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Synthesis of a novel tripodal receptor based on 1,8-naphthyridine derivatives

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Abstract

A novel tripodal receptor, 1,3,5-tri((5,7-dimethyl-1,8-naphthyridin-2-yl-amino)methyl)-2,4,6-triethylbenzene (**1**) was synthesized from starting materials 2,6-diamino-pyridine (**2**) and 1,3,5-triethylbenzene (**4**) by three steps with an overall yield of 25%, and characterized by ESI-MS, FT-IR and ^{1}H NMR spectra. Additionally, its absorption and emission spectra were investigated.

Keywords: Tripodal receptor; 1,8-Naphthyridine; Synthesis; Spectroscopy

The synthesis of effective and selective receptors for carbohydrate has been acknowledged as a subject of significant importance to chemistry and biology [1]. Although much research has been done upon host molecules [2], the recognition of carbohydrates by artificial receptors is still inadequate. The difficulty in designing these highly selective receptors is the three-dimensional complexity of sugar structures. Meanwhile, it is also important that OH groups in sugar structure as well as ring oxygen can participate host–guest interactions. 1,8-Naphthyridine derivatives that possess several inherent hydrogen-bonding sites have been chosen as the ideal building blocks for recognition of carbohydrates. Previous report has showed that 1,8-naphthyridines can form cooperative and secondary hydrogen-bond pattern like Fig. 1, when they interact with carbohydrates [3]. Therefore, 1,8-naphthyridine derivative linked with the phenyl spacer yields 1,3,5-substituted 2,4,6-triethylbenzene for matching the demand of three-dimensional recognition of sugar structures. Six identical substituents are disposed above and below the benzene plane [4], which directs the three binding arms toward the same side of the aromatic ring.

In this communication, a new tripodal receptor **1** based on 1,8-naphthyridine, was synthesized successfully by reacting 5,7-dimethyl-2-amine-1,8-naphthyridin (**3**) with 1,3,5-tris(bromomethyl)-2,4,6-triethylbenzene (**5**) (Scheme 1). **3** was obtained in 85% yield by using 2,6-diaminopyridine (**2**) and acetylacetone as starting materials in solution of acetic acid and sulfuric acid refluxed for 24 h [5]. 1,3,5-Tris-(bromomethyl)- 2,4,6-triethylbenzene (**5**) was generated directly via the threefold bromomethylation of triethylbenzene with high yield [6]. However, the desired compound **1** was not obtained by using K_2CO_3, KOH or NaH as base in CH_3CN, DMF, DMSO or toluene solution, and there was no

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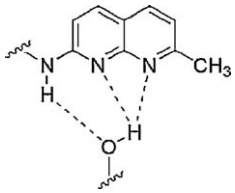
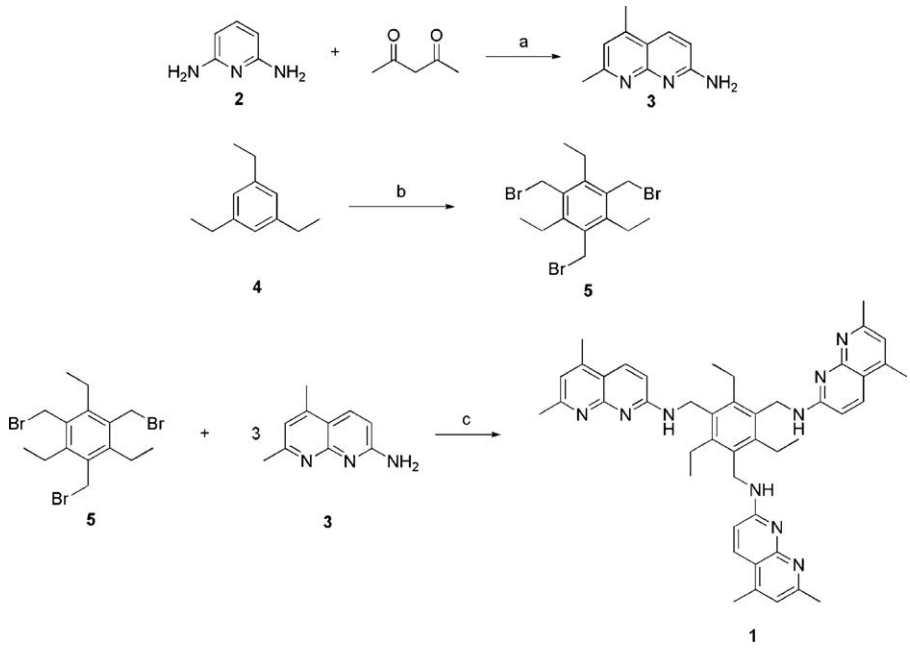


Fig. 1. Hydrogen-bond pattern for interaction of 1,8-naphthyridine with carbohydrate.



