ChemPubSoc Europe

DOI: 10.1002/chem.201805124

CHEMISTRY A European Journal Communication

Hydrocarbons

Cyclooctatetraenes through Valence Isomerization of Cubanes: Scope and Limitations

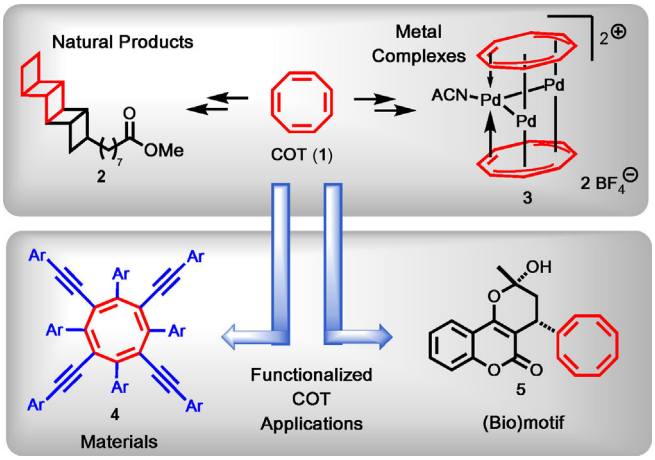
Sevan D. Houston[+],[a] Hui Xing[+],[a] Paul V. Bernhardt,[a] Timothy J. Vanden Berg,[a] John Tsanaktsidis,[b] G. Paul Savage,[b] and Craig M. Williams*[a]

Dedicated to Professor Philip Eaton

Abstract: The scope and limitations of Eaton's rhodium(I)-catalyzed valence isomerization of cubane to cyclooctatetraene (COT) were investigated in the context of functional group tolerability, multiple substitution modes and the ability of cubane-alcohols to undergo one-pot tandem Ley–Griffith Wittig reactions in the absence of a transition metal catalyst.

Since the discovery of 1,3,5,7-cyclooctatetraene (COT, **1**) in 1911 by the German Nobel laureate Willstätter and his co-worker Waser,[1] COT and its derivatives have found increasing application in diverse areas of synthetic chemistry.[2] Some important examples include the total synthesis of natural products (e.g., pentacycloanammoxic acid (**2**) by Corey and Mascitti),[3] use in organometallic chemistry (e.g., as a versatile ligand either in its neutral or anionic form[4] such as the bis-COT palladium sandwich complex **3**),[5] materials chemistry (e.g., **4** as a useful OLED emitter of blue light),[6] in polymer chemistry as a swelling agent[7] and more recently to access the archetypal fluxional hydrocarbon bullvalene on a practical scale.[8] Beyond these broad applications, our group recently identified COT as a (bio)motif (i.e., bioactive complement to cubane (bio)isosterism), which enhanced biological activity in select pharmaceutical templates, for example, the warfarin analogue **5**[9] (Scheme 1). That said, methods to access COT derivatives are limited.

The first preparation of COT (**1**) by Willstätter and Waser was by means of a low-yielding ten-step sequence starting from a tropinone derivative obtained from a pomegranate tree root bark.[1] In 1948, Reppe identified a one-step tetramerization of



Scheme 1. Cyclooctatetraene (COT, **1**) and applications thereof in natural product total synthesis, organometallics, materials chemistry, and drug lead.

acetylene using a nickel cyanide/calcium carbide catalyst, effectively making COT a readily available commodity chemical;[10] although, this method has limited scope with substituted acetylenes.[11] Monobromo-COT (**6**), reported by Huisgen et al.,[12] provided a platform for functionalizing the COT core (e.g., access to COT-carboxylic acid **7** via Grignard formation).[13] 1,2-Disubstituted COTs (e.g., **8**) can be reached by photolytic addition of substituted acetylenes to benzene, via [2+2] photocyclization followed by valence tautomerization (i.e., **9**),[14] which our group utilized previously to access bicyclo[4.2.0]octa-2,4-dienes.[15] Protocols for arriving at 1,4-disubstituted COT derivatives (e.g., **10**) are quite limited and have restricted synthetic utility, but the key advances in this area were made by Huisgen, through alkylation (e.g., **11**) of the sulfur dioxide cycloadduct of COT (i.e., **12**) (Scheme 2),[16] with further developments provided by Paquette and Streitwieser.[17] In addition, 1,4-dimetalation of COT has also been reported.[18] However, all these methods suffer from either multistep procedures, low yields, long reaction times, laborious purification protocols, and/or limited scope. Furthermore, although other poly-substitution patterns are available, including benzo and annulated derivatives,[19] rapid and routine access to mono and disubstituted COT systems are not available.

