Molbank **2010**, M662

OPEN ACCESS

molbank

ISSN 1422-8599

www.mdpi.com/journal/molbank

Short Note

Luminescent Lariat Aza-Crown Ether

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Received: 24 February 2010 / Accepted: 9 March 2010 / Published: 10 March 2010

Abstract: Lariat ethers are interesting recognition motifs in supramolecular chemistry. The synthesis of a luminescent lariat ether with triglycol chain by azide–alkyne (Huisgen) cycloaddition is presented.

Keywords: crown ether; cycloaddition; triazole; ammonium receptor; lariat ether; podand

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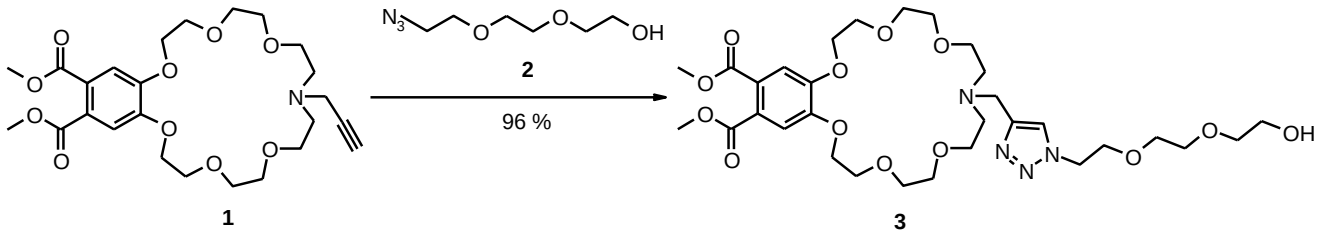
1. Introduction

Luminescent crown ether amino acids bind ammonium ions and signal the binding event by changes of their specific emission properties [1]. They are versatile building blocks for amino acid and peptide receptors [2–4]. Introduction of podand arms [5] may enhance the cation binding affinity of crown ethers [6]. The copper(I) catalyzed dipolar cycloaddition (Huisgen cycloaddition) is known to be a robust ligation method for a variety of differently substituted azides and alkynes [7–9]. We present the functionalization of a luminescent aza-crown ether with triglykol podand arm by this method. Such a compound is expected to have enhanced ammonium ion binding properties.

2. Synthesis

The lariat ether was prepared by Huisgen cycloaddition at the side chain of a propargyl-substituted crown ether (**1**) with 2-(2-(2-azidoethoxy)ethoxy)ethanol (**2**).

Scheme 1. Synthesis of a lariat ether (**3**) by copper(I) mediated dipolar cycloaddition.

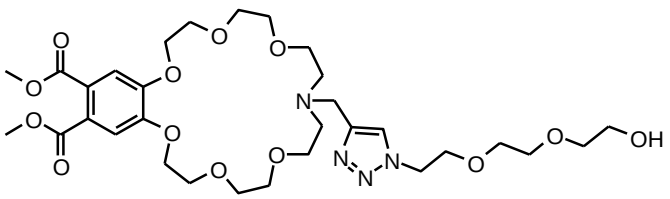


Conditions: MeOH, H_2O, $CuSO_4$ * 5 H_2O, Na-ascorbate, N_2, RT to reflux, 5h

3. Experimental

Crown ether **1** [2], and 2-(2-(2-azidoethoxy)ethoxy)ethanol (**2**) [10,11] were prepared as published.

*14-[2-(2-(2-(4-Methyl-1H-1,2,3-triazol-1-yl)ethoxy)ethoxy)ethanol]-6,7,9,10,13,14,15,16,18,19,21,22-dodecahydro-12H-5,8,11,17,20,23-hexaoxa-14-aza-benzocycloheneicosene-2,3-dicarboxylic acid dimethyl ester (**3**)*



Compound **1** (102 mg, 0.2 mmol) and compound **2** (53 mg, 0.3 mmol) were dissolved in 1.0 mL of methanol. A solution of copper(II)sulphate pentahydrate (10 mg, 0.02 mmol) in 0.5 mL of water containing 16 mg sodium ascorbate (0.1 mmol) was added drop wise. After stirring for 1 h at room temperature, the reaction mixture was heated to reflux for 4 h in a nitrogen atmosphere (TLC control). After cooling to room temperature, 9.0 mL dichloromethane were added, the aqueous layer was separated off and the organic phase was washed with 3.0 mL of brine. After drying over $MgSO_4$ the solvent was evaporated and the solid residue was purified by column chromatography with ethyl acetate/ethanol 3:1. The pure product is a yellow oil (132 mg, 0.192 mmol, 96 %).

