

The Barrier to Internal Rotation in *N*-Methylpyrrole-2-aldehyde

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The rotational barrier in *N*-methylpyrrole-2-aldehyde has been studied by nuclear magnetic resonance at 100 MHz at temperatures between +30° and -90°C. The two rotational isomers are present in highly unequal amounts (*ca.* 1:22 at -60°C). The rate parameters have been calculated from the line shape of the aldehyde proton. The data from two independent series of measurements have been evaluated and the barrier in *N*-methylpyrrole-2-aldehyde is found to be *ca.* 1 kcal/mole higher than the corresponding barrier in 2-furanaldehyde.

In two preceding communications we have reported the barriers to internal rotation in the =C-C=O bonds of 2-furanaldehyde¹ and 2-acetylfuran.² In order to elucidate the role of the heteroaromatic nuclei it is of interest to study analogous thiophene and pyrrole derivatives. Despite several attempts we have not been able to observe any sign of hindered rotation in the PMR spectra of 2-thiophenealdehyde or 2-acetylthiophene at temperatures down to -115°C. This could either mean that the rotational barrier is very low (less than about 8 kcal/mole) or that the two rotational isomers in each molecule have very unequal populations. In the case of the pyrrole analogue we were, however, more successful.

To avoid spin coupling between the NH proton and the other protons in pyrrole-2-aldehyde, which complicates the evaluation of the spectra we decided to investigate *N*-methylpyrrole-2-aldehyde. This compound may be assumed to exist in two essentially planar rotational isomers I and II (*cf.* Fig. 1).

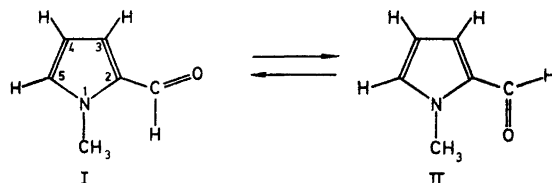


Fig. 1. The two rotational isomers of *N*-methylpyrrole-2-aldehyde.

The two isomers proved to have very unequal populations, the ratio I/II being ca 22:1 at -60°C (see below). To enable calculations of the rate constants to be made this population ratio must be known throughout the temperature region used for the evaluation, -10 to -65°C . As in the case of 2-furanaldehyde¹ the equilibrium amounts of the conformers may be expected to vary with temperature. In the present case, however, the population ratio could only be determined indirectly, and somewhat at the expense of the accuracy of the rate parameters.

Two complete series of measurements were performed independently as a check of the reproducibility of the results.

EXPERIMENTAL

The sample of *N*-methylpyrrole-2-aldehyde was prepared by methylation of pyrrole-2-aldehyde with dimethylsulphate in alkali. The first series of measurements was performed on an 8.5 % solution and the second series on a 9.9 % solution in hexadeuteroacetone (E. Merck AG, Darmstadt, Germany). To both samples ca. 5 % tetramethylsilane (TMS) was added to provide a signal for the field-frequency lock system of the NMR spectrometer. The samples also contained about 10 % chloroform for monitoring the resolutions of the spectrometer. The *N*-methylpyrrole-2-aldehyde used in the second sample was purified by preparative gas chromatography and distilled twice in vacuum before use (b.p. = $75-76^{\circ}\text{C}/12-13$ mm).

The NMR spectra were recorded at 100 MHz with a Varian HA-100 spectrometer equipped with a Varian V-4333 variable temperature probe and V-4343 temperature controller. The spectra were expanded to 0.4 Hz/cm by the use of an external precalibrated recorder. The sweep rate used was 0.1 Hz/sec and the amplitudes of the radiofrequency fields were low enough to avoid saturation of the signals.

Chemical shifts from TMS (used as internal lock signal) were measured directly with a Hewlett-Packard Model 5512 A Electronic Counter.

The temperature measurements were performed by the use of a capillary tube filled with methanol and centered in the sample tube by means of teflon plugs (Fig. 2). The temperature dependence of the shift difference between the OH and CH₃ methanol signals was separately calibrated by the use of a copper-constantan thermocouple placed inside a dummy tube (*cf.* Ref. 3). This proved to be a convenient and accurate way of measuring temperatures.

The temperature stability of the sample in a typical run was found to be quite good. When the sample temperature was monitored at short intervals during one hour at a fixed setting of the temperature controller (-43°C), we found the temperature changes of the sample to be within $\pm 0.3^{\circ}\text{C}$. At each temperature setting five to ten spectra were recorded and the sample temperature was checked three or four times during each setting.