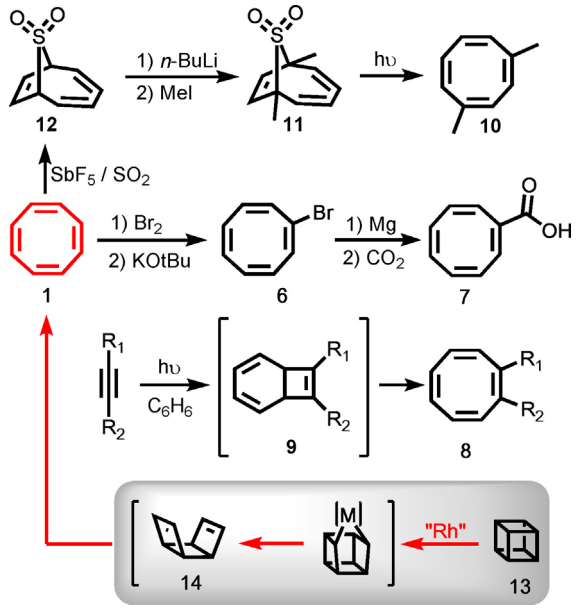
In a continuing effort to explore the fundamental reactivity of cubane (**13**),[20] Eaton discovered that the strained hydrocarbon underwent valence isomerization to COT on treatment

[a] Dr. S. D. Houston,[+] Dr. H. Xing,[+] Prof. P. V. Bernhardt, T. J. Vanden Berg, Prof. C. M. Williams
School of Chemistry and Molecular Biosciences
University of Queensland, Brisbane, 4072, Queensland (Australia)
E-mail: c.williams3@uq.edu.au

[b] Dr. J. Tsanaktsidis, Dr. G. P. Savage
CSIRO Manufacturing, Ian Wark Laboratory
Melbourne, 3168, Victoria (Australia)

[+] These authors contributed equally to this work.

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/chem.201805124.

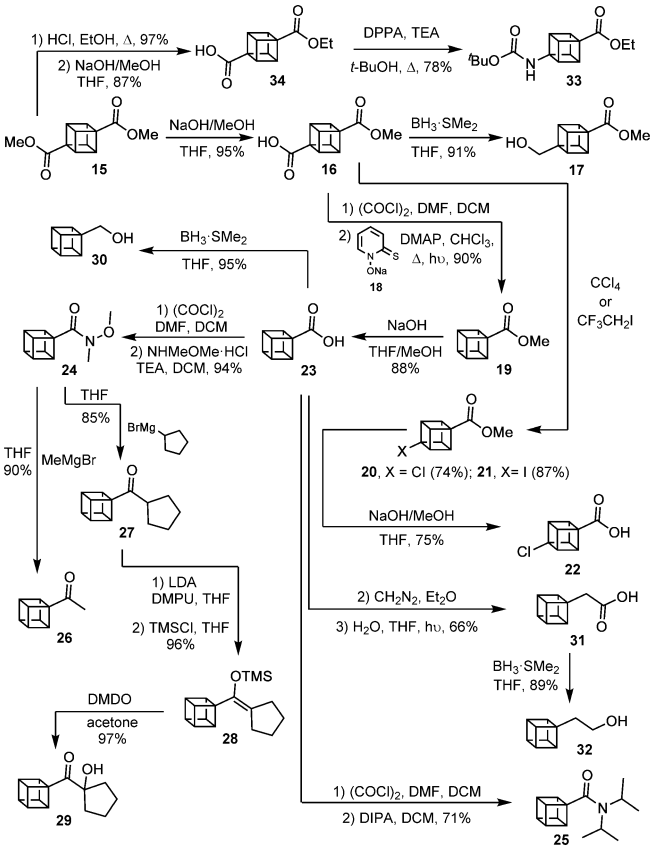


Scheme 2. Reported synthetic methods to access functionalized COT systems, including Eaton's valence isomerization of cubane (**13**) to COT (**1**).

with rhodium(I) norbornadiene chloride dimer (i.e., $[Rh(nbd)Cl]_2$) and subsequent exposure of the intermediate tricyclo[4.2.0.0^{2,5}]octa-3,7-diene (**14**) to thermal conditions (Scheme 2).[21] Interestingly, only the rearrangement of a few esoteric cubanes was reported,[22] but functional examples were never published, apart from examples in the polymer field[7,23] and supramolecular chemistry.[24] Understandably, the lack of interest in this methodological approach likely originated from the scarcity of starting cubane substrates.

However, with the advent of our improved process scale synthesis of dimethyl cubane-1,4-dicarboxylate (**15**),[25] experience in manipulating cubane drug and agrichemical candidates,[26] and the recent development of aryl coupling to cubane reported by Senge et al.,[27] Eaton's method has potential to evolve from physical organic chemistry observation to widely deployable synthetic methodology. Herein reported is a wide scope and limitations study utilizing numerous mono- and disubstituted cubane derivatives in the context of their ability to undergo valence isomerization to the corresponding COT derivatives.

