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Short Note

N,N′,N″,N‴-Tetrakis(5,7-dimethyl-1,8-naphthyridine-2-yl)-3,3',5,5'-diphenylmethanetetracarboxamide

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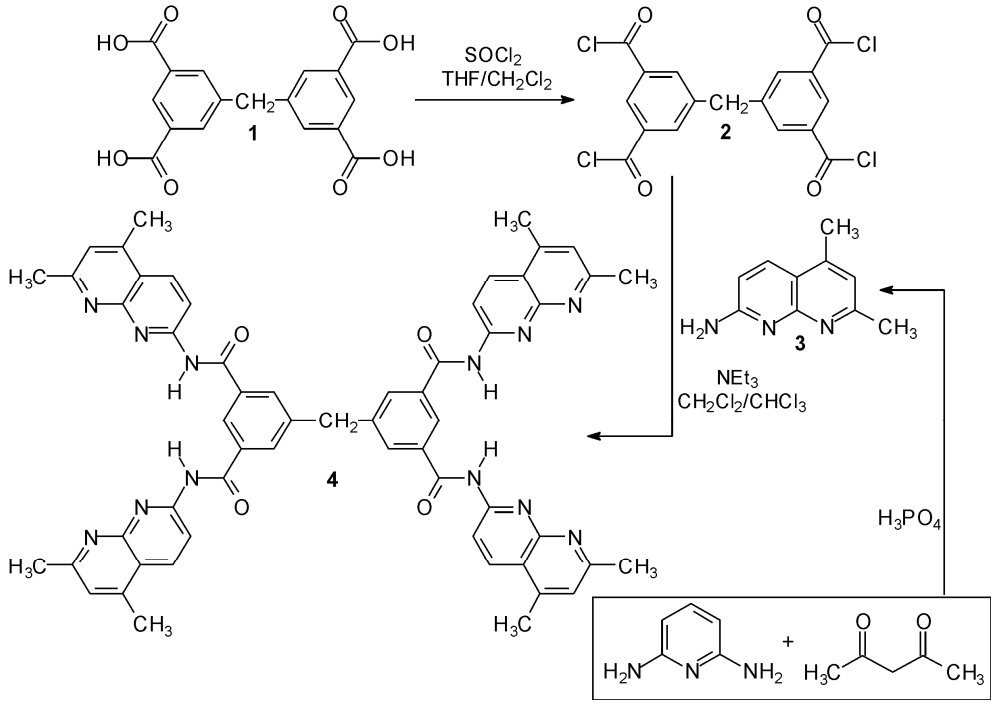
Abstract: Diphenylmethane-based compounds bearing heterocyclic recognition groups, capable to act as hydrogen bonding sites were established to be powerful receptors for carbohydrates. In this paper, we describe the synthesis of a further representative of this class of compounds, containing four 1,8-naphthyridine groups as recognition units. The title compound has been characterized by elemental analysis, ^{1}H-NMR, ^{13}C-NMR and mass spectrometry.

Keywords: 1,8-naphthyridine; diphenylmethane; receptors

Dimesitylmethane-based compounds bearing pyridine, pyrimidine, imidazole or indole groups as heterocyclic recognition groups (3,3',5,5'-substituted 2,2',4,4',6,6'-hexamethyldiphenylmethanes), attached to the dimesitylmethane-spacer via –CONHCH$_2$-, -NHCH$_2$- or –CH$_2$NHCH$_2$- linker units, were shown to be effective carbohydrate receptors, displaying interesting di- *vs.* monosaccharide binding preference [1,2]. The tetrasubstituted dimesitylmethane scaffold provides a cavity of a correct shape and size for disaccharide encapsulation and its aromatic units are able to participate in CH-π interactions with the carbohydrate [1,2]. Furthermore, a diphenylmethane-based compound, the design of which was inspired by the binding motifs found in the crystalline complex of 2-α-*O*-methyl *N*-acetylneuraminic acid with rhesus rotavirus hemagglutinin, was established to be a powerful

receptor for *N*-acetylneuraminic acid [3]. The acyclic architecture of such receptor molecules is notably easy to prepare and especially suitable for systematic variations [4,5]. The performed studies showed that the synthetic receptors provide valuable model systems to study the basic molecular features of carbohydrate recognition. In this paper, we describe the synthesis of a further representative of the class of diphenylmethane-based compounds bearing four 1,8-naphthyridine groups capable of serving as hydrogen bonding sites, which are attached to the diphenylmethane-spacer via –NHCO- linker units. The 1,8-naphthyridine group was found to be a valuable building block for the construction of receptors, which are able to bind both neutral [6] and ionic [7] carbohydrates, as shown by binding studies with compounds based on a benzene spacer (for reviews on carbohydrate recognition, see for example refs. [4,5,8,9]).

