Tetrahedron Letters 57 (2016) 979–982

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Synthesis and photophysical properties of a new BODIPY-based siloxane dye

Alexey A. Pakhomov [a,*], Yuriy N. Kononevich [b], Maria V. Stukalova [b], Evgeniya A. Svidchenko [c], Nikolay M. Surin [c], Georgy V. Cherkaev [c], Olga I. Shchegolikhina [b], Vladimir I. Martynov [a], Aziz M. Muzafarov [b,c]

[a] M.M. Shemyakin and Yu.A. Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, 117997 Moscow, Russian Federation
[b] A.N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 119991 Moscow, Russian Federation
[c] N.S. Enikolopov Institute of Synthetic Polymeric Materials, Russian Academy of Sciences, 117393 Moscow, Russian Federation

ARTICLE INFO

Article history:
Received 11 November 2015
Revised 15 January 2016
Accepted 18 January 2016
Available online 19 January 2016

Keywords:
BODIPY
Siloxane
Cyclotetrasiloxane
Hydrosilylation
Fluorescence
Solvatochromism

ABSTRACT

A fluorescent dye comprising four BODIPY derivatives conjugated to a cyclotetrasiloxane core was synthesized by consecutive hydrosilylation and esterification reactions. Photophysical properties of the dye in various organic solvents were investigated. It was shown that due to a fourfold extinction coefficient increase and a moderate quantum yield decrease the brightness of the tetra-BODIPY dye in low-polarity solvents, calculated per molecule, increased 3 times when compared to mono-BODIPY. By contrast, in polar solvents there was a dramatic drop in brightness apparently associated with intramolecular interactions of the low-polar BODIPY chromophores.

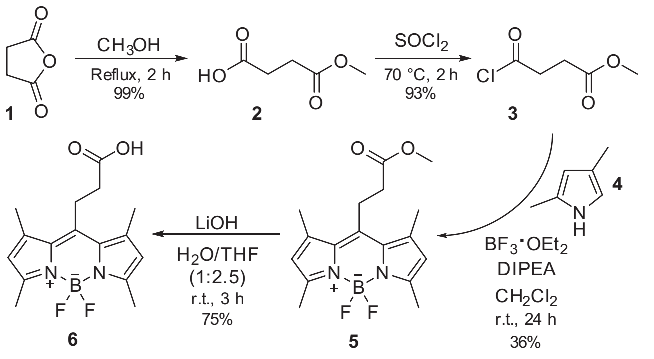
Bright and photostable fluorescent compounds are of particular interest in the fields of modern photonics, photochemistry and molecular biology. Derivatives of 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY) display outstanding photophysical properties and usually possess considerable light-absorbing capacity, high quantum yield, sharp absorption and emission bands, remarkable photostability, and solubility in organic solvents.[1] Different BODIPY derivatives span most of the visible and near infrared spectrum and offer great potential for the development of biomolecular labels,[2,3] chemosensors,[4] energy transfer cassettes,[5,6] dye-sensitized solar cells (DSSC)[7] and can be used in photodynamic therapy.[8] BODIPYs were used as a base structure in the construction of fluorescent molecular rotors[9] and fluorescent liquid-crystalline dendrimers.[10] Herein, we have synthesized a carboxylic derivative of 1,3,5,7-tetramethyl-BODIPY (TMB) and conjugated it with cyclotetrasiloxane. Cyclic and polyhedral oligosiloxanes are known to be indispensable building blocks for the preparation of a variety of organic polymer materials[11,12] improving their thermal and optical properties.[13,14] Moreover, these compounds display high chemical inertness and biocompatibility.[15,16] As might be expected, conjugation of several TMB fluorophores with the cyclosiloxane core structure would enhance the total brightness, which is proportional to the product of extinction (ε) and quantum yield (QY). Thus, combining four fluorophores at the cyclotetrasiloxane matrix might enhance the total brightness up to 4 times due to an extinction increase. On the other hand, raising of the local concentration of fluorophores may lead to the formation of nonfluorescent aggregates and in turn lead to a drop in quantum yield, which is the primary reason for fluorescence quenching of chromophore bearing dendrimers.[17] In the present work, we have attempted to design a multichromophore compound with the minimized effect of self-quenching. We presumed that the use of TMB would prevent aggregation-induced quenching owing to the BODIPY π-system being protected by four methyl groups.

