METHOXY DERIVATIVES OF 7-SULFODIMETHYLAMIDOACRIDINE

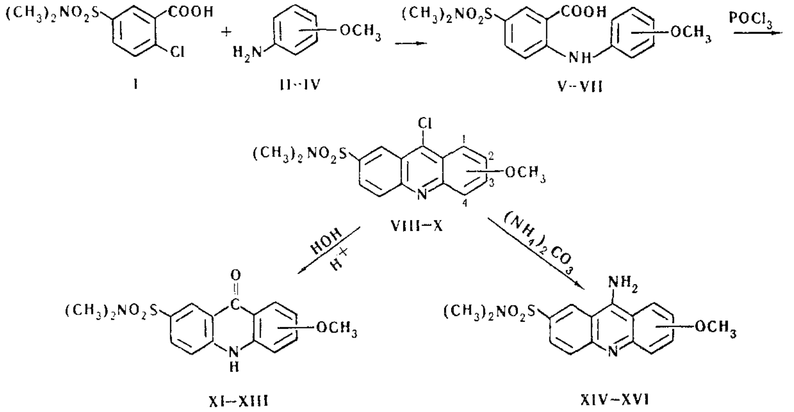
V. T. Skripkina, N. N. Dykhanov,
V. P. Maksimets, and L. D. Shcherbak

UDC 547.835:4.6

The 2'-, 3'-, and 4'-methoxy derivatives of 4-sulfodimethylamidodiphenylamine-2-carboxylic acid were synthesized by the condensation of 2-chloro-5-sulfodimethylamidobenzoic acid with o-, m-, and p-anisidines, respectively. These acids were cyclized by the action of phosphorus oxychloride to the corresponding methoxy-substituted 7-sulfodimethylamido-9-chloroacridines. The 2-, 3-, and 4-methoxy derivatives of 7-sulfodimethylamido-9-acridone and 7-sulfodimethylamido-9-aminoacridine were obtained from the latter.

The sulfamido derivatives of acridine have received only little study. The fusion of a sulfamido group and the acridine ring may be of decided interest in the search for luminescent and antimicrobial substances.

We have synthesized the 2-, 3-, and 4-methoxy derivatives of 7-sulfodimethylamido-9-chloroacridine, from which the corresponding 9-acridones and 9-aminoacridines were obtained.



The starting compounds were 2'-, 3'-, and 4'-methoxy derivatives of 4-sulfodimethylamidodiphenylamine-2-carboxylic acid (V-VII), which were obtained by the condensation of 2-chloro-5-sulfodimethylamidobenzoic acid (I) with o-, m-, and p-anisidines (II-IV) via the Ullmann reaction [1].

The 2-, 3-, and 4-methoxy derivatives of 7-sulfodimethylamido-9-chloroacridine (VIII-X) were obtained via the method in [2] by treatment of acids V-VII with excess phosphorus oxychloride. Cyclization of 3'-methoxy-4-sulfodimethylamidophenylamine-2-carboxylic acid (VI) leads to the formation of a mixture of isomeric 1- and 3-methoxy derivatives of 7-sulfodimethylamido-9-chloroacridine. Despite attempts to use the various methods for separating similar mixtures recommended in [3-6], the 1-methoxy isomer could not be isolated in view of its extremely facile hydrolizability.

The purity of 3-methoxy-7-sulfodimethylamido-9-chloroacridine was confirmed by thin-layer chromatography [with aluminum oxide as the sorbent, and benzene-heptane-methanol (5:1:1) as the solvent].*

---

*We thank M. I. Fedosyuk for conducting the thin-layer-chromatography investigations.

All-Union Scientific-Research Institute of Single Crystals, Scintillation Materials, and Very Pure Chemical Substances, Khar'kov. Khar'kov Institute of Public Nutrition. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 115-117, January, 1971. Original article submitted July 2, 1969.

TABLE 1. Characteristics of the Compounds Obtained

Compound	Position of the CH_3O group	Mp, °C*	Empirical formula	Found, %			Calculated, %			UV spectrum, λ_{max}, nm (log ε)	Yield, %
				Cl	N	S	Cl	N	S		
VIII	2	210[7]	$C_{16}H_{15}ClN_2O_3S$	—	—	—	—	—	—	238 (4,48); 266 (4,94); 340 (3,80); 356 (3,94); 390 (3,78); 408 (3,74)	88
IX	3	204—205	$C_{16}H_{15}ClN_2O_3S$	10,0	8,3	9,1	10,1	8,0	9,1	242 (4,46); 276 (5,00); 358 (3,98); 366 (3,92); 388 (3,86); 415 (infl.) (3,68)	79
X	4	230—231	$C_{16}H_{15}ClN_2O_3S$	9,9	8,2	9,0	10,1	8,0	9,1	230 (5,02); 274 (4,90); 346 (3,34); 366 (3,42); 406 (3,55)	80
XI	2	>360	$C_{16}H_{16}N_2O_4S$	—	8,7	9,8	—	8,4	9,6	242 (3,76); 256 (3,80); 290 (3,86); 324 (3,06); 396 (3,06); 418 (3,08)	98
XII	3	>360	$C_{16}H_{16}N_2O_4S$	—	8,5	9,3	—	8,4	9,6	252 (4,50); 288 (4,74); 365 (3,80); 380 (3,82)	98
XIII	4	>360	$C_{16}H_{16}N_2O_4S$	—	8,6	9,3	—	8,4	9,6	226 (4,28); 260 (4,56); 326 (3,98); 384 (3,78)	95
XIV	2	257—257,5 (dec.)	$C_{16}H_{17}N_3O_3S$	—	12,8	9,9	—	12,7	9,7	266 (4,44); 294 (4,66); 326 (3,34); 342 (3,52); 358 (3,24); 424 (3,72); 445 (3,66)	87
XV	3	281—282 (dec.)	$C_{16}H_{17}N_3O_3S$	—	12,5	9,8	—	12,7	9,7	238 (4,18); 290 (4,64); 326 (infl.) (3,15); 345 (3,40); 408 (3,80); 430 (3,65)	70
XVI	4	255 (dec.)	$C_{16}H_{17}N_3O_3S$	—	12,8	9,6	—	12,7	9,7	275 (4,74); 328 (infl. 3,52); 348 (3,50); 360 (3,78); 406 (3,72); 418 (infl.) (3,70)	68

