

研究论文

烷基修饰寡聚脱氧核苷酸磷酸残基的化学合成及稳定性研究

梁远军, 何军林, 徐亮, 张迪, 刘克良

军事医学科学院毒物药物研究所, 北京 100850

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摘要 分别采用格氏试剂和三氯化磷三步取代法合成了4个新的烷基修饰磷酸残基的亚磷酸酰胺单体, 其结构经 ^1H NMR和 ^{31}P NMR表征. 利用这些单体合成模型序列5'-dTTT_x TT-3', 考察了单体及寡聚核苷酸序列在DNA/RNA合成条件下的稳定性, 提出了固相合成含有烷基修饰磷酸残基的寡聚核苷酸序列裂解及脱保护条件.

关键词 [烷基修饰](#) [亚磷酸酰胺单体](#) [寡聚核苷酸](#) [高效液相色谱](#) [稳定性](#)

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Chemical Synthesis and Stability of Oligonucleotides Modified by Alkyl- or Alkoxy- on the Phosphonates

LIANG Yuan-Jun, HE Jun-Lin, XU Liang, ZHANG Di, LIU Ke-Liang

Beijing Institute of Pharmacology and Toxicology, The Academy of Military Medical Sciences, Beijing 100850, China

Abstract Four novel phosphoramidites with isopentyl, phenethyl, isopentoxy, phenethoxy attached to the phosphorus residue were synthesized through Grignard reaction or a sequential three-step substitution on PCl_3 respectively. Four model oligonucleotides (5'-dTTT_x TT-3', where T_x was formed by introducing each of the novel phosphoramidites above-mentioned) were prepared with high coupling yields to study the compatibility of the new building blocks to the customized DNA/RNA synthesis, and the stability of the oligonucleotides were tested under four kinds of deprotection conditions. Based on HPLC analysis and MALDI-TOF-MS measurement, the fast-deprotection strategy (concentrated ammonia, room temperature, 4 h) was suitable for the solid-phase synthesis of oligonucleotides containing above new building blocks. Undoubtedly, these novel phosphoramidites could be used as the building blocks for nucleic acids research.

Key words [Alkylation modification](#) [Phosphoramidite monomer](#) [Oligonucleotide](#) [HPLC](#) [Stability](#)

DOI:

通讯作者 刘克良 Keliangliu@yahoo.com

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