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246. ^{13}C-NMR. Spectra of 4-Substituted Quinuclidines. Polar Effects, Part V.

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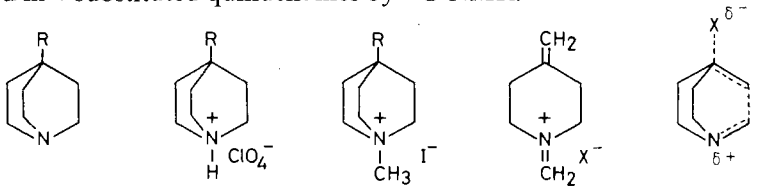
Summary

^{13}C-NMR. spectra of 37 4-substituted quinuclidinium perchlorates, 15 4-substituted quinuclidines and the corresponding 1-methylquinuclidinium iodides have been measured. The chemical shifts δ for all compounds lie in the expected range. No correlation is found between δ and the inductive substituent constant σ_I^q of the substituent. Abnormal shift differences between quinuclidines bearing a nucleofugal group and the corresponding protonated or *N*-methylated quinuclidinum salt are observed for the bridgehead carbon C(4). These differences are ascribed to incipient fragmentation, *i.e.* C,C-hyperconjugation in the ground state.

Introduction. – The importance of ^{13}C-NMR. spectroscopy in the structural elucidation of organic compounds stems from the fact that the effect of a substituent on the chemical shift of a particular carbon in a given molecule may be predicted fairly reliably by a set of empirical rules [1]. Nevertheless, carbon shielding and its dependence on various electronic and steric factors are not yet well understood [2]. Rigid models have been quite useful in the study of substituent effects, because they allow the separation, at least qualitatively, of the factors which contribute to carbon shielding, *i.e.* steric and inductive or field effects. Thus, numerous investigations have been conducted on bridgehead substituted bi- and polycyclic compounds, such as norbornanes [3], bicyclo[2.2.2]octanes [4], adamantanes [5], bicyclo[3.3.1]-nonanes [6], twistanes [7], and tricyclenes [8]. However, only a limited number of substituents were included in these studies.

Recently, a new set of inductive substituent constants σ_I^q was derived from the pK_a values of 4-substituted quinuclidines I [9] [10]. Quinuclidines are essentially strain-free and possess well-defined geometry. Owing to their symmetry, polar and steric effects of unsymmetrical substituents R at the bridgehead will be averaged and only the net effect oriented in the symmetry axis of the molecule is evaluated. Quinuclidines I are therefore well suited for the determination of substituent effects on ^{13}C-NMR. chemical shifts. In addition, the effect of a positive charge on nitrogen may be easily gauged by comparison of the shifts for I with those for the corresponding quinuclidinium salts, such as perchlorates II or *N*-methylquinuclidinium iodides III.

Quinuclidines bearing a nucleofugal group at C(4) undergo solvolytic fragmentation to *N*,4-dimethylidenepiperidinium salts IV by the concerted mechanism, *i.e.* the positive charge generated at C(4) in the transition state V[1]) is transferred to the nitrogen atom with concomitant cleavage of the C(2)–C(3) bond [11]. Later, it was suggested that electron density is already transferred from the nitrogen atom to the nucleofugal group in the ground state in order to explain the abnormal basicity order, I > Cl > F > Br, observed for the 4-haloquinuclidines [9]. The chemical shift in ^{13}C-NMR. is a sensitive probe for electron delocalization, and applications of this method to evaluate electronic effects of substituents in aromatic and some aliphatic systems are abundant [12]. It was therefore of interest to see whether incipient fragmentation, *i.e.* C,C-hyperconjugation [9] [10] could be detected and quantified in 4-substituted quinuclidines by ^{13}C-NMR.



I II III IV V

Results. – ^{13}C-NMR. spectra were recorded for the 4-substituted quinuclidinium perchlorates **II-1** to **II-37** available from earlier studies [9] *(Table 1)*. Spectra were run in D_2O and, in cases of low solubility also in $(CD_3)_2SO$. Chemical shifts were

[1]) For convenience the σ electrons of only one of the 3 ethano bridges are delocalized in V.

