

Reduced derivatives of imides of natural chlorins

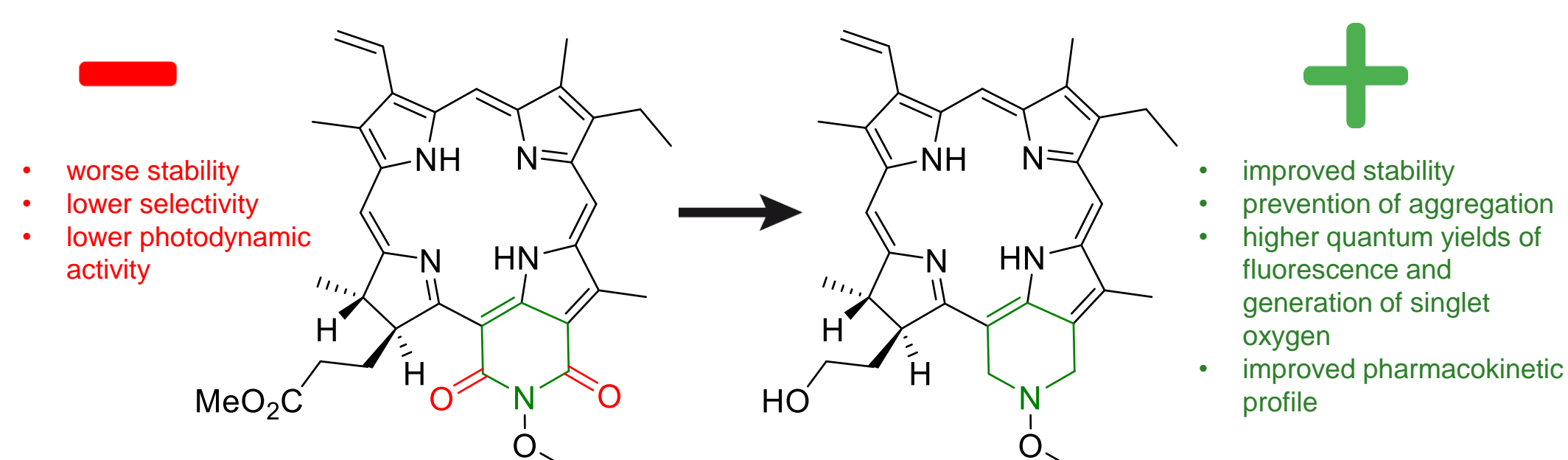
Pogorilyy V.A.* , Kartava J.S., Tandare T.F., Grin M.A.
MIREA – Russian Technological University, Moscow, Russia

