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A step toward polytwistane: synthesis and characterization of C_2-symmetric tritwistane†

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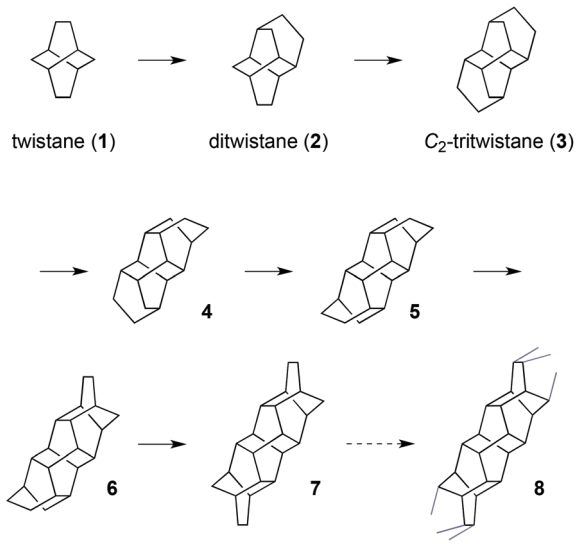
Twistane is a classic hydrocarbon with fascinating stereochemical properties. Herein we describe a series of oligomers of twistane that converges on a chiral nanorod, which we term polytwistane. A member of this series, C_2-symmetric tritwistane, has been synthesized for the first time.

Twistane (tricyclo[4.4.0.0^{3,8}]decane) (**1**) is a tricyclic hydrocarbon that has played an important role in the development of organic stereochemistry.[1] The D_2-symmetrical molecule consists of three interwoven twist boat rings, all of which have approximate D_2-symmetry with identical handedness. It can be formed, conceptually, through bridging of a *cis*-decalin with a single bond or by adding an ethano (ethane-1,2-diyl) bridge to a bicyclo[2.2.2]octane. In reality, twistane (**1**) has been synthesized numerous times, in both enantiomeric forms[1,2] and as a racemate,[3] starting with Howard Whitlock's seminal work in 1962.[4] A large variety of substituted twistanes, including unsaturated derivatives, are now known.[5]

In a "Gedankenexperiment", twistane (**1**) can be further extended by bridging its six-membered rings with additional ethano bridges mounted in a 1,4-fashion (Scheme 1). Due to geometrical constraints, the newly formed six-membered rings continue to adopt a twist boat conformation with the same handedness as the existing rings. Provided quaternary carbons are avoided, the first substitution can only proceed in one way to yield the C_2-symmetrical ditwistane (**2**). Further addition of an ethano bridge to ditwistane in a linear fashion produces C_2-symmetric tritwistane (**3**). Linear extension of C_2-tritwistane (**3**) affords tetratwistane (**4**), pentatwistane (**5**), hexatwistane (**6**), heptatwistane (**7**), and so on. All of these helical compounds are chiral molecules with C_2 symmetry.

Further extension of these oligotwistanes in a linear fashion, ideally to infinity, affords a polymer with fascinating geometrical properties, which we propose to call "polytwistane" (**8**) (Fig. 1). Ideal polytwistane has the same molecular formula, C_nH_n, as polyacetylene but it is fully saturated with all of its sp^3 hybridized carbons and hydrogens in an identical chemical environment. It is a chiral nanorod of high rigidity since none of its C,C-bonds can rotate freely and it can exist in two enantiomorphic forms, *i.e.* as a *P* or *M* helix. A more detailed description of polytwistane as a geometrical object and a prediction of its physical properties will be described elsewhere.[6]



Scheme 1 Twistane (**1**), oligotwistanes and polytwistane (**8**).

