Synthesis of 1*H*-1,2,3-triazoles from alkyne derivatives of 1,3,5-triazines by Huisgen reaction

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Abstract:

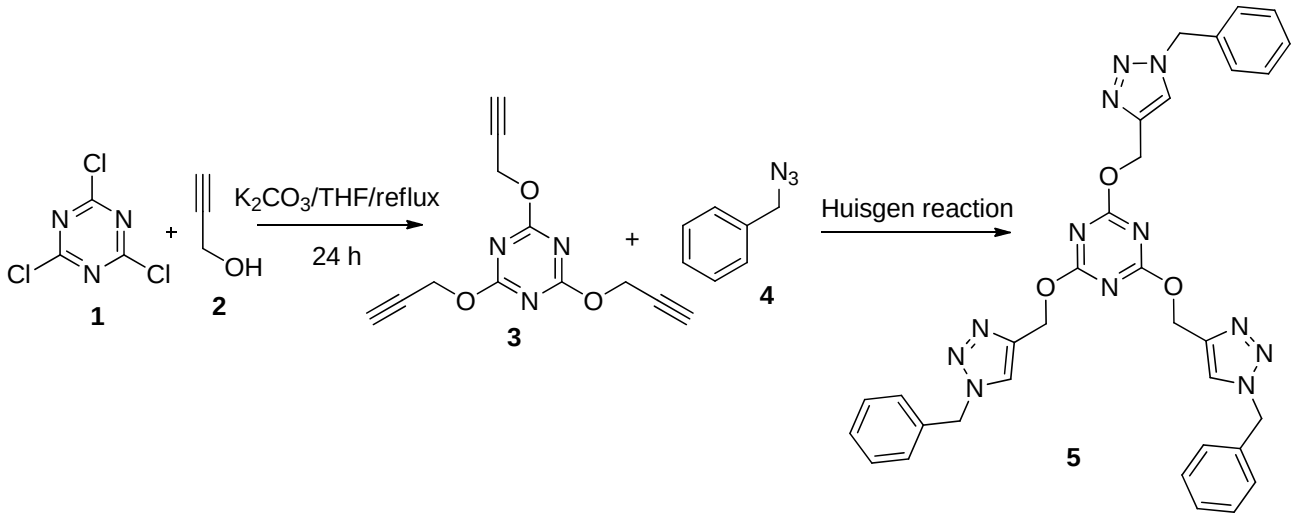
The synthesis of 2,4,6-tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methoxy]-1,3,5-triazine and N^2, N^4, N^6-tris[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]-1,3,5-triazine-2,4,6-triamine from cyanurate and melamine alkyne derivatives by Huisgen reaction is described.

Introduction

Copper catalyzed Huisgen reaction is a widespread tool in click chemistry.[1] However there are few examples about its use in the building of molecules based in a cyanurate core with C_3 symmetry.

