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METHYL CHEMICAL SHIFTS IN ^{1}H-NMR SPECTRA OF 1-R-2,4,6-TRIMETHYLPYRIDINIUM SALTS AS SIMPLE PROBES FOR THE EXISTENCE AND MAGNITUDE OF RING CURRENT IN GROUP R

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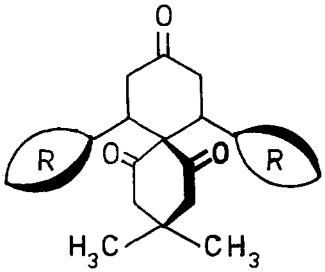
Among the physical manifestations of aromaticity, the diamagnetic ring current remains the most striking one.[1,2] Despite various criticisms aimed at its quantitative use,[3] the ring current criterion continues to be a powerful diagnostic for aromaticity, especially in the larger annulenes and heteroanalogues.[4] De Jongh and Wynberg proposed an ingenious method for ascertaining the presence and magnitude of ring current in a group *R* : they incorporated two such groups into the spiranic molecule I and measured the shielding induced in the ^{1}H-NMR peak of the methyl protons.[5] The present paper reports a similar approach which, however, is much simpler since one starts from a primary amine R-NH$_2$ and in a single reaction step one obtains the molecule III whose ^{1}H-NMR α- and γ-methyl chemical shifts subtracted from one another afford a measure for the ring current. Therefore unlike the previous method [5] which made intermolecular comparisons relative to a standard, the present method is more precise because the comparison is intramolecular relying on the difference between two chemical shifts from the same NMR spectrum. Moreover, the structure of III is simpler and contains neither cyclohexane rings which are conformationally mobile, nor two different distances between one methyl and the two *R* groups, like I.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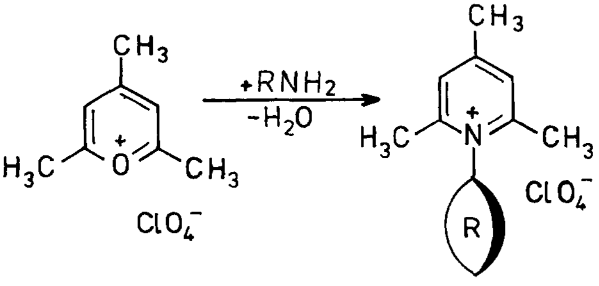

II III

2,4,6-Trimethylpyrylium perchlorate (II)[6,7] converts primary amines RNH_2 into N-substituted 2,4,6-trimethylpyridinium perchlorates (III) readily and in good yield (> 75 %).[8] The reaction is carried out with excess amine in ethanol at room or reflux temperature, or without solvent in the molten amine. The excess amine is removed with ether and the products III are recrystallized from water, ethanol or acetic acid. It had been observed earlier that unlike the initial pyrylium salt or N-alkylpyrylium salts, whose α-methyl protons resonate at lower fields than the γ-methyl protons, in N-phenyl-2,4,6-trimethylpyridinium salts (III, R = Ph) the α-methyl groups are so strongly shielded that they resonate at higher field than the γ-methyl group.[8,9] This effect was interpreted as indicating that the two rings in III, R = Ph, are not coplanar, and was confirmed by X-ray diffraction evidencing a dihedral angle of 85° in the crystal,[10] and by the presence of atropisomerism in asymmetrically substituted N-arylpyridinium salts.[11] Interestingly, unlike biphenyl which is planar when crystalline and twisted in the liquid or vapour phase, the isoelectronic unsubstituted N-phenylpyridinium chloride hydrate is twisted also in the crystal with a dihedral angle of 45°.[12]

From a systematic investigation of various N-substituted 2,4,6-trimethylpyridinium perchlorates III,[13] it appeared that the difference D between the chemical shifts of the α-methyls and the γ-methyl

$$D = \tau(\alpha\text{-methyls}) - \tau(\gamma\text{-methyl}) = \delta(\gamma\text{-methyl}) - \delta(\alpha\text{-methyls}) \qquad (1)$$

is a qualitative diagnostic, and with certain restrictions after conversion into another index, RRC (see below) a quantitative measure, of the ring current in the N-substituent R. Since D is a difference in chemical shifts, any global effects due to charge density induced by the group R cancel out. Obviously, since the two terms of relation (1) are read from the same NMR spectrum, any slight variations of the NMR instrument also cancel out, leading to enhanced precision.

The Table presents a few selected data from the NMR spectra of pyridinium salts III in trifluoroacetic acid. Perchlorates III described earlier have literature references in the Table, the remaining ones are new. Indices D and RRC are defined by relations (1) and (2), respectively. The assignments of α- and γ-methyl protons are usually straightforward since there are six protons for the α-methyl singlet and three protons for the γ-methyl singlet. If other methyl peaks due to protons in the R group appear nearby, the assignment may be checked by using a totally or selectively α- or γ-methyl deuteriated 2,4,6-trimethylpyrylium salt.[14]

It is apparent from the Table that N-alkyl (No. 1) or unconjugated cyclic N-substituents which cannot sustain an induced ring current (No. 2) have negative D values, lower than -0.20 ppm. On the other hand, typical aryl substituents (Nos. 6-16) have positive D values, higher than +0.20 ppm. It may be observed that from these aryl groups ordered according to increasing Hammett σ values, phenyl (No.13) has the highest τ and D values.* Interesting results are obtained with five-membered aromatic rings (Nos. 3-5). They have intermediate D values ranging from slightly negative (No. 3) to slightly positive (No. 5), passing through zero (No.

