

Proceeding Paper

Hexa-Substituted Hybrid C₆₀ Derivatives with Norbornadiene Fragments: Synthesis and Structure †

Arslan R. Akhmetov *, Zarema R. Sadretdinova, Arthur R. Tulyabaev and Leonard M. Khalilov

Institute of Petrochemistry and Catalysis, Ufa Federal Research Center, Russian Academy of Sciences, 450075 Ufa, Russia; zarema.hairullina18@yandex.ru (Z.R.S.); tulebeich@gmail.com (A.R.T.); khalilovlm@gmail.com (L.M.K.)

* Correspondence: akhmetov_arслан@mail.ru

† Presented at the 27th International Electronic Conference on Synthetic Organic Chemistry (ECSOC-27), 15–30 November 2023; Available online: <https://ecsoc-27.sciforum.net/>.

Abstract: New hybrid fullerene C₆₀ derivatives with five norbornadiene fragments, distant from fullerene core by several methylene groups, were synthesized for the first time. Subsequent photoirradiation of these derivatives leads to only partial (up to 20%) opening of double bonds in norbornadiene fragments to form quadricyclane substituents. It is assumed that the resulting fullerene C₆₀ derivatives can serve as the basis to create high-energy materials.

Keywords: fullerene C₆₀; norbornadiene; photoirradiation; quadricyclane

1. Introduction

Fullerenes and their derivatives attract great attention due to their unique properties that can be used as effective antioxidants [1], solar energy converters [2], semiconductor materials [3], additives for motor oils [4], and modern medicinal products [5]. Such a wide applied significance of fullerene C₆₀ derivatives is due to various methods of its functionalization, among which the most popular are currently the Prato [6] and Bingel-Hirsch reactions [7]. These approaches make it possible to selectively prepare not only mono-, bis-, tris-, but also hexa-adducts of fullerene C₆₀ [8–11] with specified symmetry types, in which addends are located almost throughout the entire fullerene sphere. Besides these studies, there are works devoted to the synthesis of various highly symmetric fullerene C₆₀ polyadducts, when a chlorofullerene C₆₀Cl₆ was used as a starting compound. Indeed, this method makes it possible to obtain various alkoxyfullerenes [12], aminofullerenes [13], sulfides [14] and arylated [15] C₆₀ derivatives, which have particular interest and application in medicine [16,17].

We reported recently [18–21] the synthesis of energy-rich methanofullerenes through the reaction of fullerene C₆₀ with mono- and bis-quadricyclane esters of malonic acid and under the Prato reaction conditions [22]. It was shown that some distance between a quadricyclane fragment and a fullerene core is necessary to maintain the metastable structure of a hybrid fullerene-quadricyclane molecule. At the same time, it seemed interesting and relevant to study the photochemical isomerization of norbornadiene fragments into quadricyclane one in the C₆₀ cycloadducts synthesized.

Considering these facts, we performed a covalent binding of fullerene C₆₀ with norbornadienes and quadricyclanes in this work, where chlorofullerene C₆₀Cl₆ was used as a starting compound. It was assumed that the selective synthesis of C₆₀ adducts containing five addends, according to the method described in the literature [12], will increase the solubility of new hybrid molecules due to a higher number of quadricyclanes attached covalently to a C₆₀ carbon core. The photochemical isomerization of norbornadiene-containing penta-derivatives of fullerene C₆₀ into quadricyclane derivatives was also studied.

Citation: Akhmetov, A.R.; Sadretdinova, Z.R.; Tulyabaev, A.R.; Khalilov, L.M. Hexa-Substituted Hybrid C₆₀ Derivatives with Norbornadiene Fragments: Synthesis and Structure. *2023*, *14*, x. <https://doi.org/10.3390/xxxxx>

