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Alternatively Modified Bingel Reaction for Efficient Syntheses of C_{60} Hexakis-Adducts

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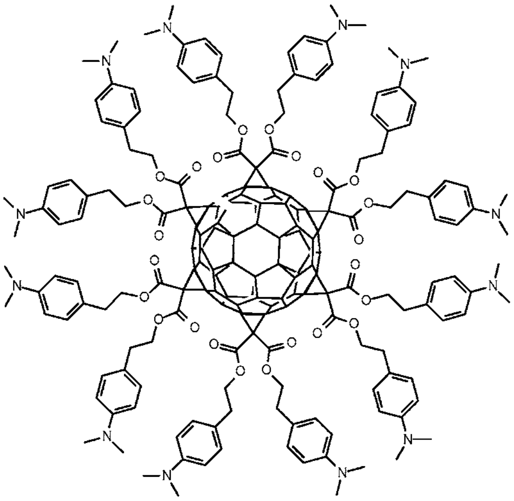
ABSTRACT



It was found that the C_{60} hexakis-adduct (T_h) bearing 12 electron-donating *N*,*N*-dimethylaniline moieties could not be synthesized by the Bingel–Hirsch method with either classical or deviated experimental parameters in a one-pot reaction. A different modification to the original Bingel reaction without the use of any templating agent was necessary for high-yield synthesis of the compound. The generalization of this alternatively modified Bingel method to the preparation of other C_{60} hexakis-adducts is demonstrated.

Hexakis-adducts of fullerene C_{60} represent a unique class of three-dimensionally symmetric (T_h) macromolecular structures,[1−5] with nanoscale dimensions and stoichiometrically defined chemical compositions. Their interesting properties as materials and their biocompatibility and potential biological applications have received much recent attention.[6−8]

Most of the available C_{60} hexakis-adducts bear the Bingel methano addition pattern.[5,9,10] However, the original Bingel reaction conditions[9] were found to be generally ineffective

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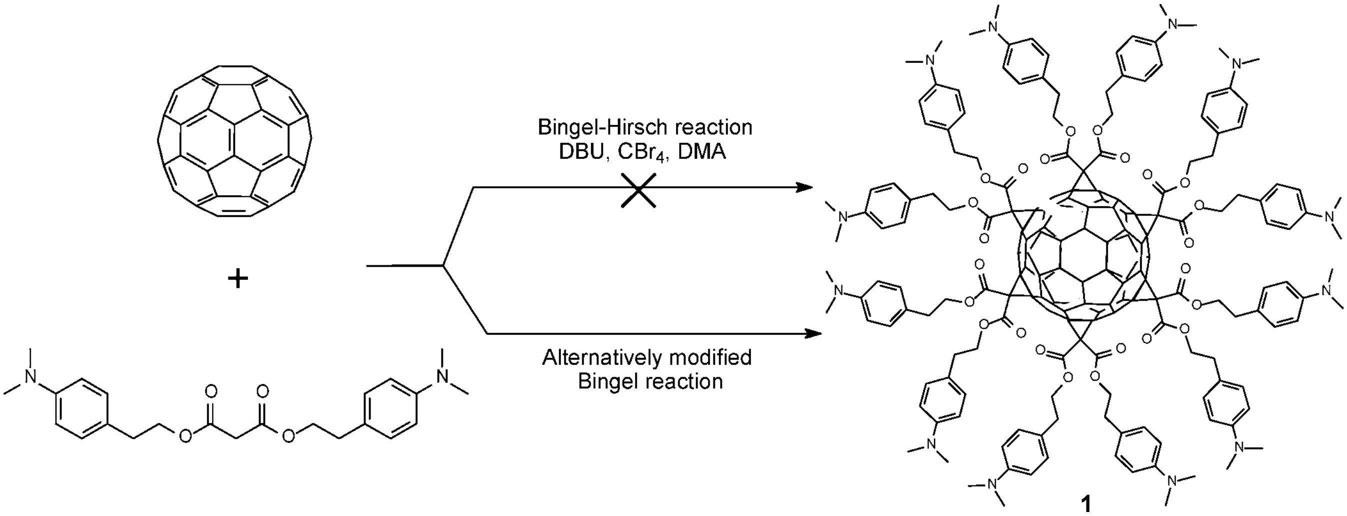
Scheme 1. Hexakis-Addition of Bis(4-(*N*,*N*-dimethylamino)phenethyl) Malonate to C_{60}



