	-320.8 <sup>c)</sup> <b>55</b>	-
$(\text{CH}_3)_2\text{CH}-\text{CH}_2-$	-355.2 <sup>c)</sup> <b>56</b>	-326.1 <b>57</b>	-330.4 <sup>c)</sup> <b>58</b>	-335.0 <b>59</b>	-
$(\text{C}_6\text{H}_5)_2\text{CH}-\text{CH}_2-$	-355.8 <sup>c)</sup> <b>60</b>	-326.6 <sup>c)</sup> <b>61</b>	-330.9 <sup>c)</sup> <b>62</b>	-335.2 <b>63</b>	-

<sup>a)</sup> Measured at  $4^\circ$ .

<sup>b)</sup> Data from [11].

<sup>c)</sup> Calculated data, *cf.* p. 1505.

<sup>2)</sup> All data are referred to the resonance of the  $\text{NO}_3^-$  ion as an external standard, and decreasing values with negative sign indicate lower shielding constants.

Table 2.  $^{15}\text{N}$ -Chemical shifts [ $\delta$ , ppm] of conjugated enamines

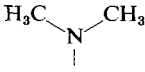

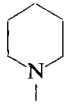
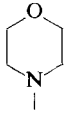
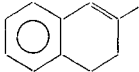
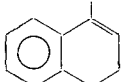
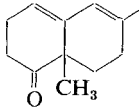
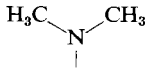

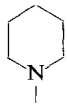
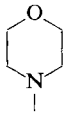

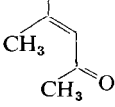
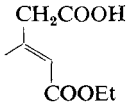
R	X			
				
$(E)\text{-C}_6\text{H}_5\text{-CH=CH-}$	-323.1 <b>14</b>	-297.4 <b>15</b>	-299.9 <b>16</b>	-306.1 <b>17</b>
$(\text{C}_6\text{H}_5)_2\text{C=CH-}$	-325.6 <b>18</b>	-298.2 <b>19</b>	-301.3 <b>20</b>	309.2 <b>21</b>
	-323.2 <b>22</b>	-	-	-
	-309.3 <b>23</b>	-	-	-
	-	-297.5 <b>24</b>	-	-

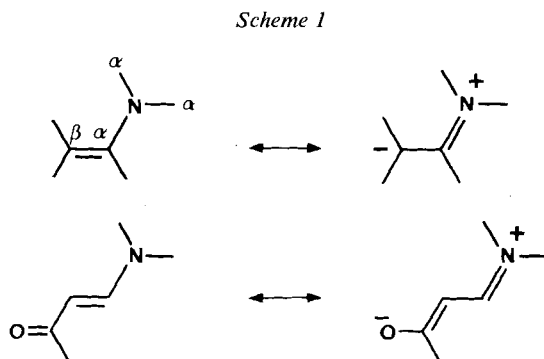
 Table 3.  $^{15}\text{N}$ -Chemical shifts [ $\delta$ , ppm] of enaminketones and related compounds

R	X				
					$\text{-NH(CH}_2)_3\text{CH}_3$
	-295.3 <b>25</b>	-270.9 <b>26</b>	-276.7 <b>27</b>	-288.0 <b>28</b>	-
	-294.2 <b>29</b>	-269.2 <b>30</b>	-273.1 <b>31</b>	-280.9 <b>32</b>	-
	-270.9 <b>33</b>	-	-	-	-
$(\text{CN})_2\text{C=C(CN)-}$	-	-	-	-	-259.8 <b>34</b>
$(E)\text{-NO}_2\text{-CH=CH-}$	-	-	-263.0 <b>35</b>	-	-

This deshielding effect is further enhanced in 'conjugated' enamines where the olefinic component is of a diene or styrene type. In this class the shift range for the present examples extends from  $-326$  to  $-298$  ppm (*Table 2*). If the olefinic component has strongly electron-withdrawing properties as, *e.g.*, in enaminketones, -esters, -nitriles *etc.*, the enamine nitrogen becomes more deshielded and the chemical shifts are now between  $-295$  and  $-260$  ppm (*Table 3*). These data extend into the range of amide resonances ( $-280$  to  $-235$  ppm) [11] which reflects the vinylogous amide nature of enaminketones.

