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Soccer goes BOXing: Synthetic access to novel [6 : 0] hexakis[(bisoxazoliny) methano]fullerenes

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The syntheses of [6 : 0] hexakis[(bisoxazoliny)methano]fullerenes are presented. Two derivatives could be directly obtained using conditions developed by the Sun group. For the remaining products, a two stage protocol had to be developed. All compounds were obtained in synthetically useful scales and were purified via column chromatography with standard achiral phase. These new fullerene adducts bear six metal-chelation sites which are aligned in the three orthogonal space directions and are disposed on a completely rigid scaffold. First experiments indicate that the generation of six-fold metal-complexes is possible with these structures. This makes them very appealing as ligands in asymmetric catalysis and as building blocks in higher supra-molecular assemblies.

Just about two decades after the discovery of C₆₀ Buckminster fullerene, carbon allotropes – fullerenes, nanotubes and graphene – have become increasingly important in material sciences^{1–9}. Fullerenes are widely known and used as electron acceptors. Beside their electro-chemical properties, several fullerene adducts also possess optical activity, which is often beneficial and sometimes essential for applications in asymmetric synthesis or racemic resolution^{10–14}.

Over the years, different methods for the functionalization of the fullerene core have appeared^{15–22}. Chiral fullerene adducts are either generated through an inherent chiral addition pattern, through chiral addends or a combination of both^{10c}. Hirsch was the first to prepare enantiomerically pure bis- and tris[bis(4-phenyl-2-oxazoline)methano]fullerenes with inherent chiral addition arrangements^{23,24}. Later, his group extended this strategy to bis(4-phenyl-2-oxazoline) derivatives bearing an inherently chiral [3 : 3] hexaaddition pattern and used these structures as auxiliaries in stereoselective cyclopropanation reactions²⁵. Related systems have also been published by Echegoyen²⁶ and Rubin²⁷.

Results

Herein, we report the syntheses of the first enantiomerically pure [6 : 0]hexakis[(bisoxazoliny)methano]fullerenes **2** and the generation of several six-fold metal-complexes based on these compounds. These fullerene structures are not only aesthetically appealing, but also the first purely organic structures offering six metal-chelating sites disposed on a completely rigid scaffold and aligned according to the three orthogonal space directions there are some other completely rigid organic compounds bearing six metal-chelation sites. These do however possess a lower symmetry than the described fullerene adducts²⁸. Potential applications should be found in asymmetric catalysis and as tectons in enantiomerically pure self-assembled supra-molecular structures.

Discussion

Derivatives **2a–c** were obtained via cyclopropanation of C₆₀ with the corresponding C₂-symmetrical enantiomerically pure bis(oxazolines) **1a–c**²⁹ followed by simple silica column chromatography. The reaction conditions initially used by Hirsch to prepare bis- and tris[bis(oxazoliny)methano]fullerene derivatives were not suitable for six-fold addition^{23,25}, as they only yielded mixtures of lower oligo adducts. The latter could not be separated on achiral stationary phases. However, using the conditions reported by Sun with a 100-fold excess of CBr₄ (Conditions A)³⁰, both enantiomers of the phenyl derivatives *all-S-2a* and *all-R-2a* were obtained in 32% and 31% yield respectively (Fig. 3 and Table 1, Entries 1,2).

SUBJECT AREAS:

STEREOCHEMISTRY

METHODOLOGY

REACTION MECHANISMS

COORDINATION CHEMISTRY

Received
29 April 2013

Accepted
21 August 2013

Published
2 October 2013

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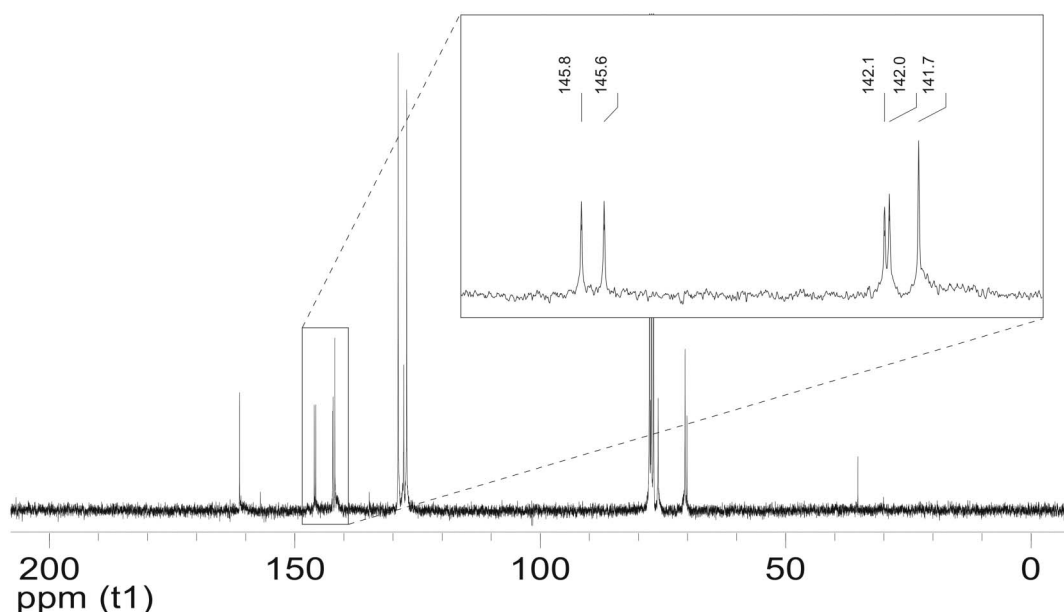


Figure 1 | ^{13}C NMR spectra of compound 2a.

Conditions A proved however to be inadequate for the preparation of compounds 2b–c. In all cases, no hexakis derivatives bearing the desired geometry could be found. One of the major products was a pentakis adduct with an addition pattern not leading to the desired octahedral hexakis adducts (results not shown)³¹. In order to circumvent this problem, we turned to the 9,10-dimethylantracene (DMA) template-directed activation developed by Hirsch, which is known to generate exclusively the desired penta- and consequently hexakis-regioisomers with an octahedral addition pattern³¹.

With this method hexakis adducts 2b–c could be obtained. However, the [5 : 1] hexakis bis(oxazoline)/DMA adduct was in all cases a major side product in these reactions and could not be completely separated from the [6 : 0] compound. These [5 : 1] adducts did not further react under the Hirsch conditions, but yielded the corresponding [6 : 0] hexakis[bis(oxazoliny)methano]fullerenes 2b–c when first heated to 60°C for 30 min and then reacted with CBr_4 (3 eq.), BOX (3 eq.) and DBU (6 eq.) in *o*-DCB (Conditions B)

(Table 1, Entries 3–5)³⁰. Hence, applying either protocols A or B gave access to a whole series of hexakis[bis(oxazoline)] adducts in good to excellent overall yields.

^1H and ^{13}C NMR analyses confirm the octahedral addition pattern of compounds 2. The four observed ^{13}C signals at 142.0, 142.1, 145.5, and 145.9 ppm are in agreement with the chiral tetrahedral (*T*) point group symmetry (Figure 1). These BOX-fullerene adducts are actually less symmetric than most [6 : 0] hexakis adducts bearing pyritohedral symmetry (T_h)³².

Hirsch proved that a fullerene multi-adduct is obtained as diastereomers if C_{60} is reacted with enantiomerically pure addends, which arrange in an inherently chiral addition pattern^{23b}. Hexakis adducts with an octahedral [6 : 0] addition pattern have achiral tetrahedral symmetry. Such adducts can consequently only exhibit axial chirality generated through their chiral addends. Thus, all [6 : 0] hexakis[bis(oxazoliny)methano]fullerenes generated from enantiomerically pure BOX 1 were obtained as single enantiomer. Optical rotation

all-(*R*)-2a (blue) and *all*-(*S*)-2a (red)