A new tetra-BODIPY-substituted siloxane fluorescent dye was synthesized from two fragments: a siloxane ring and 3-(4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-*s*-indacene-8-yl)-propionic acid (TMB-propionic acid). The latter was prepared analogously to the method described earlier.[13] Briefly, the reaction of succinic anhydride **1** with methanol followed by thionyl chloride chlorination yielded chloroanhydride **3** (Scheme 1). Product **3** was reacted with 2,4-dimethylpyrrole **4** in dry dichloromethane under argon at room temperature for 24 h followed by neutralization

---

* Corresponding author. Tel.: +7 495 336 5111.
E-mail address: alpah@mail.ru (A.A. Pakhomov).

http://dx.doi.org/10.1016/j.tetlet.2016.01.059
0040-4039/

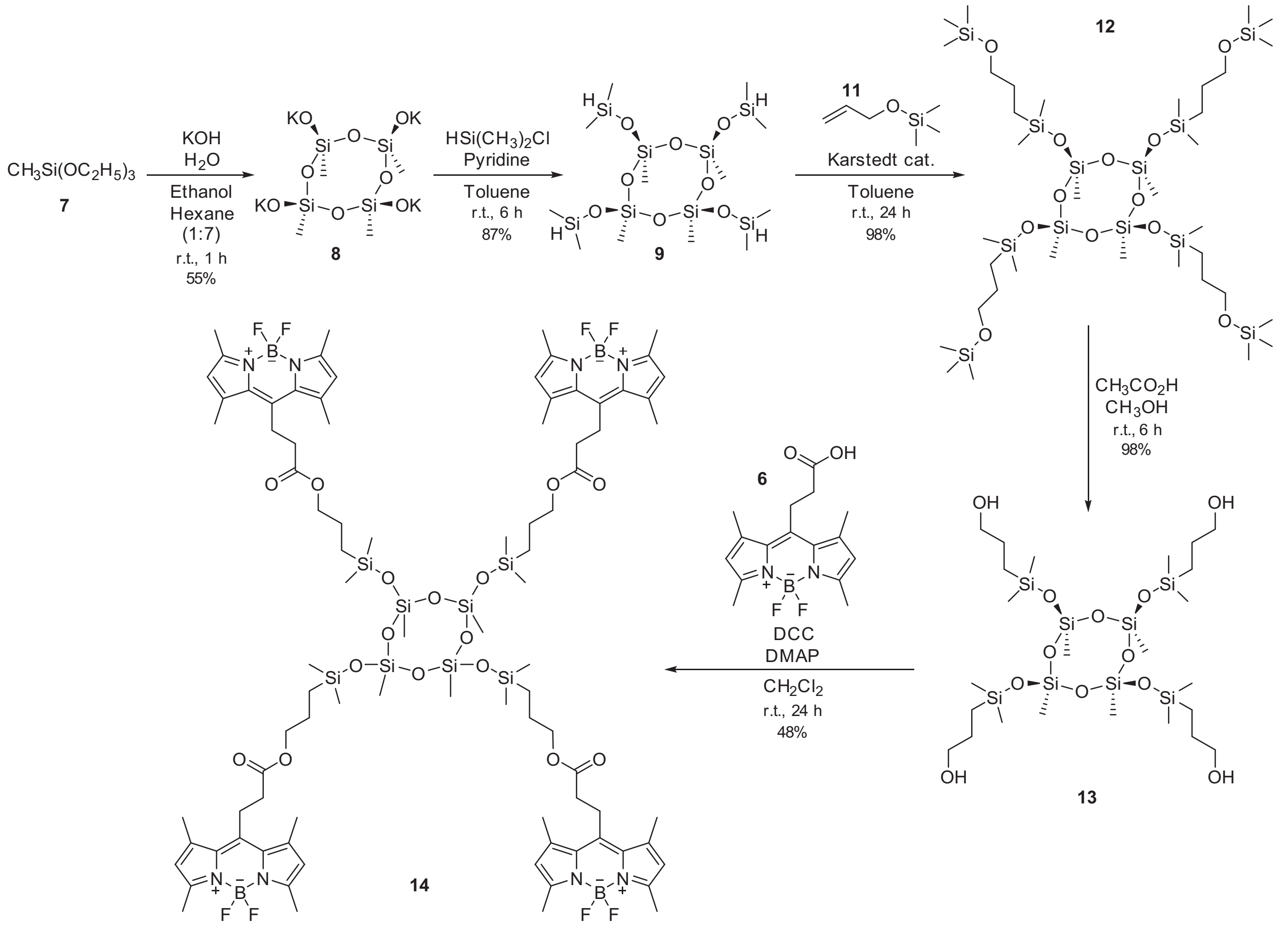


Scheme 1. Synthesis of TMB-propionic acid **6**.

using DIPEA and subsequent reaction with boron trifluoride diethyl etherate. Addition of an extra equivalent of dimethylpyrrole **4** (3:1 instead of the commonly used 2:1) drastically improved the reaction yield. After purification, the resultant TMB ester **5** was saponified using LiOH in water-THF yielding TMB-propionic acid **6**.

The synthesis of hydroxyl-bearing cyclotetrasiloxane began from methyltriethoxysilane **7** (Scheme 2). The potassium *cis*-tetramethylcyclotetrasiloxanolate **8** was synthesized in good yields by the method previously reported by our group.[18] The reaction was carried out at room temperature in a mixture of ethanol and hexane. It should be noted that in this reaction only the *cis*-isomer can be formed, which was confirmed by X-ray analysis.