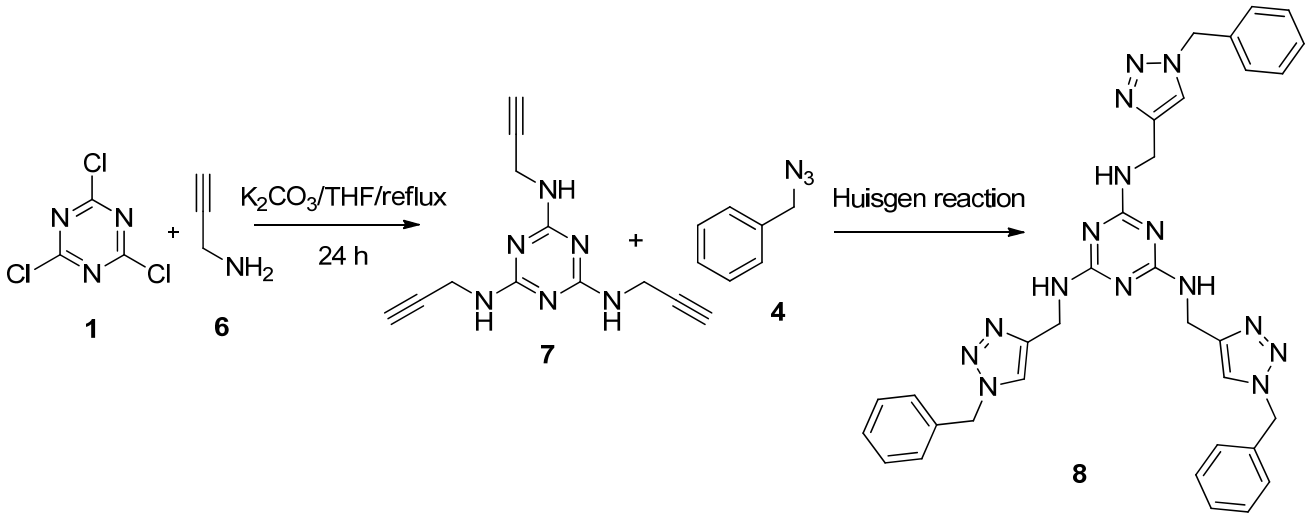
Results and discussion

In this communication we present the viability of the synthesis of 1,2,3-triazole derivatives of propargyl cyanurate, in order to check the possibility of its use as core for dendrimers. Among the various methods available in literature for the synthesis of 2,4,6-tris(prop-2-yn-1-yloxy)-1,3,5-triazine, the one using potassium carbonate and propargyl alcohol in THF under reflux was followed.[2-3] The trispropargyl cyanurate **3** was reacted with benzyl azide under Huisgen reaction conditions[4] (DMF, copper sulfate and sodium ascorbate) rendering 2,4,6-tris((1-benzyl-1*H*-1,2,3-triazol-4-yl)methoxy)-1,3,5-triazine (**5**) in 46% yield after column chromatography purification (Scheme 1). The ^{1}H-NMR of this compound shows a singlet at δ 7.63 ppm corresponding at the vinylic proton of triazole ring, but only one peak for the two CH_2 groups at δ 5.51 ppm since they have the same chemical shift, however in the ^{13}C-NMR spectrum there are two different signal for these groups one at δ 61.72 ppm and the other at δ 54.55 ppm.



Scheme 1

The synthesis of N^2,N^4,N^6-tri(prop-2-yn-1-yl)-1,3,5-triazine-2,4,6-triamine (**3**) was carried out with cyanuric chloride (**1**) and propargylamine (**6**). This tripropargyl melamine[5] was treated with benzyl azide under the same conditions yielding N^2,N^4,N^6-tris((1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl)-1,3,5-triazine-2,4,6-triamine (**8**) in 90% yield (Scheme 2). In this compound the ^{1}H-NMR spectrum shows to different signals for CH_2 groups, one as singlet at δ 5.51pp and other as broad doublet δ= 4.44 ppm. In the ^{13}C-NMR spectrum there are two peaks corresponding to two methylene groups at δ 53.36 and 35.95 ppm. This compound was not synthesized before.



Scheme 2

Conclusions

In conclusion, we have developed a straightforward method to synthesize 1*H*-1,2,3-triazoles with C_3 symmetry derived of tripropargyl cyanurate or melamine by Huisgen reaction. Now we are studying the synthesis of derivatives functionalized in the benzene

ring to obtain dendrimer compounds. This method is very promising to apply to the synthesis of dendrimers since the triazole linker has proven to be resistant under acidic or nucleophilic sol–gel conditions.

Acknowledgements

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Experimental

General Procedure. *Synthesis of 2,4,6-tris((1-benzyl-1H-1,2,3-triazol-4-yl)methoxy)-1,3,5-triazine (**5**).* Benzylazide (466 mg, 3.5 mmol) was added dropwise to a mixture of alkyne **3** (243 mg, 1mmol) and sodium ascorbate dissolved in DMF (6 mL) with stirring. Then a solution de copper(II) sulfate was slowly added. After 1 day, water (100 mL) and EtOAc (100 mL) was added, the appearing solid was isolated by filtered and purified by flash column (silica gel 3% MeOH in CH_2Cl_2). Yield 46%. ^{1}H-NMR (300 MHz, DMSO-d_6) δ 7.63 (s, 1H, C=CH), 7.35 (m, 3H), 7.26 (2H), 5.51 (s, 4H, 2 x CH_2). ^{13}C-NMR (75 MHz, DMSO-d_6) δ 172.9, 142.8, 134.6, 129.4, 129.0, 128.4, 124.0, 61.7, 54.5.

*N^2,N^4,N^6-tris((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-1,3,5-triazine-2,4,6-triamine (**8**).* ^{1}H-NMR (300 MHz, DMSO-d_6) δ 7.92 (s, 1H, C=CH), 7.32-7.26 (m, 5H), 6.85 (br s, 1H, NH), 5.51 (s, 2H, $PhCH_2$), 4.44 (d, 2H, CH_2N, J= 5.6 Hz). ^{13}C-NMR (75 MHz, DMSO-d_6) δ 166.4, 146.9, 136.6, 129.3, 128.7, 128.4, 123.7, 53.6, 36.2.

References

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