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ROTATION BARRIERS IN N-SUBSTITUTED 2,4,6-TRIMETHYLPYRIDINIUM CATIONS

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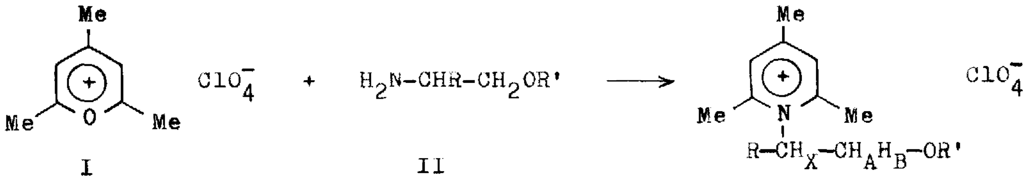
Abstract. The α-methyl and ß-protons in ^{1}H-NMR spectra, the α-methyl, α-ring, and ß-ring carbons in ^{13}C-NMR spectra of N-substituted 2,4,6-trimethylpyridinium salts III are anisochronous. Dynamic NMR spectroscopy affords appreciably higher activation enthalpies $\Delta G^{\ddagger}$ for rotation around the N(sp^2)-C(sp^3) bond than $\Delta G^{\ddagger}$ for the analogously substituted mesityl derivatives, in agreement with the shorter $\overset{+}{N}$-C than the C-C bond.

We report the first case of hindered rotation around the N(sp^2)-C(sp^3) bond in N-substituted 2,4,6-trimethylpyridinium cations (III) obtained by reacting 2,4,6-trimethylpyrylium perchlorate (I) [1] with α-aminoalcohols (IIAa, IIBa, IICa). The hydroxy groups of the resulted pyridinium alcohols (IIIa) can be easily [2] converted into esters (IIIb, IIIc, IIId).



I II III

A, R = Me ; B, R = Et ; C, R = Ph

a, R' = H ; b, R' = $COCF_3$; c, R' = $COCH_3$; d, R' = COPh

The room-temperature ^{1}H-NMR and ^{13}C-NMR spectra of III evidence chemical shift non-equivalence of the relevant nuclei bonded to, or in, the pyridinium ring, as indicated in Tables 1 and 2 (in addition to the H_A, H_B protons which are obviously diastereotopic being bonded to an asymmetric carbon atom, and which form the AB part of an ABX multiplet in the ^{1}H-NMR spectra). All chemical shifts are given in the delta scale (ppm vs. internal TMS). In compounds IIIBa--IIIBd, the methylenic protons of the ethyl group are accidentally equivalent in all solvents which were tested.

Compound IIIBa was prepared both from the racemic and from the optically active (+)-aminoalcohol IIBa ; as expected, the ^{1}H-NMR spectra are identical in achiral solvents. Assignments in the ^{1}H-NMR and ^{13}C-NMR spectra are straightforward and agree with earlier data.[2,3]

Table 1. Melting points and ^{1}H-NMR chemical shifts of pyridinium perchlorates III (at room remperature unless otherwise stated)

III	Aa[a]	Ab	Ac	Ad	Ba	Ba	Bb	Bc	Bd	Ca[b]	Cb[b]	Cc[b]
M.p.(°C)	117	[c]	109	84	[d]	[d]	[c]	96	[e]	157	[c]	156
Solvent	[f]	TFA	ACD	ACD	PyD	ACD[g]	TFA	ACD	ACD	TFA	TFA	TFA
ppm	2.88	2.98	3.05	3.10	2.93	2.82	3.05	3.04	3.09	2.61	2.72	2.70
α-Me$_2$	2.93	3.05	3.11	3.19	2.98	2.75	3.11	3.08	3.17	3.04	3.06	3.02
ppm[h]	7.34	7.68	7.94	-	7.53	-	7.83	7.91	-	-	-	-
ß-H$_2$	7.43	7.68	7.94	-	7.58	-	7.83	7.91	-	-	-	-

[a] At -10°C (see Table 3 for coalescence temperature). [b] Broadened peaks.
[c] Obtained only as solution in TFA by leaving overnight alcohols IIIa in TFA.
[d] For racemic IIIBa, m.p. 112° ; for optically active IIIBa, m.p. 98°. [e] Oily product which does not crystallize. [f] PyD-ACD (1:1). [g] With C_6H_6 added (ASIS).
[h] No values are given when the pyridinium ß-protons are obscured by other protons from the solvent or by aromatic protons within the molecule.

Table 2. ^{13}C-NMR chemical shifts of III at 40°C

III	Aa	Ac	Ad	Ba
Solvent	PyD	TFAD	TFAD	PyD
ppm	21.6	23.3	23.4	21.6
α-Me$_2$	22.7	23.9	24.0	23.2
ppm	154.6	157.3	157.5	154.7
α-C$_2$	155.8	157.9	157.9	156.2
ppm	128.6	131.4	131.3	128.7
ß-C$_2$	130.3	133.2	133.2	130.5

Abbreviations for solvents in Tables 1 - 3 : TFA = CF_3COOH ; TFAD = CF_3COOD ; ACD = D_3CCOCD_3 ; PyD = C_5D_5N.