The interconversion rate was calculated from the line shape of the aldehyde proton signal. Several hundred theoretical NMR spectra were calculated with the Swedish

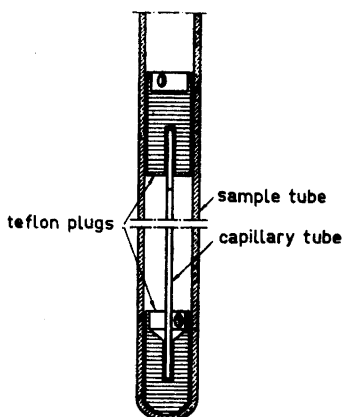


Fig. 2. The arrangement of the capillary tube used for the temperature measurement.

computer TRASK using a program based on the modified Block equations, as carried out for 2-acetylfuran.² These spectra were fitted to the recorded ones by the use of a graphical method to be described below.

THE NMR SPECTRUM OF *N*-METHYLPYRROLE-2-ALDEHYDE

The spectrum of *N*-methylpyrrole-2-aldehyde consists of five groups of signals (Fig. 3). The chemical shifts and spin coupling constants evaluated from the spectra at two different temperatures above and below the coalescence temperature of the signals from the two rotamers are given in Table 1.

The signals from the protons in the 4- and 3-positions (H4 and H3) appear as quartets due to coupling to H3, H5 and H4, H5, respectively. The signal

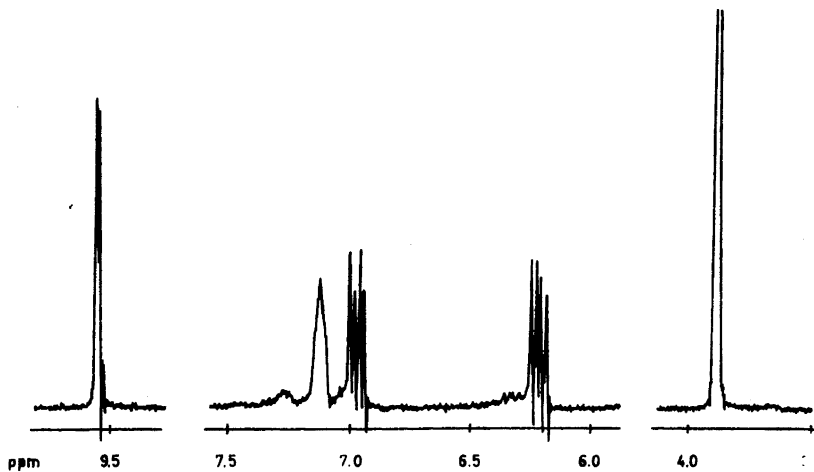


Fig. 3. 100 MHz spectrum of *N*-methylpyrrole-2-aldehyde in $(\text{CH}_3)_2\text{CO}$ recorded at room temperature.

Table 1. Chemical shifts and spin coupling constants for *N*-methylpyrrole-2-aldehyde. The superscripts I and II refer to the two rotational isomers, cf. Fig. 1.

$T^{\circ}\text{K}$	Proton	Chemical shifts (δ -values)	Spin coupling constants (Hz)
268.7	CHO	9.55	$J_{\text{CHO-5}}=0.99$ $J_{34}=4.00$ $J_{35}=1.73$ $J_{45}=2.44$
	H(3)	6.97	
	H(4)	6.20	
	H(5)	7.12	
	CH ₃	3.88	
188.2	CHO	I 9.54	$J^{\text{I}}_{\text{CHO-5}}=1.02$ $J^{\text{II}}_{\text{CHO-5}}=1.00$ $J_{34}=4.00$ $J_{35}=1.75$ $J_{45}=2.42$
		II 9.86	
	H(3)	7.09	
	H(4)	6.26	
	H(5)	7.29	
	CH ₃	I 3.93 II 4.08	

from H5 is very complex, probably due to spin coupling with all other protons in the molecule except the protons of the *N*-methyl group. The aldehyde signal appears as a doublet due to coupling with H5. The variation of the interconversion rate of the two rotational isomers is manifested in three of the signal groups, *viz.* the H3, the CHO, and the *N*-CH₃ signals. At temperatures below -10°C these signals become broadened and have their maximum widths between -40° and -50°C . At still lower temperatures the interconversion rate is slow enough to give separate NMR signals from the two isomers. Separate signals could, however, only be detected for the *N*-methyl and aldehyde protons. Since the aldehyde signal gave the most pronounced broadening effects this signal was chosen for the evaluation of the rate parameters. The temperature interval used for the rate evaluations was from -10°C to -65°C . The maximum width at half height of the aldehyde signal was only 50 % larger than the width at the ends of the temperature interval (see Fig. 4).

