

272. *4-Anilinoquinaldine Derivatives.*

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IN view of the powerful local anæsthetic action ascribed by Silberstein (D.R.-P. 137,121) to 4-anilinoquinaldine and 4-*p*-phenetidino-6-ethoxyquinaldine (J., 1931, 2814) a series of similar compounds has been synthesised, the pharmacological action of which will be investigated by Prof. J. M. Watt of this University : only one similar compound has been described (4-anilino-6-methoxyquinaldine; Slater, J., 1931, 118).

4-Chloroquinaldine or its 8-methoxy-, 6-methoxy-, 8-ethoxy-, or 6-ethoxy-derivative (1 mol.) was refluxed with aniline, *o*- or *p*-anisidine, or *o*- or *p*-phenetidine (1 mol.) in glac. AcOH for 3 hrs. The hydrochloride of 4-anilino-6-ethoxyquinaldine crystallised from the hot solution; other hydrochlorides separated, usually as a gelatinous mass of pale yellow, silky needles, only after dilution with H₂O and addition of conc. HCl; but the hydrochlorides of the condensation products of 8-methoxy- and 8-ethoxy-4-chloroquinaldine

with aniline, *o*- and *p*-anisidine did not separate under these conditions and appeared to be unstable and easily hydrolysed.

The bases formed well-defined colourless crystals from dil. EtOH, readily soluble in EtOH and sparingly soluble in Et₂O. The hydrochlorides are pale yellow, and the picrates, which crystallise well from EtOH, are bright yellow.

The condensation of other aromatic bases with 4-chloroquinaldines is being investigated.

(Nitrogen determinations were carried out by the micro-Dumas method.)

o-Phenetidine has d_{20}^{20} : 1.0513.

(1) 4-*Chloro-8-methoxyquinaldine monohydrate*, long colourless needles, m. p. 83°; dried in vac. over P₂O₅, the anhydrous base has m. p. 89° (Found: C, 58.5; H, 5.3; H₂O, 7.9. C₁₁H₁₀ONCl.H₂O requires C, 58.55; H, 5.3; H₂O, 8.0%). Picrate, m. p. 191° (decomp.).

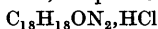
(2) 4-*Hydroxy-8-ethoxyquinaldine dihydrate*, large colourless prisms (from H₂O), becoming anhydrous at 110°; m. p. 197°. Reddish-purple coloration with FeCl₃ aq. (Found: H₂O, 15.15. C₁₂H₁₃O₂N.2H₂O requires H₂O, 15.1%. Found for anhydrous base: N, 7.0. C₁₂H₁₃O₂N requires N, 6.9%). *Hydrochloride*, m. p. 264° (decomp.) (Found: Cl, 14.9. C₁₂H₁₃O₂N.HCl requires Cl, 14.8%). Picrate, m. p. 211°.

(3) 4-*Chloro-8-ethoxyquinaldine monohydrate*, long colourless needles, m. p. 61°; dried in vac. over P₂O₅, the anhydrous base has m. p. 44° (Found: N, 5.8; H₂O, 7.6. C₁₂H₁₂ONCl.H₂O requires N, 5.85; H₂O, 7.5%). Picrate, m. p. 193° (decomp.).

(4) 4-*o-Anisidinoquinaldine*, m. p. 203° (Found: N, 10.7. C₁₇H₁₆ON₂ requires N, 10.6%). *Hydrochloride*, m. p. 252° (decomp.) (Found: Cl, 11.7. C₁₇H₁₆ON₂.HCl requires Cl, 11.8%). Picrate, chars at 276°.

(5) 4-*p-Anisidinoquinaldine*, m. p. 209° (Found: N, 10.7%). *Hydrochloride*, m. p. 286° (decomp.) (Found: Cl, 11.6%). Picrate, m. p. 223° (decomp.).

(6) 4-*o-Phenetidinoquinaldine*, m. p. 171° (Found: N, 10.2. C₁₈H₁₈ON₂ requires N, 10.1%). *Hydrochloride*, m. p. 143° (Found: Cl, 11.4.



requires Cl, 11.3%). Picrate, chars at 274°.

(7) 4-*p-Phenetidinoquinaldine*, m. p. 182° (Found: N, 10.2%). *Hydrochloride*, m. p. 277° (decomp.) (Found: Cl, 11.1%). Picrate, m. p. 223°.

(8) 4-*Anilino-8-methoxyquinaldine*, m. p. 268° (Found: N, 10.7. C₁₇H₁₆ON₂ requires N, 10.6%). Picrate, m. p. 189°.

(9) 4-*o-Anisidino-8-methoxyquinaldine*, m. p. 198° (Found: N, 9.6. C₁₈H₁₈O₂N₂ requires N, 9.5%). Picrate, m. p. 192°.

(10) 4-*p-Anisidino-8-methoxyquinaldine*, m. p. 234° (Found: N, 9.65%). Picrate, m. p. 187°.