Among the hydrocarbons shown in Scheme 1, only twistane (**1**) and ditwistane (**2**) are known compounds. Both enantiomers of ditwistane (**2**) have been synthesized[8] and dozens of compounds that incorporate the ditwistane skeleton have been described.[8] Structures containing the carbon skeleton of C_2-tritwistane[9] and C_2-hexatwistane[10] have also been reported. None of these compounds, however, have been identified as oligotwistanes, and polytwistane (**8**) does not seem to have been mentioned in the literature so far.

We now report our studies on linear oligotwistanes, which were undertaken to extend the series of known oligotwistanes and obtain spectral data that might help in the identification of polytwistane. Our initial studies were based on additions to

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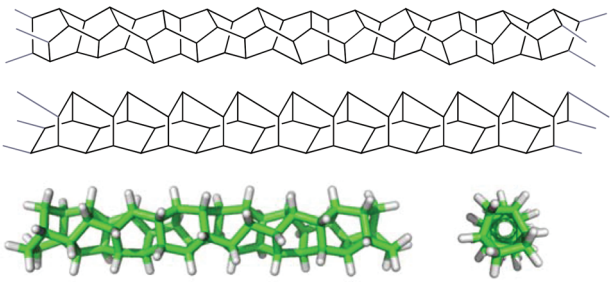
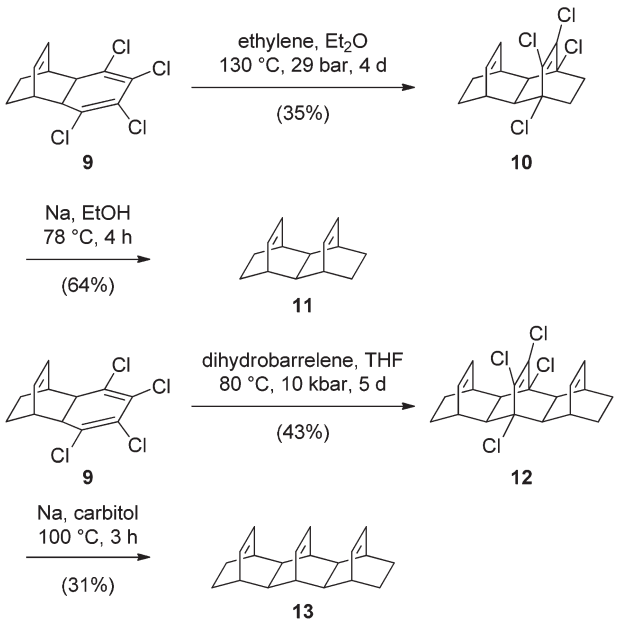


Fig. 1 Aspects of polytwistane (**8**). Top: *M* helical polytwistane (**8**) drawn in a manner that emphasizes the structural unit of twistane. Middle: *M* helical polytwistane (**8**) drawn in a manner that emphasizes the incorporated bicyclo[2.2.2]-octane units. Bottom: side view (left) and top view (right) of a $C_{52}H_{58}$-fragment of *M* helical polytwistane calculated at the B3LYP/6-31 g(d) level.[7]

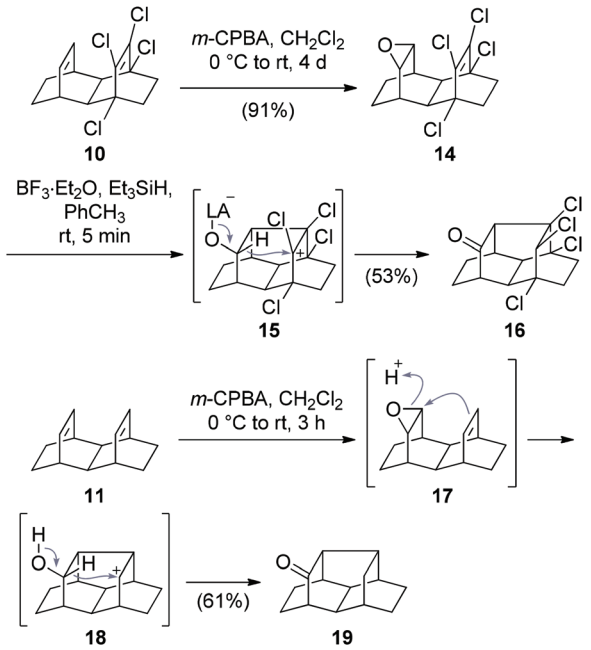


Scheme 2 Synthesis of the laticyclic conjugated precursors.