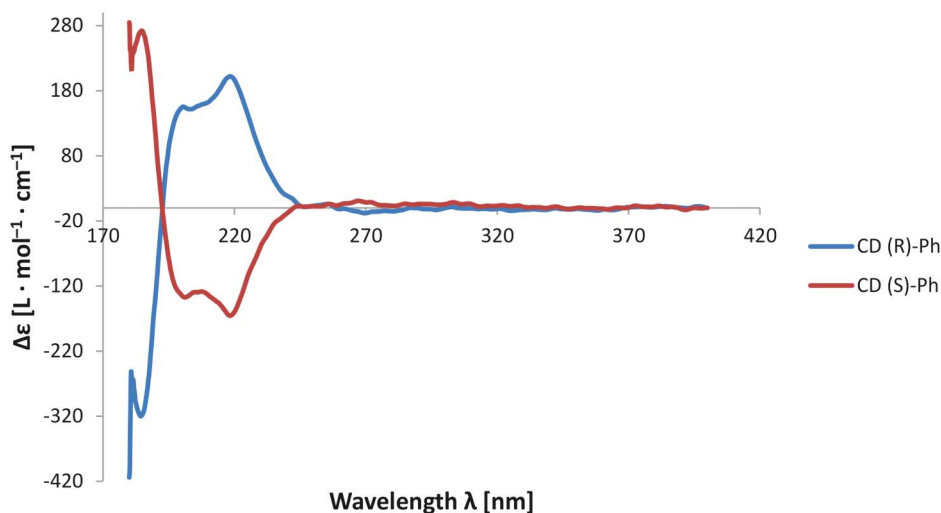


Figure 2 | CD spectra of *all*-*S*-2a (red) and *all*-*R*-2a (blue). Concentrations in trifluoroethanol (TFE): *all*-*R*-2a: 0.058 mg/mL, *all*-*S*-2a: 0.060 mg/mL.

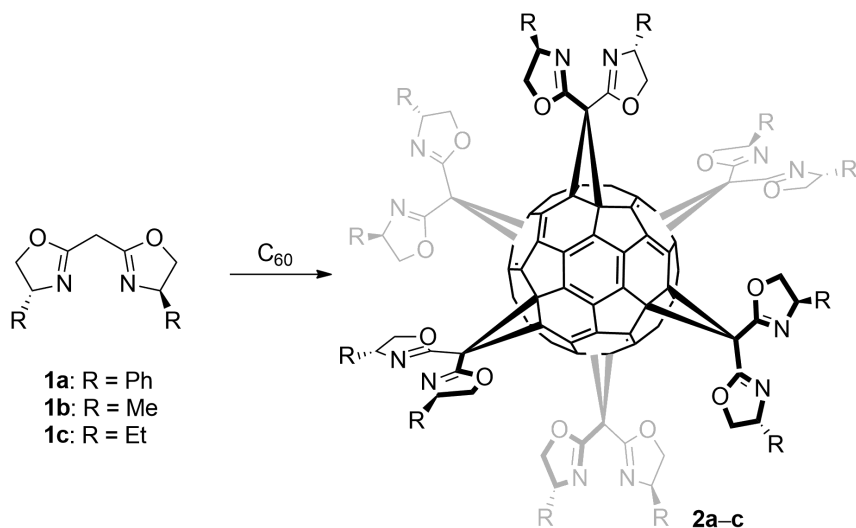


Figure 3 | (Relating to Table 1) Reagents for the six-fold cyclopropanation reaction.

and CD spectra show the enantiomeric relationship of (*all-S-2a/all-R-2a*) and (*all-S-2b/all-R-2b*) (see Figure 2 and SI).

With compounds **2** in hand, we investigated their capacity to build six-fold metal-complexes. Compounds *all-S-2a* and *all-S-2b* were treated with [(PhCN)₂PdCl₂] (10 eq.) and in a third test *all-S-2a* was reacted with [CuI] (10 eq.). In all three cases, the recovered precipitate proved to be insoluble in conventional solvents. The six-fold complexes could however be detected by mass spectrometry (see SI). In each case, several fragments containing six metal-ions and (6-*n*) chloride ions were detected (*n* = 1 to 6). This strongly indicates the formation of six-fold metal-complexes. Due to the weakly bound chloride ions it was not possible to detect the [2Pd₆Cl₁₂] species.