*E-mail: pogorilvictor@gmail.com

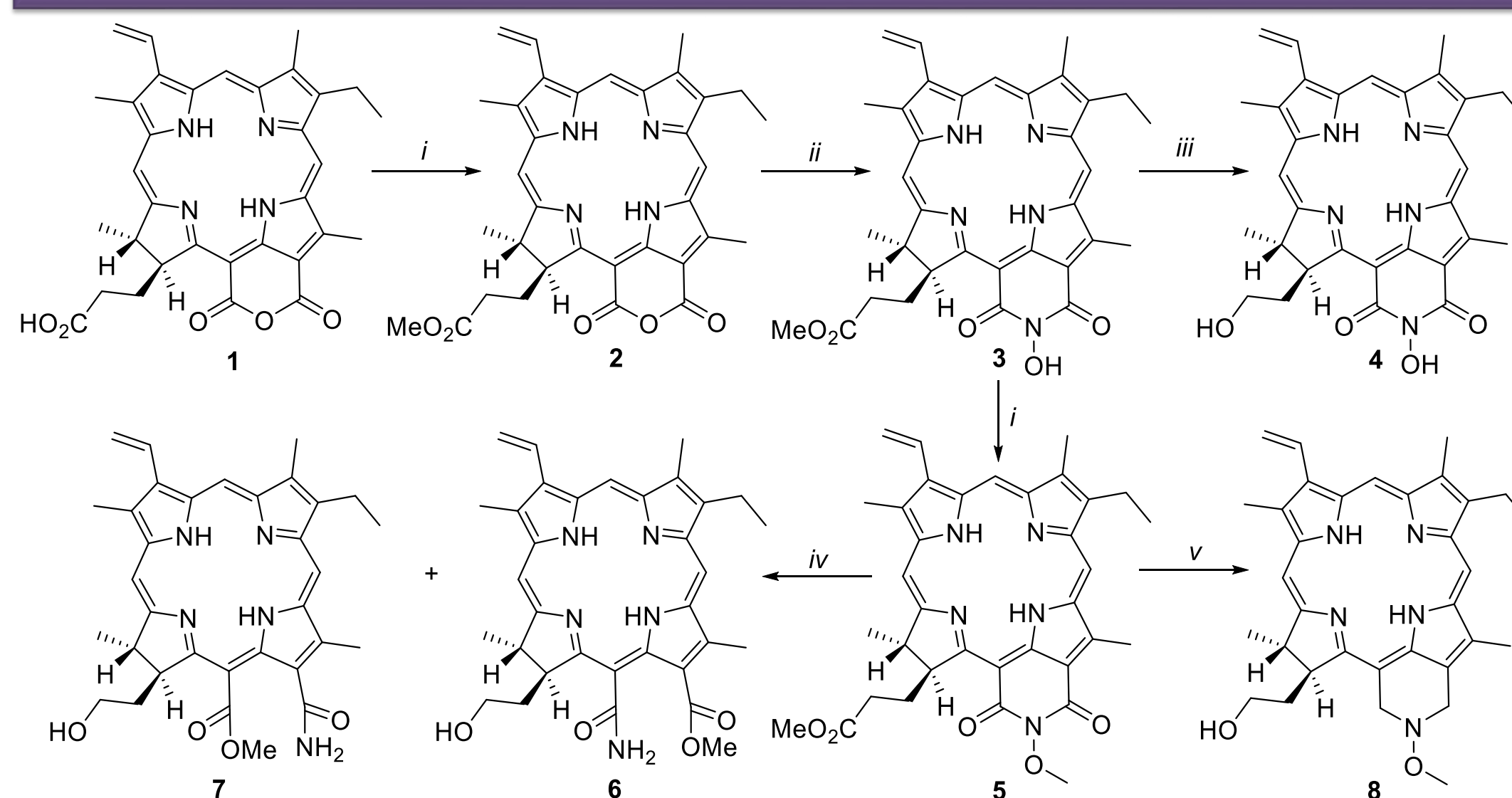
INTRODUCTION & AIM

For photodynamic therapy (PDT), special attention is paid to photosensitizers (PS) based on chlorins and their derivatives, synthetic analogues of natural pigments that combine powerful photoactivity with the possibility of subtle chemical modification. The main advantages of chlorin photosensitizers are their intense absorption in the long-wavelength region of the spectrum (650–750 nm), providing deep penetration of light into biological tissues, high quantum yield of singlet oxygen generation and the ability to selectively accumulate in pathological foci. Reduced derivatives of chlorin imides are of particular interest in this context, as they have greater stability under physiological conditions.

The purpose of this work is to develop strategies for synthesizing reduced forms of natural chlorin derivatives and to study their photophysical and biological properties *in vitro* in relation to both gram-positive (*Staphylococcus aureus*) and gram-negative (*Pseudomonas aeruginosa*) bacterial cell lines.



Synthesis



Conditions and reagents: *i* - CH_2N_2 , $(\text{Et})_2\text{O}$, CH_2Cl_2 , 0°C , 1 h; *ii* - $\text{NH}_3\text{OH}^+\text{HCl}$, Py, 20°C , 12 h; *iii* - NaBH_4 , Py/*i*-Pr, 20°C , 24 h; *iv* - LiAlH_4 , THF, 0°C , 24 h; *v* - LiAlH_4 , AlCl_3 , THF, 0°C , 2 h.