[19] At the next stage, modification of compound **8** by the dimethylsilyl group was accomplished. Reaction between salt **8** and chlorodimethylsilane was carried out in dry toluene at room temperature. The obtained compound **9** was used without further purification. Allyloxytrimethylsilane **11** was used to introduce the hydroxyl-bearing fragment into the siloxane ring. The hydrosilylation reaction was carried out in dry toluene under an inert atmosphere at room temperature. Product **12** was sufficiently pure and was used at the next stage without any purification. It should be noted that during the reaction only β-addition occurred which was confirmed by NMR. The trimethylsilyl protecting group was removed by stirring at room temperature in methanol with acetic acid. Thus, for the first time a hydroxyl-bearing *cis*-cyclotetrasiloxane **13** was prepared and characterized.

The final step of the synthesis of the star-shaped BODIPY-bearing siloxane fluorescent dye was Steglich esterification (Scheme 2). The reaction was carried out in dichloromethane at room temperature using dicyclohexylcarbodiimide (DCC) as condensing agent and 4-dimethylaminopyridine (DMAP) as catalyst. Product **14** was obtained in 48% yield and purified by silica column chromatography using toluene/ethylacetate (10:1) as eluent. It should be noted that during the reaction, isomerization of the siloxane ring with loss of the all-*cis* configuration takes place as evident from the ^{29}Si NMR spectrum (see ESI). Probably, isomerization of the all-*cis* compound is the result of DMAP base treatment. To verify this proposal we incubated *cis*-cyclotetrasiloxanolate **13** with DMAP and observed an analogous loss of the all-*cis* configuration. The obtained compounds were characterized by ^{1}H, ^{13}C, ^{19}F, ^{29}Si NMR, IR, MS, and elemental analysis.



Scheme 2. Synthesis of star-shaped cyclotetrasiloxane with four terminal TMB fluorophores.