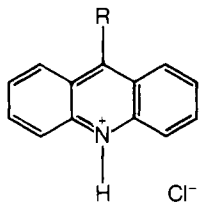
Fluorometric and Mass Spectral Data for 2-(9-Acridinyl)ethyl N-Substituted Carbamates and Their 10-*N*-Oxides

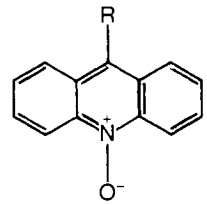
James T. Stewart,* Richard E. Gammans, and Otis J. Bouwsma
Department of Medicinal Chemistry, School of Pharmacy, University of Georgia, Athens, Georgia 30602

Fluorometric and mass spectral data for some 2-(9-acridinyl)ethyl N-substituted carbamates and 2-(10-oxido-9-acridinyl)ethyl N-substituted carbamates are presented. In addition, fluorescence data for the hydrochlorides of the 2-(9-acridinyl)ethyl N-substituted carbamates and NMR data for the 2-(9-acridinyl)ethyl N-substituted carbamates are also shown.

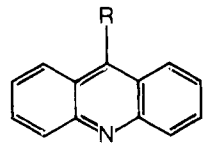
Interest in this laboratory in the anticancer activity of 2-(9-acridinyl)ethyl N-substituted carbamates (I–IV) and their 10-*N*-oxides (V–VIII) resulted in the synthesis and biological evaluation of some model compounds (*1*). A literature search revealed that little if any fluorometric or mass spectral data were available concerning these acridine carbamates and *N*-oxides. These data are of value in the identification and characterization of these compounds and their possible metabolites in biological samples.



IX, R = $-CH_2CH_2OCONH_2$
X, R = $-CH_2CH_2OCONHC_2H_5$
XI, R = $-CH_2CH_2OCONHC_6H_5$
XII, R = $-CH_2CH_2OCONHSO_2-C_6H_4$-*p*-$CH_3$
XVII, R = $-CH_3$
XVIII, R = $-CH_2CH_2OH$



V, R = $-CH_2CH_2OCONH_2$
VI, R = $-CH_2CH_2OCONHC_2H_5$
VII, R = $-CH_2CH_2OCONHC_6H_5$
VIII, R = $-CH_2CH_2OCONHSO_2-C_6H_4$-*p*-$CH_3$
XV, R = $-CH_3$
XVI, R = $-CH_2CH_2OH$



I, R = $-CH_2CH_2OCONH_2$
II, R = $-CH_2CH_2OCONHC_2H_5$
III, R = $-CH_2CH_2OCONHC_6H_5$
IV, R = $-CH_2CH_2OCONHSO_2-C_6H_4$-*p*-$CH_3$
XIII, R = $-CH_3$
XIV, R = $-CH_2CH_2OH$

Table I presents a summary of fluorescence data for these acridine derivatives. Also included in the table is information concerning the hydrochloride salts (IX–XII) of carbamates I–IV and reference compounds 9-methylacridine (XIII) and 9-(2-hydroxyethyl)acridine (XIV) and their *N*-oxides (XV, XVI) and hydrochlorides (XVII, XVIII). There was special interest in the fluorescence of all the compounds since the literature indicates that acridines are among the most intensely fluorescent compounds known (*2*). Fluorometric measurements were performed by visual examination of the dry powder using long-wavelength ultraviolet light (Ultra-Violet Products, Inc., San Gabriel, Calif.) and by determination of the excitation and emission maxima of the compounds in ethanol using a spectrophotofluorometer.