laticyclic polyenes, which are known to yield twistane motifs.[10] To this end, we synthesized the diene **11** and the triene **13** following a strategy developed by Gleiter and colleagues (Scheme 2).[11]

Addition of ethylene to triene **9** at high pressure gave tetracyclic tetrachloro diene **10**, which was dechlorinated to afford **11**. Similarly, Diels–Alder addition of dihydrobarrelene[12] to **9** gave **12**, the dechlorination of which yielded the hexacyclic triene **13**.

Our first attempts to synthesize tritwistane from dienes **10** or **11** are shown in Scheme 3. Epoxidation of tetrachloro diene **10** gave **14**. Treatment of **14** with a Lewis acid in the presence of a hydride source, however, did not yield a twistane but exclusively gave **16**. Presumably, this compound is the product of a "U-type" (instead of "N-type") nucleophilic attack, yielding intermediate **15**, followed by an intramolecular hydride shift, as evidenced by the stereochemistry of the product **16**.[13]

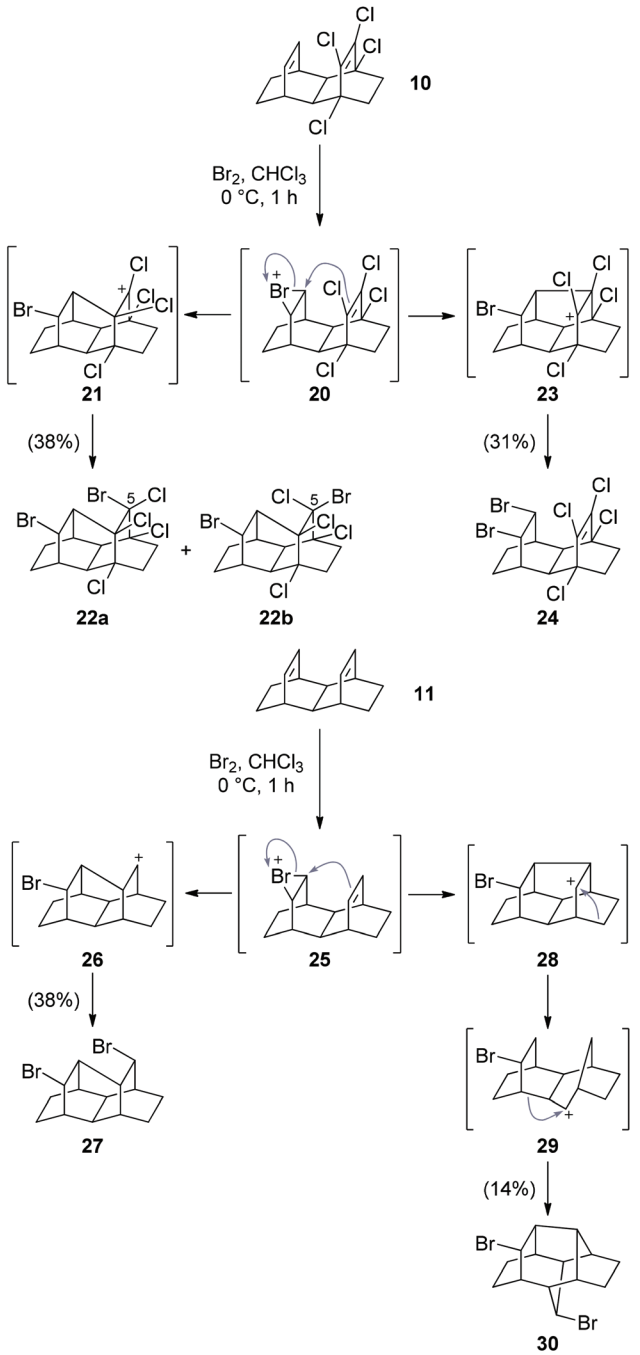


Scheme 3 Initial attempts to synthesize tritwistane *via* epoxidation of **10** and **11**.

