



Overcrowded Triply Fused Carbo[7]helicene

Albert Artigas, Florian Rigoulet, Michel Giorgi, Denis Hagebaum-Reignier,
Yannick Carissan, Yoann Coquerel

► To cite this version:

Albert Artigas, Florian Rigoulet, Michel Giorgi, Denis Hagebaum-Reignier, Yannick Carissan, et al..
Overcrowded Triply Fused Carbo[7]helicene. Journal of the American Chemical Society, 2023, 145
(28), pp.15084 - 15087. 10.1021/jacs.3c05415 . hal-04172611

HAL Id: hal-04172611

<https://hal.science/hal-04172611>

Submitted on 27 Jul 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Overcrowded Triply Fused Carbo[7]helicene

Albert Artigas,* Florian Rigoulet, Michel Giorgi, Denis Hagebaum-Reignier, Yannick Carissan, and Yoann Coquerel*

ABSTRACT: This paper presents the synthesis and comprehensive analysis of a highly contorted and doubly negatively curved multihelicene compound, composed of three carbo[7]helicene units fused within a central six-membered ring. The synthesis of this compound involved a $[2 + 2 + 2]$ cycloaddition reaction of 13,14-picnyne, employing a Ni(0) catalyst, which exhibited superior performance compared to conventional Pd(0) catalysts. The evaluation of aromaticity in this triple carbo[7]helicene, utilizing magnetic and electronic criteria, led to noteworthy insights challenging the limitations of Clar's model of aromaticity.

In 1999, Pascal and co-workers proposed that overcrowded chiral symmetric polycyclic aromatic hydrocarbons (PAHs) can be designed by dendritically fusing aromatic rings onto benzene.¹ The first generation of these dendrimers would be triphenylene (achiral, depicted in blue in Figure 1), while the

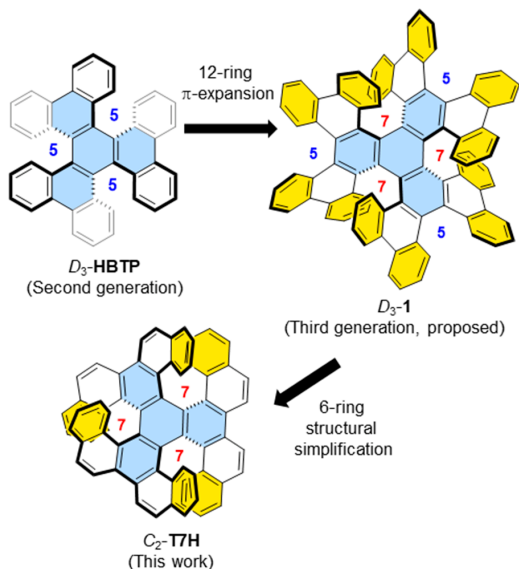


Figure 1. Overcrowded dendritic multihelicenes (top) and the first multihelicene with three carbo[7]helicene units fused in a single benzenic core (bottom).

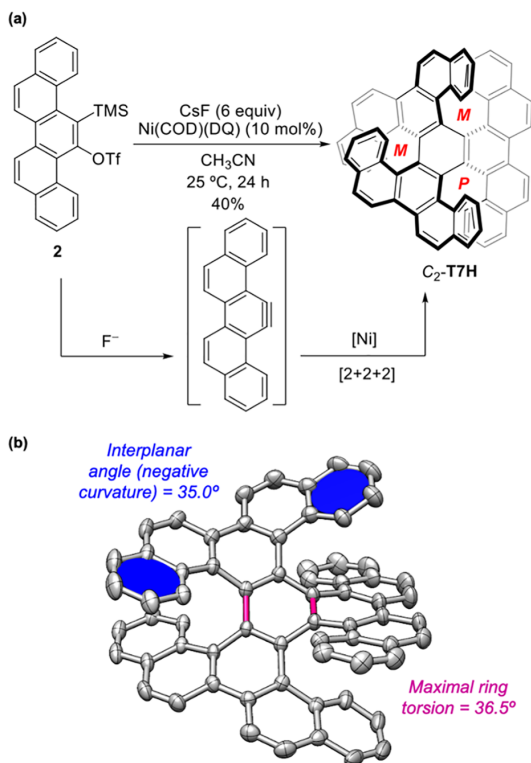
second generation features hexabenzotriphenylene (HBTP). The latter could be obtained in a 5% yield by Pascal's group through the thermolysis of phenantrene-9,10-dicarboxylic anhydride, probably involving an uncatalyzed $[2 + 2 + 2]$ cycloaddition of 9,10-phenanthryne.¹ Notably, HBTP is a severely contorted molecule that contains three carbo[5]helicene fragments fused in a benzenic core. An alternative