**3. Discussion of the results.** – An attempt is made to interpret the observed  $^{15}\text{N}$  chemical shifts in terms of  $\pi$ -electron delocalization ( $n, \pi$ -interaction) and substituent effects. The variation in the chemical shifts of both the enamines and the corresponding amines over the whole series is about 100 ppm. However, if the changes in  $\delta(\text{N})$  of a particular series of compounds is considered, the effects are considerably smaller. For this reason, we do not attempt to find a correlation with calculated shielding constants. This approach was shown to be successful only when either large chemical shift effects between different types of nitrogen functional groups are considered, or in a given series of compounds with very similar molecular geometry, in particular local geometry at the nitrogen atom [11] [12].

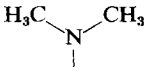

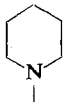
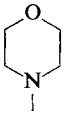
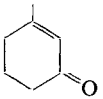
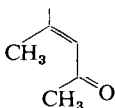
An empirical treatment of the experimental data is more suitable to deal with such effects as variation in  $\pi$ -electron delocalization and the influence of different substituents. An application of the resonance formalism to enamines and enaminketones (*Scheme 1*) illustrates that the nitrogen nucleus is expected to show a decrease of the shielding constant (*i.e.*, a low-field shift) with increasing electron delocalization.



Using this model, it is presumed that the variations in the nitrogen chemical shifts are governed by delocalization effects in the electronic ground state. From the  $^{15}\text{N}$  chemical shift data in *Tables 1, 2* and *3*, it is clear that there is a general trend towards lower field in going from the amines to enamines, and finally to enaminketones and related structures. This effect becomes particularly clear if the variation in  $\delta(\text{N})$  is considered for a series of compounds derived from the same secondary amine. Chemical shift studies of aliphatic amines [9] have already revealed that substituent effects are rather large for  $\alpha$ - ( $-8.7$  ppm) and  $\beta$ -alkyl substituents ( $-18.2$  ppm) whereas the increments for  $\gamma$ -,  $\delta$ - and  $\epsilon$ -alkyl groups are of minor importance

(1–2 ppm). In order to isolate the influence of  $\pi$ -electron delocalization in enamines from all other structural effects, the chemical shift of the enamine should be considered *relative* to the shift of the corresponding tertiary amine obtained by hydrogenation of the carbon-carbon double bond. In such  $\Delta\delta(N)$  values, inductive and steric influences due to different *N*-substitution should be cancelled. Consequently,  $\Delta\delta(N)$  values allow a comparison of enamines derived from different bases or carbonyl compounds with respect to lone-pair delocalization. The preparation, in each case, of the exactly corresponding amine is, however, not even necessary since one can take advantage of the additivity of substituent effects. The chemical shifts of the amines for the four members of a horizontal column in *Table 1* may be calculated from the experimentally determined shift value of a single member and the constant increments between dimethylamino, pyrrolidino, piperidino and morpholino derivatives. These increments were obtained from the complete series of experimental chemical shifts for the *N*-methyl and *N*-propylamines. The  $\Delta\delta(N)$  values of the compounds of *Tables 1, 2* and *3* obtained in this way are included in *Table 4*. Large  $\Delta\delta$  values indicate that for such enamines the iminium resonance structure in *Scheme 1* is of considerable importance.

Table 4. Differential chemical shifts  $\Delta\delta(N)^a$ 

R	X			
				
cyclohex-1-enyl	-18.3	-11.9	-19.8	-18.1
cyclopent-1-enyl	-10.7 <sup>b)</sup>	-5.5	-10.0	-9.2 <sup>b)</sup>
(CH <sub>3</sub> ) <sub>2</sub> C=CH-	-7.7 <sup>b)</sup>	-7.6	-8.5 <sup>b)</sup>	-8.6
( <i>E</i> )-C <sub>6</sub> H <sub>5</sub> -CH=CH-	-32.1	-28.7	-30.5	-28.9
(C <sub>6</sub> H <sub>5</sub> ) <sub>2</sub> C=CH-	-30.2 <sup>b)</sup>	-28.4 <sup>b)</sup>	-29.6 <sup>b)</sup>	-26.0
	-53.1	-44.0	-46.7	-38.5
	-54.2 <sup>b)</sup>	-45.7 <sup>b)</sup>	-50.3 <sup>b)</sup>	-45.6
( <i>E</i> )-NO <sub>2</sub> -CH=CH-			-66.7	

<sup>a)</sup>  $\Delta\delta(N) = \delta_N(\text{amine}) - \delta_N(\text{enamine})$ .