Epoxidation of diene **11** with *m*-CPBA yielded the analogous ketone **19** as the only isolable product, due to the instability of the intermediary epoxide **17** under the conditions. The X-ray structures of ketones **16** and **19**, which bear a novel carbon skeleton, as well as epoxide **14** are shown in the ESI.†

Our attempts to access the tritwistane skeleton, *via* halogen addition, using conditions reported by Chou and coworkers[9] were more successful (Scheme 4). Exposure of tetrachloro diene **10** to bromine in chloroform gave the halogenated tritwistanes **22a,b** together with the interesting *syn*-adduct **24**. The former presumably stem from an "N-type" nucleophilic attack onto bromonium ion **20**, followed by quenching of the intermediary carbocation **21** by bromide, which yielded a 7 : 3 mixture of diastereomers **22a** and **b**, respectively. The formation of **24** can be rationalized by a "U-type" nucleophilic attack, followed by an S_N2-type displacement with overall double inversion. The X-ray structures of the major diastereomer **22a** and the *syn*-dibromide **24** are shown in Fig. 2. We next investigated the bromination on laticyclic hydrocarbon **11**, which gave the dibromo tritwistane **27** as a single diastereomer, together with the unusual dibromide **30**. The former is again the product of an "N-type" cyclization, whereas the latter presumably arises from a twofold Wagner–Meerwein rearrangement of the initial "U-type" cation **28**, followed by nucleophilic interception by bromide. The X-ray structures of **27** and the rearranged **30** are also shown in Fig. 2.

Attempts to synthesize hexatwistane derivatives *via* bromination of laticyclic triene **13** were less successful and gave complex mixtures. So far, we have been unable to separate and cleanly characterize the major components of this mixture. Global dehalogenation of tetrachloro dibromo tritwistane **22** also failed under a variety of conditions. By contrast,



Scheme 4 Synthesis of tritwistanes **22a**, **b** and **27** *via* bromination of **10** and **11**.

dehalogenation of dibromo tritwistane **27** using Chatgilialoglu's reagent[14] was more successful and gave the parent hydrocarbon **3** (Scheme 5). C_2-Symmetric tritwistane (**3**) was easy to identify due to its simplified ^{1}H- and ^{13}C-NMR spectra (see ESI†).

In summary, we have described the first synthesis of racemic tritwistane (**3**), which also yielded a variety of interesting byproducts. Several of these, such as compounds **16**, **19** and **30**, bear a novel carbon skeleton. Our results indicate that

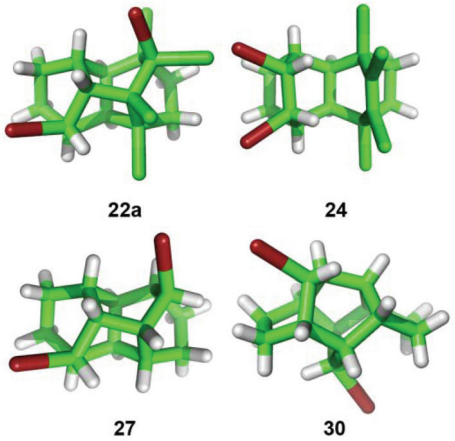
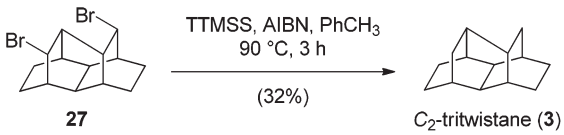


Fig. 2 X-ray structures of **22a**, **24**, **27** and **30**.