The simple synthesis of *N,N′,N″,N‴*-tetrakis(5,7-dimethyl-1,8-naphthyridine-2-yl)-diphenylmethane-3,3',5,5'-tetracarboxamide (**4**) involved the reaction of 3,3',5,5'-diphenylmethanetetracarbonyl tetrachloride (**2**) (prepared from **1** [3,10], as shown in Scheme 1) with 2-amino-5,7-dimethylnaphthyridine (**3**); the purification of **4** was carried out on the base of column chromatography. 2-Amino-5,7-dimethylnaphthyridine (**3**) was prepared through a reaction of 2,6-diaminopyridine with acetylacetone in phosphoric acid [11].



Scheme 1. Synthesis of the title compound *N,N′,N″,N‴*-Tetrakis(5,7-dimethyl-1,8-naphthyridine-2-yl)-3,3',5,5'-diphenylmethanetetracarboxamide (**4**).

Experimental

A mixture of 3,3',5,5'-tetracarboxydiphenylmethane (0.3 g, 0.87 mmol) and thionylchloride (0.55 g, 0.34 mL, 4.65 mmol) in THF/CH_2Cl_2 (20 mL/10 mL) was heated under reflux for 5 h. The solvent was removed *in vacuum*. Afterwards, CH_2Cl_2 (20 mL) was added and again the solvent was removed *in vacuum* (this procedure was repeated four times). The crude product **2** was dissolved in CH_2Cl_2 (20 mL)

and added dropwise to a solution of 2-amino-5,7-dimethyl-1,8-naphthyridine (0.67g, 3.87 mmol) and triethylamine (0.40 g, 0.55 mL, 3.96 mmol) in CH_2Cl_2/$CHCl_3$ (60 mL/40 mL). After complete addition, the mixture was stirred at room temperature for 48 h. The precipitate was filtered off and washed with dichloromethane. The filtrate was concentrated under reduced pressure and purified by column chromatography (silica gel, methanol/chloroform 1:7; v/v). The product **4** was obtained as a yellow solid in 45% yield (0.38 g, 0.39 mmol).

Mp = 238 °C (dec.). R_f = 0.49 (silica gel, methanol/chloroform 1:7 v/v).

^{1}H-NMR (400 MHz, $CDCl_3$/MeOD-d_4 4:1): δ [ppm] = 2.69 (s, 12H, 4 × CH_3), 2.70 (s, 12H, 4 × CH_3), 4.48 (s, 2H, CH_2), 7.18 (s, 4H, H_{napht}), 8.26 (s, 4H, H_{phenyl}), 8.41 (d, J = 9.0 Hz, 4H, H_{napht}), 8.62 (d, J = 9.0 Hz, 4H, H_{napht}), 8.68 (s, 2H, H_{phenyl}).

^{13}C-NMR (100 MHz, $CDCl_3$/MeOD-d_4 4:1): δ [ppm] = 18.2, 24.9, 41.6, 114.9, 118.9, 122.6, 125.9, 132.4, 135.6, 135.7, 141.6, 146.8, 154.3, 162.4, 166.6.

HRMS (ESI) calcd. for $C_{57}H_{49}N_{12}O_4$ $[M + H]^+$ 965.39942. Found 965.39959.

Anal. calcd. for $C_{57}H_{48}N_{12}O_4$: C, 70.93; H, 5.02; N, 17.42. Found: C, 70.84; H, 5.17; N, 17.28.

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Author Contributions

US performed the experimental work. MM prepared the manuscript and the overall project management was done by MM.

Conflicts of Interest

The authors declare no conflict of interest.

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