SYNTHESIS, SPECTRAL CHARACTERIZATION AND FLUORESCENCE PROPERTIES OF O-METHYL-S-ALKYL-N-(9-ACRIDINYL)IMINOTHIOCARBONATES

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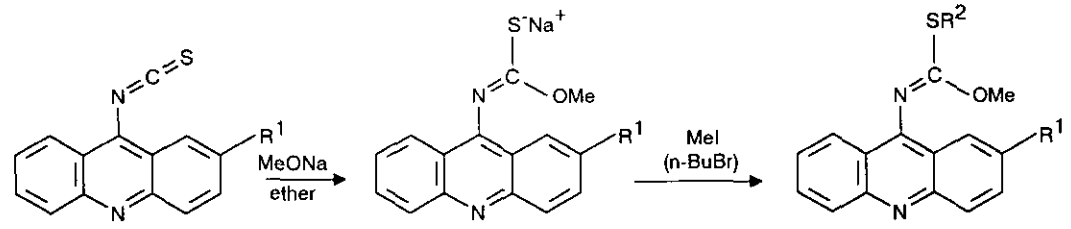
(Dedicated to Professor Rolf Huisgen on the occasion of his 75th birthday)

Abstract-A simple method for preparation of O-methyl-S-alkyl-N-(9-acridinyl)iminothiocarbonates *via* addition of sodium methoxide to 9-isothiocyanatoacridines **(1a-1d)** and subsequent alkylation of formed sodium salts **(2a-2d)** with methyl iodide and butyl bromide has been elaborated.

Intercalating [1] and fluorescent[2] properties of several acridine derivatives are utilized in important chemotherapeutics[3] and sensitive markers of biomolecules In our previous papers[4-6] we dealt with the synthesis and utilization of isothiocyanatoacridines as fluorescent agents



	R^1
1a	H
1b	Me
1c	OMe
1d	Cl

	R^1
2a	H
2b	Me
2c	OMe
2d	Cl

	R^1 (R^2=Me)		R^1 (R^2=n-Bu)
3a	H	**3e**	H
3b	Me	**3f**	Me
3c	OMe	**3g**	OMe
3d	Cl	**3h**	Cl

Scheme 1

In this work we studied the preparation of 9-acridinyl derivatives containing an activated N=C bond in order to obtain reactive intermediates with intensive fluorescence. As starting compounds we utilized the 9-isothiocyanatoacridine (**1a**) and its 2-substituted derivatives (**1b-1d**) [4] Their treatment with sodium methoxide in dry ether afforded corresponding sodium O-methyl-N-(9-acridinyl)-iminothiocarbonates (**2a-2d**) which readily reacted with alkyl halides under the formation of O-methyl-S-alkyl-N-(9-acridinyl)-iminothiocarbonates (**3a-3h**) as final products in very good yields (Scheme 1, Table 1)

Table 1 O-Methyl-S-alkyl-N-(9-acridinyl)iminothiocarbonates(**3a-3h**)

Compd	Formula	mp (^{o}C)	Analysis (%)		λ_{max}(nm)		F/F_0[a]
		Yield (%)	Calcd (Found)		log ε		
3a	$C_{16}H_{14}N_2OS$	150-151	C.68.06(68 09)	254	355	377	0.11
		82	H: 5.00(5.05)	4.88	3.79	3 82	
			N· 9.92(9 87)				
3b	$C_{17}H_{16}N_2OS$	138-140	C 68 89(68.92)	258	352	381	0 43
		69	H: 5.44(5 47)	4 66	4.00	3 62	
			N. 9.45(9 38)				
3c	$C_{17}H_{16}N_2O_2S$	129-131	C 65 36(65 43)	257	352	380	0 38
		85	H 5 16(5 14)	4.59	3 52	3.55	
			N: 8.97(8.86)				
3d	$C_{16}H_{13}N_2OClS$	128-130	C.60.66(60.75)	257	359	379	0.47
		85	H 4 14(4 27)	5.01	3 73	3.73	
			N 8 84(8 79)				
3e	$C_{19}H_{20}N_2OS$	113-114	C 70 34(70.48)	255	355	378	0.48
		65	H 6.21(6.35)	4 97	3 86	3 90	
			N 8 63(8 54)				
3f	$C_{20}H_{22}N_2OS$	104-107	C 70 97(70.96)	256	356	377	0.35
		78	H· 6 55(6 68)	5.00	3 92	3.93	
			N 8 28(8 23)				
3g	$C_{20}H_{22}N_2O_2S$	48-52	C.67 77(67 79)	258	352	380	1 06
		88	H. 6.26(6 29)	4 96	3 79	3.81	
			N 7 90(7 84)				
3h	$C_{19}H_{19}N_2OClS$	59-61	C·63 59(63 62)	258	362	381	0.54
		72	H 5 34(5 37)	4 63	3.53	3 54	
			N· 7 81(7 76)				

