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# Synthesis and effect on SMMC-7721 cells of new benzo[*c*, *d*]indole rhodanine complex merocyanines as PDT photosensitizers

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ABSTRACT

Photodynamic therapy (PDT) represents a modern and noninvasive therapeutic approach, however, it relies on the development of photosensitizers. Here five new benzo[*c*,*d*]indole rhodanine complex merocyanines (BIRCM) **D1**-**D5**, displaying low dark toxicity and significant photo toxicity, were synthesized as PDT photosensitizers, and characterized by $^1$H NMR, IR, UV–Vis and HRMS. The investigation of their absorption spectra in different solvents showed that the absorption maxima and molar extinction coefficient were in the region 507–679 nm and $0.21 \times 10^4$–$1.27 \times 10^5$ L · mol$^{-1}$cm$^{-1}$, respectively. The evaluation of PDT activity showed that only irradiation could not kill SMMC-7721 cells, and the cell survival rate and inhibition rate at the application dose and duration was 92%–87% and 78%–49%, respectively. Especially, using **D2**, absorbed in the red zone, as photosensitizer for PDT analyzed its effect on SMMC-7721 cells survival, it could be found that the cell survival rate was 92% without irradiating and the cell inhibited rate was 78% under irradiating at concentrations of $2.5 \times 10^{-6}$ mol/L, displaying low dark toxicity and high photo toxicity, which was valuable for PDT of some microvascular diseases or other superficial diseases.



## 1. Introduction

Photodynamic therapy (PDT) is a promising non-invasive modality to cure cancer specifically through combining of laser and photosensitizers.[1–3] The efficacy of PDT directly depends on photosensitizers.[4–6] Now the limitations of the available photosensitizers include few varieties, unsuitable phototherapeutic window, and low selective destruction of malignant cells.[7–9] Therefore, there is a need to design new PDT photosensitizers.

Rhodanine, having biological activity and dual functions of electrophilicity and nucleophilicitie, can be reacted with both electrophilic and nucleophilic heterocycle to give rhodanine complex merocyanines (RCM), which has two different kinds of donor-π-acceptor (D–π–A) structures, one is a neutral group (lipophilic structure), the other is a single cationic group (hydrophilic structure). In addition, RCM possesses large conjugated system, tunable spectrum, and high extinction coefficient.[10] Since most of tumor cells carry a net negative charge on the surface, cationic structures of RCM can be enriched selectively on tumor cells and entry into the tumor cells through the cell membrane.[11] And tumor cells have more low density lipoprotein receptor than normal cells, so lipophilic structures of RCM are easy to accumulate on it.[12] Besides, the hydrophilic structures of RCM can also be accumulated in the mesenchyme and vascular tissues of the tumor by the transport of albumin and serum proteins. In previous work, we reported the synthesis of two quinoline rhodanine complex merocyanines, and investigated their performance as photosensitizers for PDT.[13] Present work is a continuation of researches aimed on the search of RCM with longer absorption wavelength, low dark toxicity and high phototoxicity. In this work, we introduce benzo[*c*,*d*]indole heterocycle having larger conjugated system into RCM unit to synthesize a series of new benzo[*c*,*d*]indole rhodamine complex merocyanines (BIRCM) (Scheme 1), investigate their spectral

