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论文

抗白血病药物靛玉红以及靛蓝和异靛蓝衍生物的合成

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摘要：

靛玉红是我国用于临床治疗慢性粒细胞白血病的一个药物[1]。前报[2]已报道了N_1,取代靛玉红衍生物的合成。为了研究靛玉红分子内氢键(N_1取代)和两个吲哚环连接位置对于抗肿瘤活性的影响。我们合成了N_1-取代和双取代的靛玉红衍生物(I_1,I_2,I_3)和六个靛蓝、异靛蓝衍生物($II_{1\sim3}$,$III_{1\sim3}$)。其中,N-乙基靛蓝和N-甲基或乙基异靛蓝都对Walker癌肉癌256具有抑制作用,而它们的母体化合物则没有抗肿瘤活性。N_1-取代的靛玉红($I_{1\sim2}$)无活性,但N,N′-双甲基靛玉红确又有一定的抗肿瘤活性。

关键词： 靛玉红 靛蓝 异靛蓝 慢性粒细胞白血病

POTENTIAL ANTILEUKEMIC AGENTS, SYNTHESIS OF DERIVATIVES OF INDIRUBIN, INDIGO, AND ISOINDIGOTIN

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Abstract:

Indirubin is used clinically for the treatment of chronic granulocytic leukemic in China. Our previous paper reported the syntheses of N_1′substituted derivatives of indirubin.In an attempt to study the role of N_1-substitution and connecting position of two indole rings in the antitumor activity, two N_1-substituted and one N_1N_1, -bissubstituted derivatives of indirubin (I_1, I_2, I_3), and six bisindolinones, derivatives of indigo and isoindigotin ($II_{1\sim3}$, $III_{1\sim3}$) were synthesized.In the. preparation of compounds $I_{1\sim3}$ from N-alkyl-O-acetyl indoxyl Ⅳ (R=-CH_3 or -C_2H_5) with isatin or N-methylisatin, the self-condensation of the indoxyl to N-substituted indigo is suppressed by using strong acid, p-toluenesulfonic acid as condensing catalyst. It has been suggested that aminium formation stabilizes the indoxyl compound thus inhibits the self-condensation and facilitates the desired condensation of indoxyl with isatin to give a yield of 60%. Treatment of indigo with equimolecular quantity of sodium hydride, followed by corresponding alkyl halides, gave compounds $II_{1\sim3}$. Isoindigotin series compunds $III_{1\sim3}$ were obtained by condensation of the oxindole with corresponding N-alkylisatin.The lipid soluble N-ethyl indigo and N-methyl or N-ethyl isoindigotin exhibit inhibitory action on Walker carcinoma 256 against which their parent compounds are inactive. Substitution on N_1-position of indirubin caused loss of activity, but N_1N_1, -dimethylindirubin (I_3) exhibits certain anticancer activity.

Keywords: Indigo Isoindigotin Chronic granulocytic leukemia Indirubin

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