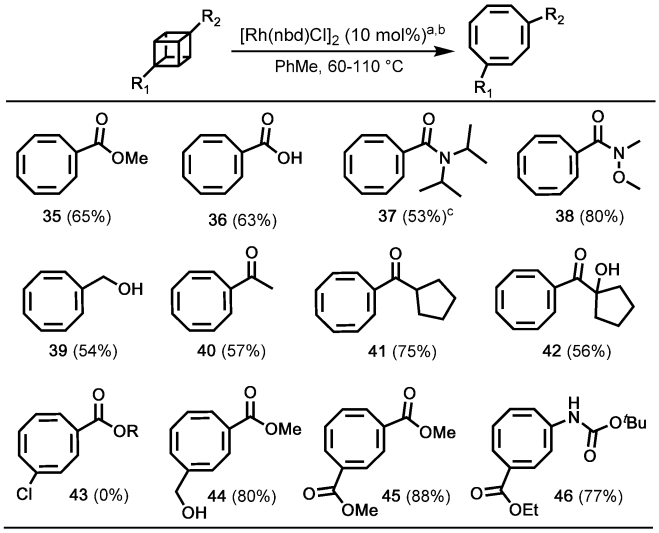
The general approach taken to build a library of candidates for performing this study focused on functionalization and derivatization of cubane diester (**15**) (Scheme 3), which is now readily available from commercial sources. Half hydrolysis of **15** proceeded smoothly and reliably to give the acid-ester **16** in 95% yield, which also underwent borane reduction to give alcohol **17**. Barton decarboxylation of **16** using our chloroform hydrogen atom donor methodology[28] in combination with the sodium salt of 1-hydroxypyridine-2(*1H*)-thione (**18**) gave the mono-ester **19** (90% yield). Substitution of chloroform with either carbon tetrachloride or 1,1,1-trifluoro-2-iodoethane when running the Barton reaction gave the 4-chloro (**20**) and 4-iodo-cubane-1-methoxycarbonyl (**21**) in good to excellent yields. Hydrolysis of the 4-chloro ester **20** gave the corresponding 4-chloro acid **22**, whilst hydrolysis of mono-ester **19** gave acid **23**, which acted as a key platform for accessing a wide range of monosubstituted cubane derivatives. Initially, valuable amides were targeted, for example, the Weinreb amide[29] **24** and the *N,N*-diisopropylamide **25**, which can be used for *ortho*-lithiation of the cubane ring system.[20] The Weinreb amide **24** was then taken through to the methyl ketone **26** and the cyclopentyl ketone **27**. Ketone **27** was further transformed, via Rubottom oxidation[30] of the TMS enol ether **28**, to the hydroxy ketone **29** (confirmed by X-ray crystal-structure analysis), in the view that this is a sensitive functional group to be explored in the valence isomerization process. Borane reduction of **23** gave cubylmethanol **30** in excellent yield. Considering that most examples thus far have a carbonyl directly attached to the cubane core, **23** was subjected to a single unit homologation to give **31** (which also underwent borane reduction to give **32**), using the Arndt–Eistert protocol,[31] which involves the Wolff rearrangement[32] as the key step. Lastly, an example with nitrogen directly attached to the cubane core was required, and thus the *t*-Boc amide **33** was prepared according to our previously reported synthesis.[26] Briefly, the synthesis of **33** involved transesterification of **15** followed by half hydroly-



Scheme 3. Synthesis of the mono- and disubstituted cubane library. [DMAP = *N,N*-(dimethylamino)pyridine, DMF = *N,N*-dimethylformamide, DPPA = diphenylphosphorylazide, TEA = triethylamine, LDA = lithium *N,N*-diisopropylamide, DCM = dichloromethane, THF = tetrahydrofuran, DMPU = 1,3-dimethyl-3,4,5,6-tetrahydro-2-pyrimidinone, TMS = trimethylsilyl, DMDO = dimethyldioxirane, DIPA = *N,N*-diisopropylamine].

sis to give acid-ester **34**, and diphenylphosphoryl azide (DPPA) mediated Curtius rearrangement[33] in *t*-butanol (Scheme 3).

With a range of mono- and 1,4-disubstituted cubane derivatives (i.e., **15**–**33**) in hand the valence isomerization to COT derivatives could be explored. [Note: There are at least 20 valence isomers with the general formula $(CH)_8$;[34] however, the only interconversion of cubane as reported by Eaton was COT].[22] Treatment of the mono-substituted cubanes with the commercially available rhodium(I) catalyst $[Rh(nbd)Cl]_2$ in toluene at temperatures between 60 and 110 °C afforded COT derivatives **35**–**46** in yields ranging from 53–88% (Scheme 4).