Table 1. *Chemical shifts and substituent shift increments of 4-substituted quinuclidinium perchlorates* II *in* D_2O *and* $(CD_3)_2SO$[a])

	R	Chemical shift δ[b])								Shift increments $\Delta\delta$		
		C(2)	C(3)	C(4)	others					α	β	γ
1	H	47.3	22.9	19.3						–	–	–
	(DMSO)	46.6	23.1	19.4						–	–	–
2	CH_3	47.6	29.5	24.7	26.2					+ 5.4	+ 6.6	+0.3
3	C_2H_5[c])	47.8	27.4	27.7	32.3	7.8				+ 8.4	+ 4.5	+0.5
4	$CH(CH_3)_2$[c])	47.5	24.9	30.6	34.5	16.8				+11.3	+ 2.0	+0.2
5	$C(CH_3)_3$[c])	47.4	22.8	33.4	33.8	24.8				+14.1	− 0.1	+0.1
	(DMSO)	46.7	23.0	33.3	34.4	25.5				+13.9	− 0.1	+0.1
6	CH_2OH	47.2	24.9	30.0	68.3					+10.7	+ 2.0	−0.1
7	CH_2Br	47.2	26.4	29.8	42.6					+10.5	+ 3.5	−0.1
8	$CH(OH)_2$[d])	47.1	22.8	e])	e])					–	− 0.1	−0.2
	(DMSO)	46.3	23.0	32.8	102.0					+13.4	− 0.1	−0.3
9	$CH=CH_2$	47.3	27.6	30.4	143.8	113.6				+11.1	+ 4.7	±0
10	$C(CH_3)=CH_2$[c])	47.4	26.7	32.7	149.8	110.8	18.9			+13.4	+ 3.8	+0.1
11	C≡CH[c])	46.8	28.7	e])	e])					–	+ 5.8	−0.5
	(DMSO)	46.2	29.0	23.9	87.3	73.5				+ 4.5	+ 5.9	−0.4
12	C_6H_5[d])	47.6	28.8	31.8	e])	125.9	129.5	127.7		+12.5	+ 5.9	+0.3
	(DMSO)[c])	47.0	29.1	31.9	146.3	126.0	129.3	127.3		+12.5	+ 6.0	+0.4
13	COOH	46.8	25.3	35.3	178.4					+16.0	+ 2.4	−0.5
14	$COOCH_3$	46.8	25.3	35.6	176.9	53.5				+16.3	+ 2.4	−0.5
15	$COOC_2H_5$[c])	46.8	25.2	35.5	176.6	63.0	13.8			+16.2	+ 2.3	−0.5
16	$CONH_2$	46.8	25.5	35.4	179.7					+16.1	+ 2.6	−0.5
17	$COCH_3$[c])	46.8	24.6	41.1	214.9	25.7				+21.8	+ 1.7	−0.5
18	$C(CH_3)=NOH$	47.0	25.5	34.3	162.8	10.3				+15.0	+ 2.6	−0.3
19	CN[c])	46.1	26.1	24.8	122.7					+ 5.5	+ 3.2	−1.2
20	$NH_3^+ClO_4^-$	47.3	26.7	47.9						+28.6	+ 3.8	±0
21	$NH_2CH_3^+ClO_4^-$	47.2	24.8	52.9	27.2					+33.6	+ 1.9	−0.1
22	$NH(CH_3)_2^+ClO_4^-$	47.2	23.3	59.3	38.6					+40.0	+ 0.4	−0.1
23	$N(CH_3)_3^+ClO_4^-$	47.3	22.4	67.7	50.0					+48.4	− 0.5	±0
24	$NHCOCH_3$	47.6	27.0	47.1	174.3	23.6				+27.8	+ 4.1	+0.3
25	NO_2[c])	47.7	27.3	79.7						+60.4	+ 4.4	+0.4
26	OH[c])	48.6	30.2	64.8						+45.5	+ 7.3	+1.3
27	OCH_3	48.5	26.7	70.3	50.0					+51.0	+ 3.8	+1.2
28	$OCOCH_3$	48.3	27.1	74.6	173.4	22.3				+55.3	+ 4.2	+1.0
29	$OSO_2C_6H_4CH_3$[c])	48.6	28.7	e])	e])					–	+ 5.8	+1.3
	(DMSO)	47.9	28.9	83.6	136.1	127.9	131.0	145.8	21.9	+64.2	+ 5.8	+1.3
30	SCH_3	47.8	28.6	36.4	9.8					+17.1	+ 5.7	+0.5
31	$SOCH_3$	47.2	22.0	49.8	31.0					+30.5	− 0.9	−0.1
32	SO_2CH_3[c])	46.7	22.3	54.9	35.2					+35.6	− 0.6	−0.6
33	$Sn(CH_3)_3$[d])	47.6	26.9	13.6	−12.7					− 5.7	+ 4.0	+0.3
	(DMSO)[f])	46.8	27.1	14.4	−11.4					− 5.0	+ 4.0	+0.2
34	F[c])	49.1	28.9	89.5						+70.2	+ 6.0	+1.8
	(DMSO)[g])	48.5	28.8	89.7						+70.3	+ 5.7	+1.9
35	Cl[c])	48.7	32.6	58.3						+39.0	+ 9.7	+1.4
	(DMSO)[c])	48.2	33.1	60.3						+40.9	+10.0	+1.6
36	Br	49.2	33.8	50.3						+31.0	+10.9	+1.9
	(DMSO)	48.7	34.2	52.9						+33.5	+11.1	+2.1
37	I[c])	49.4	36.4	25.0						+ 5.7	+13.5	+2.1
	(DMSO)	48.9	36.7	28.2						+ 8.8	+13.6	+2.3