The assignment of the signals to the two rotational isomers presents the same problem as for 2-acetylfuran. Referring to this discussion,² we ascribe the very small low field aldehyde and *N*-methyl signals to isomer II and the large high field signals to isomer I (see Fig. 5).

THE RATIO OF THE ROTATIONAL ISOMERS AND THE RATE MEASUREMENTS

The general method of estimating the populations of two rotational isomers below the coalescence temperature is to integrate the separate signals, but electronic intergration proved to be very unreliable in the present case (*cf.* Fig. 5). Integration was therefore performed at -83°C by weighing

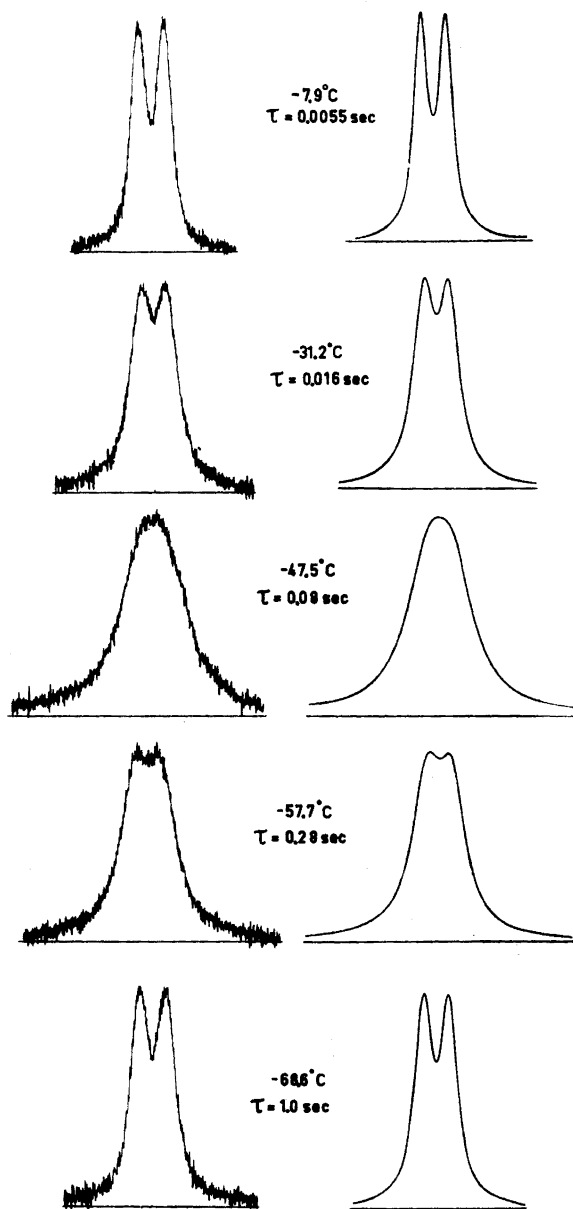


Fig. 4. The experimental and calculated shape of the aldehyde signal at five different temperatures.

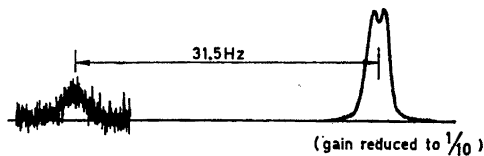


Fig. 5. The signals from the aldehyde proton in the two rotational isomers recorded at -83°C . The small signal at lower field is ascribed to isomer II and the large one at higher field to isomer I.

the cutout paper pieces corresponding to the isomeric signals, which gave the population ratio 32:1.