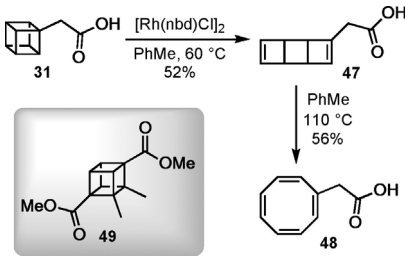
[a] Reaction conditions: Cubane derivative (0.2 mmol, 1 eq.), $[Rh(nbd)Cl]_2$ (0.02 mmol, 0.1 eq.), toluene (5 mL), 60-110 °C, 2-4 h; [b] Isolated yield; [c] Confirmed by X-ray crystal structure analysis.

Scheme 4. Functionalized cubane conversion to mono- and disubstituted COTs, through valence isomerization. [nbd = norbornadiene].

Even the tertiary free hydroxyl group present in **29** was well tolerated, giving COT **42** in 56% yield. COT alcohol **39** was only obtained after heating at 110 °C (see below). The 1,4-disubstituted cubane derivatives were generally better tolerated, giving higher yields of the 1,4-disusubstituted COT derivatives **44**–**46**, ranging from 77–88%. Difficulty was encountered isolating a pure sample of the chloro substituted system **43** either as the methyl ester (R = Me) or the carboxylic acid (R = H) from the corresponding cubanes **20** and **22** (Scheme 4).

To confirm whether $[Rh(nbd)Cl]_2$ was the optimum catalyst, a number of different rhodium based catalysts were screened using cubanes **15** and **25** as the test substrates. $[Rh(nbd)Cl]_2$ was found to be superior for both cases. However, $[Rh(COD)(MeCN)_2]BF_4$ and $[Rh(nbd)(MeCN)_2]SbF_6$ afforded COT **45** in 63 and 30% respectively, whereas for COT **37** yields were very similar, that is, 61 and 63%, respectively. The polymer-bound $[Rh(nbd)(PPh_3)]BF_4$ Fibre-cat®, and the rhodium(II) catalyst $Rh_2(OAc)_4$ gave no product.

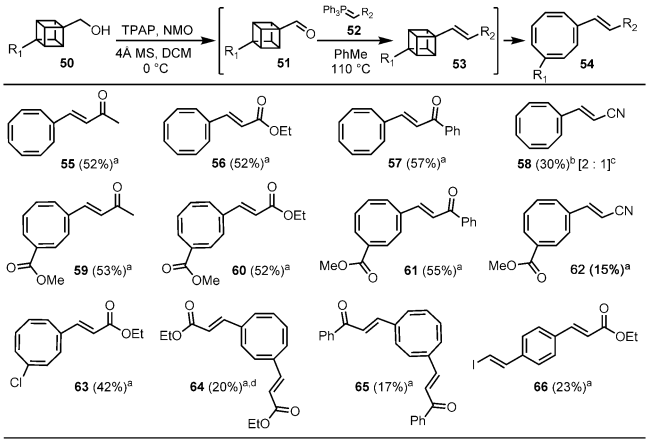
In the case of cubane **31** (Scheme 3), which does not contain an electron-withdrawing carbonyl group, treatment with the rhodium catalyst at 60 °C gave for the first time the intermediate tricyclo[4.2.0.0^{2,5}]octa-3,7-diene (**47**), which was isolated in 52% yield and found to be reasonably stable (i.e., when stored at 8 °C, only slight degradation was observed over a period of three weeks). Although stable, **47** underwent thermal rearrangement at 110 °C (in the absence of rhodium catalyst) giving the COT derivative **48** in 56% yield. Unfortunately, higher substituted cubanes, such as the 1,2,3,4-tetrasubstituted example **49**[35] led only to a complex COT product distribution (Scheme 5).



Scheme 5. Observation of the tricyclo[4.2.0.0^{2,5}]octa-3,7-diene (**47**) intermediate and tetrasubstituted cubane analogue **49**; [nbd = norbornadiene].

Encouraged by the broad substrate compatibility of Eaton's valence isomerization, a catalyst-free variant was developed. The rearrangement of 4-iodo-1-vinyl cubane to 4-iodo-1-vinyl COT (and subsequently to the corresponding *trans*-β-halo styrene) has been reported under thermally promoted conditions in the absence of $[Rh(nbd)Cl]_2$.[36] Notably, the transformation was greatly accelerated by the addition of a Lewis acid (BCl_3).[36c] Given that the valence isomerization can be performed without a rhodium catalyst and best proceeds with an electron deficient moiety appended directly to the cubane framework, an opportunity to incorporate both precepts into one contiguous methodology was envisaged. Our recent work extending the Ley–Griffith oxidation[37] [that is, tetrapropylammonium perruthenate (TPAP) oxidation][38] in the context of tandem Wittig reactions[39] was applied to cubane-alcohols **50** (see the Supporting Information for synthetic methods) to expand the mono- and 1,2-disubstituted COT derivative library. A range of mono- and 1,4-disubstituted COT derivatives were obtained (i.e., **55**–**65**) in yields ranging from 15–57%, which, considering three reactions are occurring in the one pot, was deemed satisfactory (Scheme 6). A general trend of *E* stereoselectivity was observed, based on the measurement of a large vinyl coupling constant (J = ca. 16 Hz) where possible, although the complex ^{1}H-NMR olefinic regions of **55**–**65** precluded measurement of one or both signals in some cases. An X-ray crystal structure for diester **64** was obtained unambiguously conferring *E* stereochemistry (see the Supporting Information). A notable exception was that of COT derivative **58**, which was observed as a 2:1 *E*:*Z* mixture. Reactions with the cyano phosphorane (**52**, R_2 = CN) were generally low yielding and difficult to push to completion (i.e., **58**, **62**). Reaction of (4-iodocuban-1-yl)methanol (**50**, R_1 = I, see the Supporting Information) gave the corresponding *trans*-β-halo styrene **66**.[36]