[a]) *Ca.* 1M solution in D_2O except where noted. [b]) $\delta \pm 0.07$ ppm. Internal reference: dioxane 67.17 ppm. [c]) *Ca.* 0.3M solution. [d]) *Ca.* 0.1M solution. [e]) Not observed. [f]) $^1J_{CSn}(CH_3) = 322/307$ Hz; $^2J_{CSn} < 20$ Hz; $^3J_{CSn} = 47$ Hz. [g]) $^1J_{CF} = 190$ Hz; $^2J_{CF} = 22$ Hz; $^3J_{CF} = 10$ Hz.

Table 2. *Chemical shifts, substituent shift increments, and protonation shifts of quinuclidines* I *in* $CDCl_3$[a])

	R	Chemical shift δ[b])								Shift increments $\Delta\delta$			Protonation shift δ(II)-δ(I)[c])		
		C(2)	C(3)	C(4)	others					α	β	γ	C(2)	C(3)	C(4)
1	H	47.8	26.8	20.8						-	-	-	−0.5	−3.9	− 1.5
6	CH_2OH	47.8	28.5	30.7	70.5					+ 9.9	+ 1.7	±0	−0.6	−3.6	− 0.7
7	CH_2Br	47.9	30.0	30.4	44.9					+ 9.6	+ 3.2	+0.1	−0.7	−3.6	− 0.6
15	$COOC_2H_5$	47.6	28.5	36.1	176.0	60.2	14.2			+15.3	+ 1.7	−0.2	−0.8	−3.3	− 0.6
19	CN	46.5	29.2	24.7	123.6					+ 3.9	+ 2.4	−1.3	−0.4	−3.1	+ 0.1
22	$N(CH_3)_2$	48.4	26.8	52.2	37.8					+31.4	± 0	+0.6	[d])	[d])	[d])
23	$N(CH_3)_3^+I^-$[e])	47.9	24.5	71.7	49.5					+50.9[e])	− 2.3[e])	+0.1[e])	−0.6	−2.1	− 4.0
26	OH[a])	49.5	34.6	66.6						+45.8	+ 7.8	+1.7	−0.9	−4.4	− 1.8
27	OCH_3	48.9	30.0	71.2	48.5					+50.4	+ 3.2	+0.9	−0.4	−3.3	− 0.9
29	$OSO_2C_6H_4CH_3$[f])	49.2	31.6	88.9	136.3	127.1	129.7	144.3	21.7	+68.1	+ 4.8	+1.4	−0.6	−2.9	− 5.3[f])
33	$Sn(CH_3)_3$[g])	48.6	30.9	17.4	−12.8					− 3.4	+ 4.1	+0.8	−1.0	−4.0	− 3.8
34	F[h])	49.8	32.3	92.0						+71.2	+ 5.5	+2.0	−0.7	−3.4	− 2.5
35	Cl	49.9	36.6	63.8						+43.0	+ 9.8	+2.1	−1.2	−4.0	− 5.5
36	Br	50.2	37.6	59.4						+38.6	+10.8	+2.4	−1.0	−3.8	− 9.1
37	I	50.5	40.4	39.2						+18.4	+13.6	+2.7	−0.9	−4.0	−14.2