(11) 4-*o-Phenetidino-8-methoxyquinaldine*, m. p. 191° (Found: N, 9.2. C₁₉H₂₀O₂N₂ requires N, 9.1%). *Hydrochloride*, m. p. 210° (decomp.) (Found: Cl, 10.3. C₁₉H₂₀O₂N₂.HCl requires Cl, 10.3%). Picrate, m. p. 174°.

(12) 4-*p-Phenetidino-8-methoxyquinaldine*, m. p. 228° (Found: N, 9.1%). *Hydrochloride*, m. p. 245° (decomp.) (Found: Cl, 10.25%). Picrate, m. p. 188°.

(13) 4-*o-Anisidino-6-methoxyquinaldine*, m. p. 193° (Found: N, 9.5%). *Hydrochloride*, m. p. 274° (decomp.) (Found: Cl, 10.6. C₁₈H₁₈O₂N₂.HCl requires Cl, 10.7%). Picrate, m. p. 233° (decomp.).

(14) 4-*p*-Anisidino-6-methoxyquinaldine, m. p. alone or mixed with a specimen prepared in 10% yield by Silberstein's method (*loc. cit.*), 203° (Found : N, 9.5%). *Hydrochloride*, m. p. 292° (decomp.) (Found : Cl, 10.7%). Picrate, m. p. 274° (decomp.).

(15) 4-*o*-Phenetidino-6-methoxyquinaldine, m. p. 172° (Found : N, 9.2%). *Hydrochloride*, m. p. 238° (decomp.) (Found : Cl, 10.2%). Picrate, m. p. 229°.

(16) 4-*p*-Phenetidino-6-methoxyquinaldine, m. p. 223° (Found : N, 9.1%). *Hydrochloride*, m. p. 282° (decomp.) (Found : Cl, 10.1%). Picrate, m. p. 251° (decomp.).

(17) 4-Anilino-8-ethoxyquinaldine, m. p. 245° (Found : N, 10.2. $C_{18}H_{18}ON_2$ requires N, 10.1%). Picrate, m. p. 191°.

(18) 4-*o*-Anisidino-8-ethoxyquinaldine, m. p. 203° (Found : N, 9.1. $C_{19}H_{20}O_2N_2$ requires N, 9.1%). Picrate, m. p. 163°.

(19) 4-*p*-Anisidino-8-ethoxyquinaldine, m. p. 211° (Found : N, 9.2%). Picrate, m. p. 174°.

(20) 4-*o*-Phenetidino-8-ethoxyquinaldine, m. p. 143° (Found : N, 8.7. $C_{20}H_{22}O_2N_2$ requires N, 8.7%). *Hydrochloride*, m. p. 147° (decomp.) (Found : Cl, 10.0. $C_{20}H_{22}O_2N_2.HCl$ requires Cl, 9.9%). Picrate, m. p. 164°.

(21) 4-*p*-Phenetidino-8-ethoxyquinaldine, m. p. 209° (Found : N, 8.7%). *Hydrochloride*, m. p. 240° (decomp.) (Found : Cl, 10.0%).

(22) 4-Anilino-6-ethoxyquinaldine, m. p. 223° (Found : N, 10.2%). *Hydrochloride*, m. p. 311° (decomp.) (Found : Cl, 11.3. $C_{18}H_{18}ON_2.HCl$ requires Cl, 11.3%). Picrate, m. p. 227°.

(23) 4-*o*-Anisidino-6-ethoxyquinaldine, m. p. 158° (Found : N, 9.1%). *Hydrochloride*, m. p. 255° (decomp.) (Found : Cl, 10.2. $C_{19}H_{20}O_2N_2.HCl$ requires Cl, 10.3%). Picrate, m. p. 200°.

(24) 4-*p*-Anisidino-6-ethoxyquinaldine, m. p. 194° (Found : N, 9.2%). *Hydrochloride*, m. p. 281° (decomp.) (Found : Cl, 10.25%). Picrate, m. p. 221°.

(25) 4-*o*-Phenetidino-6-ethoxyquinaldine, m. p. 177° (Found : N, 8.7%). *Hydrochloride*, m. p. 279° (decomp.) (Found : Cl, 9.7%). Picrate, m. p. 219°.

The picrates of the following known compounds were also prepared : 4-hydroxy-8-methoxyquinaldine, m. p. 217°; 4-hydroxy-6-methoxyquinaldine, m. p. 202°; 4-hydroxy-6-ethoxyquinaldine, m. p. 205°; 4-chloro-6-methoxyquinaldine, m. p. 210° (decomp.); 4-chloro-6-ethoxyquinaldine, m. p. 209°; 4-anilino-6-methoxyquinaldine, m. p. 269° (decomp.); and 4-*p*-phenetidino-6-ethoxyquinaldine, m. p. 217°.

Solubility in Benzene.—Compounds 4, 6, 9, 11, 13, 15, 18, 20, and 25 are readily soluble in cold C_6H_6 , compounds 7, 16, and 24 are sparingly soluble in cold and soluble in hot C_6H_6 , and compounds 5, 8, 10, 12, 14, 17, 19, 21, 22, and 23 are sparingly soluble in hot C_6H_6 .

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