Above the temperature of maximum broadening the isomer equilibrium constant may be calculated if there exists a stereospecific coupling to some proton involved in the interconversion. The spin coupling constant at temperatures above the coalescence temperature will then be the weighted mean value of the coupling constants in each isomeric form. However, this method makes great demands on spectral resolution at low temperatures to make the separate signals sufficiently resolved, and there must be a significant difference between the two coupling constants. In *N*-methylpyrrole-2-aldehyde stereospecific long-range couplings between H5 and the aldehyde proton are not unlikely, but the hardly detectable signal from isomer II could not be resolved. Furthermore, the difference in $J^{\text{I}}_{\text{CHO}-5}$ and $J^{\text{II}}_{\text{CHO}-5}$ is presumably too small to be of any guidance. $J^{\text{I}}_{\text{CHO}-5}$ is 1.02 Hz while the averaged value of $J^{\text{II}}_{\text{CHO}-5}$ at -5°C is 0.99 Hz.

In order to overcome these difficulties in the determination of the population of the rotamers a graphical method utilizing the "iso-F" surface⁴ was used in combination with theoretical spectra calculated on a computer. The "iso-F" surface method, which has been successfully applied to the case of 2-furanaldehyde, is based on the fact that the maximum height, F, of the appropriately normalized signals in a two-site system is a function of the lifetimes τ and the populations p when the shifts and the transverse relaxation time T_2 are kept constant. Many combinations of τ and p give the same F-

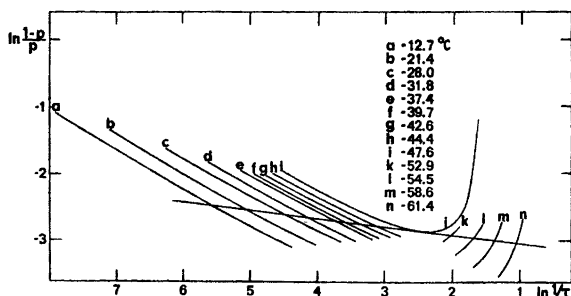


Fig. 5. The "iso-F" surface for the first series of measurements on *N*-methylpyrrole-2-aldehyde (see text).

value and a plot of these connected pairs as $\ln 1/\tau$ against $\ln (1-p)/p$ will produce a parabolic "iso-F" curve for each F-value. The "iso-F" surface for the first series of measurements is shown in Fig. 6. Only the region of the surface which is of interest for the evaluation of the thermodynamic parameters has been constructed, for example a positive value of ΔH° excludes large parts of the "iso-F" curves except for the curve referring to the coalescence temperature. Only one tangent to this curve is shown in the figure. The points of intersection of the "iso-F" curves along this tangent give pairs of connected values of $\ln 1/\tau$ and $1/T$, the corresponding plot of which has a minimum deviation from a straight line. According to the basic assumptions in the "iso-F" method this plot gives the best value of ΔE_A . The complete description of the construction of these "iso-F" curves and the evaluation of ΔE_A and ΔH° from their tangents is to be published elsewhere.⁴ It may be mentioned that in our case, where the aldehyde signal shows only a small broadening even at the coalescence temperature, it was found to be more accurate to characterize the shape of the signals by the quotient a/b , defined in Fig. 7, rather than by the maximum height at the temperatures at which the aldehyde signal was split into a doublet.

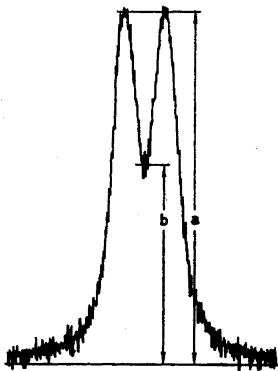


Fig. 7. Definition of the quotient a/b as a characterization of the signal shape.

The transverse relaxation time T_2 was first calculated from the aldehyde signal at -75° to -85°C , where exchange broadening could be neglected, resulting in T_2 -values between 0.5 and 0.6 sec. The values of T_2 evaluated from the aldehyde signal at room temperature were 0.67 and 0.65 sec for the two series of measurements. Since the variation of T_2 with temperature was small the room temperature values were used as constant over the temperature range -15 to -65°C . Evaluation of T_2 from the H4 quartet and the chloroform signal gave fairly constant but different values, *ca.* 0.5 and 0.4 sec, respectively, varying only *ca.* 0.05 sec over a temperature range of 50°C .

The free energy, enthalpy, and entropy of activation were calculated from the theory of absolute reaction rates assuming the transmission coefficient to be equal to unity. The results from the two independent series of measurements are summarized in Table 2 together with the corresponding data for

2-furanaldehyde and 2-acetylfuran. The errors indicated in the table are standard deviations assuming only random errors.