synthesis was proposed a few months later by Peña, Pérez, Guitián, and co-workers. The authors employed, in this case, a Pd(0)-catalyzed $[2 + 2 + 2]$ cycloaddition of 9,10-phenanthryne to afford both C_2 and D_3 symmetric diastereomers of HBTP in synthetically useful yields.^{2,3} Several π -expanded analogues of HBTP have been synthesized since then.^{4–10} All these multihelicenes embed three carbo[5]helicene units fused in a core six-membered ring. Notably, one of these molecules embeds the most twisted benzene ring reported until now, with a twist angle measure at 36.9° .⁸ Pascal envisioned a third-generation dendrimer, the hextuple helicene 1, which he acknowledged as "exceptionally crowded" and "very difficult" to synthesize. The complex structure of 1 poses the major synthetic challenge of merging three carbo[7]helicene units into a single benzenic core. This structural motif has remained synthetically inaccessible until now. In this Letter, we report the synthesis and thorough analysis of triple carbo[7]helicene C_2 -T7H, a simplified analogue of 1 that keeps its unique triply fused carbo[7]helicene core. Surprisingly, the preferred symmetry group of this novel multihelicene is C_2 , in contrast with the prediction of Pascal for 1 (Figure S1).¹ The synthesis of C_2 -T7H relied on a rare Ni(0)-catalyzed $[2 + 2 + 2]$ cycloaddition of an aryne, in this case 13,14-picnyne. The chemical and stereochemical outcomes of this reaction can be rationalized by DFT modeling. The structural analysis of C_2 -T7H revealed an extreme twist angle of 36.5° for its central ring and two picene units with strong negative curvature. The examination of aromaticity¹¹ in this molecule revealed some limitations of Clar's model of aromaticity¹² when highly contorted systems are considered.

The synthesis of C_2 -T7H is based on the transition metal catalyzed $[2 + 2 + 2]$ cyclotrimerization of 13,14-picnyne,¹⁰

which is *in situ* obtained from its *ortho*-TMS/OTf precursor **2** by a fluoride induced 1,2-elimination reaction (Scheme 1a).¹³

Scheme 1. (a) Optimized Ni(0)-Catalyzed Synthesis of Racemic C₂-T7H; (b) Structural Analysis of Racemic C₂-T7H from Its Single-Crystal X-ray Diffraction Data (CCDC 2235879)^a



^aThe (*P,M,M*) enantiomer is arbitrarily illustrated.

The synthesis of **2** was achieved in 6 steps from beta-tetralone (see section S2.1 in the Supporting Information). In early experiments, the Pd(0)-catalyzed [2 + 2 + 2] cycloaddition of the aryne derived from **2** was attempted, which allowed the isolation of the target molecule C₂-T7H, albeit in 14% yield at best, together with identified side-products (see Section S2.2 and Table S1 in the Supporting Information). When switching to the bench-stable nickel(0) precatalyst Ni(COD)(DQ),¹⁴

the target molecule C₂-T7H could be obtained in a remarkable 40% yield (Scheme 1a).

To rationalize the crucial role of the Ni(0) catalyst vs the traditional Pd(0) catalyst in this [2 + 2 + 2] cycloaddition, a mechanistic DFT modeling study was undertaken¹⁵ (see Section S3 in the Supporting Information for details). The main conclusion from this computational study is that the initial formation of the five-membered nickelacycle is seemingly largely kinetically favored over the formation of the corresponding palladacycle from the starting tris-coordinated aryne–metal complex, justifying the much more efficient formation of C₂-T7H under Ni(0)-catalysis. Also, it was found that during the subsequent formation of the metallabicyclo[3.2.1]heptatriene intermediate from the aryne-coordinated five-membered metallacycle, one *pro*-helix changes from *pro*-D₃ to *pro*-C₂ (see TS 3 in Figure S7a), justifying the observed diastereoselectivity. Notably, several agostic interactions between the metal center and C_{sp2}–H bonds could be identified in the metallacycle reaction intermediates.