Academic Editor(s): Name

Published: 15 November 2023

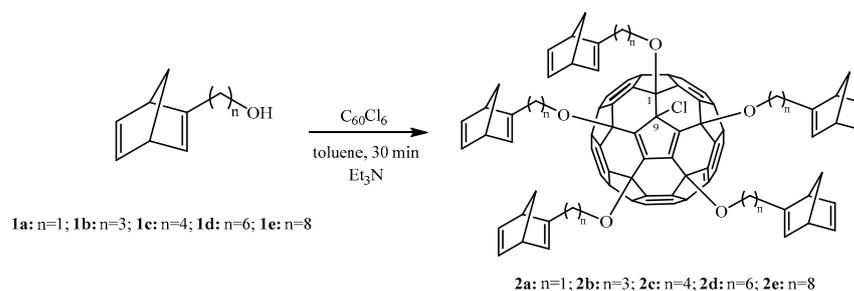


Copyright: © 2023 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

2. Results and Discussion

The interaction between hexachlorofullerene and norbornadiene alcohols **1a–1e** [23,24] at room temperature for 30 min led to the formation of hexa-substituted adducts **2a–2e**, in which the fullerene core was bound to a polycycle fragment through an ether bond. Fullerene polyadducts **2a–2e** were isolated from the reaction mass using preparative HPLC with a chromatographic purity of ~99.9%.

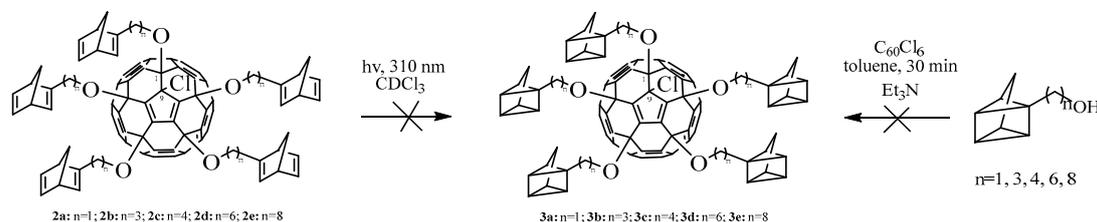
The structure of the compounds **2a–2e** was elucidated with one-dimensional (^1H and ^{13}C) and two-dimensional (^1H – ^1H COSY, ^1H – ^{13}C HSQC, ^1H – ^{13}C HMBC) NMR techniques and MALDI TOF mass spectrometry. High-frequency signals (δ 158.72, 144.39, 142.30, and 133.30 ppm), characteristic of sp^2 hybridized carbon atoms of a norbornadiene fragment, and low-frequency one (δ 73.53, 55.66 and 50.20 ppm), typical of sp^3 carbon atoms of this fragment, for example, are observed in the ^{13}C NMR spectrum of the compound **2e**, in which norbornadiene fragment is removed from a fullerene core to the greatest extent compared to the derivatives **2a–2d**. ^{13}C NMR signals of seven methylene groups appear in low-frequency region at δ 31.73, 30.57, 29.77, 29.63, 27.44, 26.67, and 26.59 ppm, and the signal of a methylene group bound to an oxygen atom is at δ 68.34 ppm. The sp^3 hybridized carbon atom of a fullerene sphere bound to a chlorine one resonates at δ 71.47 ppm in the ^{13}C NMR spectrum, and fullerene carbon atoms in the sp^3 hybridization bound to oxygen atoms give signals at δ 79.39 and 81.66 ppm, which is in agreement with previous published data [12,25]. Fullerene carbon atoms in the sp^2 hybridization give 47 signals at δ 138–154 ppm, of which seven signals have a double relative intensity and the rest have a single one. This indicates that the molecule of this derivative is assigned to a C_1 symmetry point group probably due to the asymmetric arrangement of a norbornadiene fragment at the C-1 fullerene carbon atom relative to conventional symmetry plane passing through the C-1 and C-9 carbon atoms of a fullerene sphere (see Scheme 1 for numbering of carbon atoms) [26]. A molecular ion peak in the MALDI TOF mass spectrum recorded in the negative ion mode at m/z 1851.8505 indicates that five oxooctylnorbornadiene fragments and one chlorine atom are attached to a fullerene sphere, which confirms the proposed structure of the derivative **2e**. Similarly, the molecules of the compounds **2a–2d** are assigned to the C_1 symmetry group, regardless of the length of an alkyl fragment that connects an oxygen atom and a norbornadiene fragment.



Scheme 1. Preparation of hexa-adducts of fullerene C_{60} .

We reported previously [18] that it is impossible to perform the photoisomerization of norbornadiene fragments into quadricyclane one in hybrid molecules, but it is known [11] that such compounds are capable of converting into quadricyclane derivatives under certain conditions. We converted the hybrid molecules **2a–2e** with norbornadiene fragments into those with quadricyclane one **3a–3e** via photochemical isomerization according to the method described earlier [11]. As a result, it was found that the norbornadiene fragments are only partially isomerized into quadricyclane one with a yield of no more than 20%. It was impossible to isolate and to determine the composition of new hybrid molecules because of the formation of a complex mixture of stereoisomers consisting of norbornadiene and quadricyclane fragments bound to one fullerene molecule. We

assumed that quadricyclane fullerene C_{60} derivatives can be synthesized through the reaction between chlorofullerene $C_{60}Cl_6$ and the corresponding quadricyclanes in this regard.