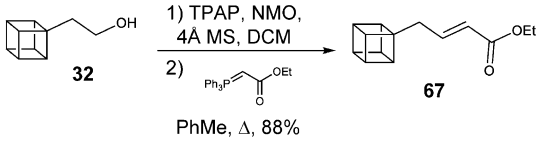
Promotion of the valence isomerization by the perruthenate catalyst was ruled out based on a series of control experi-



[a] Isolated yield; [b] Yield based on ^{1}H-NMR as product could not be purified nor fully characterised; [c] Values in [ ] represent *E* : *Z* isomer ratio; [d] Confirmed by X-ray crystal structure analysis.

Scheme 6. One-pot tandem Ley–Griffith Wittig reactions in the absence of a transition metal catalyst. [nbd = norbornadiene, TPAP = tetrapropylammonium perruthenate, NMO = *N*-methyl morpholine *N*-oxide].

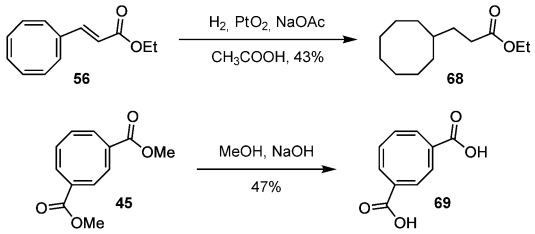
ments: 1) heating an isolated sample of **53** ($R_1 = CO_2Me$, $R_2 = CO_2Et$) in toluene at 110 °C for 6 h gave **60** in 90% yield and 2) heating cubane diester **15** to 110 °C in the presence of TPAP did not give any of the corresponding COT derivative **45** (see the Supporting Information). Electron deficient functionality directly appended to the cubane framework was found to be essential for the progress of the tandem reaction: when homologated cubane-alcohol **32** was subjected to the tandem conditions only cubane **67** was recovered (Scheme 7).



Scheme 7. Failed tandem valence isomerization reaction. [DCM = dichloromethane, TPAP = tetrapropylammonium perruthenate, NMO = *N*-methyl morpholine *N*-oxide, MS = molecular sieve].

Lastly, some basic chemistry of the COT system was explored. Hydrogenation of COT **56** was investigated.[40] The reaction proceeded in a straightforward fashion using Adams's catalyst (platinum oxide) in glacial acetic acid, giving the reduced product, ethyl 3-cyclooctylpropanoate (**68**) in moderate yield (43%). Hydrolysis of 1,4-disubstituted COT derivative **45** proceeded smoothly, giving the corresponding dicarboxylic acid (**69**) in 47% yield (Scheme 8).

In conclusion, Eaton's observation of rhodium(I)-catalyzed valence isomerization of cubane to COT has been validated, and the scope greatly extended, such that it can be used as a synthetic protocol to access a wide range of mono- and 1,4-disubstituted COT derivatives. Furthermore, a catalyst-free tandem Wittig sequence was devised based on an in situ one-step oxidation of cubane-alcohols, which further broadens the scope of the methodology. Hydrogenation of COT derivatives can provide access to substituted cyclooctyl derivatives, and generally it is possible to hydrolyze COT esters.



Scheme 8. Observed basic chemistry of the COT system.

Acknowledgements

The authors thank the University of Queensland (UQ) and the CSIRO (Melbourne) for financial support, Queensland University of Technology (QUT) for assistance with mass spectrometry (Prof. Stephen Blanksby and Mrs. Silvia Gemme), the Australian Synchrotron (Melbourne, Australia) for access to beamtime and Dr Aiden Brock for the collection of synchrotron data. The Australian Research Council for a Future Fellowship award (grant number FT110100851) to C.M.W. is also gratefully acknowledged. S.D.H. gratefully acknowledges the Northcote Trust and Britain–Australia Society for their award of the Northcote Graduate Scholarship. H.X. gratefully acknowledges the UQ Graduate School and the School of Chemistry and Molecular Biosciences for a graduate scholarship. T.J.V. gratefully acknowledges the Australian Government for a Research Training Program Scholarship. C.M.W. gratefully acknowledges financial support from the Department of Agriculture and Water Resources.