Scheme 1. Reagents and conditions: (a) HOAc and H_2SO_4, reflux, 24 h; (b) $(CH_2O)_n$ and $ZnBr_2$, HBr in HOAc (30%), 90 °C, 10 h; and (c) TBAB, toluene and 50% KOH, 80 °C, 24 h.

improvement for the nucleophilic substitution reaction via prolonging reaction time, changing reaction temperature or reagent concentration until tetrabutylammonium bromide (TBAB) was used as phase-transfer catalyst to yield the tripodal receptor **1**.

The changes of UV–vis absorption and fluorescent emission spectra for compound **1** in CH_2Cl_2 with the addition CH_3OH were shown in Fig. 2. Compound **1** displayed two absorption peaks at 341 and 355 nm

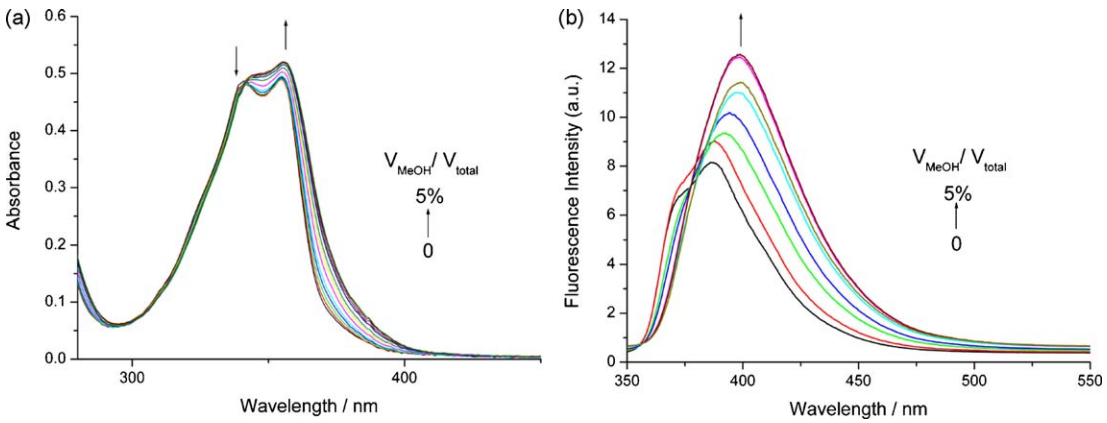


Fig. 2. Changes in the absorption (a) and emission (b) spectra of **1** (1.0×10^{-5} mol/L) in CH_2Cl_2 with addition of CH_3OH.

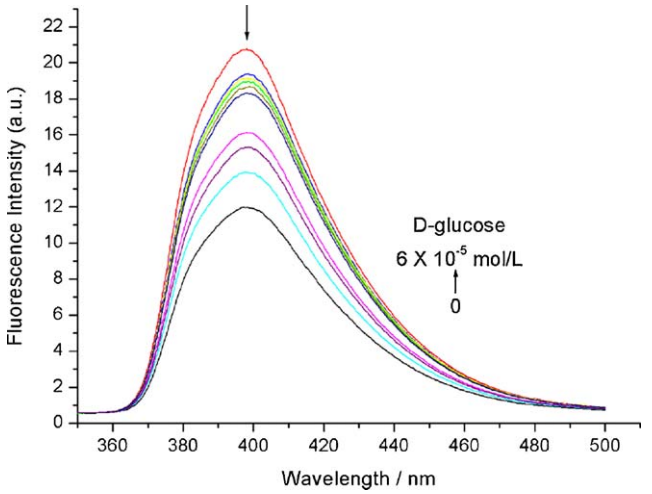


Fig. 3. Changes in emission spectra of **1** (1.0×10^{-5} mol/L) in CH_3OH with addition of D-glucose in CH_3OH (3.4×10^{-2} mol/L).

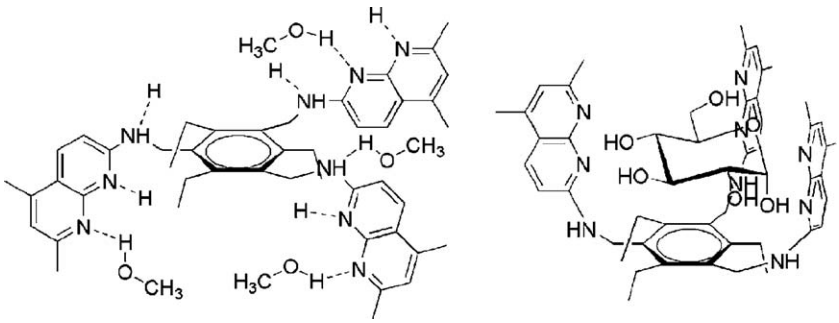


Fig. 4. Probable molecular configuration of **1** with CH_3OH or D-glucose.