Scheme 2. Synthesis of quadricyclane fullerene C_{60} derivatives.

The reaction between quadricyclane alcohols and hexachlorofullerene also led to the formation of a difficult-to-identify reaction mass of the compounds **3a–3e** under previously developed conditions [12], which is probably because of partial opening of strained C–C bonds in quadricyclane fragments.

3. Materials and Methods

All reactions were performed in argon atmosphere and in anhydrous solvent. The solvents and reagents were dried or purified according to procedures described in the literature. Commercially available fullerene C_{60} (purity of 99.5%, Sigma-Aldrich) was used.

The reaction products were analyzed on a Shimadzu SPD-20A HPLC chromatograph (Japan) equipped with a UV detector at 313 or 340 nm. The mixtures were separated on a Cosmosil Buckyprep Waters preparative column (250 × 10 mm) at a temperature of ~20 °C. Toluene was used as an eluent, and flow rate was 3.0 mL min⁻¹. ¹H, ¹³C and two-dimensional NMR spectra were acquired on a Bruker Avance III HD 500 NMR spectrometer with frequencies of 500 and 125 MHz, respectively. A mixture of $CDCl_3$ and CS_2 (1:5) was used as a solvent. ¹H and ¹³C NMR chemical shifts (δ) are given in ppm relative to internal standard $SiMe_4$. Mass spectra were recorded on a MALDI TOF/TOF mass spectrometer (Bruker Daltonik GmbH, Germany), operating in linear (TOF) and reflective (TOF/TOF) modes of positive and negative ions. S_8 and DCTB (trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]malononitrile) were used as a matrix. The solutions of the samples in toluene were used to apply them to a metal target for mass spectrometric measurements. The photoisomerization of norbornadiene derivatives into quadricyclane derivatives was performed on a HAMAMATSU LC 8 irradiator at 310 nm.

Compound 2a

Brown powder. ¹H NMR, δ : 1.60 (m, 1H), 2.06 (m, 1H), 2.19 (m, 1H), 2.21 (m, 1H), 3.59 (m, 2H), 6.12 (m, 1H), 6.77 (m, 1H), 6.78 (m, 1H). ¹³C NMR, δ : 25.84, 27.31, 29.41, 29.49, 29.56, 29.83, 31.62, 32.92, 50.11, 50.28, 51.57, 51.99, 53.59, 63.14, 66.63, 66.81, 67.04, 67.26, 67.69, 68.05, 69.10, 69.65, 70.06, 70.29, 73.50, 73.73, 76.83, 77.08, 77.34, 133.21, 137.21, 137.33, 137.45, 137.62, 137.81, 138.18, 142.36, 142.51, 142.61, 143.31, 143.40, 143.55, 143.83, 144.39, 147.28, 147.70, 148.08, 148.28, 148.46, 148.93, 149.14, 149.48, 149.57, 154.68, 154.85, 154.99, 155.14, 158.92. MALDI TOF, [M]⁻ calcd. for $C_{100}H_{45}ClO_5$ 1361.3024, found 1361.3020.

Compound 2b

Brown powder. ¹H NMR, δ : 1.62 (m, 2H), 1.71 (m, 1H), 1.99 (m, 2H), 2.07 (m, 1H), 3.02 (m, 2H), 3.52 (m, 2H), 6.13 (m, 1H), 6.76 (m, 2H). ¹³C NMR, δ : 22.96, 26.49, 28.15, 29.47, 29.93, 30.43, 30.62, 31.56, 32.10, 42.00, 50.34, 50.58, 50.87, 53.71, 60.47, 65.95, 67.73, 67.99, 68.16, 68.33, 68.58, 68.80, 73.61, 133.81, 134.00, 134.17, 134.44, 136.12, 136.32, 136.39, 136.48, 142.20, 142.26, 142.32, 143.84, 143.92, 143.99, 146.94, 147.00, 147.10, 147.16, 147.32, 147.50, 147.76, 147.86, 147.93, 148.07, 148.14, 148.42, 148.55, 148.92, 149.06, 149.21, 157.74. MALDI TOF, [M]⁻ calcd. for $C_{110}H_{65}ClO_5$ 1501.4657, found 1501.4662.

