242. 2-*Anilinolepidine Derivatives.*

By O. G. Backeberg.

In a previous communication (J., 1932, 1984) a number of 4-anilinoquinaldine derivatives was described, and their possible use as local anæsthetics indicated. The isomeric 2-anilinolepidine derivatives have now been prepared, and their pharmacological action is to be investigated. 2-Chlorolepidine, its 6-methoxy- or 6-ethoxy-derivative was condensed with aniline, *o*- or *p*-anisidine, or *o*- or *p*-phenetidine; of the condensation products, 2-anilinolepidine only has been previously described (Knorr, *Annalen*, 1886, **236**, 103).

Acetoacet-*o*-anisidide and -*o*-phenetidide could not be made to undergo ring closure either by the action of sulphuric acid, hydrochloric acid, phosphoric acid, phosphoric oxide, phosphoryl chloride, or acetic anhydride, which is surprising in view of the fact that the -*o*-chloroanilide (Kermack and Muir, J., 1933, 302) and -*o*-toluidide (Ewins and King, J., 1913, **103**, 104) readily undergo ring closure to the corresponding 2-hydroxylepidines. It was therefore not possible to prepare the 8-methoxy- and 8-ethoxy-2-anilinolepidine derivatives.

There appears to be uncertainty as regards the melting point of 2-hydroxy-6-methoxy-4-methylquinoline and its picrate. The base was prepared by treating acetoacet-*p*-anisidide with concentrated or 90% sulphuric acid or glacial phosphoric acid, and in each case the product melted at 272° and the picrate at 204°. The base has been described by Rabe and his co-workers (*Ber.*, 1931, **64**, 2492), who gave m. p. 253°; Monti and Verona (*Gazzetta*, 1932, **62**, 14), who gave m. p. 268°, picrate, m. p. 196—198°; and Kermack and Muir (*loc. cit.*), who gave m. p. 255°, picrate, m. p. 191°. The last authors report that on attempting to reconvert its 2-methoxy-derivative into the original 2-hydroxy-compound, they obtained a product, m. p. 271°, picrate, m. p. 165—166°, which appeared to be different from the original material, although the analytical data indicated the same empirical formula.

Experimental.

All analyses were done by Pregl's micro-methods.

The following acetoacetanilides were prepared by the method of Limpach (*Ber.*, 1931, **64**, 970) : acetoacet-anilide, -*o*-anisidide, m. p. 87° (D.R.-P. 256621 gives 84°), -*p*-anisidide, -*o*-phenetidide, m. p. 87° (Daines and Harger, *J. Amer. Chem. Soc.*, 1918, **40**, 564, give 92°), and -*p*-phenetidide, m. p. 105° (D.R.-P. 268318 gives 103°).

Ring closure was effected by heating the acetoacetanilides to 100° with an equal weight of concentrated sulphuric acid for 2 hours, and the 2-hydroxylepidines formed were converted into the corresponding 2-chloro-compounds by refluxing with phosphoryl chloride for ½ hour without addition of phosphorus pentachloride; the chloro-compounds were condensed with the aniline bases mentioned by the method used for 4-anilinoquinaldine derivatives (*loc. cit.*). The products crystallise well from dilute or absolute alcohol and form well-defined picrates; unlike the isomeric 4-anilinoquinaldines, they are readily soluble in dilute mineral acids.

2-*Hydroxy*-6-*methoxy*-4-*methylquinoline*, m. p. 272° from dilute acetic acid or alcohol, is sparingly soluble in dilute sodium hydroxide solution, and its dilute alcoholic solution gives a reddish-brown coloration with ferric chloride (Found: C, 70·01; H, 5·75. $C_{11}H_{11}O_2N$ requires C, 69·84; H, 5·82%); picrate, from alcohol, m. p. 204°. 2-*Hydroxy*-6-*ethoxy*-4-*methylquinoline*, m. p. 232° from dilute acetic acid; it had the same properties as the preceding compound (Found: C, 70·79; H, 6·28. $C_{12}H_{13}O_2N$ requires C, 70·94; H, 6·40%); picrate, m. p. 179°. 2-*Chloro*-6-*ethoxy*-4-*methylquinoline*, colourless needles from dilute alcohol, m. p. 123°; it is slowly volatile in steam (Found: C, 65·30; H, 5·31. $C_{12}H_{12}ONCl$ requires C, 65·02; H, 5·42%).

2-o-*Anisidinolepidine*, m. p. 140° (Found: N, 10·70. $C_{17}H_{16}ON_2$ requires N, 10·60%); picrate, m. p. 223°. 2-p-*Anisidinolepidine*, m. p. 129° (Found: N, 10·72%); picrate, m. p. 190°. 2-o-*Phenetidinolepidine*, m. p. 127° (Found: N, 10·20. $C_{18}H_{18}ON_2$ requires N, 10·07%); picrate, m. p. 226°. 2-p-*Phenetidinolepidine*, m. p. 165° (Found: N, 10·23%); picrate, m. p. 215°. 2-*Anilino*-6-*methoxylepidine*, m. p. 139° (Found: N, 10·68. $C_{17}H_{16}ON_2$ requires N, 10·60%); picrate, m. p. 213°. 2-o-*Anisidino*-6-*methoxylepidine*, m. p. 151° (Found: N, 9·62. $C_{18}H_{18}O_2N_2$ requires N, 9·53%); picrate, m. p. 228°. 2-p-*Anisidino*-6-*methoxylepidine*, m. p. 137° (Found: N, 9·51%); picrate, m. p. 216°. 2-o-*Phenetidino*-6-*methoxylepidine*, m. p. 119° (Found: N, 9·09. $C_{19}H_{20}O_2N_2$ requires N, 9·09%); picrate, m. p. 237°. 2-p-*Phenetidino*-6-*methoxylepidine*, m. p. 149° (Found: N, 9·14%); picrate, m. p. 183°. 2-*Anilino*-6-*ethoxylepidine*, m. p. 127° (Found: N, 10·21. $C_{18}H_{18}ON_2$ requires N, 10·07%); picrate, m. p. 236°. 2-o-*Anisidino*-6-*ethoxylepidine*, m. p. 158° (Found: N, 9·22. $C_{19}H_{20}O_2N_2$ requires N, 9·09%); picrate, m. p. 241°. 2-p-*Anisidino*-6-*ethoxylepidine*, m. p. 172° (Found: N, 9·22%); picrate, m. p. 203°. 2-o-*Phenetidino*-6-*ethoxylepidine*, m. p. 141° (Found: N, 8·71. $C_{20}H_{22}O_2N_2$ requires N, 8·70%); picrate, m. p. 224°. 2-p-*Phenetidino*-6-*ethoxylepidine*, m. p. 128° (Found: N, 8·87%); picrate, m. p. 218°. 2-Anilinolepidine picrate, m. p. 228°.

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