[a] Relative fluorescence F/F_0, where F_0=1 for 1.6 . 10^{-5} mol l^{-1} solution of 9-isothiocyanatoacridine. Excitation wavelength λ_{ex}~395 nm

Pure products are crystalline compounds exhibiting intensive green fluorescence in the uv light. Physicochemical and spectral characteristics of compounds (**3a-3h**) are listed in Table 2 Fluorescent spectra were measured in acetonitrile with 50% quenching effect, compared to Hepes-acetonitrile (7.3) buffer used in our previous paper.[4] From the values of relative fluorescent intensities F/F_0 (Table 2) it follows that the highest fluorescence, comparable with 9-isothiocyanatoacridine was exhibited by derivative (**3g**).

Table 2 Spectral characteristics of O-methyl-S-alkyl-N-(9-acridinyl)iminothiocarbonates(**3a-3h**)

	ir	^{1}H nmr (δ , $CDCl_3$)			^{13}C nmr (δ , $CDCl_3$)			
Compd	ν_{as} (N=C)		SMe	2-Me[a]		SMe		
		OMe	SBu-n	2-OMe	OMe	SBu-n		N=C
3a	1634	4 30s	2.33s	-	56 92	13.59		160 47
3b	1639	4.29s	2.31s	2.56s	56.89	13 59		160 32
3c	1640	4 28s	2.31s	3 94s	56.92	13.62		160.58
3d	1618	4.27s	2.35s	-	57.07	13 62		161.07
3e	1623	4.26s	0.84t 2.87t	-	56.74	13.40	21.62	160 51
			J=6.9 Hz J=6.9 Hz			30.68	31 95	
			1 09-1.60m					
3f	1625	4 29s	0.86t 2.89t	2 57s	56.70	13 44	21.61	160 40
			J=6 8 Hz J=7.0 Hz			30.68	32 03	
			1 09-1.60m					
3g	1632	4 28s	0 84t 2 88t	3 94s	56.66	13.40	21.58	160 52
			J=6 7 Hz J=6.9 Hz			30 61	32.10	
			1 15-1 67m					
3h	1620	4.20s	0 79t 2 83t	-	56.89	13 40	21 61	161 25
			J=6 8 Hz J=7 0 Hz			30 76	31 92	
			1.01-1.56m					

[a] Other signals 7.05-8 50m (acridine H).

EXPERIMENTAL

Melting points were determined on a Kofler hot apparatus and are uncorrected. ^{1}H and ^{13}C nmr spectra (δ , ppm) were measured on Tesla BS 487 (80 MHz) and Tesla BS 567 (25.156 MHz) instruments at 298 K Chemical shifts are expressed in ppm relative to TMS as internal standard Infrared spectra were taken on a Specord M-85 (Zeiss, Jena) using KBr technique (0.8 mg / 300 mg KBr, ν in cm^{-1}). The uv spectra were run on a uv-3000 Shimadzu spectrophotometer (concentration 1 6 . 10^{-5} mol l^{-1}) and fluorescence spectra on a RF 5000 Shimadzu spectrofluorimeter (concentration 1 6 . 10^{-5} mol l^{-1}) in acetonitrile. Fluorescence emission spectra

were measured at excitation wavelength λ_{ex} 395 nm. Microanalyses were measured on a Perkin-Elmer analyzer and were in satisfactory agreement with the calculated values. The starting compounds (**1a-1d**) were prepared according to ref.[4]

*Preparation of O-methyl-S-alkyl-N-(9-acridinyl)iminothiocarbonates (**3a-3h**) General procedure*

A solution of 9-isothiocyanatoacridine (0.01 mol) in ether (25 ml) was added to an intensively stirred suspension of sodium methoxide (0.54 g, 0.01 mol) in dry ether (30 ml) at room temperature and the mixture was stirred for 30 min. Separated sodium O-methyl-N-(9-acridinyl)iminothiocarbonate (**2a-2d**) (0.01 mol) was suspended in dry acetonitrile (25 ml) and 0 01 mol of methyl iodide or butyl bromide was added with stirring at room temperature. The mixture was stirred for 45 min, separated NaI or NaBr was filtered off and washed with a small amount of acetonitrile and the solvent evaporated in vacuo The residue was crystallized from ether-hexane mixture. Purity of the obtained compounds (**3a-3h**) was confirmed by thin-layer chromatography on silica plates, eluent benzene-hexane (5.1), uv detection at 366 nm

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