[a]) *Ca.* 1M solution except **26** (0.3M). [b]) $\delta \pm 0.07$ ppm. Internal reference dioxane 67.17 ppm, TMS 0.00 ppm. [c]) Includes solvent shift $CDCl_3/D_2O$ except for **23**, **29** (C(4)). [d]) Not comparable. In II-**22**, the substituent $N(CH_3)_2$ is also protonated. [e]) In D_2O. Shift increments include solvent shift. $^1J_{CN}(CH_3) = 4$ Hz; $^1J_{CN}(C(4)) = 2$ Hz; $^2J_{CN}$, $^3J_{CN} < 1$ Hz. [f]) −55°. Protonation shift for C(4) includes solvent shift $CDCl_3/(CD_3)_2SO$. [g]) $^1J_{CSn}(CH_3) = 307/294$ Hz; $^2J_{CSn} = 9$ Hz; $^3J_{CSn} = 46$ Hz. [h]) $^1J_{CF} = 187$ Hz; $^2J_{CF} = 14$ Hz; $^3J_{CF} = 6$ Hz.

Table 3. *Chemical shifts, substituent shift increments, and methylation shifts of 1-methylquinuclidinium iodides* III *in* D_2O *and* $(CD_3)_2SO$[a])

	R	Chemical shift δ[b])									Shift increments $\Delta\delta$				Methylation shift δ(III)–δ(I)[c])		
		CH_3	C(2)	C(3)	C(4)	others					α	β	γ	$CH_3(\varepsilon)$	C(2)	C(3)	C(4)
1	H	52.7	57.7	24.2	19.2						–	–	–	–	+ 9.9	−2.6	−1.6
	(DMSO)	52.0	56.6	24.1	19.4						–	–	–	–	+ 8.8	−2.7	−1.4
6	CH_2OH	52.4	57.7	26.3	30.1	68.0					+10.9	+ 2.1	±0	−0.3	+ 9.9	−2.2	−0.6
7	CH_2Br	52.4	57.7	27.8	29.8	42.5					+10.6	+ 3.6	±0	−0.3	+ 9.9	−2.2	−0.6
15	$COOC_2H_5$	52.5	57.2	26.6	35.5	176.2	63.2	14.1			+16.3	+ 2.4	−0.5	−0.2	+ 9.6	−1.9	−0.6
19	CN	53.0	56.3	27.3	24.7	122.5					+ 5.5	+ 3.1	−1.4	+0.3	+ 9.8	−1.9	±0
22	$N(CH_3)_2$	52.4	58.2	25.1	51.9	38.0					+32.7	+ 0.9	+0.5	−0.3	+ 9.8	−1.7	−0.3
23	$N(CH_3)_3^+I^-$	52.4	57.5	23.9	67.2	50.6					+48.0	− 0.3	−0.2	−0.3	+ 9.6	−0.6	−4.5
	(DMSO)	51.8	56.9	23.7	67.2	50.3					+47.8	− 0.4	+0.3	−0.2	+ 9.0	−0.8	−4.5
26	OH	52.4	59.2	31.3	64.5						+45.3	+ 7.1	+1.5	−0.3	+ 9.7	−3.3	−2.1
27	OCH_3	52.4	59.0	27.8	70.1	50.5					+50.9	+ 3.6	+1.3	−0.3	+10.1	−2.2	−1.1
29	$OSO_2C_6H_4CH_3$																
	(DMSO)	51.7	58.0	29.7	82.7	135.9	127.8	130.9	145.6	21.9	+63.5	+ 5.6	+1.4	−0.3	+ 8.8	−1.9	−6.2
33	$Sn(CH_3)_3$[g])	52.6	57.5	28.4	14.1	−11.2					− 5.1	+ 4.2	−0.2	−0.1	+ 8.9	−2.5	−3.3
34	F	52.4	59.5	29.5	89.1						+69.9	+ 5.3	+1.8	−0.3	+ 9.7	−2.8	−2.9
35	Cl	52.6	59.0	33.7	57.9						+38.7	+ 9.5	+1.3	−0.1	+ 9.1	−2.9	−5.9
36	Br[d])	52.7	59.4	34.9	[f])						–	+10.7	+1.7	±0	+ 9.2	−2.7	–
	(DMSO)	52.2	58.8	35.1	52.3						+32.9	+11.0	+2.2	+0.2	+ 8.6	−2.5	−7.1
37	I[d])	[f])	59.6	37.6	[f])						–	+13.4	+1.9	–	+ 9.1	−2.8	–
	(DMSO)[e])	52.8	59.2	37.9	26.6						+ 7.2	+13.8	+2.6	+0.8	+ 8.7	−2.5	−12.8