Scheme 5 Synthesis of tritwistane (**3**).

N-type additions across laticyclic polyenes are not a viable way to access longer oligotwistanes or polytwistane (**8**) due to a variety of possible side reactions and difficulties associated with the procurement of precursors. Attempts to synthesize polytwistane in a more direct fashion from acetylene itself are ongoing in our laboratory and will be reported in due course. The relationship of polytwistane to recently reported diamond nanowires[15] and ultra-small carbon nanotubes[16] is also under investigation.

Experimental section

Pentacyclo[6.2.2.2^{3,6}.0^{2,7}.0^{5,9}]tetradecan-4-one (19)

To a solution of tetracyclotetradecadiene **11** (30.0 mg, 0.161 mmol, 1.00 eq.) in CH_2Cl_2 (2.50 mL) at 0 °C was added *m*-CPBA (70–75 wt%, 37.5 mg, 0.161 mmol, 1.00 eq.). The reaction mixture was stirred at 0 °C for 1 h, was then allowed to warm to room temperature and stirred at room temperature for an additional 2 h. After dilution with CH_2Cl_2 (15 mL) the reaction mixture was poured into 10% aqueous NaOH (10 mL) and the organic layer was washed with H_2O (2 × 7.5 mL), brine (7.5 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (hexanes–EtOAc = 9 : 1) afforded ketone **19** (20.0 mg, 61%) as a colorless solid. Recrystallization from hexanes afforded crystals suitable for X-ray analysis.

R_f 0.36 (hexanes–EtOAc = 9 : 1); mp 95–97 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.80–2.71 (m, 1H), 2.40–2.29 (m, 1H), 2.27–2.19 (m, 1H), 2.17–2.10 (m, 1H), 2.07–2.01 (m, 1H), 2.00–1.88 (m, 2H), 1.85–1.72 (m, 4H), 1.67–1.53 (m, 5H),

1.52–1.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 222.7, 58.9, 47.1, 42.5, 40.6, 39.1, 38.3, 37.4, 29.5, 28.6, 28.3, 27.2, 19.8, 19.8; IR ν_{max} 2925, 2859, 1721, 1260, 1090, 1063, 1025, 994, 909, 886, 858, 812, 798, 732; HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{14}H_{18}O^+$ 202.1352; found: 202.1348.

Bromination of *syn*-3,4,5,6-tetracyclo[6.2.2.2^{3,6}.0^{2,7}]tetradeca-4,9-diene (11)

To a solution of diene **11** (49.9 mg, 268 μmol, 1.00 eq.) in $CHCl_3$ (3.00 mL) at 0 °C was added a solution of bromine in $CHCl_3$ (1.253 mL of a 1.37 vol% solution, 335 μmol, 1.25 eq.). The reaction mixture was stirred at 0 °C for 1 h and the reaction was then quenched by addition of diluted aqueous $Na_2S_2O_3$. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (3 × 15 mL). The combined organic layer was washed with $NaHCO_3$ (30 mL), brine (30 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Purification of the residue by flash column chromatography (hexanes–Et_2O = 95 : 5) afforded rearranged dibromide **30** (15 mg, 14%) and dibromotritwistane **27** (35 mg, 38%) as colorless solids. Recrystallization from hexanes afforded crystals suitable for X-ray diffraction experiments for both compounds.