---

*The solvents used to crystallize the compounds were as follows: VIII ethanol, IX benzene, X acetone, XI-XIII 60% aqueous dimethylformamide, and XIV-XVI aqueous ethanol.

The corresponding 9-acridones (XI-XIII) were obtained from VIII-X by refluxing with 1 N hydrochloric acid, while the derivatives of 9-aminoacridine (XIV-XVI) were obtained by treatment of VIII-X with ammonium carbonate.

XI-XIII have the following fundamental bands in the IR spectra*: ν_{CO} 1626 cm^{-1} (XI), 1630 cm^{-1} (XII), and 1628 cm^{-1} (XIII); the valence vibrations of the associated NH groups are represented by several bands from 2800 to 3260 cm^{-1}; ν_{SO_2} 1160 and 1334 cm^{-1} (XI), 1174 and 1335 cm^{-1} (XII), 1175 and 1340 cm^{-1} (XIII); $\nu_{=C-O-C}$ bands (methoxy group) at 1034 and 1252 cm^{-1} (XI), 1032 and 1258 cm^{-1} (XII), 1078 and 1252 cm^{-1} (XIII).

The UV absorption of VIII-X differs from that of the corresponding 9-acridones (XI-XIII, Table 1), which also confirms the oxo structure for the latter.

The characteristics of the compounds obtained are presented in Table 1.

EXPERIMENTAL

Condensation of 2-Chloro-5-sulfodimethylamidobenzoic Acid (I) with Anisidines (II-IV). A mixture of 26.4 g (0.1 mole) of I, 18.5 g (0.15 mole) of either II, III, or IV, 15.2 g (0.11 mole) of potassium carbonate, and 1 g of copper powder was heated in 250 ml of n-butanol at 125-135° for 4-5 h. The alcohol and excess amine were removed by steam distillation, the solution was refluxed with activated charcoal and filtered. Hydrochloric acid was added until the mixture was neutral, and the resulting precipitate of V-VII was crystallized from glacial acetic acid.

V [14 g (40%)] had mp 191-192°, which was in agreement with the melting point reported in [7].

VI [12.9 g (37%)] had mp 179-180°. Found %: N 8.1; S 9.3. $C_{16}H_{18}N_2O_5S$. Calc. %: N 8.0; S 9.1.

VII [10.2 g (29%)] had mp 173-174°. Found %: N 7.8; S 9.2. $C_{16}H_{18}N_2O_5S$. Calc. %: N 8.0; S 9.1.

2-, 3-, and 4-Methoxy Derivatives of 7-Sulfodimethylamido-9-chloroacridine (VIII-X). V-VII [3.5 g (0.01 mole)] was heated on a water bath with 6.1 g (0.04 mole) of phosphorus oxychloride for 3-4 h. The solution was cooled and poured into a mixture of ice and ammonium hydroxide, and the resulting precipitate was separated and dried in vacuo over potassium hydroxide.

2-, 3-, and 4-Methoxy Derivatives of 7-Sulfodimethylamido-9-acridone (XI-XIII). The appropriate 9-chloroacridine (VIII-X)[1.75 g (0.005 mole)] was refluxed with 30 ml of 1 N hydrochloric acid for 2-2.5 h. The mixture was made alkaline with ammonia, and the resulting precipitate was separated and crystallized.

2-, 3-, and 4-Methoxy Derivatives of 7-Sulfodimethylamido-9-aminoacridine (XIV-XVI). VIII-X [3.5 g (0.01 mole)] was dissolved at 70° in 9.4 g (0.1 mole) of phenol, and 1.7 g of finely ground ammonium carbonate was added in portions with stirring; the mixture was heated at 100° for 1.5 h, and 10% sodium hydroxide was added with cooling. The resulting precipitate was separated, extracted with hot 5% acetic acid, and XIV-XVI were isolated from the acetic acid filtrate by the addition of ammonia.

LITERATURE CITED

1. F. Ullmann, Ann., 355, 312 (1907).
2. O. Yu. Magidson and A. M. Grigorovskii, Zh. Obshch. Khim., 3, 615 (1933).
3. K. Lehmstedt and K. Schrader, Ber., 70, 838 (1937).
4. A. Albert, The Acridines, London, (1951), pp. 28, 40.
5. A. F. Bekhli, Zh. Obshch. Khim., No. 2, 1130 (1953).
6. A. K. Sukhomlinov and V. P. Maksimets, Khim. Geterotsikl. Soedin., 99 (1965).
7. F. Mietzsch, H. Mauss, and J. Klarer (I. G. Farbenindustrie AG), German Patent No. 642,758 (1935); P. Friedländer, Fortschritte der Teerfarbenfabrikation and verwandter Industrie Zweige, Berlin, 23, 541 (1936).

---

*The IR spectra of KBr pellets were measured with a UR-10 spectrometer.