(ε_{max} = 65,048 L mol^{-1} cm^{-1}) as depicted in Fig. 2a, which could be ascribed to intraligand charge transfer (ILCT) $\pi \rightarrow \pi^*$ transition. Upon addition CH_3OH to the CH_2Cl_2 solution of **1**, the absorption was red-shifted, and emission intensity increased. The emission spectrum with λ_{max} at 386 nm was red-shifted to 398 nm upon excitation at 340 nm (Fig. 2b), indicating the presence of weak interaction between **1** and polar solvent CH_3OH.

As shown in Fig. 3 fluorescence intensity of **1** in CH_3OH changed with addition of D-glucose in the same solvent. **1** exhibits one emission peak at 398 nm in CH_3OH, the fluorescence intensity decreased obviously with increasing D-glucose concentration while absorption spectrum remained unaltered. As the flexible framework of **1**, the mutual repulsion of methanol molecules and the three-dimensional feature of D-glucose structure lead to changes in molecular configuration of **1** as depicted in Fig. 4. The quenched luminescence can be tentatively assigned to the intermolecular interaction of **1** and D-glucose.

In conclusion, an effective method for synthesis of the new tripodal receptor bearing 1,8-naphthyridine via *N*-alkylation was performed. The advantages of this approach are few by-product and easy experiment. And the recognition of D-glucose in CH_3OH by this tripodal receptor was realized. Detail mechanism of quenching effect on fluorescence emission of **1** in CH_3OH with addition of D-glucose and further applications of this new tripodal receptor in recognition of other carbohydrate are in progress.

1. Experimental

^{1}H NMR spectrum was recorded on Bruker DPX-400 (400 MHz) at 298 K and chemical shifts (δ) were obtained relative to tetramethylsilane (TMS). Mass spectra were recorded on BIFLEX-III MALDI-TOF mass spectrometer for matrix-assisted laser desorption/ionization (MALDI). UV–vis absorption spectra were taken on a Hitachi U-3010

spectrophotometer and emission spectra were recorded with a Hitachi F-4500 fluorescence spectrophotometer. IR spectra were measured on Varian 3100 FT-IR System at 298 K.

A solution of **3** (0.590 g, 3.4 mmol) TBAB (0.137 g, 0.85 mmol) and **5** (0.375 g, 0.85 mmol) in toluene (50 mL) and 50% aqueous KOH (8.5 mL) was stirred at 80 °C for 24 h under nitrogen atmosphere. Then organic phase was separated after cooled, washed with water for three times and dried over anhydrous sodium sulfate. After filtration and removal of the solvent under reduced pressure, the crude product was purified by chromatography on silica gel (200–300 mesh), using CH_2Cl_2/C_2H_5OH (v/v, 20/1) as eluent to give the pure product as pale yellow powder. Yield: 30%. MALDI-TOF-MS: $[M+H]^+$, 718.1; $[M+Na]^+$, 740.1; $[M+K]^+$, 756.1. FT-IR (KBr, cm^{-1}): 3427.5, 2960.4, 2923.6, 2361.3, 2337.7, 1630.6, 1570.3, 1385.1, 1097.9. ^1H NMR (400 MHz, DMSO-d_6, 298 K, relative to Me_4Si): δ 1.51 (t, 9H, CH_3), 2.57 (s, 18H, CH_3), 2.82 (q, 6H, CH_2), 4.41 (s, 6H, CH_2), 4.52 (br, 3H, NH), 7.00 (d, 3H, $J = 9.12$ Hz, naphthyl-H), 7.14 (s, 3H, naphthyl-H), 8.11 (d, 3H, $J = 9.12$ Hz, naphthyl-H).

Acknowledgments

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References

[1] (a) B. Ernst, G.W. Hart, P. SinaK, Carbohydrates in Chemistry and Biology, Part I, vol. 2, Wiley–VCH, Weinheim, 2000;
(b) B. Ernst, G.W. Hart, P. SinaK, Carbohydrates in Chemistry and Biology, Part II, vol. 4, Wiley–VCH, Weinheim, 2000.
[2] (a) R.P. Bonar-Low, J.K.M. Sanders, J. Am. Chem. Soc. 117 (1995) 259;
(b) A.P. Davis, R.S. Wareham, Angew. Chem. Int. Ed. 37 (1998) 2270;
(c) J.C. Morales, S. Penades, Angew. Chem. Int. Ed. 37 (1998) 654;
(d) A.P. Davis, R.S. Wareham, Angew. Chem. Int. Ed. 38 (1999) 2978;
(e) M. Inouye, K. Takahashi, H. Nakazumi, J. Am. Chem. Soc. 121 (1999) 341.
[3] M. Mazik, W. Sicking, Chem. Eur. J. 7 (2001) 664.
[4] For a recent review on benzene-based tripodal receptor, see: G. Hennrich, E.V. Anslyn, Chem. Eur. J. 8 (2002) 2218.
[5] R.A. Henry, P.R. Hammond, J. Heterocyclic Chem. 14 (1977) 1109.
[6] A. Vacca, C. Nativ, M. Cacciarini, R. Pergoli, S. Roelens, J. Am. Chem. Soc. 126 (2004) 16456.