Highly Diastereoselective Synthesis of a Novel Functionalized Benzocyclotrimer

Musa Erdoğan,[a] **Selçuk Eşsiz,**[a] **Fabrizio Fabris,**[b] **and Arif Daştan** [a,]*

[a]*Department of Chemistry, Ataturk University, Faculty of Sciences, Erzurum, Turkey*

[b]*Dipartimento di Scienze Molecolari e Nanosistemi, Università Ca' Foscari di Venezia, Venezia, Italy*

**Corresponding author: +90(442)2314109, adastan@atauni.edu.tr*

Abstract: The high yielding synthesis of a novel benzocyclotrimer is herein presented. The *syn*-diastereomer is obtained as major product, presumably in virtue of the presence of oxa-bridge of the bicylic components. The three oxa-bridges can be used for further functionalization, as well as the six bromine atoms of the three aromatic rings, as demonstrated in the aromatization of the a mixture of *anti*-**6** and *syn*-**6** (3:7) leading to trinaphthylene **7**.

Keywords: Cyclotrimerization, copper, cup-shaped molecules

1. Introduction

Benzocyclotrimers[1] are rigid molecules characterized by one or two cavities, which have been successfully employed in supramolecular chemistry.[2] amongst these, benzocyclotrimers bearing aromatic rings are characterized by large stiff cavities. The cavities are particularly deep and suitable for supramolecular applications in the case of the more symmetrical *syn*-diastereomer, which is generally obtained in lower amounts. In this report we describe the highly diastereoselective synthesis of the benzocyclotrimer *syn*-**6**, displaying one rigid and functionalized hemi-cavity in the bottom of the structure, concomitantly with three relatively reactive oxa-bridges (Figure 1). The reactivity of these moieties can be conveniently used for further functionalization of the less valuable diastereomer *anti*-**6**, which furnished the more symmetrical trinaphtylene **7** (Figure 1).

2. Experimental

*Cyclotrimerization of the vinylstannane (**5**) and Synthesis of syn- and anti-7,8,17,18,27,28-hexabromo-31,32,33-trioxadecacyclo[22.6.1.1^{4,11}.1^{14,21}.0^{2,23}.0^{3,12}.0^{5,10}.0^{13,22}.0^{15,20}.0^{25,30}]tritriaconta-2,5,7,9,12,15,17,19,22,25,27,29-dodecaene (syn-**6**) and (anti-**6**)*

In a flame dried 50-ml two-necked round-bottomed flask fitted with a nitrogen inlet, copper(I) 2-thiophenecarboxylate (CuTC) (0.13 g, 0.69 mmol) was introduced, purging with nitrogen and capping with a rubber septum. The reactor was cooled to -20° and consecutively dry NMP (15 ml) and bromostannyl-olefin **5** (0.25 g, 0.46 mmol) were added via syringe. The reaction evolution was monitored by ^{1}H-NMR spectroscopy. After 30 min, an aqueous 10% NH_3 solution (20 ml) was added and the mixture was stirred until the brown solid disappeared. The mixture was extracted with diethyl ether (3 × 20 ml) and the combined ethereal extracts were dried over $MgSO_4$. Volatile materials were removed in *vacuo*, and the residue was purified by column chromatography on neutral aluminum oxide with EtOAc/*n*-hexane (3:7) as eluent and cyclotrimers *syn*-**6** and *anti*-**6**-was obtained.

3. Results and discussion

The starting material for the synthesis of the benzocyclotrimers *syn*-**6** and *anti*-**6** is *vic*-bromostannane **5**, which obtained from commercially available 1,2,4,5-tetrabromobenzene **1**. The key reagent **5** for the cyclotrimerization is obtained either by lithium-de-protonation of halide **3** with lithium diisopropylamide (LDA), or by lithium-de-bromination of the dibromide **4** with *n*-butyl lithium, followed in both cases by *trans*-metalation with trimethyltin chloride, furnishing the desired stannane **5** in 96% yields in both cases. The high chemo-selectivity of the lithium-de-bromination observed in the second approach is surprisingly high: indeed, the bromine atoms of the aromatic ring resulted completely unaffected by the metalating agent.