5,10-Dibromopentacyclo[6.2.2.2^{3,6}.0^{2,7}.0^{4,9}]tetradecane (27). R_f 0.25 (hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.63 (d, *J* = 5.9 Hz, 1H), 4.49 (d, *J* = 5.4 Hz, 1H), 2.67–2.63 (m, 1H), 2.50–2.46 (m, 1H), 2.43–2.38 (m, 1H), 2.33–2.26 (m, 1H), 2.18–2.12 (m, 2H), 2.02–1.95 (m, 2H), 1.82–1.76 (m, 2H), 1.73–1.66 (m, 2H), 1.61–1.52 (m, 2H), 1.48–1.38 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 56.0, 54.9, 42.3, 39.8, 37.8, 37.7, 36.1, 35.6, 32.3, 27.5, 25.9, 21.5, 21.4, 21.2; IR ν_{max} 2939, 2868, 745; HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{14}H_{18}Br_2^+$ 345.9750; found: 345.9568.

9,13-Dibromopentacyclo[6.2.2.1^{2,7}.1^{3,6}.0^{10,14}]tetradecane (30). R_f 0.35 (hexanes); mp 130–136 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.12 (m, 1H), 4.78 (ddd, *J* = 5.4, 5.4, 1.3 Hz, 1H), 2.82–2.79 (m, 1H), 2.79–2.74 (ddd, *J* = 13.5, 9.6, 4.4 Hz, 1H), 2.52–2.46 (m, 2H), 2.43–2.38 (m, 2H), 2.38–2.31 (m, 4H), 2.27 (dddd, *J* = 14.4, 11.4, 4.7, 1.9 Hz, 1H), 2.11 (dddd, *J* = 14.9, 11.4, 6.0, 6.0 Hz, 1H), 1.83–1.76 (m, 2H), 1.75–1.68 (m, 1H), 1.56–1.53 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 56.3, 53.2, 52.9, 51.9, 47.3, 47.0, 43.1, 41.5, 38.0, 37.2, 28.9, 26.9, 24.0, 18.8; IR ν_{max} 2933, 823, 803, 770, 741, 719; HRMS (EI) *m*/*z*: $[M - Br]^+$ calcd for $C_{14}H_{18}Br^+$ 265.0586; found: 265.0594.

***C*$_2$-Tritwistane (3)**

To a solution of dibromide **27** (34.6 mg, 0.100 mmol, 1.00 eq.) in toluene (3.00 mL) was added TTMSS (0.075 mL, 59.7 mg, 0.240 mmol, 2.40 eq.) and one crystal of AIBN (2.50 mg, 0.015 mmol, 0.150 eq.). The resulting mixture was heated to 90 °C for 3 h and was then allowed to cool to room temperature and was concentrated *in vacuo*. The residue was purified by flash column chromatography (2 × 20 cm, *n*-pentane, 8 mL) to afford tritwistane (**3**) contaminated with some silicon species as a colorless oil. A solution of this oil in $CDCl_3$ (1.50 mL) was stirred over a fluoride polymer at room temperature for 8 d. The solution was filtered over a short silica column and the solvent was removed *in vacuo* to afford tritwistane (**3**) (6 mg, 32%) as a waxy amorphous solid.

R_f 0.92 (hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.72 (m, 2H), 1.70–1.63 (m, 6H), 1.52–1.44 (m, 10H), 1.36 (dd, *J* = 12.1, 5.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 35.4, 33.6, 29.1, 28.6, 27.3, 24.8, 22.8; IR ν_{max} 2921, 2908, 2871, 2860; HRMS (EI) *m*/*z*: $[M]^+$ calcd for $C_{14}H_{20}^+$ 188.1560; found: 188.1549.

