

Synthesis of a Novel Conjugate of Dibenzoyldiazomethane and Polyamide Containing *N*-Methylimidazoles

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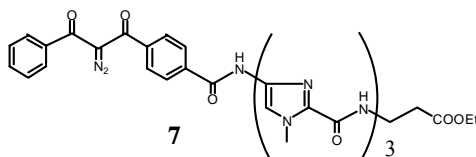
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Abstract: A novel conjugate of dibenzoyldiazomethane and polyamide containing *N*-methylimidazoles was synthesized by a chloroform reaction and a DCC/HOBT coupling reaction.

Keywords: Dibenzoyldiazomethane, polyamide, chloroform reaction.

Photoinduced DNA cleaving agents have generated considerable interest because they are chemically stable and can be activated by photoirradiation. Under UV light, dibenzoyldiazomethane(DBDM)^{1,2} undergoes Wolff rearrangement to produce electrophilic ketene which cleaves single-stranded DNA by alkylation. Polyamides containing *N*-methylimidazoles and *N*-methylpyrroles show high affinity and specificity to sequences of DNA nucleobases. Dibenzoyldiazomethane and polyamide was conjugated in order to increase the selective photocleaving of dibenzoyldiazomethane and decrease the distance between cleavager and DNA to gain higher photocleaving efficiency. In this research, a novel conjugate of dibenzoyldiazomethane and polyamide was designed and synthesized for recognition of 5'-TTAGGG-3' sequence according to Dervan's recognizing rules².

Scheme 1 Structure of the conjugate **7**

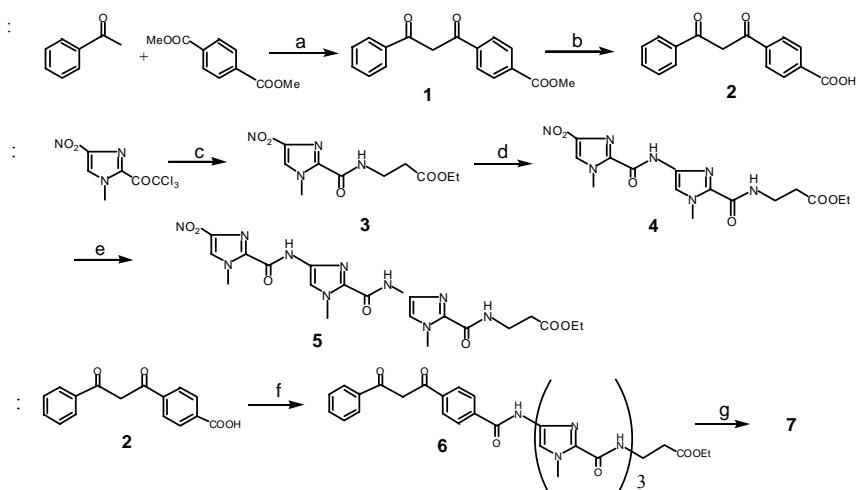


In this synthetic process, dibenzoyldiazomethane derivative **2** was synthesized by condensation and saponification reactions. $\text{NO}_2\text{ImImIm}\beta\text{OEt}$ **5** (where Im=*N*-methylimidazole, β = β -alanine) was synthesized by a convenient chloroform reaction³ and the compound could precipitate from the solution without any further separation.

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Then **2** and **5** was conjugated by the DCC/HOBT coupling reaction³. In the last step, diazo transfer from tosyl azide to compound **6** under the catalysis of Et₃N could successfully produce the conjugate **7**.

Scheme 2 The synthetic routes



Reagents and conditions: a=NaH, THF, 63% yield; b=LiOH/H₂O, 6N HCl, 87% yield; c=NH₂CH₂CH₂COOEt, 64% yield; d=H₂, Pd-C/EtOAc, NO₂ImCOCCl₃, 80% yield; e=H₂, Pd-C/DMF, NO₂ImCOCCl₃, 65% yield; f=HOBT, DCC/DMF, NH₂ImImIm/βOEt, 30% yield; g= TsN₃, Et₃N/CH₃CN, 57% yield.

Experimental

Compound **6** was synthesized by the DCC/HOBT coupling reaction³. 0.10 g (0.14 mmol) compound **6** and 0.053 mL (0.28 mmol) Et₃N was dissolved in 4 mL CH₃CN, then

0.057 g (0.16 mmol) TsN₃ was added to the solution dropwise. After stirring for 4 hr, the mixture was washed by brine and water, dried over anhydrous Na₂SO₄, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography to give a yellow solid **7** (0.057 g, 57% yield). IR: >C=N₂ (2152 cm⁻¹, 2118 cm⁻¹); ¹H-NMR

(CDCl₃, δppm): 9.76 (s, 1H), 9.63 (s, 1H), 9.43 (s, 1H), 7.98 (d, 2H, *J*=6.5 Hz), 7.91 (t, 1H, *J*=6.4 Hz), 7.71-7.60 (m, 5H), 7.42-7.35 (m, 5H), 4.10 (q, 2H, *J*=7.1 Hz), 4.06 (s, 3H), 3.98 (s, 3H), 3.95 (s, 3H), 3.57 (q, 2H, *J*=6.1 Hz), 2.57 (t, 2H, *J*=6.7 Hz), 1.20 (t, 3H, *J*=6.8 Hz); FAB-MS: calcd. for C₃₆H₃₅N₁₂O₈ (MH⁺)763, found 763.

Acknowledgments

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