Table I. Summary of Fluorescence Data of 2-(9-Acridinyl)ethyl N-Substituted Carbamates, Their Hydrochlorides, and 10-*N*-Oxides

	Fluorescence			
Compd	Solid[a]	Soln[b] excit max	Soln[b] emiss max	Rel fluores QRU[c]
I	Yellow	384	412	0.116
II	Bluish white	370	425	0.119
III	Green	360	424	0.070
IV	Yellowish orange	360	425	0.150
XIII	Yellow	370	420	0.080
XIV	Greenish yellow	394	412	0.123
V	Dull orange	395	448	0.088
VI	Dull orange	425	468	0.136
VII	Dull orange	425	468	0.134
VIII	Dull orange	423	468	0.168
XV	Dull orange	410	448	0.069
XVI	Dull orange	425	470	0.479
IX	Bluish green	398	455	0.090
X	Green	398	482	0.053
XI	Green	380	435	0.046
XII	Yellowish green	380	455	0.106
XVII	Bluish green	397	475	0.059
XVIII	Bluish green	397	458	0.061

[a] Ascertained by visual observation of the dry powder when exposed to UV light from a long-wavelength UV lamp. [b] Measurements were recorded on a Perkin-Elmer MPF-4 spectrophotofluorometer using ethanol as solvent. [c] Quinine Reference Unit, see ref 3.

All the compounds possessed varied fluorescent intensities in both the solid state and ethanol solution. A comparison of the fluorescent intensity of the acridines to quinine sulfate via the quinine reference unit (QRU) was performed (*3*). It was concluded that the compounds possessed only moderate to weak fluorescence in solution compared to quinine sulfate. However, the fluorescence intensity is still sufficient to allow fluorometric analysis of these compounds with sensitivity in the nanogram per milliliter range.

Table II presents a summary of electron impact (EI) mass spectral data. Also included in this table for comparison purposes are EI data for 9-methylacridine (XIII), 9-(2-hydroxyethyl)acridine (XIV), and 9-(2-hydroxethyl)acridine 10-*N*-oxide (XVI). Fragmentation patterns for the carbamates I–IV give major ions at *m/e* 223, 205, and 193. These indicate loss of RNCO, H_2O, and CH_2O, respectively, from the molecular ion. Additional ions at *m/e* 166 and 151 result from loss of HCN from the acridine ring to give a 8-methylcyclopent(a)indene ion (*m/e* 166) and subsequent loss of CH_3 to yield a cyclopent(a)indene ion (*m/e* 151). Most of these ions can also be observed in the fragmentation patterns for both 9-methyl- and 9-(2-hydroxyethyl)acridines. Carbamate IV does not give a molecular ion (*m/e* 420) indicating relative ease of loss of *p*-toluenesulfonyl isocyanate.

The *N*-oxides V–VIII give EI data suggesting that loss of oxygen occurs at various stages. This is shown by the occurrence of major ions at *m/e* $[M - 16]^+$, 239, 221, and 209. The *m/e* 239, 221, and 209 ions are presumably due to the 9-(2-hydroxyethyl)acridine 10-*N*-oxide, the 9-vinylacridine 10-*N*-oxide, and the 9-methylacridine 10-*N*-oxide ions, respectively. The remaining ions are similar to those observed in the carbamates

Table II. Mass Spectral Data [a] for 2-(9-Acridinyl)ethyl N-Substituted Carbamates and Their 10-*N*-Oxides

