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Full Papers

利用脱镁叶绿酸甲酯的化学修饰合成红紫素酰亚胺衍生物

韩光范*,[1],王进军[2], 吕俊华[3], 汪芳明[1], 瞿艳[1], 沈荣基[4]

[1]江苏科技大学材料科学与工程学院 镇江 212003

[2]烟台大学应用化学系 烟台 264005

[3]暨南大学药学院广州 510632

[4]仁济大学微工程学院 釜山321-749 韩国

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摘要 光动力疗癌的离体和在体实验表明，理想的光动力疗癌光敏剂应具有较长的吸收波长，分子应具有亲水区和疏水区，以及较高的单线态氧的产率。红紫素酰亚胺3-位烃基醚的衍生物已经证明具有良好的疗效。为了获得理想的光敏剂，我们以脱镁叶绿酸甲酯为原料，利用OsO_4和 $NaIO_4$氧化3-位乙烯基，得到3-(甲酰基)-去乙烯基脱镁叶绿酸甲酯，体系在氮气的保护下，控制反应条件，通过Grignard

反应合成了对应的3-(1-羟基烷基)-去乙烯基脱镁叶绿酸甲酯，在分子中同时引入亲水性的羟基和疏水性的烷基。^{1}H NMR光谱数据中两个甲氧基的单峰和13^{2}位的氢的存在可以证明产物的结构。通过空气氧化将*E*环转变成酸酐环得到红紫素衍生物，他们具有693nm的吸收波长同时具有亲水性的羟基和疏水性的烷基。对3-羟基进行脱水得到*trans*-3-(2-烷基)红紫素衍生物。为了克服酸酐环的不稳定性和增加化合物的吸收波长，

上述红紫素衍生物用盐酸羟胺处理得到的*N*-羟基红紫素酰亚胺衍生物，氧化3^1-位羟基得到3-(1-氧代烷基)-*N*-羟基红紫素酰亚胺衍生物，将*N*-羟基乙酰化得到酰化产物。合成的一系列化合物具有长波长的紫外吸收，其中3-(1-氧代烷基)-*N*-羟基红紫素酰亚胺的吸收波长达到733 nm, 同时具有亲水性的羟基和亲脂性的分子侧链，根据QSAR研究，上述合成的具有长波长吸收和兼有亲水性和疏水性基团的红紫素酰亚胺衍生物，有望成为理想的光动力疗癌光敏剂。

关键词 合成的新化合物均由核磁共振、红外光谱、元素分析予以证实。

分类号

Synthesis of Purpurin Imide Derivatives by Modification of Peripheral Functional Groups of Methyl Pheophorbide-*a*

HAN Guang-Fan*,[1], WANG Jin-Jun[2], LÜ, Jun-Hua[3], WANG Fang-Ming[1], QU Yan[1], SHIM Young-Key[4]

[1] *School of Material Science and Engineering, Jiangsu University of Science and Technology, Zhenjiang, Jiangsu 212003, China*

[2] *Department of Applied Chemistry, Yantai University, Yantai, Shandong 264005, China*

[3] *School of Pharmaceutical Sciences, Jinan University, Guangzhou, Guangdong 510632, China*

[4] *School of Nano Engineering, Inji University, Gyongnam 621-749, Korea*

Abstract A series of novel purpurin-18 imide derivatives exhibiting long wavelength absorption and amphiphilicity were obtained from methyl pheophorbide-*a* (MPa) by modification of the peripheral functional groups. The vinyl group at 3-position was oxidized with OsO_4 and $NaIO_4$ to form the formyl group and the Grignard reaction of this aldehyde with the alkyl magnesium bromide was carried out to give the corresponding 3-(1-hydroxylalkyl) pheophorbide-*a*. The *E*-ring of these chlorines was converted into anhydride ring to give purpurin derivatives by air oxidation. The *trans*-3^2-alkyl purpurin derivatives were obtained by dehydration of hydroxyl group at 3^1-position. The *N*-hydroxyl purpurin imide was generated by treatment of the anhydride ring with hydroxylamine hydrochloride. The 3^1-alkylacyl-*N*-hydroxyl purpurin imides were obtained by oxidation of hydroxyl group at 3^1-position. The acylation of *N*-hydroxyl group was completed to afford *N*-acyloxy purpurin imides. The photocytoxicity of several compounds *in vitro* were tested.

Key words methyl pheophorbide-*a* purpurin-18 imide photosensitizer photodynamic therapy

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通讯作者 韩光范 gf552002@yahoo.com.cn