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# Improved method for the preparation of nonyl acridine orange analogues and utilization in detection of cardiolipin

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### S3





	RT	Area	%Area	Height	EP Plate Count	Width@50%	Resolution	Selectivity
1	1.490	65125	0.16	10416	1176	0.10		
2	2.067	25345	0.06	3153	1775	0.12	3.13	-57.80
3	2.730	8301	0.02	1226	3467	0.11	3.48	2.17
4	3.032	44289	0.11	4233	2396	0.15	1.40	1.25
5	3.558	220028	0.55	33704	5581	0.11	241	1.34
6	3.741	381701	0.95	56658	6303	0.11	0.97	1.09
7	4.034	39544492	98.03	2110970	1002	0.30	0.84	1.13
8	5.061	48257	0.12	3085				1.41
Sum		40337538.0						

S5







<sup>1</sup>H NMR spectra of 10-nonyl-3,6-bis(dimethylamino)acridin-10-ium iodide (3)



S8











<sup>1</sup>H NMR spectra of 10-dodecyl-3,6-bis(dimethylamino)acridin-10-ium iodide (4)







1	6.057	94523	0.40	10831	12749	0.1263		
2	10.392	55180	0.23	1748	1970	0.5510	7.552	1.951
3	10.952	10708	0.05	1024	22490	0.1719	0.915	1.063
4	11.332	20791	0.09	1999				1.040
5	11.536	15685	0.07	1734				1.021
6	12.024	122957	0.52	12651	36525	0.1481		1.049
7	12.478	44432	0.19	4730	39783	0.1472	1.814	1.043
8	12.790	22786691	96.98	2446136	46498	0.1396	1.287	1.028
9	13.692	92874	0.40	5768	16580	0.2503	2.728	1.080
10	16.112	253357	1.08	5698	2690	0.7311	2.910	1.199
Sum		23497196.8						





<sup>1</sup>H NMR spectra of 10-(3-(trimethylsilyl)propyl)-3,6-bis(dimethylamino)acridin-10-ium iodide (5)







- - -0 -20 f1 (ppm) 180 160 140 120 100 80 60 40 20 -40 -60 -80 -100 -120 -140 -160 -180 -200











S23



<sup>1</sup>H NMR spectra of 10-(3-(silatranyl)propyl)-3,6-bis(dimethylamino)acridin-10-ium iodide (6)













Apollo C18-11(4.6 x 150mm)



## Stereo view of 5



Table 1. Crystal data and structure refinement for 5.

Empirical formula	C <sub>23</sub> H <sub>34</sub> IN <sub>3</sub> Si
Formula weight	507.52
Temperature	150.0(2) K
Wavelength	0.71073 A
Crystal system, space g	roup Monoclinic, I 2/a
Unit cell dimensions	a = 19.4926(7) A alpha = 90 deg.
	b = 9.8565(4) A beta = 102.680(4) deg.
	c = 25.4939(11) A gamma = 90 deg.
Volume	4778.7(3) A^3
Z, Calculated density	8, 1.411 Mg/m^3
Absorption coefficient	1.404 mm^-1
F(000) 2	2080
Crystal size	0.17 x 0.09 x 0.06 mm
Two-theta max. for dat	a 60.0 deg.
Limiting indices	-28<=h<=29, -14<=k<=12, -35<=l<=35
Reflections collected /	unique 27563 / 7979 [R(int) = 0.0544]
Completeness to theta	= 30.0 99 %
Absorption correction	Multi-scan
Max. and min. transmis	ssion 0.9241 and 0.7378
Refinement method	Full-matrix least-squares on F^2
Data / restraints / para	meters 7979 / 0 / 260
Goodness-of-fit on F^2	1.117
Final R indices [I>2sigm	a(I)] R1 = 0.0345, wR2 = 0.0886
R indices (all data)	R1 = 0.0563, wR2 = 0.1050
Largest diff. peak and h	nole 1.417 and -1.232 e.A^-3