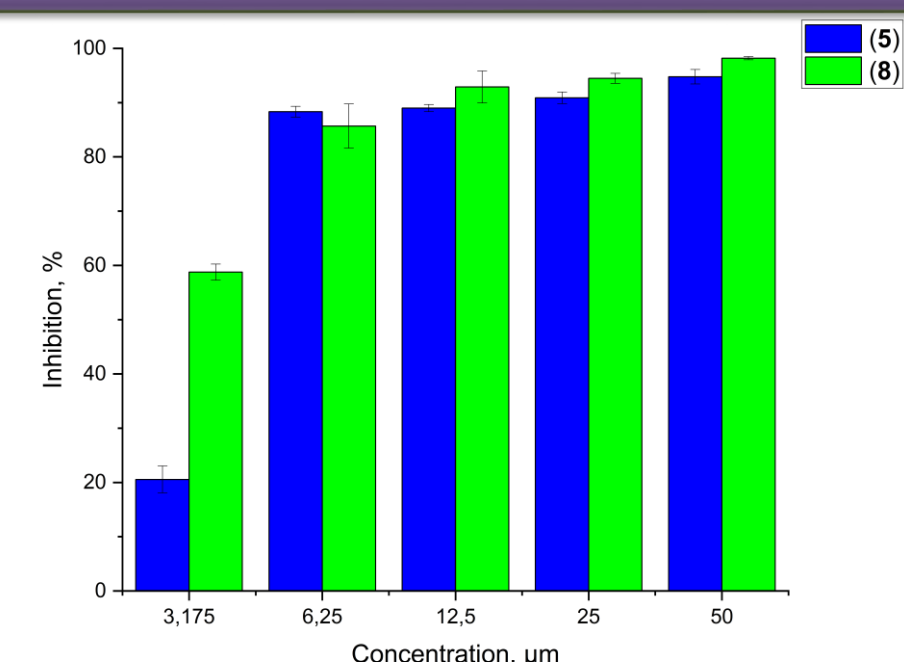
Table 1. Conditions for the reduction of purpurinimides

Compound/Conditions	Reagents	Solvent	Temperature, $^\circ\text{C}$	Time, h	Reaction product
3	NaBH_4	Py/ <i>i</i> -Pr	20	24	4
5	LiAlH_4	THF	0	24	6 and 7
5	LiAlH_4 , AlCl_3	THF	0	2	8

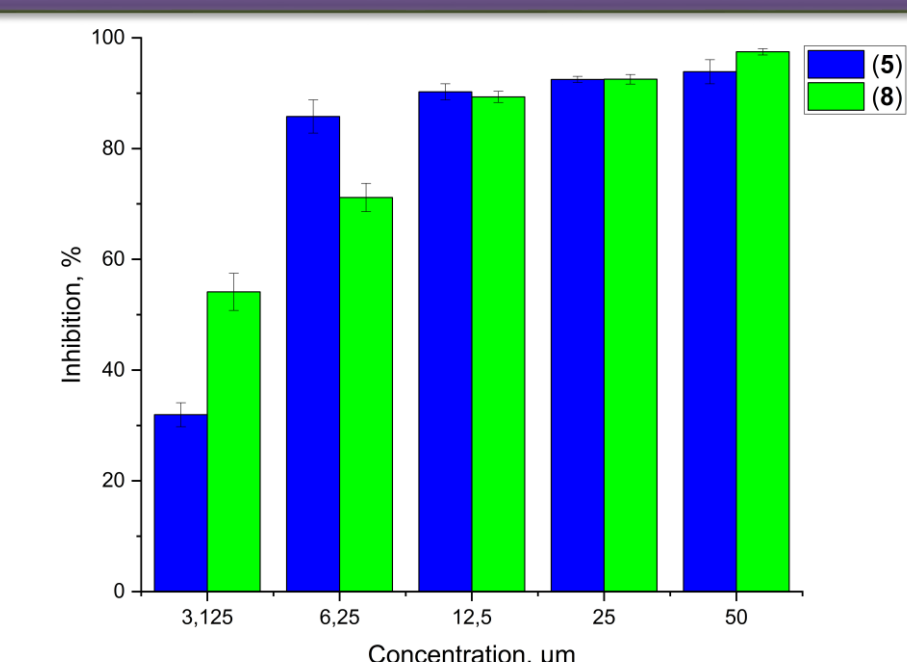
Biological research *in vitro*

Table 2. Results of the study of biological activity of synthesized compounds (5) and (8) *in vitro*