Conflict of interest

CSIRO (J.T. and G.P.S.) and UQ (C.M.W.) have a formal relationship with Boron Molecular Pty Ltd. who supply cubane intermediates.

Keywords: cubanes · cyclooctatetraenes · rhodium · tandem · valence isomerization

[1] a) H. Hopf, *Classics in Hydrocarbon Chemistry: Syntheses, Concepts, Perspectives, Vol. 1*, Wiley-VCH, Weinheim, **2000**; b) R. Willstätter, E. Waser, *Ber. Dtsch. Chem. Ges.* **1911**, *44*, 3423–3445.
[2] a) K. W. Glaeske, W. A. Donaldson, *Mini-Rev. Org. Chem.* **2012**, *9*, 31–43; b) T. Nishinaga, in *Chemical Science of π-Electron Systems, Vol. 1*, 1st ed. (Ed.: T. Akasaka), Springer, Japan, **2015**, pp. 46–67.
[3] V. Mascitti, E. J. Corey, *J. Am. Chem. Soc.* **2004**, *126*, 15664–15665.
[4] P. W. Roesky, *Eur. J. Inorg. Chem.* **2001**, 1653–1660.
[5] T. Murahashi, S. Kimura, K. Takase, T. Uemura, S. Ogoshi, K. Yamamoto, *Chem. Commun.* **2014**, *50*, 820–822.
[6] P. Lu, H. Hong, G. Cai, P. Djurovich, W. P. Weber, M. E. Thompson, *J. Am. Chem. Soc.* **2000**, *122*, 7480–7486.
[7] A. E. McGonagle, G. P. Savage, *Aust. J. Chem.* **2009**, *62*, 145–149.
[8] O. Yahiaoui, L. F. Pašteka, B. Judeel, T. Fallon, *Angew. Chem. Int. Ed.* **2018**, *57*, 2570–2574; *Angew. Chem.* **2018**, *130*, 2600–2604.
[9] a) H. Xing, S. D. Houston, X. Chen, S. Ghassabian, T. Fahrenhorst-Jones, A. Kuo, C.-E. P. Murray, K.-A. Conn, K. N. Jaeschke, D.-Y. Jin, C. Pasay, P. V. Bernhardt, J. M. Burns, J. Tsanaktsidis, G. P. Savage, G. M. Boyle, J. J. De Voss, J. McCarthy, G. H. Walter, T. H. J. Burne, M. T. Smith, J.-K. Tie, C. M. Williams, *Chem. Eur. J.* DOI: https://doi.org/10.1002/chem.201806277; b) see also: T. A. Reekie, C. M. Williams, L. M. Rendina,

M. Kassiou, *J. Med. Chem.* DOI: https://doi.org/10.1021/acs.jmedchem.8b00888; c) see also: S. D. Houston, B. A. Chalmers, G. P. Savage, C. M. Williams, *Org. Biomol. Chem.* DOI: https://doi.org/10.1039/c8ob02959h; d) P. K. Mykhailiuk, *Org. Biomol. Chem.* DOI: https://doi.org/10.1039/C8OB02812E.

[10] W. Reppe, O. Schlichting, K. Klager, T. Toepel, *Justus Liebigs Annn Chem.* **1948**, *560*, 1 – 92.

[11] J. R. Leto, M. F. Leto, *J. Am. Chem. Soc.* **1961**, *83*, 2944 – 2951.

[12] J. Gasteiger, G. E. Gream, R. Huisgen, W. E. Konz, U. Schnegg, *Chem. Ber.* **1971**, *104*, 2412 – 2419.

[13] a) J. F. M. Oth, R. Merényi, T. Martini, G. Schröder, *Tetrahedron Lett.* **1966**, *7*, 3087 – 3093; b) L. A. Paquette, K. A. Henzel, *J. Am. Chem. Soc.* **1973**, *95*, 2726 – 2728.

[14] a) E. Grovenstein, T. C. Campbell, T. Shibata, *J. Org. Chem.* **1969**, *34*, 2418 – 2428; b) A. C. Cope, J. E. Meili, *J. Am. Chem. Soc.* **1967**, *89*, 1883 – 1886; c) D. Bryce-Smith, J. E. Lodge, *J. Chem. Soc.* **1963**, 695 – 701; d) E. Grovenstein, D. V. Rao, *Tetrahedron Lett.* **1961**, *2*, 148 – 150; e) D. Bryce-Smith, J. E. Lodge, *Proc. Chem. Soc.* **1961**, 333 – 334; f) L. A. Paquette, R. S. Beckley, *Org. Photochem. Synth.* **1976**, *2*, 45 – 46.

[15] R. L. Grange, M. J. Gallen, H. Schill, J. P. Johns, L. Dong, P. G. Parsons, P. W. Reddell, V. A. Gordon, P. V. Bernhardt, C. M. Williams, *Chem. Eur. J.* **2010**, *16*, 8894 – 8903.