<sup>b)</sup> Obtained with the aid of calculated amine data, *cf.* p. 1505.

At this point the question arises as to what extent the  $\Delta\delta(\text{N})$  values defined in the above way are a quantitative measure of  $\pi$ -electron delocalization in enamines. In search of independent support we determined the barrier to internal rotation about the N–C( $\alpha$ ) bond in the conjugated system. Free enthalpies of activation ( $\Delta G^\ddagger$ ) were obtained from the temperature dependence of the C( $\alpha$ ) carbon signals in the amine moiety of the enamines and enaminketones **14**, **15**, **25**, **28**, **29**, **32**, and **35**. Figure 1 shows a satisfactory linear correlation between the  $\Delta G_c^\ddagger$  and  $\Delta\delta(\text{N})$  data. Regression analysis (correlation coefficient 0.94) gave the equation

$$\Delta G_c^\ddagger [\text{kcal/mol}] = -0.19 (\Delta\delta(\text{N})[\text{ppm}]) + 2.91$$

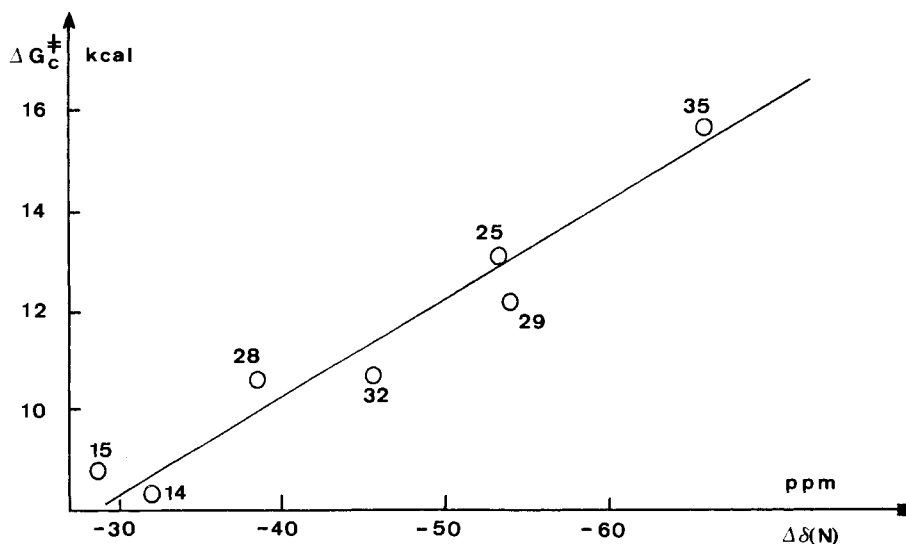
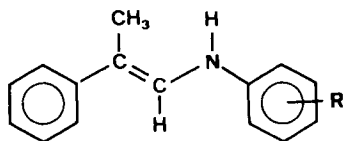


Fig. 1. Correlation of the free enthalpy of activation  $\Delta G_c^\ddagger$  for rotation about the N–C( $\alpha$ ) bond with the differential chemical shift  $\Delta\delta(\text{N})$

Since the height of the barrier to rotation will be largely determined by the C( $\alpha$ )–N  $\pi$ -bond order, this correlation supports the significance of  $\Delta\delta(\text{N})$  values as a measure for  $n, \pi$ -interaction, provided that the entropy term in  $\Delta G^\ddagger$  is small over the whole range of coalescence temperatures. In a similar treatment *Martin et al.* [13] have recently correlated *Arrhenius* activation energies  $E_a$  with  $^{15}\text{N}$  chemical shifts in amides and thioamides. These authors have also advanced a *semi-empirical* ex-

Scheme 2



planation for the validity of such correlations. It should be noted that enamino-ketones may be considered as vinylogous amides and, consequently, our results lend further support to this approach.