Monocrystalline samples of C₂-T7H could be obtained by slow evaporation of diluted EtOAc/pentane solutions at room temperature, which allowed us to ascertain its structure by X-ray diffraction analysis (see Scheme 1b and Section S2.11 in the Supporting Information). The two most remarkable structural features of the triple carbo[7]helicene C₂-T7H are (1) it embeds two largely negatively curved picene units, an oddity for PAH made exclusively of 6-membered rings,¹⁶ and (2) the central benzene ring is extremely twisted, with a twist angle of 36.5°. The crystalline solid-state structure of C₂-T7H agreed well with its DFT optimized gas-phase geometry (Figure S3). The geometry of its D₃-symmetric diastereomer was optimized using the same level of theory, and its Gibbs free energy was determined to be 25.8 kJ·mol^{−1} higher than that of C₂-T7H (Figure S1). This, combined with the experimental synthetic results and the mechanistic study (Section S3 in the Supporting Information), indicates that C₂-T7H is both the kinetic and thermodynamic diastereomer of the reaction. So, it appears unlikely that the diastereomer D₃-T7H can be obtained by the synthetic approach proposed herein.

From its single-crystal X-ray resolved structure, looking only at bond lengths, one can imagine a Clar structure for C₂-T7H containing nine π -sextets and six isolated double bonds, with three aromatic π -sextets located in each of the three picene blades, the core six-membered ring being nonaromatic (see Figure S4). This structural analysis of aromaticity in C₂-T7H

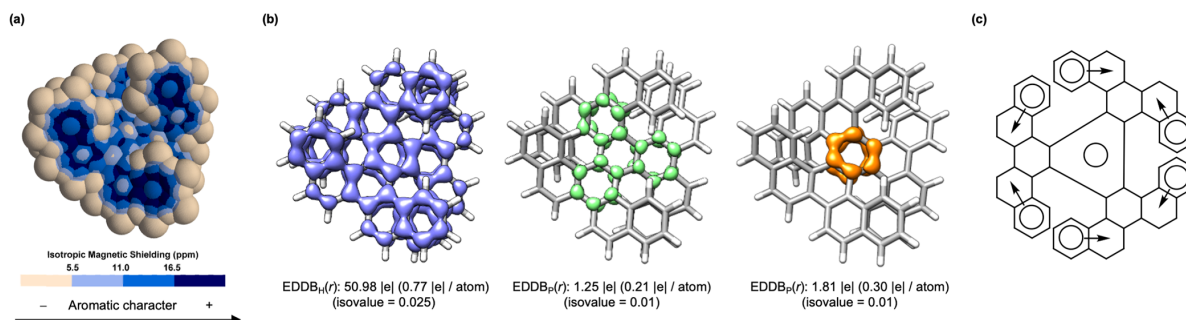


Figure 2. (a) 3D IMS map of C₂-T7H. (b) EDDB(r) analyses for C₂-T7H. (c) The most representative Clar structure of C₂-T7H.

however turned out to be wrong following magnetic and electronic criteria (Figure 2). Indeed, from the 3D IMS map¹⁷ of C_2 -T7H (Figure 2a), one can easily appreciate that electron delocalization and aromaticity are most intense in the two external rings of each picene moiety (naphthalene-like ring systems). This can be visualized by circular dark blue areas over these rings. The three central rings of each picene unit exhibit nonaromatic or poorly aromatic character, as visualized by discontinuous dark blue areas over the rings and a large neutral color area at the center of each ring. Because of the chiral nature of C_2 -T7H, both faces of each ring must be considered for a complete analysis. A 3D IMS map of C_2 -T7H is provided in the Supporting Information (.vtk file) for the best appreciation of this. From the 3D IMS map of C_2 -T7H, it can also be inferred that its core ring, a “benzene” ring embedding severe torsion, shows 1,3,5-cyclohexatriene character, with the three double bonds visualized by tiny dark blue areas located at the fused ring junctions. To complement the analysis, Electron Density of Delocalized Bonds [EDDB(*r*)] calculations¹⁸ were carried out (Figure 2b). The resulting EDDB(*r*) isosurfaces support the results obtained by 3D IMS analysis. The effect of molecular contortion in the triphenylene core is again evident from the EDDB(*r*) perspective, with none of its four rings exhibiting continuous isosurfaces. Notably, dissected EDDB_P(*r*) calculations on each individual six-membered ring of C_2 -T7H and comparison with analogous isosurfaces over triphenylene and picene (Figure S10) showed an inversion of Clar’s π -sextets in the triphenylene core. That is, the three external rings (green) are visibly less aromatic than the central one (orange). The same conclusions were drawn from EDDB_P(*r*) isosurfaces (Figure S11). Overall, the analysis of aromaticity in C_2 -T7H revealed the limitations of Clar’s model when highly contorted systems are considered. Based on the 3D IMS maps and EDDB(*r*) results, one may propose a more representative Clar structure of C_2 -T7H (Figure 2c), with two migrating π -sextets at the end of each picene unit, a weak but existing π -sextet at the core ring, and no isolated double bonds. The existence of a π -sextet in the central ring combined with the preferred C_2 symmetry group over the D_3 one for T7H is a violation of Pascal’s “rule of thumb” about the relationship between aromaticity and geometry in this class of molecules.

