

Synthesis and study of chlorophyll *a* diamide derivatives with an aromatic substituent at the amide nitrogen atom

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Keywords: pheophorbide *a*, pheophorbide *a* exocycle, pheophorbide *a* phenylamide, pyropheophorbide *a*, 13(2)-hydroxyeoporphide *a*, acid chloride, mixed anhydride, di-*tert*-butylpyrocarbonate, aniline, 2-aminopyridine, 13,17-diamides.

Abstract

In the present work, the interaction of a number of phorbins derivatives of chlorophyll *a* (pheophorbide *a*, pyropheophorbide *a*, 13(2)-hydroxypheophorbide *a*) with aromatic compounds (aniline and 2-aminopyridine), having an electron-deficient amino group. Synthesis of amides was carried out by activating the carboxyl groups of natural chlorins with thionyl chloride and di-*tert*-butylpyrocarbonate (Boc₂O). It has been established that changing of thionyl chloride to di-*tert*-butylpyrocarbonate in carboxyl groups activation of the studied phorbins derivatives allows to increase the yield of the desired amides in cases of pheophorbide *a* and pyropheophorbide *a* and obtain the amide of 13(2)-hydroxypheophorbide, which can't be synthesized upon activation with thionyl chloride. In addition, in order to synthesize chlorins with two hydroxy groups, the pheophorbide *a* activated carboxyl group amidation with diethanolamine was studied. Amide with diethanolamine fragment was obtained only by activating the carboxyl group with di-*tert*-butylpyrocarbonate, and, contrary to expectations, only one of the hydroxyl groups of the diethanolamine molecule reacts with the mixed anhydride. To obtain diamide derivatives of chlorophyll *a* with an aromatic substituent at the amide nitrogen atom, the exocycle of the pheophorbide *a* phenyl and pyridyl amides was expanded to form an additional amide group at position 13 by the action of methylamine to the corresponding 17-monoamides. It was found that the substituent at the nitrogen atom of the amide group at the position 17 of the compounds investigated is not changed during the reaction. It has been shown by ¹H NMR spectroscopy that 17-amides of chlorophyll *a* phorbins derivatives aggregation in the chloroform solution is much more pronounced than in the case of similar esters and non-aromatic amides, and the enhancement of aggregation can be explained by the possibility of formation of intermolecular hydrogen bonds involving the amide group of the substituent in position 17.

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