That relative  $^{15}\text{N}$  chemical shifts  $\Delta\delta(\text{N})$  are a reliable parameter in studies of  $\pi$ -electron delocalization is further illustrated by the following investigation. In a series of substituted anilino-styrenes (*Scheme 2*) the nitrogen lone-pair is also involved in the mesomeric system of the aniline moiety. It can be expected that the nature of the substituents R will affect the extent of enamine polarization, *i.e.*, there should be a *Hammert*-type relationship between substituent constants and  $\Delta\delta(\text{N})$  values. Furthermore, the  $^{13}\text{C}$  shift of  $\text{C}(\beta)$  should be affected by roughly the same steric and inductive factors throughout the series if substituents in *para*- or *meta*-position only are included. Hence, in this series the  $\text{C}(\beta)$  chemical shift too should be a useful probe for enamine polarization<sup>3</sup>). The results of this study are summarized in *Table 5*.

Table 5.  $^{15}\text{N}$ -Chemical shifts [ $\delta$ , ppm],  $^1\text{J}(\text{N}, \text{H})$  coupling constants [ $J$ , Hz] and  $^{13}\text{C}$ -chemical shifts [ $\delta(\text{C}_\beta)$ , ppm] of substituted anilino-styrenes<sup>a</sup>) (*Scheme 2*)

R	$\delta(\text{N})$	$^1\text{J}(\text{N}, \text{H})$	$\delta(\text{N})_{\text{aniline}}$	$\Delta\delta(\text{N})$	$\sigma$	$\delta(\text{C}_\beta)$
<i>p</i> -NO <sub>2</sub>	-269.4	90.4	-300.1	-30.7	0.78	112.4
<i>m</i> -NO <sub>2</sub>	-278.2	92.3	-313.9	-35.7	0.71	112.2
<i>m</i> -Cl	-279.5	91.7	-317.6	-38.1	0.37	111.4
<i>p</i> -Cl	-280.6	91.2	-318.8	-38.2	0.24	110.6
<i>m</i> -OCH <sub>3</sub>	-279.5	90.6	-318.5	-39.0	0.08	109.9
H	-280.1	90.8	-319.4	-39.3	0	109.8
<i>p</i> -OCH <sub>3</sub>	-284.2	92.9	-324.8	-40.6	-0.11	108.4
<i>p</i> -CH <sub>3</sub>	-281.4	90.2	-321.5	-40.1	-0.13	108.6

a) Solvent: dimethylsulfoxide-d<sub>6</sub>.

The  $^{15}\text{N}$  chemical shifts of the corresponding substituted anilines are also listed and were subtracted from the shifts of the anilino-styrenes to give  $\Delta\delta(\text{N})$ . This parameter is expected to reflect the influence of R upon  $\pi$ -electron delocalization in the enamine moiety (*Table 5*). In fact, the  $\Delta\delta(\text{N})$  values show a linear correlation with *Hammert* constants (*Fig. 2*) and with the  $^{13}\text{C}$  shifts of  $\text{C}(\beta)$  (*Fig. 3*). The one-bond N, H coupling constants lie in the range typical for  $\text{sp}^2$ -hybridized nitrogen [14] and show only a very small and non-systematic variation<sup>4</sup>) with a change in R, in contrast to the large effects observed in substituted anilines [16]. This demonstrates that hybridization of the nitrogen is mainly determined by the enamine nature of these compounds and that the substituents R only influence the extent of enamine polarization.

<sup>3</sup>) It must be pointed out that this is generally not the case and leads to the well-known limitation of the utility of  $^{13}\text{C}$  shifts in enamine studies [3].

<sup>4</sup>) Observed also for substitution in the styrene ring [15].

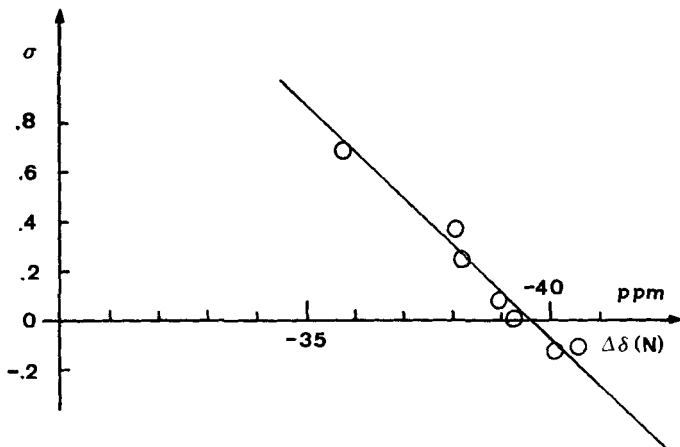


Fig. 2. Correlation of the differential chemical shift  $\Delta\delta(N)$  with the chemical shift of  $C(\beta)$  in substituted anilinostryrenes (cf. Table 5). The data of the *p*-nitro derivative are omitted