We have presented the first synthetic access to [6:0] hexakis[(bisoxazoliny)methano]fullerenes. These compounds provide an all organic rigid scaffold bearing six metal-chelation sites, which are orthogonally directed. Preliminary experiments indicate that the generation of six-fold metal-complexes is possible. We are currently working to improve the solubility of such metal-complexes in order to purify and completely characterize them.

Methods

Synthesis of *all-(R)-2a*. BOX derivative (*R,R*)-**1a** (1.28 g, 4.16 mmol, 10.0 eq.), CBr₄ (13.8 g, 41.6 mmol, 100 eq.), C₆₀ (300 mg, 416 μmol, 1.00 eq.) and DBU (1.25 g, 8.32 mmol, 20.0 eq.) were reacted in dry *o*-DCB (90.0 mL) as described above. After 72 h of stirring at ambient temperature, the reaction mixture was poured into 300 mL of cyclohexane to remove the *o*-DCB. The precipitate was filtered off and abundantly washed with cyclohexane. After column chromatography (toluene/ethyl acetate (9:1) + 5% EtOH + 0.2% NEt₃) the hexakis fullerene adduct *all-(R)-2a* was obtained as a brown solid in 31% yield. – Mp: decomposition at T > 286°C. – IR (KBr): $\tilde{\nu}$ = 2896 (vw), 2161 (vw), 2043 (vw), 1657 (vw), 1493 (vw), 1452 (vw), 1355 (vw), 1188 (vw), 1082 (vw), 980 (vw), 928 (vw), 749 (vw), 698 (w), 594 (vw), 526 (vw), 420 (vw)

cm⁻¹. – UV/VIS (CHCl₃): λ_{\max} (log ϵ) = 181 (7.7), 186 (7.7), 211 (7.4), 272 (6.9) nm. – [α]_D²⁰ (c = 0.038, THF): –101° mL·dm⁻¹·g⁻¹. – ¹H-NMR (500 MHz, CDCl₃): δ = 4.29 (dd, ³J = 8.3 Hz, 12 H, 5-*H*), 4.80 (dd, ²J = 10.0 Hz, ³J = 8.7 Hz, 12 H, 5-*H*), 5.44 (dd, ²J = 10.0 Hz, ³J = 8.3 Hz, 12 H, 4-*H*), 7.32–7.35 (m, 60 H, Ph-*H*) ppm. – ¹³C-NMR (125 MHz, CDCl₃): δ = 34.9 (Cp-C_{ap}), 69.8 (C-5), 70.2 (C₆₀-C_{sp3}), 75.1 (C-4), 127.0 (Ph-C_m), 127.6 (Ph-C_p), 128.7 (Ph-C_o), 141.7 (Ph-C_i), 142.0 (C₆₀-C_{sp2}), 142.1 (C₆₀-C_{sp2}), 145.6 (C₆₀-C_{sp2}), 145.8 (C₆₀-C_{sp2}), 161.1 (C = N) ppm. – MS (FAB, 3-NBA) *m/z* (%): 2544 (55) [M]⁺, 2412 (9), 2240 (4), 769 (28), 719 (100).

