

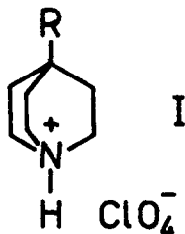
4-SUBSTITUTED QUINUCLIDIUM PERCHLORATES IN THE DETERMINATION
OF POLAR SUBSTITUENT EFFECTS

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(Received in UK 10 July 1973; accepted for publication 3 August 1973)

The superiority of 4-substituted quinuclidines over other models for the determination of polar substituent constants by pK_a measurements of corresponding salts has been recognized for some time ^{1) 2) 3)}. Now that these compounds are more easily accessible ³⁾ measurements can be carried out on a broader basis. The following Table lists the pK_a values of the quinuclidinium perchlorates (I) measured to date in our laboratory ⁴⁾.



0.1 millimole of the salt in 10 ml of water were titrated with 0.1 N NaOH at 25° C ($\pm 0.05^\circ$) under N_2 employing a precision pH-compensator (Metrohm E 388) and a glass electrode (Metrohm EA 109/UX). From the concentration of the salt c and the ml of added 0.1 N NaOH the pK_a values were calculated by the formula:

$$pK_a = pH + \log \frac{c((0.1 - 0.1 \times ml)/0.1) - [H^+] + [OH^-]}{c(0.1 \times ml/0.1) + [H^+] - [OH^-]}$$

The standard deviation corrected for a confidence limit of 99 % was computed from an average of 20 points. Duplicate runs gave pK_a values within the above limits of ca. ± 0.02 .

Table. pK_a values of 4-substituted quinuclidinium perchlorates in water at 25° C

Nr.	R	pK_a	$pK_a^R - pK_a^H$
1	H	10.96 ± 0.02	
2	CH ₃	10.88 ± 0.03 a)	-0.08
3	CH ₂ CH ₃	10.95 ± 0.03 a)	-0.01
4	CH(CH ₃) ₂	11.02 ± 0.04 a)	0.06
5	C(CH ₃) ₃	11.07 ± 0.03 a)	0.11
6	CH=CH ₂	10.60 ± 0.01	-0.36
7	C ₆ H ₅	10.20 ± 0.04	-0.76
8	CH ₂ OH	10.45 ± 0.01	-0.51
9	CH ₂ OCH ₃	10.50 ± 0.01	-0.46
10	CH ₂ OCOCH ₃	10.27 ± 0.03	-0.69
11	CH ₂ OTs b)	9.87 ± 0.03	-1.09
12	CH ₂ Cl	10.19 ± 0.02	-0.77
13	CH ₂ Br	10.13 ± 0.02	-0.83
14	CH ₂ J	10.12 ± 0.02	-0.84
15	CH(OH) ₂	9.90 ± 0.03 c)	-1.06
16	COO ⁻	10.55 ± 0.02 d)	-0.41
17	COOCH ₃	9.46 ± 0.02	-1.50
18	COOC ₂ H ₅	9.44 ± 0.01	-1.52
19	COCH ₃	9.45 ± 0.01	-1.51
20	CONH ₂	9.38 ± 0.01	-1.58
21	CN	8.07 ± 0.01	-2.89

a) literature ref. 3 and 5

b) Ts = p-CH₃C₆H₄SO₂

c) the corresponding aldehyde is completely hydrated

d) pK_a^1 of the carboxylic acid is 3.64 ± 0.03

Table continued

Nr.	R	pK_a	$pK_a^R - pK_a^H$
22	OH	9.44 ± 0.01	-1.52
23	OCH ₃	9.31 ± 0.01	-1.65
24	OCOCH ₃	8.99 ± 0.01	-1.97
25	Cl	8.62 ± 0.01 e)	-2.34
26	Br	8.49 ± 0.02 e)	-2.47
27	J	8.70 ± 0.03 e)	-2.26
28	NH ₂	10.10 ± 0.02 f)	-0.86
29	NHCH ₃	10.28 ± 0.02 g)	-0.68
30	N(CH ₃) ₂	10.11 ± 0.03 h)	-0.85
31	NHCOCH ₃	9.54 ± 0.01	-1.42
32	NHCOOC ₂ H ₅	9.57 ± 0.01	-1.39
33	NO ₂	7.65 ± 0.02	-3.31

e) due to fragmentation of the free base only part of the titration curve can be used.

f) pK_a^1 of the bis-hydroperchlorate 6.92 ± 0.02 .

g) pK_a^1 of the bis-hydroperchlorate 7.03 ± 0.02 .

h) pK_a^1 of the bis-hydroperchlorate 6.57 ± 0.02 .

Column 4 of the Table lists values of $pK_a^R - pK_a^H$, the difference between the pK_a of the 4-substituted and the unsubstituted quinuclidine perchlorate. A negative sign indicates an electron withdrawing -I effect relative to hydrogen, a positive sign an electron repelling +I effect.

The following facts are readily discernible from the Table:

- a) The range of pK_a values covers 3.42 pK_a units i.e., from 11.07 for the weakest conjugate acid (I, R = t.butyl, Nr. 5) to 7.65 for the strongest conjugate acid (I, R = NO_2 , Nr. 33).
- b) Only the isopropyl (Nr. 4) and t.butyl group (Nr. 5) are distinctly electron repelling relative to hydrogen, as noted previously ⁵⁾.
- c) The vinyl (Nr. 6) and the phenyl group (Nr. 7) have marked -I effects, the latter being twice as large as the first.
- d) The -I effects of an ester, acetyl and amide group (Nr. 17 - 20) are roughly equal.
- e) In spite of its negative charge the carboxylate group (Nr. 16) has an acid-strengthening -I effect.
- f) The -I effects of halogens increase in the order $I < Cl < Br$. (Nr. 25 - 27), in the CH_2Hal series $Cl < Br \sim I$ (Nr. 12 - 14).
- g) The OCH_3 group is more electron withdrawing than OH (Nr. 22 and 23). In the case of CH_2OCH_3 and CH_2OH the order is reversed (Nr. 8 and 9).
- h) The -I effect of some representative groups increases in the order $H \sim alkyl < -CH=CH_2 < CH_2Cl \sim C_6H_5 < NH_2 < COOalk \sim OH < CONH_2 < Cl < CN < NO_2$.

A full account of this work will be given elsewhere.

References

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