O-Methyl-*S*-allyl-*N*-(2- and 4-Substituted 9-Acridinyl)iminothiocarbonates – New Reactive Intermediates with Fluorescence Properties

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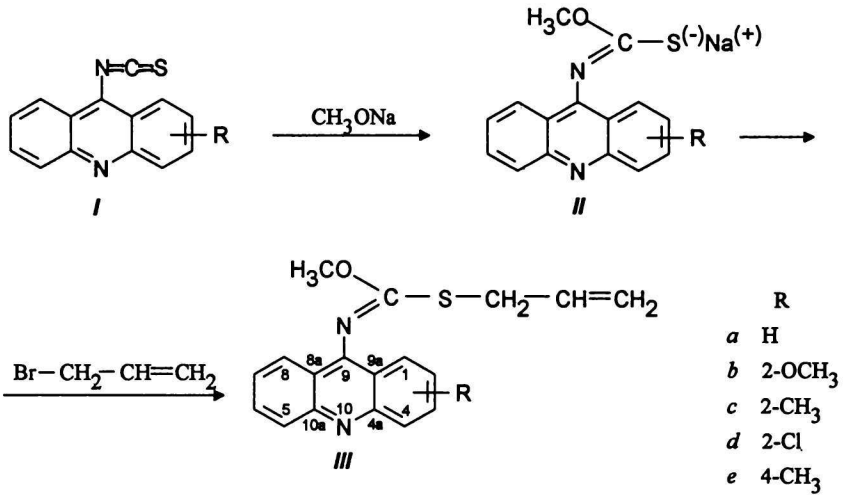
A series of *O*-methyl-*S*-allyl-*N*-(2- and 4-substituted 9-acridinyl)iminothiocarbonates *IIIa*—*IIIe* has been prepared in good yields by alkylation of corresponding sodium iminothiocarbonates *IIa*—*IIe* which were obtained by addition of sodium methoxide to 9-isothiocyanatoacridines *Ia*—*Ie*. Relative fluorescence intensity measurements of *IIIa*—*IIIe* showed that 2-methoxy derivative *IIIb* exhibited threefold higher intensity of fluorescence than 9-isothiocyanatoacridine. The structure of *IIIa*—*IIIe* was corroborated by the CHN elemental analysis, IR and mass spectra, and completely assigned ^{1}H and ^{13}C NMR spectra.

Acridines represent a group of compounds with a great variability of biological effects [1—3]. Due to a marked fluorescence, many of them, *e.g.* 9-acridinyl derivatives [4], have been utilized as fluorescence reagents [5].

In this paper we have focused our attention on the study of functionalized 9-acridinyl derivatives which may serve as reactive intermediates in organic synthesis and fluorogenes or intercalators in biochemistry. As starting compounds for their synthesis, 9-isothiocyanatoacridines *Ia*—*Ie* previously described in our papers [6, 7] were chosen. The final products *O*-methyl-*S*-allyl-*N*-(9-acridinyl)iminothiocarbonates *IIIa*—*IIIe* were obtained by addition of an excess of sodium methoxide to *Ia*—*Ie* in dry ether under formation of intermediate sodium *O*-methyl-*N*-(2- or 4-substituted 9-acridinyl)iminothiocarbonates *IIa*—*IIe* which were then alkylated with allyl bromide to give *IIIa*—*IIIe* (Scheme 1). If an equimolar amount of sodium methoxide was used, the reaction mix-



Scheme 1

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ture contained unreacted isothiocyanate even after a longer time and the isolation of pure products was difficult. The crystallization from a mixture ether—hexane afforded crystalline products *IIIa*, *IIIc*, and *IIIe*, whereas *IIIb* and *IIId* were obtained as oils.

Electronic absorption spectra of 9-acridinyliminothiocarbonates *IIIa*—*IIIe* measured in acetonitrile exhibited a broad absorption band with the high resolution in the λ-region 320—450 nm, the intensity of which was markedly influenced by the effect of substituents on the acridine skeleton (Fig. 1, Table 1). Relative values of fluorescence intensities (F/F_0) of compounds *IIIa*—*IIIe* given for the maxima of emission bands are expressed in Table 1. They show that the highest fluorescence, more than threefold higher than that of 9-isothiocyanatoacridine, was observed with 2-methoxy derivative *IIIb*. On the contrary, all other substituents decreased the fluorescence intensity. Fig. 2 presents a fluorescence emission spectrum of *O*-methyl-*S*-allyl-*N*-(2-methoxy-9-acridinyl)iminothiocarbonate (*IIIb*) normalized to that of 9-isothiocyanatoacridine.