Synthesis of *all-R-2b*. C₆₀ (360 mg, 500 μmol, 1.00 eq.) and DMA (1.03 g, 5.00 mmol, 10.0 eq.) were stirred for 1 h in dry toluene (210 mL). Then bisoxazolone (*R,R*)-**1b** (911 mg, 5.00 mmol, 10.0 eq.) and CBr₄ (1.66 g, 5.00 mmol, 10.0 eq.) were added and during 20 min DBU (1.52 g, 10.0 mmol, 20.0 eq.) was dropped into the solution. After 72 h of stirring under argon, the solvent was evaporated and the crude product was subjected to column chromatography (toluene/ethyl acetate (9:1) + 20% EtOH + 0.2% NEt₃). The product obtained that way was dissolved in dichloromethane (3 mL) and precipitated by dropping the solution into diethyl ether (100 mL) to remove the silica that was dissolved by the EtOH. That way, besides the pure product, a mixture consisting of the hexakis derivative and some lower adducts was isolated. In a further reaction under conditions c), the latter was converted into the hexakis adduct *vide supra*. The purification of the crude product was carried out as for the first product batch by chromatography and precipitation. Finally the hexakis BOX methanofullerene *all-(R)-2b* was isolated in 19% (168 mg, 90.0 μmol) overall yield. – Mp: decomposition at T > 235°C. – IR (KBr): $\tilde{\nu}$ = 3272 (br, vw), 2965 (w), 2895 (vw), 1657 (w), 1447 (vw), 1354 (w), 1288 (w), 1195 (w), 1103 (w), 1064 (w), 1022 (w), 976 (w), 942 (w), 844 (vw), 709 (w), 665 (vw), 539 (w), 523 (w) cm⁻¹. – UV/VIS (CHCl₃): λ_{\max} (log ϵ) = 213 (7.0) nm. – ¹H-NMR (400 MHz, CDCl₃): δ = 1.29 (d, ³J = 6.5 Hz, 36 H, CH₃), 3.94 (dd, ²J = 7.4 Hz, 12 H, 5-*H*), 4.32–4.37 (m, 12 H, 4-*H*), 4.43 (dd, ²J = 9.2 Hz, ³J = 8.0 Hz, 12 H, 5-*H*) ppm. – ¹³C-NMR (100 MHz, CDCl₃): δ = 21.3 (CH₃), 34.4 (Cp-C_{ap}), 62.0 (C-5), 69.7 (C₆₀-C_{sp3}), 74.7 (C-4), 141.9 (C₆₀-C_{sp2}), 142.1 (C₆₀-C_{sp2}), 145.1 (C₆₀-C_{sp2}), 145.3 (C₆₀-C_{sp2}), 160.0 (C₆₀-C_{sp2}) ppm. – MS (FAB, 3-NBA) *m/z* (%): 1801 (13) [M]⁺, 1621 (8) [M–C₉H₁₂N₂O₂]⁺, 745 (13), 720 (29), 154 (100) [3-NBA].

Table 1 | Reagents and yields for the six-fold cyclopropanation reaction

Entry	R	Conditions	Product	Yield (%)
1	Ph	A	<i>all-S-2a</i>	32
2	Ph	A	<i>all-R-2a</i>	31
3	Me	B	<i>all-S-2b</i>	19
4	Me	B	<i>all-R-2b</i>	19
5	Et	B	<i>all-S-2c</i>	13

A: C₆₀ (1 eq.), CBr₄ (100 eq.), BOX-**2** (10 eq.), DBU (20 eq.), rt, *o*-DCB.

B: C₆₀ (1 eq.), DMA (10 eq.), *o*-DCB, 1 h, r.t., BOX-**2** (10 eq.), CBr₄ (10 eq.), DBU (20 eq.), after column chromatography and heating at 60°C for 30 min. in *o*-DCB, CBr₄ (3 eq.), BOX-**2** (3 eq.), DBU (6 eq.).

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Acknowledgements

This work has been supported by the DFG excellence cluster Center for Functional Nanostructures (CFN), project C1.6.

Author contributions

T.M., C.R. and S.B. wrote the main manuscript text. S.T.S. prepared all the figures and schemes and wrote the supporting information text. All authors reviewed the manuscript.

Additional information

Supplementary information accompanies this paper at <http://www.nature.com/scientificreports>

Competing financial interests: The authors declare no competing financial interests.

How to cite this article: Seifermann, S.M., Réthoré, C., Müller, T. & Bräse, S. Soccer goes BOXing: Synthetic access to novel [6:0] hexakis[bisoxazolynyl]methano]fullerenes. *Sci. Rep.* **3**, 2817; DOI:10.1038/srep02817 (2013).



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