In conclusion, the synthesis of **1** proposed by Pascal in 1999 is yet an unsolved challenge, but significant progress has been made with the contribution presented herein. Notably, the approach presented in this article based on Ni(0) catalysts to achieve [2 + 2 + 2] aryne cycloadditions appears as a suitable alternative to the archetypical Pd(0)-based protocols when overcrowded molecules are targeted. It allowed, for the first time, three carbo[7]helicene units to fuse efficiently on a core benzene ring. Much is yet to be discovered and understood on the properties of multihelices, especially extremely contorted ones, from their electron delocalization to their interaction with light. Efforts in these directions are underway in our laboratory.

■ ASSOCIATED CONTENT

Data Availability Statement

All computational data concerning reaction mechanisms and conformational analyses was also uploaded to the ioChem-BD repository and is available through the following link: [10.19061/iochem-bd-6-208](https://doi.org/10.19061/iochem-bd-6-208).

Accession Codes

CCDC [2235876](https://www.ccdc.cam.ac.uk/data_request/cif) and [2235879](https://www.ccdc.cam.ac.uk/data_request/cif) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Authors

Albert Artigas – Aix Marseille Univ, CNRS, Centrale Marseille, ISM2, 13397 Marseille, France; Present Address: Facultat de Ciències, Campus Montilivi, Carrer de Maria Aurèlia Capmany i Farnés, 69, 17003 Girona, Catalunya, Spain; orcid.org/0000-0002-7351-0066; Email: albert.artigas@udg.edu

Yoann Coquerel – Aix Marseille Univ, CNRS, Centrale Marseille, ISM2, 13397 Marseille, France; orcid.org/0000-0003-0646-006X; Email: yoann.coquerel@univ-amu.fr

Authors

Florian Rigoulet – Aix Marseille Univ, CNRS, Centrale Marseille, ISM2, 13397 Marseille, France

Michel Giorgi – Aix Marseille Univ, CNRS, Centrale Marseille, FSCM, 13397 Marseille, France; orcid.org/0000-0002-4367-1985

Denis Hagebaum-Reignier – Aix Marseille Univ, CNRS, Centrale Marseille, ISM2, 13397 Marseille, France; orcid.org/0000-0001-8761-1047

Yannick Carissan – Aix Marseille Univ, CNRS, Centrale Marseille, ISM2, 13397 Marseille, France; orcid.org/0000-0002-9876-0272

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was funded by the French Agence Nationale de la Recherche – ANR (ANR-19-CE07-0041). Institutional financial support from Aix-Marseille University, Centrale Marseille and the CNRS is acknowledged. A.A. acknowledges the Spanish Ministerio de Universidades and the EU for a Margarita Salas grant (REQ2021_A_02). We thank Mrs. R. Rosas (AMU) and Dr. G. Herbette (CNRS) for assistance in NMR spectroscopy, and the Centre Régional de Compétences en Modélisation Moléculaire (AMU) for computing facilities.

■ REFERENCES

- (1) Barnett, L.; Ho, D. M.; Baldridge, K. K.; Pascal, R. A. The Structure of Hexabenzotriphenylene and the Problem of Over-

crowded “D_{3h}” Polycyclic Aromatic Compounds. *J. Am. Chem. Soc.* **1999**, *121*, 727–733.

(2) Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. Synthesis of Hexabenzotriphenylene and Other Strained Polycyclic Aromatic Hydrocarbons by Palladium-Catalyzed Cyclotrimerization of Arynes. *Org. Lett.* **1999**, *1*, 1555–1557.

(3) Peña, D.; Cobas, A.; Pérez, D.; Guitián, E.; Castedo, L. Kinetic Control in the Palladium-Catalyzed Synthesis of C₂-Symmetric Hexabenzotriphenylene. A Conformational Study. *Org. Lett.* **2000**, *2*, 1629–1632.

(4) Yanney, M.; Fronczek, F. R.; Henry, W. P.; Beard, D. J.; Sygula, A. Cyclotrimerization of Corannulyne: Steric Hindrance Tunes the Inversion Barriers of Corannulene Bowls. *Eur. J. Org. Chem.* **2011**, *2011*, 6636–6639.

(5) Hosokawa, T.; Takahashi, Y.; Matsushima, T.; Watanabe, S.; Kikkawa, S.; Azumaya, I.; Tsurusaki, A.; Kamikawa, K. Synthesis, Structures, and Properties of Hexapole Helicenes: Assembling Six [5]Helicene Substructures into Highly Twisted Aromatic Systems. *J. Am. Chem. Soc.* **2017**, *139*, 18512–18521.