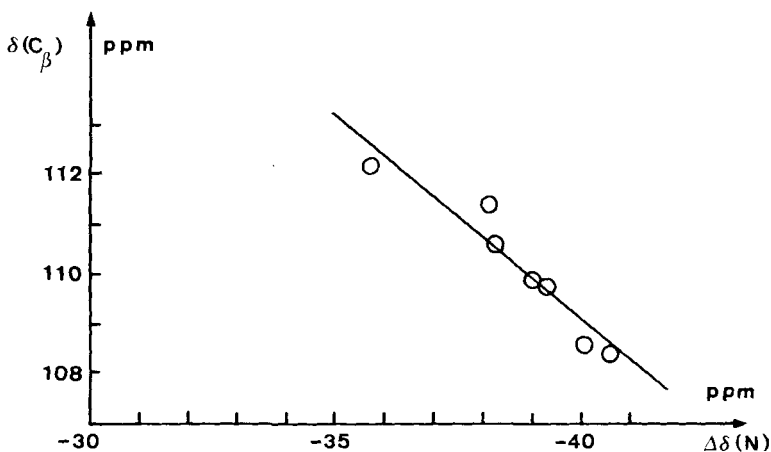


Fig. 3. Correlation of the differential chemical shift  $\Delta\delta(N)$  with Hammett  $\sigma$ -values for substituted anilinostryrenes (cf. Table 5). The data of the *p*-nitro derivative are omitted

In conclusion, nitrogen chemical shifts, unlike carbon chemical shifts [3], reflect in a quantitative way the extent of  $n,\pi$ -interaction in enamines and they can be correlated with other parameters which are sensitive to the same effect. The better results obtained with  $^{15}\text{N}$ -NMR, are rationalized by the facts that this nucleus exhibits a much larger variation in the shielding constant and that substituent effects can be largely eliminated in the differential shifts  $\Delta\delta(N)$ .

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## Experimental Part

The  $^{15}\text{N}$ -NMR. spectra were measured in natural isotope abundance at 10.1 MHz on a *Varian* XL-100-15 spectrometer (12 mm sample tubes) in the pulsed mode. The substrates were dissolved in benzene- $d_6$  (approx. 80%  $v/v$ ) if not otherwise specified. In those cases where the NOE was unfavorable, chromium acetylacetonate ( $\text{Cr}(\text{acac})_3$ ) was added at concentrations up to 0.1M. Chemical shifts are referred to external nitrate ion (31.3 mg  $\text{NH}_4^{15}\text{NO}_3$  per ml  $\text{H}_2\text{O}$ ). Chemical shift effects arising from variations in substrate concentration or the addition of  $\text{Cr}(\text{acac})_3$ , do not exceed  $\pm 0.5$  ppm.

The temperature-dependent  $^{13}\text{C}$ -NMR. spectra of the compounds in *Fig. 1* were obtained on a *Varian* XL-100-12 spectrometer (10 mm sample tubes) at 25.2 MHz in the pulsed and proton-noise-decoupled mode. Sample temperatures ( $\pm 2^\circ$ ) were determined by means of a reference tube containing the same solvent and a precision thermometer. The substrate concentration was  $(40 \pm 10)\%$   $v/v$  in acetone- $d_6$  or methylene chloride- $d_2$ . Free enthalpies of activation ( $\Delta G^\ddagger$ ) were calculated from the rate constants at the coalescence point with the use of the *Eyring* equation.

The majority of the compounds was prepared following standard procedures. The enamines **1** to **9**, **22** and **24** were kindly supplied by Prof. *U. K. Pandit* and the amines **44** to **47** by Dr. *P. Fischer*.

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