[a]) *Ca.* 1M solution in D_2O except where noted. [b]) $\delta \pm 0.07$ ppm. Internal reference: dioxane 67.17 ppm. [c]) Includes solvent shift $CDCl_3/D_2O$ or $CDCl_3/(CD_3)_2SO$ except for **23**. [d]) *Ca.* 0.1M solution. [e]) *Ca.* 0.3M solution. [f]) Not observed. [g]) $^1J_{SnC}(CH_3) = 326/311$ Hz; $^2J_{SnC} < 10$ Hz; $^3J_{SnC} = 47$ Hz. [h]) $^1J_{CF} = 192$ Hz; $^2J_{CF} = 23$ Hz; $^3J_{CF} = 11$ Hz; $^5J_{CF} = 3.5$ Hz.

referenced to internal dioxane. The concentration dependence of the chemical shift was low (<0.05 ppm) in the range studied (0.1–1 M), however, considerable solvent dependence was noticed.

Assignment of resonance to individual carbon atoms was unambiguous in all cases. Carbon atoms α to the nitrogen atom, C(2), C(6) and C(7)[2]), resonate at 48 ± 2 ppm, whereas the chemical shift of C(3), C(5) and C(8)[2]) lies in the range of 22 to 37 ppm. The signal for the bridgehead C(4) is readily assigned from off-resonance ^{1}H-decoupled spectra and by its low intensity. The chemical shift of C(4) shows the largest variation because of the directly bonded substituent. The substituent shift increments, *i.e.* the differences between the shifts of a substituted compound and those of the parent quinuclidinium perchlorate (**II-1**) are found in the expected range in all cases.

^{13}C-NMR. shift data in $CDCl_3$ for 15 quinuclidines as the free bases I are presented in *Table 2* together with substituent shift increments and shifts due to protonation. All carbon atoms of the quinuclidine skeleton are more shielded in the protonated form II than in the free base I. Shift differences are less than -1.2 ppm at C(2) α to the nitrogen atom; they range from -2.1 to -4.4 ppm at C(3), and from 0 to -14.2 ppm at the bridgehead C(4). These protonation shifts include a solvent shift; care must therefore be exercised in comparing them to literature values [13].

Table 3 contains ^{13}C-NMR. shift data for 15 *N*-methylquinuclidinium iodides III measured in D_2O and partly in $(CD_3)_2SO$, together with substituent shift increments and *N*-methylation shifts. The signal for the methylene carbon atoms α to the nitrogen atom (C(2)) is shifted to 58 ± 2 ppm, and the additional methyl carbon atom appears between 52 and 53 ppm. C(3) is more deshielded by approximately 1 ppm than in the quinuclidinium perchlorates II, and the chemical shift of C(4) remains almost unaltered.

Both methyl and methylene carbon atoms α to quaternary nitrogen atom show ^{14}N, ^{13}C coupling constants $^1J_{CN}$ of 4 (± 0.5) Hz and 3 (± 0.5) Hz, respectively. No coupling is observed with the β carbon atom ($^2J_{CN} < 2$ Hz), however, the bridgehead carbon atom is split with a coupling constant $^3J_{CN}$ of 4.5 (± 1) Hz. These coupling phenomena are general in the spectra of tetraalkylammonium compounds [14]. The size of the coupling constants are in accord with ^{15}N, ^{13}C couplings measured on quinuclidinium chloride enriched in ^{15}N [15]. The 3-bond coupling constant $^3J_{CN}$ is exceptionally large [16], but corresponds to the large coupling constant $^3J_{CP}$ found for the phosphine oxide of 1-phosphabicyclo[2.2.2]octane [17].

Discussion. – *Substituent effects at C(4).* The chemical shift of the bridgehead carbon atom α to the substituent lies in the expected range for all compounds except for the quinuclidines bearing a nucleofugal group. These will be discussed separately. Reasonable correlation is found between shift increments in quinuclidines and in other bridgehead substituted compounds, *e.g.* 1-substituted adamantanes [5], bicyclo[2.2.2]octanes [4], and norbornanes [3], and to some extent with shift increments in *t*-butyl derivatives [1] and equatorial isomers of substituted cyclohexanes [18].

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[2]) Since C(2), C(6) and C(7) on the one hand, and C(3), C(5) and C(8) on the other, are equivalent, for simplicity these positions will be referred to as C(2) and C(3), respectively.