Table 2. Summary of thermodynamic data and activation parameters for *N*-methylpyrrole-2-aldehyde at 298.2°K, 2-furanaldehyde⁽¹⁾ at 216°K and 2-acetylfuran⁽²⁾ at 203°K.

Compound	 I II		 I II		 I II	
	1st series	2nd series				
ΔE_{AI}	10.5 ± 0.3	12.5 ± 0.4	11.9 ± 0.2		9.9 ± 0.2	
kcal/mole						
ΔE_{AII}	9.2 ± 0.3	11.0 ± 0.4	10.9 ± 0.2		»	
kcal/mole						
ΔH°	1.32 ± 0.04	1.57 ± 0.05	1.1 ± 0.1		≈ 0	
kcal/mole						
ΔH_I^*	9.9 ± 0.3	11.9 ± 0.4	11.5 ± 0.2		9.5 ± 0.2	
kcal/mole						
ΔH_{II}^*	8.6 ± 0.3	10.4 ± 0.4	10.5 ± 0.2		»	
kcal/mole						
ΔF°	1.27 ± 0.01	1.28 ± 0.01	0.58 ± 0.04		≈ 0	
kcal/mole						
ΔF_I^*	12.5 ± 0.3	12.0 ± 0.4	10.9 ± 0.2		9.0 ± 0.2	
kcal/mole						
ΔF_{II}^*	11.3 ± 0.3	10.7 ± 0.4	10.3 ± 0.2		»	
kcal/mole						
ΔS°	0.2 ± 0.1	1.0 ± 0.2	2.2 ± 0.2		≈ 0	
cal/mole, deg.						
ΔS_I^*	-8.9 ± 1.9	-0.2 ± 2.9	2.7 ± 1.9		1.5 ± 1.3	
cal/mole, deg.						
ΔS_{II}^*	-9.1 ± 1.9	-1.2 ± 2.9	0.9 ± 1.9		»	
cal/mole, deg.						

^a Average of CHO and H-3 proton at 216°K.

DISCUSSION

The differences between the results of the two series of measurements are not negligibly small, but in view of the very unfavourable rotamer equilibrium they may be considered acceptable.

The values of the free energy of activation agree well with each other but the values of enthalpy and activation energy differ somewhat less than 20 % between the two series. The first series included recordings at 21 different temperatures and the second at 8 temperatures. The calculations of the thermodynamic parameters included 13 (-12.7° to -61.2°C) and 5 (-19.2° to -57.7°C) different temperatures, respectively. Intuitively, the first series would thus be regarded the most reliable but the large negative entropy of activation in this series is difficult to explain.

The uncertainty in the entropy of activation must arise from the very unfavourable population ratios of the rotational isomers, which made it

necessary to record only the large isomer signal and involves a loss of valuable information. The uncertainty of the results cannot be due to the temperature measurements. These are accurate to $\pm 0.5^\circ\text{C}$ by the capillary method, which according to the general relation

$$\Delta S_I^* = (\Delta H_I^* - \Delta F_I^*)/T$$

gives an error in ΔS^* less than 0.1 e.u. for an error in T of 1° at 223°K .

The uncertainty in the entropy of activation caused by errors in the evaluation of τ (as a result of the unfavourable rotamer equilibrium) can be estimated from the formula⁵

$$\Delta(\Delta S^*) = \pm \frac{R}{T_2 - T_1} [(T_2 r_2 / k_2)^2 + (T_1 r_1 / k_1)^2]^{\frac{1}{2}}$$

where R is the ideal gas constant and T_1 and T_2 are the two end temperatures of an interval with corresponding rate coefficients k_1 and k_2 with errors $\pm r_1$ and $\pm r_2$, respectively. If we set $\Delta(\Delta S^*)$ equal to ± 5 e.u. we obtain an error in the k -values of 34 %. This is not impossible since a change in a of this amount cannot always be easily detected. The weak broadening effects of the single signal means a high sensitivity for disturbances in magnetic field homogeneity and other spectrometer phenomena.

The free energy of activation for internal rotation in *N*-methylpyrrole-2-aldehyde is found to be 10 % higher than the corresponding value for 2-furanaldehyde and 30 % higher than that for 2-acetylfuran.

The molecule is assumed to exist in two essentially planar isomeric forms as in the case of 2-acetylfuran, since the conjugative interaction between the ring and the aldehyde group will favour a planar structure. From reasonable molecular models and calculations of nonbonded interactions⁶ according to Scott-Scheraga⁷ it appears that the steric interactions between the CHO-group and the ring are small, but there may be some deviation from exact planarity. A certain degree of steric interaction in *N*-methylpyrrole-2-aldehyde is possibly reflected in the equilibrium constant for the isomer equilibrium, which is about 30 % higher than the corresponding value for 2-furanaldehyde.