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in the hexakis-addition, and the modification by Hirsch and co-workers to include a templating agent such as 9,10-dimethylanthracene in one-pot addition reactions has since become classical.[5] The modified Bingel (often called the Bingel−Hirsch method) has generally been successful for relatively simple hexakis-adducts, such as those from the addition of dialkyl malonates, with yields up to 50−60%.[5,10−12] For structurally more complicated hexakis-adducts, the Bingel−Hirsch reaction conditions suffer from generally low product yields or even negligible yields in some cases.[5,6,12,13] For example, the yields in the hexakis-addition of first- and second-generation trisubstituted benzene-based dendra to C_{60} were 5.4% and 2%, respectively.[13] Recently, it was shown that a relatively simple deviation from the classical Bingel−Hirsch reaction parameters could improve substantially the yields in the one-pot preparation of C_{60} hexakis-adducts bearing 12 tethered pyrene moieties,[12] suggesting that there is still great potential in further developing the hexakis-addition method to efficiently produce C_{60}-centered T_h-symmetric macromolecules of diverse tethers and functionalities.

In the synthesis of the C_{60} hexakis-adduct bearing 12 electron-donating *N*,*N*-dimethylaniline units (**1**), we found that the compound could not be made in a meaningful yield by the Bingel−Hirsch method with either the classical or deviated experimental parameters. A different modification to the original Bingel reaction without the use of any templating agent was necessary for high-yield synthesis of the compound. The generalization of this alternatively modified Bingel method to the preparation of other C_{60} hexakis-adducts is demonstrated.

For the addition, bis(4-(*N*,*N*-dimethylamino)phenethyl) malonate was synthesized and fully characterized. Despite repeated attempts, however, the classical Hirsch modification to the Bingel reaction with 9,10-dimethylanthracene as the templating agent (Scheme 1) resulted in no detectable yield of the targeted compound **1**. Instead, the compound was readily synthesized in a different modification to the original Bingel reaction with the use of a larger excess of carbon tetrabromide but without any templating agent (Scheme 1). In a typical experiment, a solution of C_{60} (36 mg, 0.05 mmol) in *o*-dichlorobenzene (10 mL) was prepared, and to the solution were added bis(4-(*N*,*N*-dimethylamino)phenethyl) malonate (200 mg, 0.5 mmol), CBr_4 (1.67 g, 5 mmol), and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 150 mg, 0.1 mmol). The mixture was stirred for 24 h, followed by the removal of the solvent *o*-dichlorobenzene. The resulting sample was separated on a silica-gel column (chloroform with 3 vol % of pyridine as eluent) in a relatively straightforward fashion to obtain **1** (105 mg, 68% yield). The chemical structure of **1** was confirmed in terms of NMR and matrix-assisted laser desorption−time-of-flight (MALDI−TOF) MS analyses. Both ^{1}H and ^{13}C NMR spectra (Figure 1) of the compound in $CDCl_3$ solution are characteristic of a hexakis-adduct of C_{60}.[5,14] For example, the simple ^{13}C NMR signals of only three peaks for the fullerene cage (145, 141,

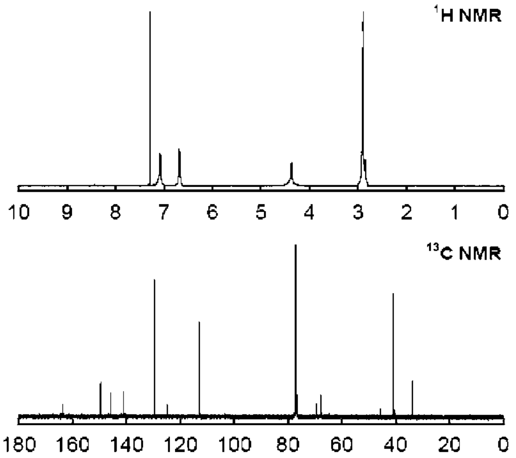


Figure 1. ^{1}H (top) and ^{13}C NMR (bottom) spectra of **1**.