Some interesting features of the data in *Tables 1–3* may be noted. In the alkyl derivatives II-**2** to II-**5** each additional methyl group β to the bridgehead deshields this carbon atom by 2.9 ($\pm$0.1) ppm. A similar difference (2.3 ppm) is observed for C(4) in the vinyl (II-**9**) and the α-methylvinyl compound (II-**10**). Shielding resulting from steric crowding considerably diminishes the usual β-effect of a methyl group (*ca.* 9 ppm). However, in the homologuous series of ammonio compounds II-**20** to II-**23**, one additional methyl group deshields by 5.0, 6.4 and 8.4 ppm respectively, considerably more than one would expect on the ground of steric shielding.

Deshielding increases when replacing the hydroxy group (shift increment 45 ppm in **26**) by the methoxy (51 ppm in **27**) or the acetoxy group (55 ppm in **28**) as generally observed [1]. The *p*-toluenesulfonyloxy group (II-**29** and III-**29**) deshields by 64 ppm, more than the strongly electron-withdrawing nitro group (60 ppm in **25**). Deshielding increases from the methyl thioether (shift increment 17 ppm in **30**) to the corresponding sulfoxide (30 ppm in **31**) and sulfone (36 ppm in **32**), but is small in comparison to that caused by substituents containing oxygen and nitrogen atoms. The carboxyl group and its derivatives (**13** to **16**) give rise to similar shift increments (16 ppm). The acetyl group is somewhat more deshielding (22 ppm in **17**). Only small downfield shifts are observed with triple bonded functional groups (4–5 ppm in **11** and **19**). The only shielding substituent studied is the trimethyltin group (-5 ppm in II-**33** and III-**33**). The halogens show the usual effects: strong deshielding by fluorine (shift increment 70 ppm in II-**34** and III-**34**), intermediate deshielding by chlorine (*ca.* 39 ppm in II-**35** and III-**35**) and bromine (*ca.* 31 ppm II-**36** and III-**36**), and small deshielding by iodine (*ca.* 6 ppm in II-**37** and III-**37**).

Substituent effects at C(3). Shift increments of carbon atoms β to the substituent show good correlation with values for the corresponding positions in other bridgehead substituted compounds [3–5]. Large differences are noted for the cyano and vinyl group, when compared to *t*-butyl derivatives. Both these substituents show magnetic anisotropy; hence small differences in bond angles and bond lengths between the *t*-butyl and quinuclidyl compounds may cause large shift differences.

Increasing the number of methyl groups γ to C(3) leads to the expected shielding effect, namely 2.1–2.5 ppm for the alkyl derivatives II-**2** to II-**5** and 0.9–1.9 ppm for the ammonio compounds II-**20** to II-**23**. Shielding increments are observed for the sulfoxide **31** and the sulfone **32**. This is probably also a steric effect of the oxygen atoms γ to C(3), similar to that observed for the dihydroxymethyl derivative **8**. The expected large downfield shifts are measured at the carbon atom β to chlorine (10 ppm in **35**), bromine (11 ppm in **36**), and iodine (14 ppm in **37**).

Substituent effects at C(2). Many efforts have been made lately to determine substituent effects on γ-carbon atoms with exclusion of steric interactions [19–21]. A fixed anti-periplanar arrangement of C(2) and the substituent R is present in 4-substituted quinuclidines I, II and III. Direct steric perturbation is therefore excluded; hence the chemical shift increments should be the result of inductive and hyperconjugative effects only.

No correlation is found between inductive substituent constants σ_I^q of R [10] and the chemical shift at C(2) in I, II and III. This is generally the case in aliphatic

systems, although a correlation between the electronegativity of substituents and shifts at γ-carbon atoms is often claimed, as in [19]. *Eliel et al.* [20] suggested that the shielding observed for a carbon atom γ to a heteroatom and held in a fixed anti-periplanar orientation is the result of hyperconjugation, the effect being more prominent for the first row atoms F, O and N than for the second row elements Cl and S. This interpretation is in line with many shift increments determined with monocyclic compounds of comparatively rigid geometry. However, in the case of 4-substituted quinuclidines, substantial *shielding* γ-effects ($\geqslant 0.5$ ppm relative to H, $\geqslant 0.8$ ppm relative to CH_3) are found only with the ethinyl- (**11**), carbonyl- (**13–17**), cyano- (**19**) and methylsulfonyl-derivatives (**32**). On the contrary, the halogen (**34–37**) (including the first-row atom F) and oxygen substituents (**26–29**) show *deshielding* γ-effects of more than 1 ppm (relative to H). All other substituents including the N-containing groups (**20–25**) and the trimethylthin group (**33**) show small γ-effects only.