[16] J. Gasteiger, R. Huisgen, *J. Am. Chem. Soc.* **1972**, *94*, 6541 – 6543.

[17] a) L. A. Paquette, *Tetrahedron* **1975**, *31*, 2855 – 2883; b) L. A. Paquette, G. J. Hefferon, R. Samodral, Y. Hanzawa, *J. Org. Chem.* **1983**, *48*, 1262 – 1266; c) M. J. Miller, M. H. Lyttle, A. Streitwieser, Jr., *J. Org. Chem.* **1981**, *46*, 1977 – 1984.

[18] a) N. C. Burton, F. G. N. Cloke, S. C. P. Joseph, H. Karamallakis, A. A. Sameh, *J. Organomet. Chem.* **1993**, *462*, 39 – 43; b) J. M. Bellama, J. B. Davison, *J. Organomet. Chem.* **1975**, *86*, 69 – 74.

[19] a) *Product Class 8: Cyclooctatetraenes, Vol. 45a*, 1st ed., Thieme, Stuttgart, **2009**; b) P. A. Wender, J. P. Christy, A. B. Lesser, M. T. Gieseler, *Angew. Chem. Int. Ed.* **2009**, *48*, 7687 – 7690; *Angew. Chem.* **2009**, *121*, 7823 – 7826; c) S. Blouin, R. Pertschi, A. Schoenfelder, J. Suffert, G. Blond, *Adv. Synth. Catal.* **2018**, *360*, 2166 – 2171.

[20] a) P. E. Eaton, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1421 – 1436; *Angew. Chem.* **1992**, *104*, 1447 – 1462; b) K. F. Biegasiewicz, J. R. Griffiths, G. P. Savage, J. Tsanaktsidis, R. Priefer, *Chem. Rev.* **2015**, *115*, 6719 – 6745; c) G. W. Griffin, A. P. Marchand, *Chem. Rev.* **1989**, *89*, 997 – 1010; d) see also zincate metalation of cubane: Y. Kato, C. M. Williams, M. Uchiyama, S. Matsubara, *Org. Lett.* **2019**, *21*, 473 – 475.

[21] L. Cassar, P. E. Eaton, J. Halpern, *J. Am. Chem. Soc.* **1970**, *92*, 3515 – 3518.

[22] a) P. E. Eaton, E. Galoppini, R. Gilardi, *J. Am. Chem. Soc.* **1994**, *116*, 7588 – 7596; b) P. E. Eaton, D. Stossel, *J. Org. Chem.* **1991**, *56*, 5138 – 5142.

[23] N.-H. Yeh, C.-W. Chen, S.-L. Lee, H.-J. Wu, C.-h. Chen, T.-Y. Luh, *Macromolecules* **2012**, *45*, 2662 – 2667.

[24] R. M. Moriarty, D. Pavlović, *J. Org. Chem.* **2004**, *69*, 5501 – 5504.

[25] M. J. Falkiner, S. W. Littler, K. J. McRae, G. P. Savage, J. Tsanaktsidis, *Org. Process Res. Dev.* **2013**, *17*, 1503 – 1509.

[26] a) B. A. Chalmers, H. Xing, S. Houston, C. Clark, S. Ghassabian, A. Kuo, B. Cao, A. Reitsma, C.-E. P. Murray, J. E. Stok, G. M. Boyle, C. J. Pierce, S. W. Littler, D. A. Winkler, P. V. Bernhardt, C. Pasay, J. J. De Voss, J. McCarthy, P. G. Parsons, G. H. Walter, M. T. Smith, H. M. Cooper, S. K. Nilsson, J. Tsanaktsidis, G. P. Savage, C. M. Williams, *Angew. Chem. Int. Ed.* **2016**, *55*, 3580 – 3585; *Angew. Chem.* **2016**, *128*, 3644 – 3649; b) B. A. Chalmers, A. P.-J. Chen, G. P. Savage, C. M. Williams, *Aust. J. Chem.* **2010**, *63*, 1108 – 1110.

[27] S. S. R. Bernhard, G. M. Locke, S. Plunkett, A. Meindl, K. J. Flanagan, M. O. Senge, *Chem. Eur. J.* **2018**, *24*, 1026 – 1030.

[28] a) J. Ho, J. Zheng, R. Meana-Pañeda, D. G. Truhlar, E. J. Ko, G. P. Savage, C. M. Williams, M. L. Coote, J. Tsanaktsidis, *J. Org. Chem.* **2013**, *78*, 6677 – 6687; b) E. J. Ko, G. P. Savage, C. M. Williams, J. Tsanaktsidis, *Org. Synth.* **2012**, *89*, 471 – 479; c) E. J. Ko, G. P. Savage, C. M. Williams, J. Tsanaktsidis, *Org. Lett.* **2011**, *13*, 1944 – 1947.