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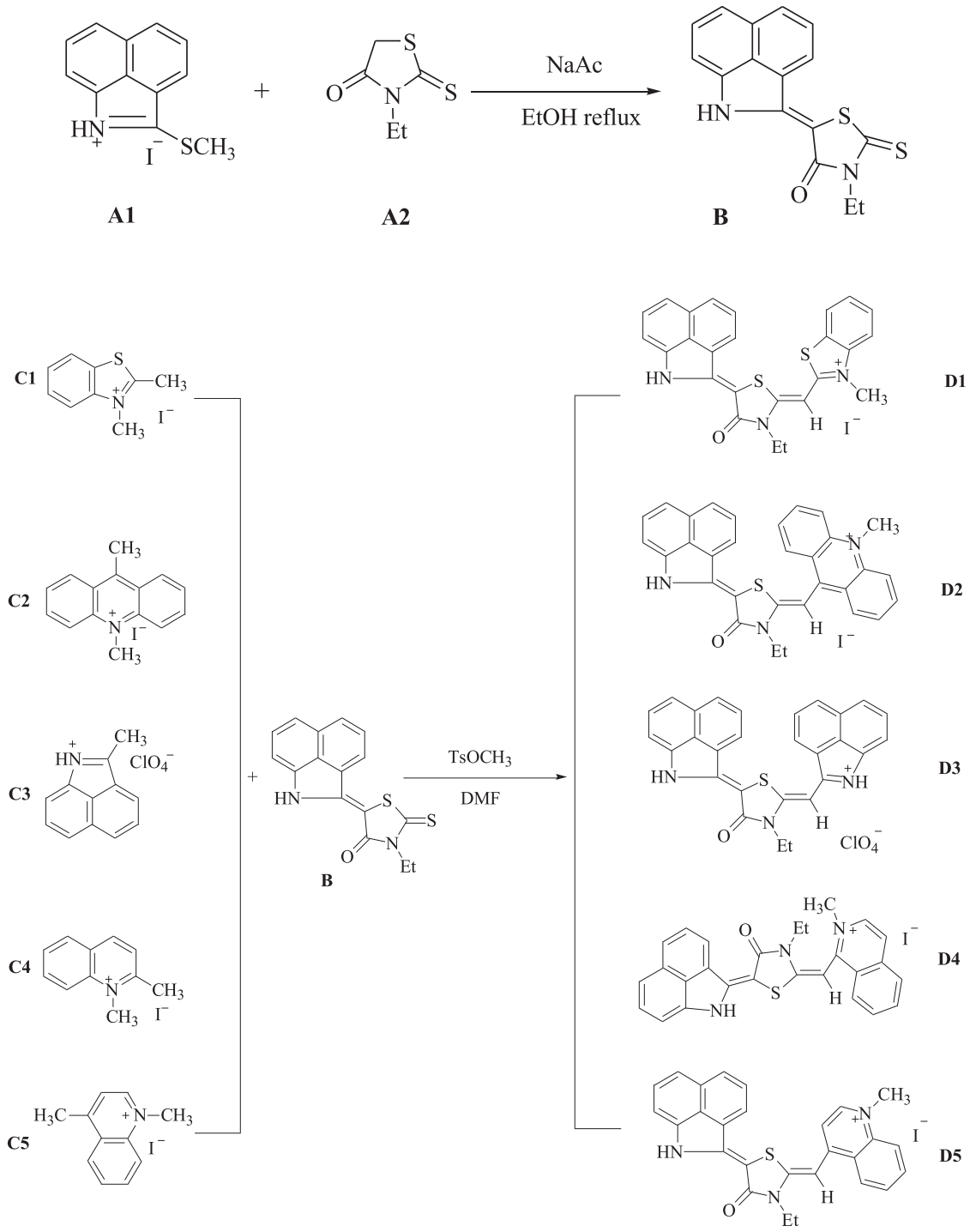


**Scheme 1.** Synthesis of dyes **D1-D5**.

properties, dark toxicity and photo toxicity. As expected, prepared BIRCM absorbed yellow-orange light and exhibited low dark toxicity and significant photo toxicity. Especially, using BIRCM **D2,** absorbed in the red zone, as photosensitizers for PDT analyzed its effect on SMMC-7721 cells survival, it could be found that the cell survival rate was 92% without irradiating and the cell inhibited rate was 78% under irradiating at concentrations of $2.5 \times 10^{-6}$ mol/L, displaying low dark toxicity and high photo toxicity, which was valuable for PDT of some microvascular diseases or other superficial diseases.[14]

## 2. Experimental

### 2.1. Reagents and apparatus

All of the necessary reagents were commercially available, and used without further purification.

The absorption spectra were recorded on a Purkinje General UV-1900 UV–vis spectrometer. NMR measurements were recorded with a 400 MHz spectrometer for $^1$H NMR. IR spectra in $cm^{-1}$ were recorded on Bruker Equiox-55 spectrometer. Melting points were