Compd	Mol wt	M^+ (RI)[b]	Major ions, *m/e* (RI)		
I	266	266 (12)	223 (25)	205 (100)	193 (51)
			166 (11)	151 (4)	43 (11)
II	294	294 (5.3)	223 (8.8)	205 (100)	193 (28)
			166 (8.8)	151 (5.3)	71 (8.8)
III	342	342 (1.7)	223 (54)	205 (39)	193 (100)
			166 (13)	151 (3.4)	119 (58)
IV	420	223 (1)	205 (24.5)	193 (3.9)	155 (100)
			197 (31.4)		
XIII	193	193 (100)	179 (2)	166 (7)	151 (1.4)
XIV	223	223 (59)	205 (8.4)	193 (100)	166 (12.6)
			151 (2.1)		
V	282	282 (4)	266 (4)	239 (20)	223 (30)
			209 (36)	205 (100)	193 (36)
			166 (12)	151 (8)	
VI	310	310 (6.3)	294 (3.8)	239 (3.8)	221 (50)
			209 (13.8)	205 (100)	193 (25)
			166 (7.5)	151 (6.3)	71 (6.3)
VII	358	358 (5.9)	342 (4.4)	239 (38.7)	221 (51.5)
			209 (100)	205 (91)	193 (64.7)
			166 (11.8)	151 (14.7)	119 (73.5)
VIII	436	239 (45)	223 (27)	209 (100)	205 (31)
			193 (62)	166 (11)	155 (75)
			151 (11)	197 (38)	
XVI	239	239 (43.3)	223 (37.3)	209 (100)	205 (13.4)
			193 (74.6)	166 (13.4)	151 (10.5)

[a] Electron impact data obtained on LKB-9000 mass spectrometer using 70 eV and probe introduction. [b] RI = relative intensity.

Table III. NMR Data[a] for 2-(9-Acridinyl)ethyl N-Substituted Carbamates

Compound	Solvent	NMR (δ, ppm)
I	Me_2SO-d_6	4.03 (t, CH_2(O))
		4.30 (t, CH_2(acr))
		6.52 (s, NH_2)
		7.77 (m, arom acr)
		8.37 (t, arom acr)
II	$CDCl_3$	1.1 (t, CH_3)
		2.6 (s, NH)
		3.2 (m, CH_2(NH))
		3.9 (t, CH_2(O))
		4.4 (t, CH_2(acr))
		7.9 (m, arom acr)
III	Me_2SO-d_6	4.06 (t, CH_2(O), J = 7 Hz)
		4.54 (t, CH_2(acr), J = 7 Hz)
		7.43 (b, phenyl)
		7.80 (m, arom acr)
		8.36 (t, arom acr)
		9.38 (s, NH)
IV	Me_2SO-d_6	1.9 (s, CH_3)
		3.9 (t, CH_2(O))
		4.4 (t, CH_2(acr))
		7.37 (a/b 7.19, a/b 7.54)
		7.93 (m, arom acr)
		8.87 (s, NH)
XIII	Me_2SO-d_6	3.08 (s, CH_3)
		7.65 (m, arom acr)
		8.22 (t, arom acr)
XIV	Me_2SO-d_6	3.52 (b, CH_2(O))
		3.60 (b, CH_2(acr))
		5.00 (b, OH)
		7.79 (m, arom acr)
		8.43 (t, arom acr)

[a] Measurements were recorded on a Perkin-Elmer-Hitachi Model R20A NMR spectrometer.

I–IV. In addition compound VIII shows no molecular ion (*m/e* 436) due to the ready loss of *p*-toluenesulfonyl isocyanate. The fragmentation pattern of VIII also shows a *m/e* 155 ion, suggesting loss of *p*-toluenesulfonyl ion. The pattern for the carbamate *N*-oxides closely resembles the fragmentations seen for 9-(2-hydroxyethyl)acridine 10-*N*-oxide (XVI).

In addition to the fluorometric and mass spectral information, NMR data for compounds I–IV, XIII, and XIV were collected and are shown in Table III.

In summary, fluorometric, mass spectral, and NMR data have been presented to aid in the identification and characterization of these compounds and their metabolites in various analytical samples.

Experimental Section

Fluorescence spectra were determined with a Perkin-Elmer Model MPF-4 spectrophotofluorometer equipped with a corrected spectra accessory.

Mass spectra data were obtained on a LKB-9000 instrument using probe introduction of the sample. Electron energy of 70 eV, ion source temperature of 200 °C, and ionizing current of 60 μA were employed.

Nuclear magnetic resonance data were obtained in an appropriate solvent with a Perkin-Elmer-Hitachi Model R20A spectrometer operating at 60 MHz.

Literature Cited

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