The interpretation of anti γ-effects therefore remains debatable. Neither hyperconjugative electron-transfer [20], nor back-lobe overlap [21] and electronegativity [19] alone provide a consistent interpretation of substituent effects at the γ-position in different systems. Rather, the overall chemical shift increment at the γ-carbon atom appears to result from opposing electronic effects, magnetic anisotropy and secondary steric effects, the latter arising from small angle variations due to the remote substituent.

N-*protonation and* N-*methylation shifts.* Protonation shifts are negative, *i.e.* all carbon atoms are more shielded in the protonated form than in the free base. The shifts are generally 1 ppm or less at C(2) and 3–4 ppm at C(3), which agrees with protonation shifts found for other amines [22]. Quaternization with methyl iodide leads to compounds which display analoguous shifts. C(2) is deshielded by 9–10 ppm relative to the tertiary amine, which corresponds to the deshielding shift induced by an additional methyl group in an all-carbon system. C(3) is shielded by 2–3 ppm, *i.e.* somewhat less than on protonation. This is the result of a small deshielding anti-γ-effect of the methyl group.

A positive charge on the nitrogen atom leads to widely varying shifts at the bridgehead C(4). Considerable shielding is observed with the nucleofugal groups iodo (13–14 ppm in **37**), bromo (7–9 ppm in **36**), chloro (6 ppm in **35**) and *p*-toluenesulfonyloxy (5–6 ppm in **29**). The effects are less pronounced for fluoro- (3 ppm in **34**), trimethylammonio- (4 ppm in **23**), and trimethyltinquinuclidine (3–4 ppm in **33**), whereas all other compounds show shifts of less than 2 ppm.

Because *N*-protonation and *N*-methylation shifts are similar at C(4), it is safe to conclude that they result from the positive charge on nitrogen or from the absence of a free electron pair on nitrogen. Only compounds bearing a nucleofugal group at the bridgehead show large effects. This means that *the ability of quinuclidines* I *to fragment under solvolytic conditions is reflected in abnormal shifts in the* ^{13}C-*NMR.* The partial transmission of electrons from nitrogen through the σ-bonds to the nucleofugal groups in the ground state, *i.e.* C, C-hyperconjugation [9][10], as in **V**, leads to deshielding of the bridgehead C(4). The bond between C(4) and the nucleofugal group X is loosened, whereas the C(3)–C(4) bond should acquire some double bond character. No effect of

Table 4. *Elemental analyses and melting points of 4-substituted 1-methylquinuclidinium iodides* III

	R	Formula	Molecular weight	Calc. %			Found %			M.p.	Recrystallyzed from
				C	H	N	C	H	N		
6	CH_2OH	$C_9H_{18}INO$	283.16	38.17	6.40	4.94	38.24	6.49	4.87	243–4°	ethanol/ether
7	CH_2Br	$C_9H_{17}BrIN$	346.07	31.23	4.95	4.04	31.08	4.96	4.01	143–4°	ethanol/ether
22	$N(CH_3)_2$	$C_{10}H_{21}IN_2$	296.20	40.55	7.15	9.46	40.42	7.40	9.61	169–70°	ethanol/ether
23	$N^+(CH_3)_3I^-$	$C_{11}H_{24}I_2N_2$	438.15	30.15	5.52	6.39	29.87	5.65	6.12	240–2°	methanol/acetone
27	OCH_3	$C_9H_{18}INO$	283.16	38.17	6.40	4.94	38.11	6.56	4.86	195–7°	2-propanol
29	$OSO_2C_6H_4CH_3$	$C_{15}H_{22}INO_3S$	423.32	42.55	5.23	3.30	42.31	5.30	3.26	186–7°	2-propanol
33	$Sn(CH_3)_3$	$C_{11}H_{24}INSn$	415.93	31.76	5.81	3.36	31.75	5.97	3.56	203–4°	ethanol/ether
34	F	$C_8H_{15}FIN$	271.13	35.43	5.57	5.16	35.39	5.68	5.15	245–8°	2-propanol
35	Cl	$C_8H_{15}ClIN$	287.58	33.41	5.25	4.87	33.60	5.30	4.82	277–8°	ethanol/ether
37	I	$C_8H_{15}I_2N$	379.04	25.34	3.98	3.69	25.63	4.15	3.72	276–7°	ethanol

N-protonation and *N*-methylation is detected by ^{13}C-NMR. at C(2) and C(3). This implies that loosening of the bond between the bridgehead C(4) and the nucleofugal group X is more advanced than bond reorganization elsewhere in the molecule. A similar conclusion was reached concerning the transition state for concerted fragmentation of 4-haloquinuclidines [11].