	x y	Z	U(eq)	
 I(1)	4255(1)	6018(1)	1157(1)	45(1)
Si(24)	6061(1)	6085(1)	4528(1)	34(1)
N(10)	7234(1)	4326(2)	-920(1) 2944(1)	25(1)
N(10)	257(1)	1128(2)	/2344(1)	22(1)
N(19)	6090(1)	7996(2)	1835(1)	37(1)
C(11)	7193(1)	5220(2)	2517(1)	26(1)
C(12)	7717(1)	5134(2)	2206(1)	28(1)
C(12)	7811(1)	3497(2)	3123(1)	25(1)
C(5)	6652(1)	6165(2)	2387(1)	29(1)
C(13)	8347(1)	3460(2)	2820(1)	27(1)
C(9)	8277(1)	4251(2)	2360(1)	30(1)
C(3)	8462(1)	1860(2)	3763(1)	27(1)
C(1)	8926(1)	2574(2)	3002(1)	31(1)
C(4)	7876(1)	2712(2)	3585(1)	27(1)
C(6)	6595(1)	7027(2)	1940(1)	31(1)
C(22)	6673(1)	5219(2)	3670(1)	29(1)
C(7)	7094(1)	6867(2)	1608(1)	34(1)
C(8)	7633(1)	5974(2)	1741(1)	33(1)
C(21)	6627(1)	4237(2)	3200(1)	27(1)
C(17)	7980(1)	1150(2)	4526(1)	36(1)
C(2)	8991(1)	1794(2)	3450(1)	31(1)
C(23)	5976(1)	5319(2)	3847(1)	32(1)
C(20)	5597(1)	8156(3)	2180(1)	41(1)
C(16)	9108(1)	194(2)	4414(1)	40(1)
C(19)	5953(2)	8766(2)	1336(1)	45(1)
C(25)	6479(1)	4778(3)	5026(1)	52(1)
C(26)	5175(1)	6546(4)	4629(1)	56(1)
C(27)	6629(2)	7617(3)	4587(1)	63(1)

Table 2. Atomic coordinates (  $x 10^{4}$ ) and equivalent isotropic displacement parameters (A<sup>2</sup>  $x 10^{3}$ ) for **5**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Table 3. Bond lengths [A] and angles [deg] for 5.

Si(24)-C(27)	1.858(3)	N(10)-C(14)-C(13)	118.22(17)
Si(24)-C(26)	1.858(2)	C(4)-C(14)-C(13)	120.11(18)
Si(24)-C(25)	1.865(3)	C(11)-C(5)-C(6)	121.30(18)
Si(24)-C(23)	1.869(2)	C(11)-C(5)-H(5)	119.4