Compound 2c

Brown powder. ^1H NMR, δ : 1.29 (m, 2H), 1.56 (m, 2H), 1.78 (m, 1H), 1.99 (m, 2H), 2.03 (m, 1H), 3.29 (m, 1H), 3.32 (m, 1H), 3.51 (m, 2H), 6.18 (m, 1H), 6.76 (m, 2H). ^{13}C NMR, δ : 24.12, 29.96, 30.10, 31.48, 50.29, 53.65, 67.83, 68.06, 68.45, 73.59, 133.78, 133.90, 134.00, 142.26, 143.86, 146.96, 147.08, 147.23, 147.36, 147.55, 147.77, 147.89, 148.18, 148.31, 148.41, 148.53, 149.02, 149.16, 149.46, 149.56, 158.07, 158.35. MALDI TOF, $[\text{M}]^-$ calcd. for $\text{C}_{115}\text{H}_{75}\text{ClO}_5$ 1571.5337, found 1571.5331.

Compound 2d

Brown powder. ^1H NMR, δ : 1.30 (m, 2H), 1.33 (m, 2H), 1.39 (m, 2H), 1.47 (m, 2H), 1.81 (m, 1H), 1.98 (m, 2H), 2.06 (m, 1H), 3.28 (m, 2H), 3.48 (m, 2H), 6.12 (m, 1H), 6.74 (m, 2H). ^{13}C NMR, δ : 26.48, 27.46, 28.67, 29.56, 30.03, 30.54, 31.77, 33.43, 50.31, 53.72, 67.77, 67.93, 68.12, 68.32, 73.60, 133.52, 142.25, 143.85, 144.40, 145.13, 145.30, 145.50, 145.63, 147.13, 147.30, 147.53, 147.71, 147.81, 148.08, 148.21, 148.41, 148.71, 148.88, 149.06, 149.21, 149.38, 149.51, 158.47. MALDI TOF, $[\text{M}]^-$ calcd. for $\text{C}_{125}\text{H}_{95}\text{ClO}_5$ 1711.6943, found 1711.6939.

Compound 2e

Brown powder. ^1H NMR, δ : 1.34 (m, 10H), 1.43 (m, 2H), 1.82 (m, 1H), 1.97 (m, 2H), 2.00 (m, 1H), 2.21 (m, 2H), 3.49 (m, 2H), 6.12 (m, 1H), 6.75 (m, 2H). ^{13}C NMR, δ : 26.60, 26.69, 27.45, 29.64, 29.72, 29.78, 30.58, 31.74, 50.20, 53.66, 68.34, 68.71, 73.54, 133.30, 142.30, 143.83, 144.05, 144.26, 144.39, 144.69, 144.81, 145.14, 145.29, 145.47, 145.63, 145.93, 146.93, 147.14, 147.35, 147.56, 147.68, 147.96, 148.11, 148.33, 149.14, 149.32, 149.44, 158.71. MALDI TOF, $[\text{M}]^-$ calcd. for $\text{C}_{135}\text{H}_{115}\text{ClO}_5$ 1851.8515, found 1851.8505.

4. Conclusions

In summary, we synthesized the hybrid molecules containing five norbornadiene or quadricyclane fragments bound covalently to fullerene core through one, three, four, six, and eight oxymethylene units for the first time. The stereoselectivity of this reaction was studied thoroughly with spectral methods. It was shown for the first time that quadricyclane alcohols, reacting with C_{60}Cl_6 , are converted under selected conditions into the corresponding norbornadiene derivatives.

Author Contributions: Conceptualization, data curation, synthetic investigation, writing—original draft, review and editing, A.R.A., A.R.T. and Z.R.S.; supervision, L.M.K. All authors have read and agreed to the published version of the manuscript.

Funding: This work was financially supported by the Russian Ministry of Science and Higher Education (Government themes FMRS-2022-0075 and FMRS-2022-0081).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data available on request.

Acknowledgments: The structural studies of the compounds **2a–3e** were performed on an equipment of the “Agidel” Collective Usage Center located at the Institute of Petrochemistry and Catalysis (Ufa Federal Research Center, Russian Academy of Sciences).