and 69 ppm) represent a classic indication for the high molecular symmetry (T_h). Shown in Figure 2 is a comparison of the MALDI−TOF MS pattern of **1** with the prediction on the basis of isotopic populations (IsoPro 3.0). It is an excellent match, with the expected peak mass of 3097 Da ($C_{198}H_{168}O_{24}N_{12}$).

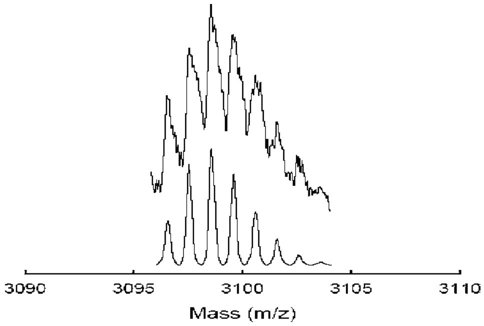
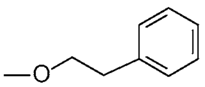
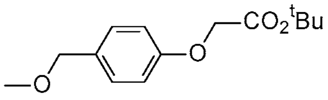
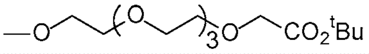


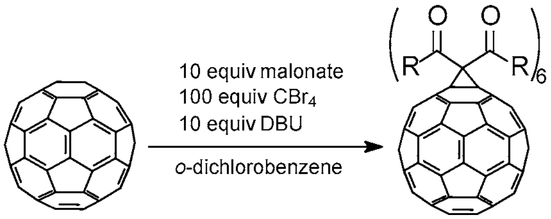
Figure 2. MALDI-TOF MS spectra of **1**: top (observed), bottom (calculated from IsoPro 3.0).

The successful synthesis of **1** in the absence of 9,10-dimethylanthracene suggests that the use of a templating agent to activate and regulate the hexakis-addition onto the C_{60} core is hardly mandatory, as widely accepted in the literature. In fact, its presence impairs the hexakis-addition in the specific case shown in Scheme 1. This may be related to the fact that *N*,*N*-dimethylaniline moieties are strong electron donors, with their known redox interactions with the C_{60} cage in ambient solution.[15,16] On the other hand, the large excess in CBr_4 obviously promotes the hexakis-addition, as also observed in the synthesis of other hexakis-adducts.[12] Even in the monoaddition experiment, the use of the same large excess in CBr_4 resulted in **1** in 15% yield instead of the intended monoadduct. Other control experiments suggest that a lower concentration of either CBr_4 or DBU corresponds to a lower yield of **1**.

This alternatively modified Bingel reaction is applicable to the synthesis of other C_{60} hexakis-adducts that may or may not be obtained by the classical Hirsch modification. As shown in Table 1, the product yields are generally high.

Table 1. C_{60} Hexakis-Addition with Different Malonates

compound	—R	yield (%)
2		68
3		65
4		40



In summary, the alternatively modified Bingel reaction reported here is necessary for the synthesis of some structurally unique C_{60} hexakis-adducts. It at least complements the classical Bingel−Hirsch method for efficient one-pot hexakis-addition. With the demonstrated efficient synthesis of several C_{60} hexakis-adducts, the general applicability of the reported reaction to C_{60} hexakis-adducts that can otherwise be prepared by the classical Bingel−Hirsch method may be expected. Nevertheless, further investigations are required for a more systematic verification.

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Supporting Information Available: Experimental procedures and spectral characterization for bis(4-(*N*,*N*-dimethylamino)phenethyl)malonate and hexakis-adducts **1**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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