N(10)-C(14)	1.385(3)	C(6)-C(5)-H(5)	119.4
N(10)-C(11)	1.388(2)	C(9)-C(13)-C(1)	122.98(17)
N(10)-C(21)	1.475(2)	C(9)-C(13)-C(14)	119.64(19)
N(15)-C(3)	1.350(3)	C(1)-C(13)-C(14)	117.37(18)
N(15)-C(17)	1.453(3)	C(12)-C(9)-C(13)	121.12(17)
N(15)-C(16)	1.462(3)	C(12)-C(9)-H(9)	119.4
N(18)-C(6)	1.354(3)	C(13)-C(9)-H(9)	119.4
N(18)-C(20)	1.448(3)	N(15)-C(3)-C(4)	120.71(17)
N(18)-C(19)	1.454(3)	N(15)-C(3)-C(2)	120.76(18)
C(11)-C(5)	1.392(3)	C(4)-C(3)-C(2)	118.53(18)
C(11)-C(12)	1.427(3)	C(2)-C(1)-C(13)	122.96(17)
C(12)-C(9)	1.385(3)	C(2)-C(1)-H(1)	118.5
C(12)-C(8)	1.425(3)	C(13)-C(1)-H(1)	118.5
C(14)-C(4)	1.390(3)	C(14)-C(4)-C(3)	121.43(17)
C(14)-C(13)	1.431(2)	C(14)-C(4)-H(4)	119.3
C(5)-C(6)	1.406(3)	C(3)-C(4)-H(4)	119.3
C(5)-H(5)	0.9300	N(18)-C(6)-C(5)	120.76(19)
C(13)-C(9)	1.389(3)	N(18)-C(6)-C(7)	121.28(19)
C(13)-C(1)	1.421(3)	C(5)-C(6)-C(7)	117.95(19)
C(9)-H(9)	0.9300	C(21)-C(22)-C(23)	111.65(16)
C(3)-C(4)	1.409(3)	C(21)-C(22)-H(22A)	109.3
C(3)-C(2)	1.437(3)	C(23)-C(22)-H(22A)	109.3
C(1)-C(2)	1.360(3)	C(21)-C(22)-H(22B)	109.3
C(1)-H(1)	0.9300	C(23)-C(22)-H(22B)	109.3
C(4)-H(4)	0.9300	H(22A)-C(22)-H(22B)	108.0
C(6)-C(7)	1.432(3)	C(8)-C(7)-C(6)	120.94(19)
C(22)-C(21)	1.526(3)	C(8)-C(7)-H(7)	119.5
C(22)-C(23)	1.526(3)	C(6)-C(7)-H(7)	119.5
C(22)-H(22A)	0.9700	C(7)-C(8)-C(12)	121.77(19)
C(22)-H(22B)	0.9700	C(7)-C(8)-H(8)	119.1
C(7)-C(8)	1.355(3)	C(12)-C(8)-H(8)	119.1
C(7)-H(7)	0.9300	N(10)-C(21)-C(22)	113.22(15)
C(8)-H(8)	0.9300	N(10)-C(21)-H(21A)	108.9
C(21)-H(21A)	0.9700	C(22)-C(21)-H(21A)	108.9
C(21)-H(21B)	0.9700	N(10)-C(21)-H(21B)	108.9
C(17)-H(17A)	0.9600	C(22)-C(21)-H(21B)	108.9
C(17)-H(17B)	0.9600	H(21A)-C(21)-H(21B)	107.7
C(17)-H(17C)	0.9600	N(15)-C(17)-H(17A)	109.5
C(2)-H(2)	0.9300	N(15)-C(17)-H(17B)	109.5
C(23)-H(23A)	0.9700	H(17A)-C(17)-H(17B)	109.5
C(23)-H(23B)	0.9700	N(15)-C(17)-H(17C)	109.5
C(20)-H(20A)	0.9600	H(17A)-C(17)-H(17C)	109.5
C(20)-H(20B)	0.9600	H(17B)-C(17)-H(17C)	109.5
C(27)-H(27C)	0.9600	C(1)-C(2)-C(3)	119.58(18)
		C(1)-C(2)-H(2)	120.2
		C(3)-C(2)-H(2)	120.2
		C(22)-C(23)-Si(24)	113.43(14)

C(27)-Si(24)-C(	26) 110.18(1	L6)	C(22)-C(23)-H(23A)	108.9
C(27)-Si(24)-C(	25) 110.10(1	L5)	Si(24)-C(23)-H(23A)	108.9
C(26)-Si(24)-C(	25) 110.78(1	L2)	C(22)-C(23)-H(23B)	108.9
C(27)-Si(24)-C(	23) 109.48(1	L3)	Si(24)-C(23)-H(23B)	108.9
C(26)-Si(24)-C(	23) 109.34(1	L2)	H(23A)-C(23)-H(23B)	107.7
C(25)-Si(24)-C(	23) 106.90(1	12)	N(18)-C(20)-H(20A)	109.5
C(14)-N(10)-C(	11) 122.46(	15)	N(18)-C(20)-H(20B)	109.5
C(14)-N(10)-C(2	21) 119.43(	16)	H(20A)-C(20)-H(20B)	109.5
C(11)-N(10)-C(2	21) 118.08(	16)	N(18)-C(20)-H(20C)	109.5
C(3)-N(15)-C(1	7) 121.09(1	.7)	H(20A)-C(20)-H(20C)	109.5
C(3)-N(15)-C(1	6) 123.23(1	.8)	H(20B)-C(20)-H(20C)	109.5
C(17)-N(15)-C(	16) 115.53(	18)	N(15)-C(16)-H(16A)	109.5
C(6)-N(18)-C(2	0) 120.41(1	.9)	N(15)-C(16)-H(16B)	109.5
C(6)-N(18)-C(19	9) 121.8(2)	C(20)-	H(16A)-C(16)-H(16B)	109.5
N(18)-C(19)	117.1(2)	N(10)-	N(15)-C(16)-H(16C)	109.5
C(11)-C(5)	121.50(17)	N(10)-	H(16A)-C(16)-H(16C)	109.5
C(11)-C(12)	118.22(18)	C(5)-	H(16B)-C(16)-H(16C)	109.5
C(11)-C(12)	120.27(18)	C(9)-	N(18)-C(19)-H(19A)	109.5
C(12)-C(8)	122.70(18)	C(9)-	N(18)-C(19)-H(19B)	109.5
C(12)-C(11)	119.75(18)	C(8)-	H(19A)-C(19)-H(19B)	109.5
C(12)-C(11)	117.55(19)	N(10)-	N(18)-C(19)-H(19C)	109.5
C(14)-C(4)	121.67(16)		H(19A)-C(19)-H(19C)	109.5
			H(19B)-C(19)-H(19C)	109.5
			Si(24)-C(27)-H(27B)	109.5
			H(27A)-C(27)-H(27B)	109.5
			Si(24)-C(27)-H(27C)	109.5