Results of NMR spectral measurements which correspond with the structure of synthesized compounds *IIIa*—*IIIe* are given in Tables 2 and 3. Analysis of

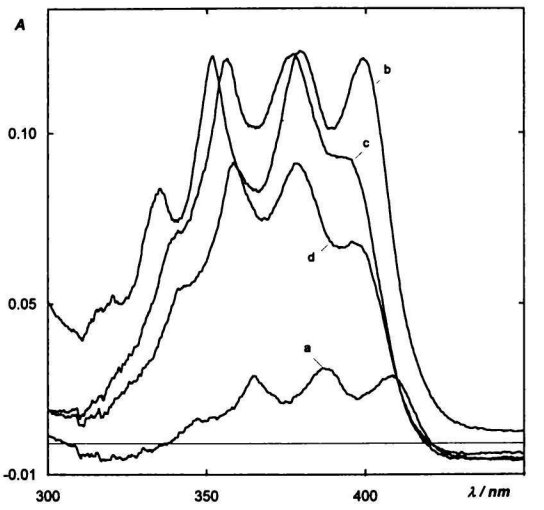

Fig. 1. Electronic absorption spectra of 9-isothiocyanatoacridine *Ia* and 9-acridinyliminothiocarbonates *IIIb*, *IIIc*, and *IIId* measured in acetonitrile.

the multiplet shapes in ^{1}H NMR spectra enabled the assignment of the chemical shifts of all acridine protons. ^{13}C NMR spectra of *IIIa*—*IIIc* and *IIIe* have been interpreted by means of comparison with those

Table 1. Characterization of *O*-Methyl-*S*-allyl-*N*-(2- and 4-Substituted 9-Acridinyl)iminothiocarbonates *IIIa*—*IIIe*

Compound	Formula M_r	w_i(calc.)/% w_i(found)/%			M.p./°C Yield/%	$\tilde{\nu}(\nu(N{=}C))$ / cm^{-1}	λ_{max}/nm log (ε/(m^2 mol^{-1}))			F/F_0^a
		C	H	N						
IIIa	$C_{18}H_{16}N_2OS$	70.10	5.23	9.08	87—90	1635	365	381	397	1.79
H[b]	308.41	70.02	5.29	8.96	75		2.92	2.95	2.78	
IIIb	$C_{19}H_{18}N_2O_2S$	67.43	5.36	8.28		1634	348	382	407	3.18
2-OCH_3	338.43	67.18	5.52	8.31	66		2.89	2.90	2.89	
IIIc	$C_{19}H_{18}N_2OS$	70.78	5.63	8.69	67—70	1628	347	378	398	0.22
2-CH_3	322.43	70.55	5.52	8.47	90		2.90	2.90	2.77	
IIId	$C_{18}H_{15}N_2ClOS$	63.06	4.41	8.17		1620	356	379	397	0.49
2-Cl	342.85	62.80	4.60	8.10	66		2.76	2.76	2.62	
IIIe	$C_{19}H_{18}N_2OS$	70.78	5.63	8.69	68—70	1624	360	372	395	0.35
4-CH_3	322.43	70.66	5.75	8.52	57		2.88	2.95	2.80	

a) Relative fluorescence.
b) Mass spectrum, m/z (I_r/%): 308 (86) [$M^{+\cdot}$], 98 (100) [$CH_2{=}CHCHNCS^{+\cdot}$], 41 (36) [$CH_2{=}CHCH_2^{+\cdot}$].

Table 2. ^{1}H NMR Chemical Shifts of *IIIa*—*IIIe*

Compound	δ_i												
	CH_2	CH	CH_2	OCH_3	R	H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-8
IIIa	3.52	5.78	4.92—5.33	4.28		7.95	7.45	7.76	8.25	8.25	7.76	7.45	7.95
IIIb	3.51	5.79	4.92—5.33	4.28	3.94	7.04		7.44	8.09	8.14	7.68	7.44	7.89
IIIc	3.52	5.79	4.95—5.33	4.28	2.55	7.64		7.57	8.08	8.15	7.70	7.41	7.91
IIId	3.54	5.80	4.97—5.35	4.28		7.90		7.65	8.12	8.15	7.74	7.46	7.91
IIIe	3.32	5.63	4.75—5.17	4.06	2.94	7.78	7.25	7.50		8.26	7.64	7.46	7.90

Table 3. ^{13}C NMR Chemical Shifts of *IIIa*—*IIIc* and *IIIe*

Compound	δ_i								
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
IIIa	124.0	124.6	130.1	129.7	129.7	130.1	124.6	124.0	149.5
IIIb	99.6	156.6	124.8	131.3	129.6	129.0	124.8	123.6	147.3
IIIc	122.0	134.3	133.0[a]	129.4[b]	129.6[b]	129.6[b]	124.5	123.9	148.5
IIIe	121.9	124.3[d]	129.5[e]	137.2	130.2	129.5[e]	124.5[d]	123.8	149.2[f]

Compound	δ_i									
	C-8a	C-9a	C-4a	C-10a	C=N	CH_2	CH	CH_2	OCH_3	R
IIIa	118.3	118.3	149.7	149.7	159.7	33.8	133.0	118.2	56.8	
IIIb	118.5	118.8	146.6	148.0	159.8	33.7	133.2	118.1	56.8	55.4
IIIc	118.4[c]	118.2[c]	148.5	149.1	159.6	33.8	133.1[a]	118.1	56.8	22.0
IIIe	118.0	118.0	149.1[f]	148.8	159.5	33.7	133.0	118.0	56.7	18.6

a—*f*) The assignments may be reversed.