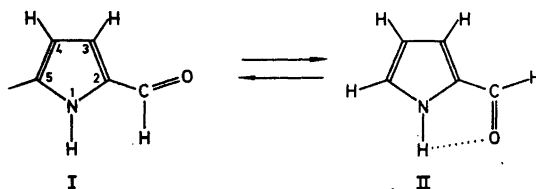


Fig. 8. The rotational isomers of 2-pyrrolealdehyde.

In this connection the conformer equilibrium of pyrrole-2-aldehyde is worth mentioning. It is an old belief that this compound is stabilized by a hydrogen bond in the isomeric form II (Fig. 8). A preliminary investigation of pyrrole-2-aldehyde shows this compound to have an isomer ratio similar to that found for the *N*-methyl analogue, *i.e.* ca. 5 % of the pyrrole-2-aldehyde

exists as conformer II at -70°C as judged from the relative intensities and chemical shifts of the two aldehyde signals observable at -70°C . Even a very weak hydrogen bond of *ca.* 1/3 kcal/mole would give an isomer ratio II/I twice as large as that found. It thus appears that the isomer ratio in pyrrole-2-aldehyde is not determined by intramolecular hydrogen bonding. This interpretation is independent of the assignment of the NMR spectrum of the two isomers of pyrrole-2-aldehyde (*cf.* Ref. 2), since a difference of a factor of two between the isomer ratio for pyrrole-2-aldehyde and that for *N*-methylpyrrole-2-aldehyde, should have been possible to observe by the NMR method.

The higher rotational barrier in *N*-methylpyrrole-2-aldehyde compared to 2-furanaldehyde is predominantly ascribed to increased electronic interaction between the CHO group and the ring. Steric interference by the *N*-methyl group would decrease instead of increase the barrier since the initial-state energy should thus be raised. The methyl group is expected to donate electrons to the aromatic pyrrole ring, thus increasing the electron density of the ring and making it easier for the positive carbonyl carbon atom to attract electrons from the ring. This would lead to a higher bond order in the bond connecting the ring and the aldehyde group in *N*-methylpyrrole-2-aldehyde as compared with the unmethylated analogue.

Attempts were made to estimate the barrier to internal rotation in *N*-methylpyrrole-2-aldehyde using MO calculations of the simple Hückel type and the Extended Hückel type. In the simple Hückel calculations the methyl group was considered using the inductive model,* but this indicates that inductive donation of electrons to the bond connecting the ring and the aldehyde group is very weak. The change in the pertinent bond order upon consideration of the methyl group was only 0.001 units.

The more elaborate Extended Hückel Theory⁹ gives values of the change in total energy** upon rotation which agree very well with the calculated

Table 3. Comparison between experimental and calculated barriers to internal rotation in *N*-methylpyrrole-2-aldehyde.

	ΔH^* kcal/mole 1st series	ΔH^* kcal/mole 2nd series	ΔE^* kcal/mole Ext. Hückel	$\Delta \pi^a$ kcal/mole Hückel MO
$0^{\circ} \rightarrow 90^{\circ}$,	9.9	11.9	11.9	
$180^{\circ} \rightarrow 90^{\circ}$, isomer II	8.6	10.4	10.8	10.2

^a $\beta = -18$ kcal/mole.

* The Hückel parameters used in the calculations are $\alpha_{\text{N}} = \alpha_{\text{C}} + 1.5\beta$ and $\beta_{\text{C-N}} = 0.8\beta_{\text{C-C}}$, *cf.* Ref. 8.

** The valence state parameters¹⁰ used for the Extended Hückel calculations are C_{2s} : -20.78 , O_{2s} : -34.35 , N_{2s} : -27.70 and C_{2p} : -11.31 , O_{2p} : -17.86 , N_{2p} : -14.78 e.V. The Slater orbital exponents¹¹ are $\zeta_{\text{H}} = 1.00$, $\zeta_{\text{C}} = 1.625$, $\zeta_{\text{O}} = 2.275$ and $\zeta_{\text{N}} = 1.950$.

free energies of activation (see Table 3). Unfortunately this must to some degree be regarded as fortuitous.

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