Table 4. Anisotropic displacement parameters ( $A^2 \times 10^3$ ) for **5**. The anisotropic displacement factor exponent takes the form:

H(27A)-C(27)-H(27C)

H(27B)-C(27)-H(27C)

109.5

109.5

-2 pi^2 [ h^2 a\*^2 U11 + ... + 2 h k a\* b\* U12 ]

	U11	U22	U33	U23	U13	U12
1(1)	37(1)	56(1)	46(1)	-16(1)	20(1)	-5(1)
Si(24	) 34(1)	41(1)	27(1)	1(1)	10(1)	12(1)
N(10	) 25(1)	30(1)	22(1)	-3(1)	8(1)	-5(1)
N(15	) 30(1)	32(1)	34(1)	1(1)	9(1)	1(1)
N(18	) 37(1)	41(1)	31(1)	4(1)	2(1)	-4(1)
C(11	) 30(1)	29(1)	21(1)	-6(1)	6(1)	-10(1)
C(12	) 32(1)	33(1)	21(1)	-7(1)	8(1)	-11(1)
C(14	) 25(1)	26(1)	24(1)	-8(1)	8(1)	-7(1)

C(5)	29(1)	34(1)	24(1)	-2(1)	5(1)	-7(1)
C(13)	27(1)	31(1)	25(1)	-8(1)	9(1)	-8(1)
C(9)	32(1)	35(1)	26(1)	-10(1)	13(1)	-9(1)
C(3)	27(1)	26(1)	28(1)	-6(1)	8(1)	-5(1)
C(1)	26(1)	40(1)	28(1)	-11(1)	10(1)	-5(1)
C(4)	27(1)	29(1)	27(1)	-5(1)	10(1)	-5(1)
C(6)	33(1)	32(1)	25(1)	-3(1)	1(1)	-10(1)
C(22)	27(1)	35(1)	27(1)	-3(1)	9(1)	-3(1)
C(7)	43(1)	37(1)	23(1)	-1(1)	7(1)	-14(1)
C(8)	41(1)	38(1)	23(1)	-5(1)	11(1)	-14(1)
C(21)	25(1)	32(1)	27(1)	-2(1)	10(1)	-5(1)
C(17)	38(1)	40(1)	35(1)	5(1)	15(1)	2(1)
C(2)	25(1)	37(1)	31(1)	-8(1)	7(1)	-1(1)
C(23)	26(1)	42(1)	30(1)	-3(1)	8(1)	2(1)
C(20)	37(1)	45(1)	40(1)	1(1)	6(1)	1(1)
C(16)	37(1)	37(1)	45(1)	5(1)	9(1)	6(1)
C(19)	51(1)	44(1)	36(1)	9(1)	2(1)	-3(1)
C(25)	39(1)	80(2)	42(1)	22(1)	16(1)	25(1)
C(26)	46(1)	86(2)	37(1)	3(1)	12(1)	35(1)
C(27)	72(2)	49(2)	63(2)	-17(1)	7(2)	-2(1)