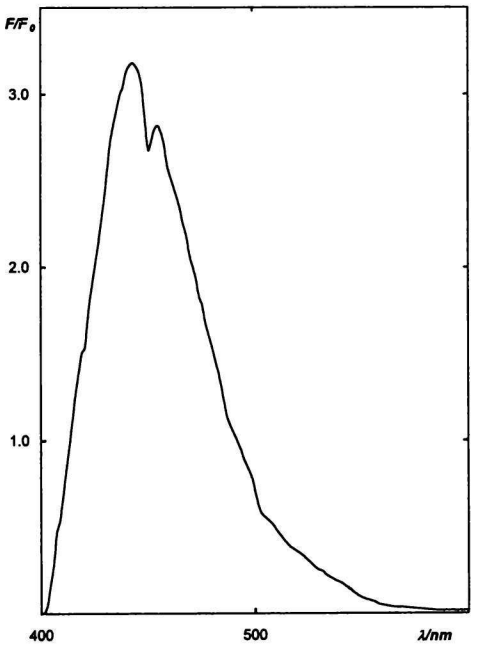

Fig. 2. Fluorescence emission spectrum of *O*-methyl-*S*-allyl-*N*-(2-methoxy-9-acridinyl)iminothiocarbonate *IIIb* in acetonitrile.

of 9-isothiocyanatoacridines *Ia*—*Ie* [8]. They showed similar effects of 2- and 4-substituents bound to the acridine skeleton on the chemical shifts of the acridine carbons in both series *I* and *III*. Considerably different ^{13}C chemical shifts were observed for carbon C-9 of iminothiocarbonates *IIIa*—*IIIc* and *IIIe* (δ = 147.3—149.5) when compared with those of isothiocyanates *Ia*—*Ie* (δ = 130.1—132.4) [8]. This fact proves that the iminothiocarbonic methoxy group does not take part in a mesomeric interaction with conjugated system of the acridine moiety but acts as an electron acceptor.

EXPERIMENTAL

Infrared spectra were measured with a Specord 75 IR spectrometer (Zeiss, Jena) in chloroform. Electron spectra were obtained on a spectrophotometer UV-3000 Shimadzu and fluorescence spectra on a spectrofluorimeter Shimadzu RF-5000 in acetonitrile, the concentration was 1.6×10^{-5} mol dm^{-3} Fluorescence emission spectra were recorded at the excitation wavelength $\lambda_{ex} \approx 395$ nm. ^1H NMR spectra of compounds *IIIa*—*IIIe* and ^{13}C NMR spectra of compounds *IIIa*—*IIIc* and *IIIe* were determined at the laboratory temperature in deuteriochloroform on an NMR spectrometer Tesla BS 587 (80 MHz) and Tesla BS 567 (25 MHz), respectively. Chemical shifts are given as δ values with reference to tetramethylsilane. An elemental analyzer Perkin—Elmer CHN 2400 was used for CHN analysis. Mass spectrum of *IIIa* was taken on a mass spectrometer SSQ 710 Finnigan equipped with direct inlet, E_e = 70 eV, θ = 150°C, I_e = 200 μA.

9-Isothiocyanatoacridines *Ia*—*Ic* and *Ie* were prepared by refluxing corresponding 9-chloroacridines and AgSCN in toluene [6]. 2-Chloro-9-isothiocyanatoacridine was obtained by reaction of 2,9-dichloroacridine with KSCN at room temperature in a mixture of dichloromethane and water containing tetrabutylammonium iodide [9].

General Procedure for Preparation of *O*-Methyl-*S*-allyl-*N*-(2- or 4-Substituted 9-Acridinyl)iminothiocarbonates *IIIa*—*IIIe*

Sodium *O*-methyl-*N*-(2- or 4-substituted 9-acridinyl)iminothiocarbonates *IIa*—*IIe* [10] (1 mmol) were suspended in dry acetonitrile (20 cm^3) and allyl bromide (1 mmol) dissolved in dry acetonitrile (10 cm^3) was added at room temperature with stirring. After 2.5 h of stirring NaBr formed was filtered off and the solvent was evaporated under diminished pres-

sure. Crude products were recrystallized from ether—hexane. Compounds *IIIb*, *IIId* were isolated as oils.

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