MF: $C_{31}H_{48}N_4O_{13}$–**FW:** 684.75 g/mol; -**IR** (neat): ν (cm^{-1}) = 3040 (w), 2970 (m), 2870 (m), 1720 (s), 1599 (m), 1519 (m), 1435 (m), 1351 (m), 1323 (m), 1287 (m), 1247 (m), 1198 (m), 1122 (s), 1052 (m), 978 (m), 961 (m), 923 (m), 889 (m), 748 (s), 665 (m); -**MS** (ESI-MS, CH_2Cl_2/MeOH + 10 mmol NH_4OAc): e/z (%) = 685.3 (100 %, MH^+); -**HRMS** (PI-LSIMS Glycerine): calc. for $C_{31}H_{49}N_4O_{13}^+$: 685.3296, found: 685.3283; -^{1}**H-NMR** (300 MHz, $CDCl_3$): δ [ppm] = 2.87 (m, 4 H), 3.17 (bs, 1 H), 3.54 (t, 2 H, *J* = 4.1 Hz), 3.59 (m, 4 H), 3.61–3.78 (m, 14 H), 3.82–3.87 (m, 2 H), 3.86 (s, 6 H), 3.90 (m, 4 H), 3.96 (s, 2 H), 4.18 (m, 4 H), 4.48 (t, *J* = 4.95 Hz, 2 H), 7.17 (s, 2 H), 7.94 (s, 1 H); -^{13}**C-NMR** (75 MHz, $CDCl_3$): δ [ppm] = 49.9 (-, 1 C), 50.0 (-, 1 C), 52.6 (+, 2 C), 53.3 (-, 2 C), 61.5 (-, 1 C), 68.9 (-, 1 C), 69.2 (-, 1 C), 69.3 (-, 2 C), 69.5 (-, 2 C), 70.2 (-, 1 C), 70.3 (-, 1 C), 70.5 (-, 2 C), 71.1 (-, 2 C), 72.6 (-, 2 C), 113.5 (+, 2 C), 124.9 (+, 1 C), 125.4 (C_{quat}, 2 C), 140.3 (C_{quat}, 1 C), 150.4 (C_{quat}, 2 C), 167.8 (C_{quat}, 2 C); -**UV** (MeOH): λ (ε) = 268 (7600), 224 (31400);

Acknowledgements

We thank the Deutsche Forschungsgemeinschaft (GRK 760) and the University of Regensburg for support of this work.

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11. The product can be easily prepared by a simplified procedure: Thoroughly dried triethylenglykol monotosylate (3.33 g, 10.0 mmol) is mixed with 10.0 mL of dry DMF. Sodium azide (0.78 g, 12.0 mmol) was added and the mixture was stirred over night at 40 ℃ under nitrogen. The solvent was evaporated and the residue was extracted with ethyl acetate (50 mL). After filtration over celite and subsequent washing of the filter cake with ethyl acetate, all volatiles were removed to give the product as pale yellow oil (1.71 g, 9.75 mmol, 89%).; **^{1}H-NMR** (300 MHz, $CDCl_3$): δ [ppm] = 2.64 (bs, 1 H), 3.31 (t, *J* = 5.4 Hz, 2 H), 3.56 (t, *J* = 5.4 Hz, 2 H), 3.58 – 3.71 (m, 8 H); -**^{13}C-NMR** (75 MHz, $CDCl_3$): δ [ppm] = 50.6 (-, 1 C), 61.7 (-, 1 C), 70.1 (-, 1 C), 70.3 (-, 1 C), 70.7 (-, 1 C), 72.5 (-, 1 C); - **IR** (neat): ν (cm^{-1}) = 3300 (bm), 2920 (m), 2871 (m), 2094 (s), 1520 (w), 1456 (m), 1347 (m), 1285 (s), 1118 (s), 1065 (s), 928 (m), 887 (m), 821 (m), 632 (m).