Acknowledgements

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Notes and references

1 M. Tichý, *Tetrahedron Lett.*, 1972, **13**, 2001.
2 (*a*) K. Adachi, K. Naemura and M. Nakazaki, *Tetrahedron Lett.*, 1968, **9**, 5467; (*b*) M. Nakazaki, H. Chikamatsu and M. Taniguchi, *Chem. Lett.*, 1982, 1761; (*c*) M. Tichý and J. Sicher, *Tetrahedron Lett.*, 1969, **10**, 4609.
3 (*a*) J. Gauthier and P. Deslongchamps, *Can. J. Chem.*, 1967, **45**, 297; (*b*) A. Bélanger, J. Poupart and P. Deslongchamps, *Tetrahedron Lett.*, 1968, **9**, 2127; (*c*) E. Osawa, P. v. R. Schleyer, L. W. K. Chang and V. V. Kane, *Tetrahedron Lett.*, 1974, **15**, 4189; (*d*) D. P. G. Hamon and R. N. Young, *Aust. J. Chem.*, 1976, **29**, 145.
4 (*a*) H. W. Whitlock, *J. Am. Chem. Soc.*, 1962, **84**, 3412; (*b*) H. W. Whitlock and M. W. Siefken, *J. Am. Chem. Soc.*, 1968, **90**, 4929.
5 (*a*) H.-G. Capraro and C. Ganter, *Helv. Chim. Acta*, 1980, **63**, 1347; (*b*) H. Greuter and H. Schmid, *Helv. Chim. Acta*, 1972, **55**, 2382; (*c*) A. Bélanger, Y. Lambert and P. Deslongchamps, *Can. J. Chem.*, 1969, **47**, 795.
6 M. Olbrich, H. Quanz, S. Barua, P. R. Schreiner, D. Trauner and W. D. Allen, *Chem.–Eur. J.*, 2013, DOI: 10.1002/chem.201303081.
7 The Gaussian 03 reference is included in the ESI.†
8 (*a*) K.-I. Hirao, T. Iwakuma, M. Taniguchi, E. Abe, O. Yonemitsu, T. Date and K. Kotera, *J. Chem. Soc., Chem. Commun.*, 1974, **22**, 691; (*b*) K. Hirao, T. Iwakuma, M. Taniguchi, O. Yonemitsu, T. Date and K. Kotera, *J. Chem. Soc., Perkin Trans. 1*, 1980, 163; (*c*) M. Nakazaki, K. Naemura, Y. Kondo, S. Nakahara and M. Hashimoto, *J. Org. Chem.*, 1980, **45**, 4440.
9 (*a*) E. LeGoff and S. Oka, *J. Am. Chem. Soc.*, 1969, **91**, 5665; (*b*) E. Osawa, K. Aigami and Y. Inamoto, *Tetrahedron*, 1978, **34**, 509; (*c*) C.-T. Lin, N.-J. Wang, Y.-L. Yeh and T.-C. Chou, *Tetrahedron*, 1995, **51**, 2907; (*d*) C.-T. Lin, H.-C. Hsu and T.-C. Chou, *J. Org. Chem.*, 1999, **64**, 7260.
10 C.-T. Lin, N.-J. Wang, H.-Z. Tseng and T.-C. Chou, *J. Org. Chem.*, 1997, **62**, 4857.
11 W. Grimme, J. Wortmann, J. Frowein, J. Lex, G. Chen and R. Gleiter, *J. Chem. Soc., Perkin Trans. 2*, 1998, 1893.

12 D. A. Lightner, J. K. Gawronski and T. D. Bouman, *J. Am. Chem. Soc.*, 1980, **102**, 5749.
13 S. B. Soloway, A. M. Damiana, J. W. Sims, H. Bluestone and R. E. Lidov, *J. Am. Chem. Soc.*, 1960, **82**, 5377.
14 C. Chatgilialoglu, D. Griller and M. Lesage, *J. Org. Chem.*, 1988, **53**, 3641.
15 J. Zhang, Z. Zhu, Y. Feng, H. Ishiwata, Y. Miyata, R. Kitaura, J. E. P. Dahl, R. M. K. Carlson, N. A. Fokina, P. R. Schreiner, D. Tománek and H. Shinohara, *Angew. Chem., Int. Ed.*, 2013, **52**, 3717.
16 X. Zhao, Y. Liu, S. Inoue, T. Suzuki, R. O. Jones and Y. Ando, *Phys. Rev. Lett.*, 2004, **92**, 125502.