Table 5. Hydrogen coordinates ( x 10^4) and isotropic displacement parameters (A^2 x 10^3) for  ${\bf 5}.$ 

	х	y z	U(eq)			
H(5)	6322	6228	2599	35		
H(9)	8613	4186	2152	36		
H(1)	9275	2526	2806	37		
H(4)	7526	2750	3780	33		
H(22A)	6805	6110	3564	35		
H(22B)	7037	4914	3970	35		
H(7)	7048	7383	1297	41		
H(8)	7956	5907	1523	40		
H(21A)	6593	3318	3328	33		
H(21B)	6200	4425	2933	33		
H(17A)	7896	2070	4620	54		
H(17B)	8129	625	4848	54		
H(17C)	7555	772	4314	54		
H(2)	9377	1222	3554	37		
H(23A)	) 5777	4417	3847	39		
H(23B)	5652	5861	3587	39		
H(20A)	5300	7370	2151	62		
H(20B)	5314	8947	2074	62		

H(20C)	5851	8257	2546	62
H(16A)	8993	-686	4258	60
H(16B)	9189	127	4799	60
H(16C)	9525	527	4315	60
H(19A)	6385	9148	1281	67
H(19B)	5626	9482	1356	67
H(19C)	5758	8176	1041	67
H(25A)	6178	3998	4997	79
H(25B)	6549	5146	5383	79
H(25C)	6924	4517	4955	79
H(26A)	4967	7210	4366	83
H(26B)	5216	6914	4983	83
H(26C)	4883	5751	4589	83
H(27A)	7078	7374	4519	94
H(27B)	6691	7985	4943	94
H(27C)	6410	8283	4329	94

Table 6. Torsion angles [deg] for 5.

C(14)-N(10)-C(11)-C(5)	-171.64(17)
C(21)-N(10)-C(11)-C(5)	10.3(3)
C(14)-N(10)-C(11)-C(12)	9.3(3)
C(21)-N(10)-C(11)-C(12)	-168.71(16)
N(10)-C(11)-C(12)-C(9)	-5.1(3)
C(5)-C(11)-C(12)-C(9)	175.79(18)
N(10)-C(11)-C(12)-C(8)	174.56(17)
C(5)-C(11)-C(12)-C(8)	-4.5(3)
C(11)-N(10)-C(14)-C(4)	173.26(17)
C(21)-N(10)-C(14)-C(4)	-8.8(3)
C(11)-N(10)-C(14)-C(13)	-6.9(3)
C(21)-N(10)-C(14)-C(13)	171.12(16)
N(10)-C(11)-C(5)-C(6)	-177.15(17)
C(12)-C(11)-C(5)-C(6)	1.9(3)
N(10)-C(14)-C(13)-C(9)	0.2(3)
C(4)-C(14)-C(13)-C(9)	-179.89(17)
N(10)-C(14)-C(13)-C(1)	-178.28(16)
C(4)-C(14)-C(13)-C(1)	1.6(3)
C(8)-C(12)-C(9)-C(13)	179.11(18)
C(11)-C(12)-C(9)-C(13)	-1.2(3)
C(1)-C(13)-C(9)-C(12)	-177.90(18)
C(14)-C(13)-C(9)-C(12)	3.7(3)
C(17)-N(15)-C(3)-C(4)	2.6(3)
C(16)-N(15)-C(3)-C(4)	177.95(19)
C(17)-N(15)-C(3)-C(2)	-177.74(18)
C(16)-N(15)-C(3)-C(2)	-2.4(3)