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Piotrovsky, L.B.; Dumpis, M.A.; Litasova, E.V.; Safonova, A.F.; Selina, E.N.; Bulion, V.V.; Rodionova, O.M.; Saponov, N.S. Toxicology of carbon nanostructures. *Med. Acad. J.* **2010**, *10*, 125–134.
2. Rubio Arias, J.J.; Vieira Marques, M.d.F. Performance of poly(3-hexylthiophene) in bulk heterojunction solar cells: Influence of polymer size and size distribution. *React. Funct. Polym.* **2017**, *113*, 58–69.
3. Nakatsuji, S.i.; Ogawa, Y.; Takeuchi, S.; Akutsu, H.; Yamada, J.-i.; Naito, A.; Sudo, K.; Yasuoka, N. Novel photo-responsive organic spin systems: Preparation and properties of norbornadienes and spiropyran with TEMPO radical substituents. *J. Chem. Soc. Perkin Trans. 2* **2000**, 1969–1975. <https://doi.org/10.1039/B001993N>.

4. Tuktarov, A.R.; Akhmetov, A.R.; Kirichenko, G.N.; Glazunova, V.I.; Khalilov, L.M.; Dzhemilev, U.M. Synthesis of functionally substituted methanofullerenes and study of their tribological properties. *Russ. J. Appl. Chem.* **2010**, *83*, 1238–1242.
5. Castro, E.; Garcia, A.H.; Zavala, G.; Echegoyen, L. Fullerenes in biology and medicine. *J. Mater. Chem. B* **2017**, *5*, 6523–6535.
6. Maggini, M.; Scorrano, G.; Prato, M. Addition of azomethine ylides to C₆₀: Synthesis, characterization, and functionalization of fullerene pyrrolidines. *J. Am. Chem. Soc.* **1993**, *115*, 9798–9799.
7. Camps, X.; Hirsch, A. Efficient cyclopropanation of C₆₀ starting from malonates. *J. Chem. Soc. Perkin Trans. 1* **1997**, 1595–1596. <https://doi.org/10.1039/A702055D>.
8. Lamparth, I.; Hirsch, A. Water-soluble malonic acid derivatives of C₆₀ with a defined three-dimensional structure. *J. Chem. Soc., Chem. Commun.* **1994**, 1727–1728. <https://doi.org/10.1039/c39940001727>
9. Hirsch, A.; Vostrowsky, O. C₆₀ Hexakisadducts with an Octahedral Addition Pattern—A New Structure Motif in Organic Chemistry. *Eur. J. Org. Chem.* **2001**, *2001*, 829–848.
10. Yan, W.; Seifermann, S.M.; Pierrat, P.; Bräse, S. Synthesis of highly functionalized C₆₀ fullerene derivatives and their applications in material and life sciences. *Org. Biomol. Chem.* **2015**, *13*, 25–54.
11. Lorenz, P.; Hirsch, A. Photoswitchable Norbornadiene–Quadricyclane Interconversion Mediated by Covalently Linked C₆₀. *Chem. Eur. J.* **2020**, *26*, 5220–5230.
12. Khakina, E.A.; Kraevaya, O.G.A.; Popova, M.L.; Peregudov, A.S.; Troyanov, S.I.; Chernyak, A.V.; Martynenko, V.M.; Kulikov, A.V.; Schols, D.; Troshin, P.A. Synthesis of different types of alkoxy fullerene derivatives from chlorofullerene C₆₀Cl₆. *Org. Biomol. Chem.* **2017**, *15*, 773–777.
13. Kornev, A.B.; Khakina, E.A.; Troyanov, S.I.; Kushch, A.A.; Peregudov, A.; Vasilchenko, A.; Deryabin, D.G.; Martynenko, V.M.; Troshin, P.A. Facile preparation of amine and amino acid adducts of [60]fullerene using chlorofullerene C₆₀Cl₆ as a precursor. *Chem. Commun.* **2012**, *48*, 5461–5463.
14. Khakina, E.A.; Yurkova, A.A.; Peregudov, A.S.; Troyanov, S.I.; Trush, V.V.; Vovk, A.I.; Mumyatov, A.V.; Martynenko, V.M.; Balzarini, J.; Troshin, P.A. Highly selective reactions of C₆₀Cl₆ with thiols for the synthesis of functionalized [60]fullerene derivatives. *Chem. Commun.* **2012**, *48*, 7158–7160.
