Synthesis and NMR Characterisation of Mono- and Bis-methano[60]fulleryl Amino Acid Derivatives and their Reductive Ring-Opening Retro-Bingel Reactions

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The pioneering investigations into the chemical reactivity of [60]fullerene have provided a precedent towards the design and synthesis of novel and sophisticated architectures that may have applications in medicinal chemistry and the material sciences.[1,2] Further, with the increasing degree of complexity of fulleryl derivatives comes the necessity for a larger range of reliable techniques for the unequivocal characterization of such molecules. Such techniques should rely heavily on direct methods of characterization (*e.g.* NMR spectroscopy) rather than the current, well used comparative techniques.

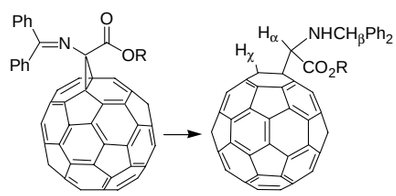
With these principles in mind we embarked on a program to investigate the regioselective synthesis and characterization of fulleryl derivatives with multiple amino acid functionalities with a view to utilize such molecules as templates for molecules to be used in nanotechnology.

Therefore, the addition of *N*-(diphenylmethylene)glycinate esters ($Ph_2C{=}NCH_2CO_2R$) to [60]fullerene under Bingel conditions gives methano[60]fulleryl iminoesters (**1**, Figure 1)which upon treatment of with sodium cyanoborohydride, in the presence of a protic or a Lewis acid results in a novel reductive ring-opening reaction giving the corresponding 1,2-dihydro[60]fulleryl glycine derivatives (**2**, Figure 1).[3]

Using the corresponding tethered bis-*N*-(diphenylmethylene)glycinate esters derived from *meta*- and *para*-benzenedimethanol scaffolds, the corresponding bis-methano[60]fulleryl iminoesters were synthesised under double Bingel reaction conditions. The *meta*-benzenedimethanol derivative gave the *trans*-4 and *cis*-3 regioisomeric bisadducts (see **3**, Figure 2) whereas the analogous *para*-tethered derivative afforded the *trans*-3 and *trans*-4 regioisomers.[4] The regiochemistry of the major bisadducts were unequivocally determined using 2D INADEQUATE and C-C TOCSY NMR experiments.[5] The regiochemistry of these bis-additions were unexpected based on literature precedents. These results unequivocally show that the regiochemistry of tethered bis-additions is not solely dependent on the nature of the tether alone.

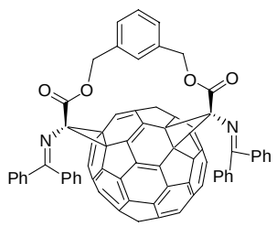
Additionally, a mixture of the *trans*-4 and *cis*-3 non-symmetrical bisadducts was obtained from the double Bingel cyclopropanation of a bis-*N*-(diphenylmethylene)glycinate tether based on a 1,3-naphthyldimethanol scaffold. The regiochemistry of these compounds were identified by correlation with the corresponding diethyl esters derivatives prepared by trans-esterification. Reductive ring-opening reactions on the napthyl-tethered bis-methano[60]fullerenes gave none of the expected bis-fullerylglycinates rather the reductive ring-opening-retro-Bingel products, the 1,2-dihydro[60]fullerylglycinates. These compounds resulted from the reductive ring-opening of one methanoimino ester moiety and a retro-Bingel reaction of the other.[6] Under analogous reductive ring-opening-retro-Bingel conditions, the non-tethered bis-methano[60]fullerene derivative afforded the 1,2-dihydro[60]fullerylglycinate. Thus it was concluded that the tether was not the driving force for the reductive elimination of one of the methano groups

This study clearly demonstrates that much has yet to be understood about tethered fullerene reactions before generalizations on regiochemical outcomes can be made. These differences in regiochemistry may indicate that these reactions proceed *via* different mechanisms and experiments are in progress to understand these differences. Futhermore, we have demonstrated the importance of 2D INADEQUATE NMR experiments for the unequivocal assignment of the regiochemistry of [60]fulleryl bisadducts which are more superior than the more widely used comparative techniques (UV-visible).



1 **2**

Figure 1: Fulleryl amino acids and the reductive ring-opened products.



3
cis-3, C_2

Figure 2: Bisaddition yielding bis-methano[60]fulleryl iminoesters.

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