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* If systems without ortho-substituents are considered (see next page).

Table of ^{1}H-NMR peaks of α- and γ-methyl protons in III and of indices D and RRC[a]

No.	N-Substituents in III	Ref.	τ(α-CH_3)	τ(γ-CH_3)	D	T	RRC
1.	Methyl	8,15	7.18	7.42	-0.24	0	2
2.	3,4-Dihydrothiazol-2-yl	13	7.05	7.30	-0.25	0	0
3.	5-Methylisoxazol-3-yl	13	7.26	7.38	-0.08	0	34
4.	2,3-Dimethyl-1-phenylpyrazol-5-on-4-yl	13	7.27	7.27	0.00	22	28
5.	Thiazol-2-yl	-	7.39	7.22	+0.17	0	84
6.	p-Anisyl	-	7.50	7.29	+0.21	0	92
7.	2,3-Xylyl [b]	-	7.56	7.23	+0.33	22	94
8.	2,6-Xylyl	-	7.57	7.22	+0.35	26	94
9.	3,4-Xylyl	-	7.51	7.29	+0.22	0	94
10.	p-Tolyl	8	7.59	7.36	+0.23	0	96
11.	o-Tolyl	-	7.57	7.25	+0.32	22	92
12.	m-Tolyl	-	7.50	7.27	+0.23	0	96
13.	Phenyl	8,15	7.61	7.36	+0.25	0	100
14.	o-Carbomethoxyphenyl	-	7.55	7.23	+0.32	22	92
15.	p-Carbethoxyphenyl	-	7.51	7.27	+0.24	0	98
16.	p-Nitrophenyl	16	7.46	7.24	+0.22	0	94
17.	3-Pyridyl	17	7.47	7.24	+0.23	0	96
18.	2-Pyridyl	-	7.44	7.20	+0.24	0	98
19.	β-Naphthyl	-	7.46	7.22	+0.24	0	98
20.	α-Naphthyl	-	7.57	7.14	+0.43	22	114

[a] Chemical shifts ( ) and D (in ppm) of NMR spectra in $F_3C-COOH$ at room temp.

[b] For a 20-fold variation of concentration chemical shifts vary negligibly.

4). This ordering of D values (isoxazole < thiazole < phenyl derivatives) parallels accepted [2,5] ideas on the "aromaticity" of these compounds. Since, however, the twist angle and the ring area are a little smaller than with six-membered rings, it is safer to make quantitative comparisons only for rings of the same size.

Thus, for examining the existence of ring current in a group R, the amine $R-NH_2$ is converted into the pyridinium salt III whose ^{1}H-NMR spectrum yields the chemical shift difference D ; for non-aromatic R groups, $D \cong -0.25$. An approximate measure of the magnitude of the relative ring current is given by index RRC:

$$RRC = 200(D + 0.25) - T \qquad \text{with } T = 71.7x/(1 + 2.26x) \qquad (2)$$

where x is the number of o-standing groups in R (excluding carbonyl oxygen).

Indeed, a definite effect is exerted by ortho-substituents (compare Nos. 7-9, 10-12, or 14-15), probably by increasing the average twist angle between the planes of the two rings. Therefore a correction term T in (2) was necessary to counter this ortho-effect.

There are several limitations of the present method : the amine $R-NH_2$ must be sufficiently (i) stable, (ii) nucleophilic, (iii) sterically non-crowded (it was shown [8] that t-butylamine does not form with I a pyridinium salt III but a ring-opened product), and (iv) devoid of other closely placed groups which could exert shielding or deshielding effects (unless these groups are part of the aromatic system like the carbonyl group in No. 4). Though β-naphthyl behaves like a normal benzenoid ring (No. 19), α-naphthyl (No. 20) has RRC = 114 despite the correction term T ; therefore equation (2) does not apply to α-naphthyl.

In conclusion, as indicated in the Table, non-aromatic R groups have index

RRC in the range from -5 to +5. Six-membered benzene derivatives have RRC = 90 - 100, with benzene conventionally chosen as standard with RRC = 100 as in ref.[5] The present data are in good agreement with those of ref.[5] for five-membered aromatic heterocyclics : those in the above Table have RRC = 28 - 90. With the RRC values quantitative comparisons of relative ring currents may be made.

Further work will investigate a larger number of aromatic R groups by means of ^{1}H-NMR and ^{13}C-NMR spectroscopy, and will attempt quantitative correlations between measured indices D and RRC, calculated ring currents, and theoretically derived resonance energies. Samples of amines ($\sim$2 g) would be welcome.

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