In order to accomplish the cyclotrimerization, the *vic*-bromostannane **5** is treated with copper(I) 2-thiophenecarboxylate (CuTC) in dry NMP at low temperature. The two isomeric benzocyclotrimers are obtained in a highly favourable 7:3 *syn* to *anti* ratio and in a very good isolated yield (92%).

The cyclotrimers *syn*-**6** and *anti*-**6** are a potential source of polyaromatic rings. When *syn*-**6** and *anti*-**6** is treated with titanium(III), generated *in situ* from TiCl$_4$, lithium aluminumhydride (LAH) and triethylamine (TEA) in refluxing THF, a quantitative yield of trinaphthylene **7** is obtained.

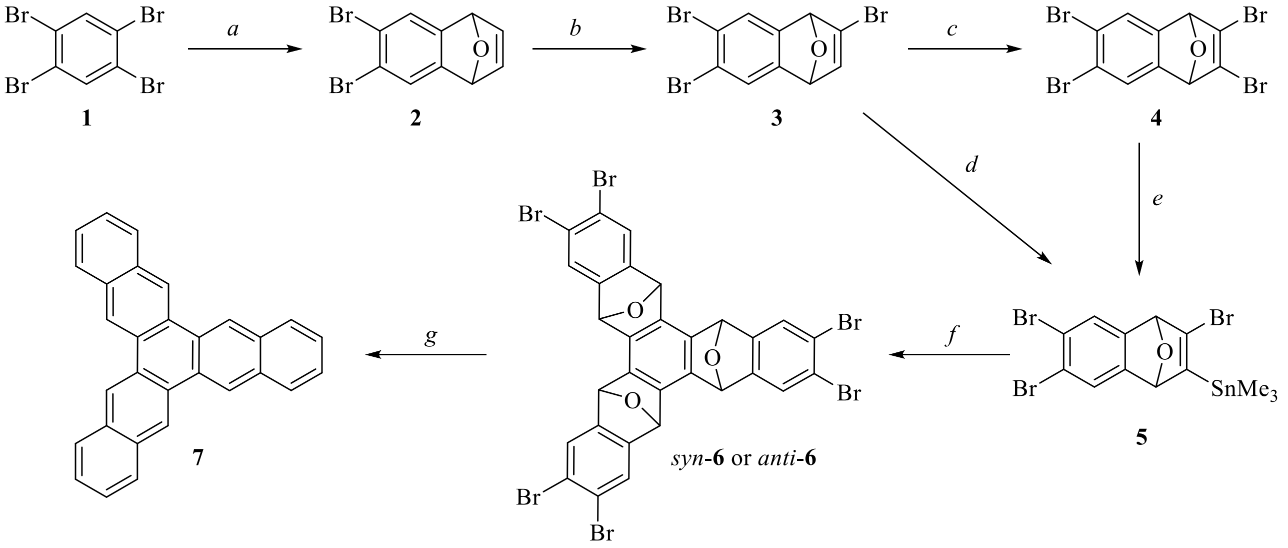

Figure 1.

a) *i*) *n*-BuLi; *ii*) furan in toluene, -78° to r.t.) *b*) *i*) DBTCE, in CCl$_4$, hυ ; *ii*) *t*-BuOK in THF, reflux. *c*) *i*) Br$_2$ in CCl$_4$, reflux. ; *ii*) *t*-BuOK in THF, reflux d) *i*) LDA; *ii*) Me$_3$SnCl in THF, -78° to r.t. *e*) *i*) *n*-BuLi; *ii*) Me$_3$SnCl in THF, -78° to r.t. *f*) CuTC in NMP, -20° *g*) TiCl$_4$, LAH, TEA in THF, reflux.

4. Conclusions

In conclusion, a straightforward and high yielding synthesis of a new benzocyclotrimer was studied. The cyclotrimerization reaction afforded the two possible diastereomers *syn* to *anti* in a very favourable 7:3 ratio. The more valuable *syn*-diastereomer will be considered for supramolecular applications. In the other hand, *anti* and *syn* diastereomers can be conveniently employed for the preparation of polyaromatic structures.

References

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