C(9)-C(13)-C(1)-C(2)	-179.55(19)
C(14)-C(13)-C(1)-C(2)	-1.1(3)
N(10)-C(14)-C(4)-C(3)	179.41(17)
C(13)-C(14)-C(4)-C(3)	-0.5(3)
N(15)-C(3)-C(4)-C(14)	178.47(17)
C(2)-C(3)-C(4)-C(14)	-1.2(3)
C(20)-N(18)-C(6)-C(5)	-0.3(3)
C(19)-N(18)-C(6)-C(5)	-170.9(2)
C(20)-N(18)-C(6)-C(7)	-178.97(19)
C(19)-N(18)-C(6)-C(7)	10.5(3)
C(11)-C(5)-C(6)-N(18)	-176.21(18)
C(11)-C(5)-C(6)-C(7)	2.5(3)
N(18)-C(6)-C(7)-C(8)	174.4(2)
C(5)-C(6)-C(7)-C(8)	-4.3(3)
C(6)-C(7)-C(8)-C(12)	1.6(3)
C(9)-C(12)-C(8)-C(7)	-177.54(19)
C(11)-C(12)-C(8)-C(7)	2.8(3)
C(14)-N(10)-C(21)-C(22)	91.2(2)
C(11)-N(10)-C(21)-C(22)	-90.7(2)
C(23)-C(22)-C(21)-N(10)	167.83(17)
C(13)-C(1)-C(2)-C(3)	-0.6(3)
N(15)-C(3)-C(2)-C(1)	-177.96(19)
C(4)-C(3)-C(2)-C(1)	1.7(3)
C(21)-C(22)-C(23)-Si(24)	163.28(15)
C(27)-Si(24)-C(23)-C(22)	45.3(2)
C(26)-Si(24)-C(23)-C(22)	166.06(17)
C(25)-Si(24)-C(23)-C(22)	-73.97(18)

# Cardiolipin / DOPC liposomes size

Sample Details						
Sample Name:	CL/DOPC 20 mM HEPES p	H 7.4				
SOP Name:	Disposable cuvette.sop					
General Notes:	Average result created from re	ecord number(s): 13	33 134 135			
File Name:	cardiolinin fluorimetrija dts	Dispersant Nar	me: Water			
Record Number:	155	Dispersant	RI: 1.330			
Material RI:	1.59	Viscosity (cP): 0.8872				
Material Absorption:	0.010 Measuren	Measurement Date and Time: tradiena 2020 cada 25				
material resolution.			ne. according,			
System						
Temperature (°C):	25,0 Duration Used (s): 25					
Count Rate (kcps):	249,1 Measurer	ment Position (m	m): 4,65			
Cell Description:	Disposable sizing cuvette	Attenuator: 6				
Results		Class (cl. and	% Intensity	Ct Daw (d a		
		Size (d.nm	% intensity.	St Dev (d.n		
Z-Average (d.nm):	115,2 Peak 1:	127,7	100,0	40,63		
Pdl:	0,089 Peak 2:	0,000	0,0	0,000		
Intercept:	0,960 Peak 3:	0,000	0,0	0,000		
Result quality	Good					
	Size Distribution	r by mensky				
20						
†		$\wedge$				
£ 15		1	:			
Per						
10 10	:	1: 1	:	:		
1 ag						
		/ = \				
0						
0.1	1 10	100	1000	10000		
	Size	(d.nm)				
	Record 155- CI /DO	PC 20 mM HEDES -	H74			
	Record 155: CL/DO	PO 20 mm HEPES p	AT 7.4			

## Cardiolipin / PI/PE/DOPC liposomes size

# Sample Details Sample Name: CL/PI/DOPE/DOPC 20mM HEPES pH 7.4 SOP Name: Disposable cuvette.sop General Notes: Average result created from record number(s): 139 140 141 File Name: cardiolipin fluorimetrija.dts Dispersant Name: Water Record Number: 154 Dispersant RI: 1,330 Material RI: 1,59 Viscosity (cP): 0,8872 Material Absorbtion: 0,010 Measurement Date and Time: trešdiena, 2020. gada 25. ...

### System

Temperature (°C):	25,1	Duration Used (s):	25
Count Rate (kcps):	243,0	Measurement Position (mm):	4,65
Cell Description:	Disposable sizin	g cuvette Attenuator:	6

### Results

			Size (d.nm	% Intensity:	St Dev (d.n
Z-Average (d.nm):	115,4	Peak 1:	131,9	100,0	48,55
Pdl:	0,117	Peak 2:	0,000	0,0	0,000
Intercept:	0,953	Peak 3:	0,000	0,0	0,000
Result quality	Good				

