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The interaction of methyl pheophorbide *a* with diethanolamine

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Abstract

At present work, the interaction of methyl pheophorbide *a* with diethanolamine was studied in order to synthesize the 13-amide chlorin e_6 derivative with two hydroxyl groups in the molecule to carry out the nucleophilic opening reaction of the exocycle E. This reaction does not require additional activation of the starting compound, and it usually occurs in mild conditions and with good yields. Carrying out such a reaction with diethanolamine containing two hydroxyl groups allowed the introduction of two hydroxyl groups into the molecule of the 13-amide chlorin e6 derivative in one step. The presence of two hydroxyl groups in the compound can promote the overall hydrophilicity of the corresponding derivative, improve the solubility in water and physiological fluids when used. The interaction of methyl pheophorbide a with diethanolamine was studied in chloroform and tetrahydrofuran at room temperature. The formation of new compounds occurs only when the reaction is carried out in chloroform, in the case of tetrahydrofuran, the formation of new compounds has not been observed. When the reaction was carried out in chloroform, the yield of the desired compound – chlorin e_6 13-*N,N*-di-(2-hydroxyethylamide)-15,17-dimethyl ether – was 10%. It was found that, in addition to the target compound, a side product, *N*-(2-hydroxyethyl)imide of the purpurin methyl ester 18, was formed. The formation of *N*-hydroxyethylimide purpurin 18 appears to occur when monoethanolamine, present in small amounts in diethanolamine, is added to the purpurin methyl ester 18, which in turn can be formed by oxidation of methyl pheophorbide with air oxygen in the presence of a base. Disclosure of the exocycle E in methyl pheophorbide *a* and the formation of the main product of the reaction tertiary amine 13-*N,N*-di-(2-hydroxyethylamide)-15,17-dimethyl chlorin e_6 and the side product of the reaction of *N*-hydroxyethylimide purpurin 18 was confirmed by IR, electronic (UV-Vis), and NMR spectroscopy. According to NMR 13-*N,N*-di-(2-hydroxyethylamide)-15,17-dimethyl ester of chlorin e_6, like all tertiary 13-amides of chlorin e_6, forms two atropisomers differing from each other by the mutual arrangement of the planes of the amide group and a chlorine macrocycle.

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