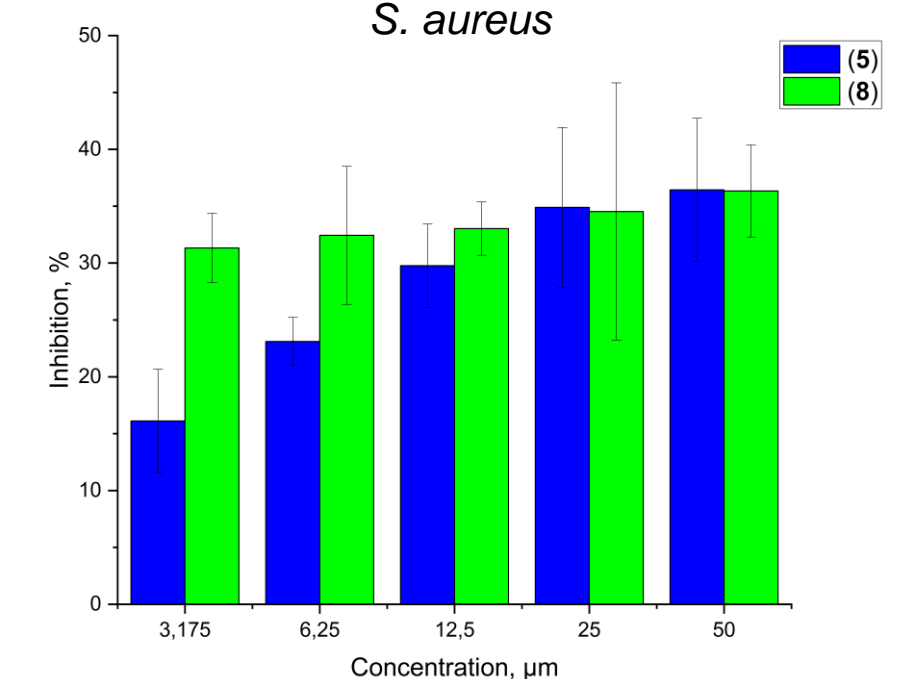
Bacterial line	Compound	Irradiation (yes/no)	MIC, μM
<i>S. aureus</i>	(5)	yes	4,45
		no	596,68
	(8)	yes	7,30
		no	2714
<i>P. aeruginosa</i>	(5)	yes	4,59
		no	756,37
	(8)	yes	20,32
		no	2632



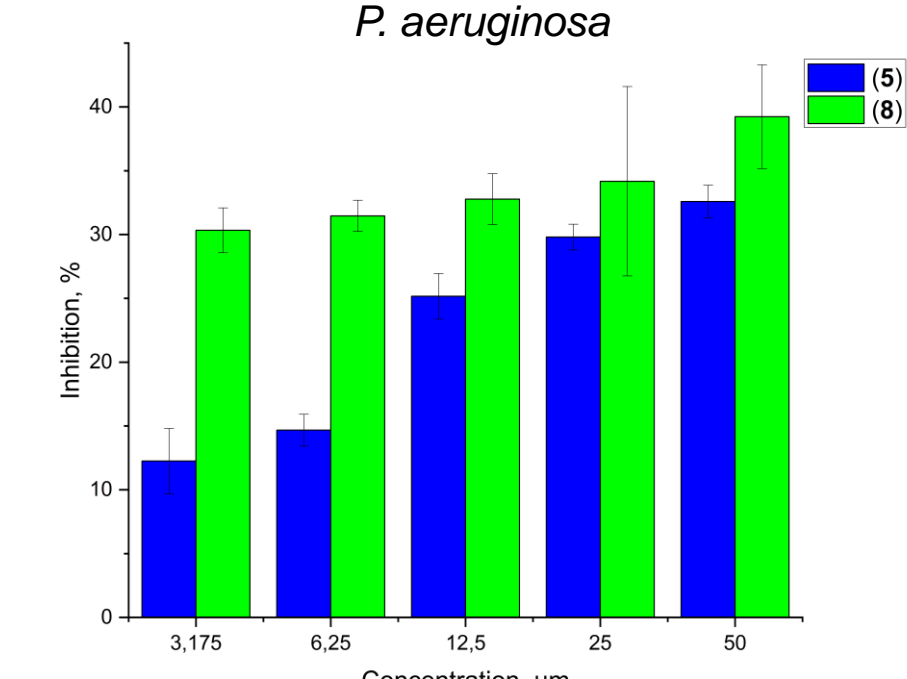
Photoinduced cytotoxicity of the compounds on *S. aureus*