(6) Bereznaia, V.; Roy, M.; Vanthuyne, N.; Villa, M.; Naubron, J. V.; Rodriguez, J.; Coquerel, Y.; Gingras, M. Chiral Nanographene Propeller Embedding Six Enantiomerically Stable [5]Helicene Units. *J. Am. Chem. Soc.* **2017**, *139*, 18508–18511.

(7) Zuzak, R.; Castro-Esteban, J.; Brandimarte, P.; Engelund, M.; Cobas, A.; Piątkowski, P.; Kolmer, M.; Pérez, D.; Guitián, E.; Szymonski, M.; Sánchez-Portal, D.; Godlewski, S.; Peña, D. Building a 22-Ring Nanographene by Combining in-Solution and on-Surface Syntheses. *Chem. Commun.* **2018**, *54*, 10256–10259.

(8) Roy, M.; Bereznaia, V.; Villa, M.; Vanthuyne, N.; Giorgi, M.; Naubron, J. V.; Poyer, S.; Monnier, V.; Charles, L.; Carissan, Y.; Hagebaum-Reignier, D.; Rodriguez, J.; Gingras, M.; Coquerel, Y. Stereoselective Syntheses, Structures, and Properties of Extremely Distorted Chiral Nanographenes Embedding Hextuple Helicenes. *Angew. Chem., Int. Ed.* **2020**, *59*, 3264–3271.

(9) Zhang, F.; Michail, E.; Saal, F.; Krause, A. M.; Ravat, P. Stereospecific Synthesis and Photophysical Properties of Propeller-Shaped C₉₀H₁₈ PAH. *Chem.—Eur. J.* **2019**, *25*, 16241–16245.

(10) Pozo, I.; Guitián, E.; Pérez, D.; Peña, D. Synthesis of Nanographenes, Starphenes, and Sterically Congested Polyarenes by Aryne Cyclotrimerization. *Acc. Chem. Res.* **2019**, *52*, 2472–2481.

(11) Merino, G.; Solà, M.; Fernandez, I.; Foroutan-Nejad, C.; Lazzaretto, P.; Frenking, G.; Anderson, H. L.; Sundholm, D.; Cossio, F. P.; Petrukhina, M. A.; Wu, J.; Wu, J. I.; Restrepo, A. Aromaticity: Quo Vadis. *Chem. Sci.* **2023**, *14*, 5569–5576.

(12) Solà, M. Forty Years of Clar’s Aromatic π -Sextet Rule. *Front. Chem.* **2013**, *1*, 22.

(13) Shi, J.; Li, L.; Li, Y. O-Silylaryl Triflates: A Journey of Kobayashi Aryne Precursors. *Chem. Rev.* **2021**, *121*, 3892–4044.

(14) Tran, V. T.; Li, Z. Q.; Apolinar, O.; Derosa, J.; Joannou, M. V.; Wisniewski, S. R.; Eastgate, M. D.; Engle, K. M. Ni(COD)(DQ): An Air-Stable 18-Electron Nickel(0)–Olefin Precatalyst. *Angew. Chem., Int. Ed.* **2020**, *59*, 7409–7413.

(15) Roglans, A.; Pla-Quintana, A.; Solà, M. Mechanistic Studies of Transition-Metal-Catalyzed [2 + 2 + 2] Cycloaddition Reactions. *Chem. Rev.* **2021**, *121*, 1894–1979.

(16) Hu, Y.; Wang, X. Y.; Peng, P. X.; Wang, X. C.; Cao, X. Y.; Feng, X.; Müllen, K.; Narita, A. Benzo-Fused Double [7]Carbohelicene: Synthesis, Structures, and Physicochemical Properties. *Angew. Chem., Int. Ed.* **2017**, *56*, 3374–3378.

(17) Artigas, A.; Hagebaum-Reignier, D.; Carissan, Y.; Coquerel, Y. Visualizing Electron Delocalization in Contorted Polycyclic Aromatic Hydrocarbons. *Chem. Sci.* **2021**, *12*, 13092–13100.

(18) Szczepanik, D. W.; Andrzejak, M.; Dominikowska, J.; Pawelek, B.; Krygowski, T. M.; Szatyłowicz, H.; Solà, M. The Electron Density of Delocalized Bonds (EDDB) Applied for Quantifying Aromaticity. *Phys. Chem. Chem. Phys.* **2017**, *19*, 28970–28981.