15. Kraevaya, O.A.; Peregudov, A.S.; Godovikov, I.A.; Shchurik, E.V.; Martynenko, V.M.; Shestakov, A.F.; Balzarini, J.; Schols, D.; Troshin, P.A. Direct arylation of C₆₀Cl₆ and C₇₀Cl₈ with carboxylic acids: A synthetic avenue to water-soluble fullerene derivatives with promising antiviral activity. *Chem. Commun.* **2020**, *56*, 1179–1182.
16. Huang, H.-J.; Chetyrkina, M.; Wong, C.-W.; Kraevaya, O.A.; Zhilenkov, A.V.; Voronov, I.I.; Wang, P.-H.; Troshin, P.A.; Hsu, S.-h. Identification of potential descriptors of water-soluble fullerene derivatives responsible for antitumor effects on lung cancer cells via QSAR analysis. *Comput. Struct. Biotechnol. J.* **2021**, *19*, 812–825.
17. Troshina, O.A.; Troshin, P.A.; Peregudov, A.S.; Kozlovskiy, V.I.; Balzarini, J.; Lyubovskaya, R.N. Chlorofullerene C₆₀Cl₆: A precursor for straightforward preparation of highly water-soluble polycarboxylic fullerene derivatives active against HIV. *Org. Biomol. Chem.* **2007**, *5*, 2783–2791.
18. Tuktarov, A.R.; Akhmetov, A.R.; Khuzin, A.A.; Dzhemilev, U.M. Synthesis and Properties of Energy-Rich Methanofullerenes Containing Norbornadiene and Quadricyclane Moieties. *J. Org. Chem.* **2018**, *83*, 4160–4166.
19. Dzhemilev, U.M.; Akhmetov, A.R.; Khuzin, A.A.; D'yakonov, V.A.; Dzhemileva, L.U.; Yunusbaeva, M.M.; Khalilov, L.M.; Tuktarov, A.R. A new original approach to the design of anticancer drugs based on energy-rich quadricyclanes. *Russ. Chem. Bull.* **2019**, *68*, 1036–1040.
20. Dzhemilev, U.M.; Khuzin, A.A.; Akhmetov, A.R.; D'yakonov, V.A.; Dzhemileva, L.U.; Yunusbaeva, M.M.; Tuktarov, A.R. Synthesis of C₆₀ Fullerene–Quadricyclane Hybrid Compound and Its Preliminary In Vitro Antitumor Activity in Combination with Cisplatin. *ACS Omega* **2019**, *4*, 15929–15934.
21. Dzhemilev, U.M.; Akhmetov, A.R.; D'yakonov, V.A.; Dzhemileva, L.U.; Yunusbaeva, M.M.; Tuktarov, A.R. Synthesis and anti-tumor activity of methanofullerenes equipped with norbornadiene and quadricyclane moieties. *Mendeleev Commun.* **2020**, *30*, 150–152.
22. Akhmetov, A.R.; Tuktarov, A.R.; Sadretdinova, Z.R.; Khalilov, L.M.; Dzhemilev, U.M. New norbornadiene-tethered fulleropyrrolidines. *Mendeleev Commun.* **2020**, *30*, 352–354.
23. Yip, C.; Handerson, S.; Tranmer, G.K.; Tam, W. Intramolecular 1,3-Dipolar Cycloadditions of Norbornadiene-Tethered Nitrile Oxides. *J. Org. Chem.* **2001**, *66*, 276–286.
24. Tranmer, G.K.; Tam, W. Intramolecular 1,3-Dipolar Cycloadditions of Norbornadiene-Tethered Nitrones. *J. Org. Chem.* **2001**, *66*, 5113–5123.
25. Avent, A.G.; Birkett, P.R.; Darwish, A.D.; Houlton, S.; Taylor, R.; Thomson, K.S.T.; Wei, X.-W. Formation and characterisation of alkoxy derivatives of [60]fullerene. *J. Chem. Soc. Perkin Trans. 2* **2001**, 782–786. <https://doi.org/10.1039/B009673N>.
26. Birkett, P.R.; Avent, A.G.; Darwish, A.D.; Kroto, H.W.; Taylor, R.; Walton, D.R.M. Preparation and ¹³C NMR spectroscopic characterisation of C₆₀Cl₆. *J. Chem. Soc. Chem. Commun.* **1993**, 1230–1232. <https://doi.org/10.1039/C39930001230>.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.