2-Methoxy-6-chloro-9-(dialkylaminoalkylamino)-acridines

By G. Bryant Bachman and D. E. Welton[1]

These compounds were prepared from 2-methoxy-6,9-dichloroacridine (I) and the appropriate dialkylaminoalkylamines by the general procedure of Magidson and Grigorovskii.[2] The products are listed in Table I.

Table I

2-Methoxy-6-chloro-9-(dialkylaminoalkylamino)-acridines

No.	Substituent, —R	Salt	M. p.,[a] °C.	Yield, % method	Crystallization solvent–diluent	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
1	$—CH_2C(CH_3)_2CH_2N(CH_3)_2$	2HCl	255–256	64	Water–dioxane	56.67	56.68 56.25	6.30	6.44 6.51
2	$—CH_2C(CH_3)_2CH_2N(C_2H_5)_2$	2HCl + $^1/_3H_2O^{b,c}$	243–245	29	Water–dioxane	57.66	57.63 57.75	6.89	7.84 7.01
3	$—CH_2C(CH_3)_2CH_2N(n\text{-}C_4H_9)$	2HCl	215–220	33	Water–dioxane	61.27	61.07 60.77	7.56	7.44 7.71
4	$—CHCH_3CH_2N(n\text{-}C_4H_9)_2$	2HCl + $^2/_3H_2O^{b,d}$	217–221	83	95% Ethanol–diethyl ether	58.30	58.39 58.37	7.33	7.45 7.65
5	$—(CH_2)_6N(CH_3)_2$	2HCl	281–282	64	Water–dioxane	57.55	57.41 57.37	6.58	6.72 6.73
6	$—CH[—CH_2N(CH_3)_2]_2{}^e$	3HCl + ·HOAc[f]	247–248	69	Acetic acid–none	49.62	49.49 49.63	6.14	6.08 6.38
7	$—CH[—CH_2N(n\text{-}C_3H_7)_2]_2{}^g$	3HCl	220–221	43	Methanol–diethyl ether	57.59	57.02 56.90	7.51	7.46 7.59

[a] Corrected; all melted with decomposition. [b] Dried to constant weight at 140° over phosphorus pentoxide. [c] Calcd.: N, 8.77. Found: N, 8.63. Ionizable Cl: Calcd., 14.83; found, 14.55. [d] % Ionizable Cl: Calcd., 13.85; found, 13.86. [e] Free base, m. p. 120–121°. %C: Calcd., 65.17; found, 65.19. %H: Calcd., 7.03; found, 7.13. [f] Dried to constant weight over calcium oxide at 100°. [g] Free base, m. p. 99–100°. %C: Calcd., 69.91; found, 69.77. %H: Calcd., 8.50; found, 8.64.

In spite of their general structural similarity, the products show considerable differences in ease of hydrolysis. Those in which the substituted ethylenediamine structure is present in the substituent group (Table I, nos. 4, 6 and 7) hydrolyze immediately in hot dilute hydrochloric acid solution to give a precipitate of 2-methoxy-6-chloroacridone, whereas those in which the amino groups are further separated are not affected under these conditions for at least one hour.

Only the 1,3-bis-(dialkylamino)-2-propylamine derivatives (Table I, nos. 6 and 7) form crystalline free bases, but all yield crystalline polyhydrochlorides which form hydrates of varying stabilities; the derivatives listed in Table I are the most nearly anhydrous materials obtainable in each case. Recrystallization of these salts from a mixture of solvents generally gives much more effective purification and recovery than a single solvent.

Pharmacological Testing.—All of the acridine derivatives listed in Table I were submitted for testing as antimalarial agents. The results of these tests will be reported in detail elsewhere. It may be noted, however, that compounds 1, 2, 3 and 5 showed activity against *P. lophurae* in ducks. Compounds 2, 3, 6 and 7 showed little or no trypanocidal activity. Compounds 3 and 7 were inactive toward *Streptococcus hemolyticus*, influenza-virus and Tetanus toxemia.

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[2] O. Y. Magidson and A. M. Grigorovskii, *Ber.*, **69B**, 396–412 (1936).

The Freezing Point of Pure Phthalic Anhydride

By D. E. Debeau

Phthalic anhydride is an article of great commercial importance and is sold on the basis of purity as determined by freezing point. Hence, it is important to know accurately the freezing point of this material with zero impurity. The values to be found in the literature vary from 130.84[1] to 131.60°.[2]

To reach a decision as to which of these values is the more reliable it was necessary to make the measurements reported below.

The phthalic anhydride used was supplied by the Oronite Chemical Company and was manufactured from *o*-xylene by air oxidation. Several methods of purification of the phthalic anhydride were tried. They were slow fractional crystallization, recrystallization from acetone, and sublimation at atmospheric pressure. Samples prepared by sublimation had the highest freezing points and gave the most reproducible results.

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