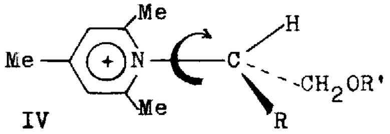
Table 1 shows that ß-protons in III are often accidentally equivalent even when α-methyl protons are not. In CH_2Cl_2 in most cases both α-methyl- and ß-protons are degenerate, but all these accidental degeneracies of ^{1}H-NMR α-methyl or ß-ring peaks in CH_2Cl_2 can be resolved with 0.1 - 0.2 moles of Eu(fod)$_3$ per mole of compound III.

Variable-temperature ^{1}H-NMR spectroscopy evidences coalescence of corresponding peaks as indicated in Table 3. In pyridine-d$_5$, ^{13}C-NMR spectra present coalescence temperatures for IIIAa and IIIBa of 70–75°C and >110°C, respectively (for IIIAa, the coalescence of α-Me_2 carbons occurs at 70°, that of β-C_2 carbons at 75°, and that of α-C_2 carbons at an intermediate temperature).

Table 3. Coalescence temperatures for ^{1}H-NMR α-methyl peaks, temperature range for line shape analysis, and average rotation barriers ($\Delta G^{\ddagger}$) in this range

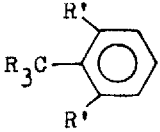
Compound	Solvent	Coalescence temp.(°C)	Temp. range (°C)	$\Delta G^{\ddagger}$ (kcal/mole)
IIIAa	PyD-ACD(1:1)	25	21 - 26	16.9
IIIAc	ACD	41	30 - 40	17.1
IIIBa	PyD	67	50 - 70	19.3

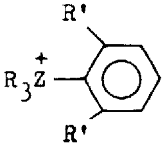
These findings indicate that the reason for the anisochronism is hindered rotation around the $N(sp^2)-C(sp^3)$ bond. The lowest-energy conformation IV, according to literature data,[4-9] has the smallest substituent of the sp^3 carbon, namely the hydrogen atom, in or nearly in, the plane of the pyridinium ring ; thus the two "sides" of this ring have different environments below the coalescence temperature.

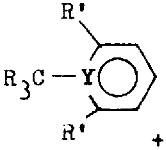

IV

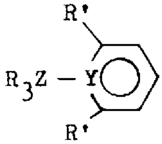
The energy barrier of the internal rotation was calculated by line shape analysis,[10-12] with the necessary corrections,[13,14] from the ^{1}H-NMR spectra. The ^{1}H-NMR chemical shift difference in the absence of exchange of corresponding non-equivalent protons is small (3-5 Hz) ; this contributes to the narrow temperature range over which the line shape analysis can be effected and does not allow meaningful correlations of $\Delta G^{\ddagger}$ versus temperature.

The activation enthalpies from Table 3 are appreciably higher than all data reported so far by Mannschreck et al. for analogous mesityl or 2,6-dimethylphenyl derivatives V,[5,6] and by other authors for related systems [7-9,15,16]. Therefore a third type, III = VII, of system with restricted rotation around an sp^2-sp^3 bond must be added to those already discussed in the literature, namely to V and VI.[15]


V, R' = Me, OMe


VI, Z = N,P,As,Sb,Bi


VII, Y = $\overset{+}{N}$


VIII

The difference in $\Delta G^{\ddagger}$ is probably due to the shorter C-$\overset{+}{N}$ bond distance in VII than in V ; indeed, similarly for VI with Z = $\overset{+}{N}$, $\Delta G^{\ddagger}_c$ = 15.9 kcal/mole at coalescence (26°C), higher than for V, $\Delta G^{\ddagger}_c$ = 12.8 kcal/mole at -35°C, all other factors being equal (phenyl-ZHMe, with R' = Me and Z = C or $\overset{+}{N}$).[5] The generalized formula VIII allows a rationalization of parameters affecting $\Delta G^{\ddagger}$ for internal rotation : bulk of R and R' groups, electronegativities and covalent radii of Z and Y.

So far, rotation barriers for VII with R' = Me were observed with at most one of the R groups being hydrogen ; results for N-isopropyl-2,4,6-trimethylpyridinium and other related cations which show at room temperature in TFA broadened α-methyl ^{1}H-NMR peaks will be reported separately.

The practically equal rotation barriers found for the pyridinium alcohol IIIAa and its acetate IIIAc, both with R = Me, indicate that remote flexible groups (like acetate) do not enhance appreciably the barrier ; however, the sensibly higher barrier found for the alcohol IIIBa with R = Et shows that slight structural variations in the proximity of the $N(sp^2)-C(sp^3)$ bond influence detectably the barrier for internal rotation.

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