[29] a) B. Qu, D. B. Collum, *J. Org. Chem.* **2006**, *71*, 7117 – 7119; b) S. Nahm, S. M. Weinreb, *Tetrahedron Lett.* **1981**, *22*, 3815 – 3818.

[30] a) M. J. Gallen, C. M. Williams, *Eur. J. Org. Chem.* **2008**, 4697 – 4705; b) G. M. Rubottom, J. M. Gruber, R. K. Boeckman Jr, M. Ramaiah, J. B. Medwid, *Tetrahedron Lett.* **1978**, *19*, 4603 – 4606.

[31] a) P. E. Eaton, Y. C. Yip, *J. Am. Chem. Soc.* **1991**, *113*, 7692 – 7697; b) F. Arndt, B. Eistert, *Ber. Dtsch. Chem. Ges.* **1935**, *68*, 200 – 208.

[32] W. Kirmse, *Eur. J. Org. Chem.* **2002**, 2193 – 2256.

[33] T. Shioiri, K. Ninomiya, S. Yamada, *J. Am. Chem. Soc.* **1972**, *94*, 6203 – 6205.

[34] L. T. Scott, M. Jones, *Chem. Rev.* **1972**, *72*, 181 – 202.

[35] M. Bliese, D. Cristiano, J. Tsanaktsidis, *Aust. J. Chem.* **1998**, *51*, 593.

[36] a) P. J. Heaphy, J. R. Griffiths, C. J. Dietz, G. P. Savage, R. Priefer, *Tetrahedron Lett.* **2011**, *52*, 6359 – 6362; b) J. R. Griffiths, J. Tsanaktsidis, G. P. Savage, R. Priefer, *Thermochim. Acta* **2010**, *499*, 15 – 20; c) V. M. Carroll, D. N. Harpp, R. Priefer, *Tetrahedron Lett.* **2008**, *49*, 2677 – 2680.

[37] For oxidation and oxidant developments see a) P. W. Moore, C. D. G. Read, P. V. Bernhardt, C. M. Williams, *Chem. Eur. J.* **2018**, *24*, 4556 – 4561; b) P. W. Moore, Y. Jiao, P. M. Mirzayans, L. N. Q. Sheng, J. P. Hooker, C. M. Williams, *Eur. J. Org. Chem.* **2016**, 3401 – 3407; c) P. W. Moore, P. M. Mirzayans, C. M. Williams, *Chem. Eur. J.* **2015**, *21*, 3567 – 3571. d) For mechanistic aspects, see: T. J. Zerk, P. W. Moore, J. S. Harbort, S. Chow, L. Byrne, G. A. Koutsantonis, J. R. Harmer, M. Martínez, C. M. Williams, P. V. Bernhardt, *Chem. Sci.* **2017**, *8*, 8435 – 8442; e) T. J. Zerk, P. W. Moore, C. M. Williams, P. V. Bernhardt, *Chem. Commun.* **2016**, *52*, 10301 – 10304.

[38] a) M. Pagliaro, S. Campestrini, R. Ciriminna, *Chem. Soc. Rev.* **2005**, *34*, 837 – 845; b) S. V. Ley, J. Norman, W. P. Griffith, S. P. Marsden, *Synthesis* **1994**, 639 – 666; c) W. P. Griffith, *Chem. Soc. Rev.* **1992**, *21*, 179 – 185; d) W. P. Griffith, S. V. Ley, *Aldrichimica Acta* **1990**, *23*, 13.

[39] C. D. G. Read, P. W. Moore, C. M. Williams, *Green Chem.* **2015**, *17*, 4537 – 4540.

[40] A. C. Cope, M. Burg, S. W. Fenton, *J. Am. Chem. Soc.* **1952**, *74*, 173 – 175.

Manuscript received: October 11, 2018
Version of record online: ■■ ■■, 0000

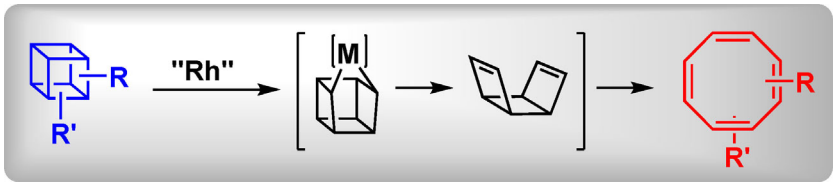
COMMUNICATION

Hydrocarbons

*S. D. Houston, H. Xing, P. V. Bernhardt, T. J. Vanden Berg, J. Tsanaktsidis, G. P. Savage, C. M. Williams**

■■ – ■■

Cyclooctatetraenes through Valence Isomerization of Cubanes: Scope and Limitations



Releasing the strain! This work aims to take Eaton's rhodium(I)-catalyzed valence isomerization of cubane to cyclooctatetraene (COT) to the next level. Functional group tolerability, scope, and limitations of this reaction were investigated in the context of developing deployable methodology for the increasing number of applications involving the COT ring system.