It is tempting to look for a quantitative relationship between *N*-protonation and *N*-methylation shifts in the ^{13}C-NMR. spectra and the rate of solvolytic fragmentation. The rate order of the 4-haloquinuclidines **34–37**, F < Cl < Br < I [11], is correctly reflected in the protonation shift *(Table 2)*. 4-Trimethylammonioquinuclidine (I-**23**) fragments only when refluxed in aqueous solution [23]. It is therefore less reactive than the chloride I-**35**, as is borne out by a smaller protonation and methylation shift.

The relationship between ^{13}C-NMR. shifts and fragmentation breaks down with the *p*-toluenesulfonate I-**29**. This is the solvolytically most reactive compound studied, but the induced shift is less than that for the bromide I-**36**. Therefore other effects, such as substituent polarizability, play an important role in determining the size of the induced shift at C(4). Substituent polarizability, prominent for iodine and to some extent for bromine, could also explain the induced shift in the 4-trimethyltinquinuclidine (**33**). Trimethyltin is an electrofugal rather than a nucleofugal group [24], and hyperconjugation as depicted in **V** would therefore not be expected.

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Experimental Part

4-Substituted quinuclidinium perchlorates II-**1** to II-**37** were available from previous work (see ref. in [9]). The free amines I were liberated from the perchlorates II with saturated aqueous K_2CO_3 and extracted with ether. 4-Trimethylammonioquinuclidine (I-**23**) was extracted with $CHCl_3$ after anion exchange with KI. The quinuclidines I were distilled in a bulb tube at reduced pressure (except the salt I-**23**) and characterized by their ^{1}H-NMR. spectra in $CDCl_3$ (chemical shift δ in ppm relative to tetramethylsilane (TMS)): 2.8–3.0 (*t*, J = 8 Hz, 6 H, H–C(2^2)); 1.4–2.4 (*t*, J = 8 Hz, 6 H, H–C(3^2)). 1-Methylquinuclidinium iodides III [25] were obtained by reacting the quinuclidines I with methyl iodide in ether and characterized by their melting points, elemental analyses (new compounds see *Table 4*), and ^{1}H-NMR. spectra in D_2O: 3.4–3.8 (*t*, J = 8 Hz, 6 H, H–C(2)); 2.9–3.1 (*s*, 3 H, CH_3); 1.8–2.6 (*t*, J = 8 Hz, 6 H, H–C(3)).

^{13}C-NMR. spectra were obtained at natural ^{13}C abundance with a *Bruker HX-90* spectrometer operating at 22.63 MHz in a *Fourier* Transform mode using 8K data set, which gives chemical shifts correct to ±0.02 ppm. Owing to slow relaxation of C(4), spectra were run at low pulse angle (10–15°) and a repetition time of 2.5 sec. Unless indicated, samples were approximately 1M in D_2O, $(CD_3)_2SO$, or $CDCl_3$ containing dioxane as an internal reference. The chemical shift was calculated for dioxane δ = 67.17 ppm, the value obtained in $CDCl_3$ relative to TMS. With this standard, the signal for TMS appeared at −0.83 ppm in $(CD_3)_2SO$, and that for the methyl carbon atoms in sodium 3-trimethylsilylpropanesulfonate at −1.47 ppm in D_2O. The dependence of the chemical shift of quinuclidinium perchlorate (II-**1**) upon concentration was less than 0.05 ppm in the range used for substituted quinuclidines, 0.1M to 1M. Spectra were run between 30 and 40° except for 4-*p*-toluenesulfonyloxyquinuclidine (I-**29**), which fragments under these conditions. I-**29** was measured at −55° on a *Varian XL-100* at 25.2 MHz by courtesy of *Mr. A. Borer* of *CIBA-GEIGY AG*, Basel.

The spectra were run by *Mr. K. Aegerter*. Elemental analyses were carried out by *Mr. E. Thommen*.

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247. Synthese von Nor-β-cyclocitral, Norsafranal und 2,2′-Dinor-β-carotin

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Synthesis of nor-β-cyclocitral, norsafranal, and 2,2′-dinor-β-carotene

Summary

The synthesis of 2,2′-dinor-β-carotene (**10**) *via* norsafranal (**5**) and nor-β-cyclocitral (**6**) is described.