Photoinduced cytotoxicity of the compounds on *P. aeruginosa*



Cytotoxicity of the compounds on *S. aureus*



Cytotoxicity of the compounds on *P. aeruginosa*

Spectral characteristics

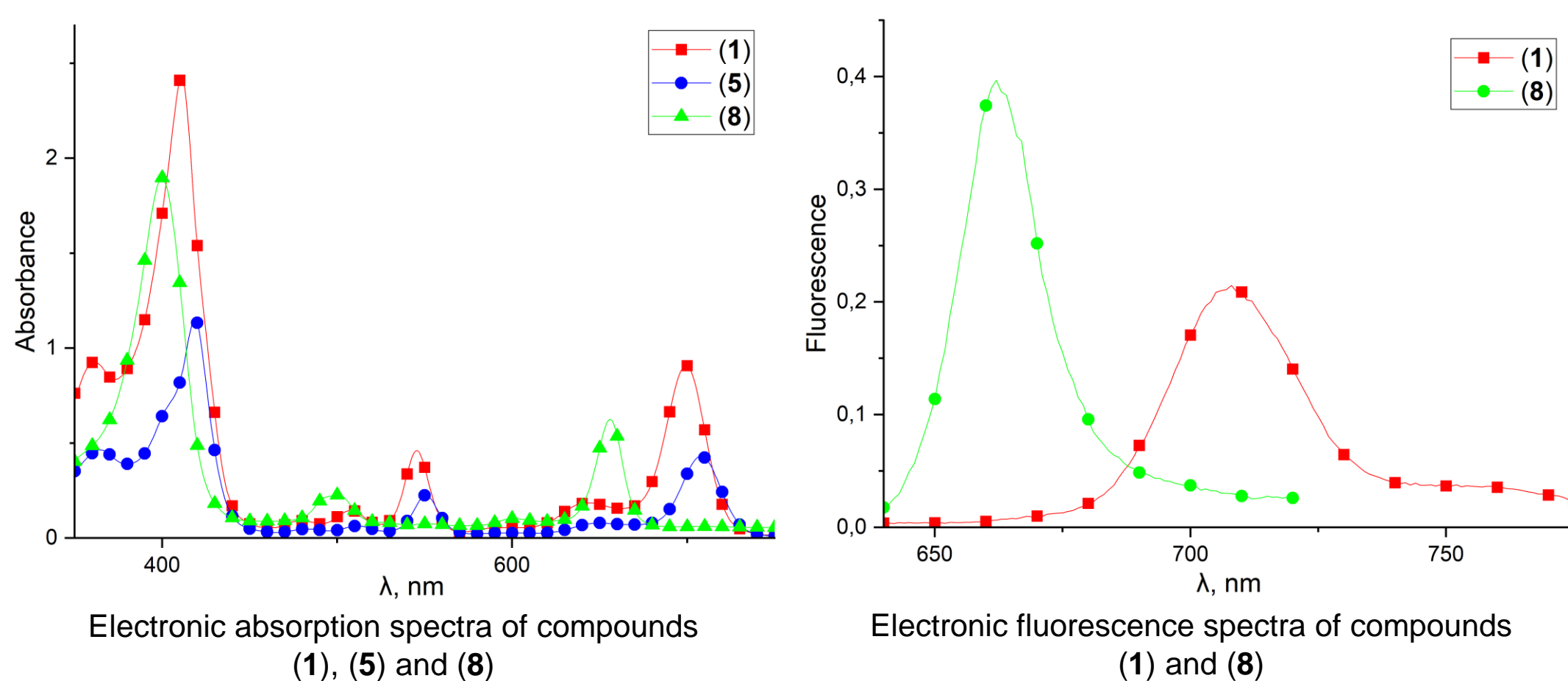


Table 3. Results of studying the photophysical properties of compounds

Compound/Parameter	$\lambda_{a, \max}$, nm	$\lambda_{f, \max}$, nm	Φ_f	Φ_Δ
(1)	700	708	0.12	0.30
(7)	656	662	0.25	0.37

$\lambda_{a, \max}$ – wavelength of the absorption maximum, $\lambda_{f, \max}$ – wavelength of the fluorescence maximum, Φ_f – quantum yield of fluorescence, Φ_Δ – quantum yield of singlet oxygen generation

CONCLUSION

The resulting reduced imide derivative combines absorption in the therapeutic window (656 nm) and high photoactivity (compared to the parent compound). The reduction of carbonyl groups of exocycle E can lead to an improvement in pharmacokinetic parameters and a more effective modification of the nitrogen atom. This compound is a promising candidate for the development of new effective drugs for PDT.

FUTURE WORK / REFERENCES

The work was carried out with the support of the Ministry of Science and Higher Education of the Russian Federation (government assignment №075-00727-25-05 dated 20/03/2025; FSFZ-2024-0013).