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An expedient synthesis of tetrakis(cyclopropylmethyl)methane

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Synthesis of tetrakis(cyclopropylmethyl)methane, a new symmetric product has been described using the radical mediated *gem*-diallylation of cyclopropylmethyl xanthate as a key step and its single crystal X-ray analysis established its C_2-symmetry.

The art of organic synthesis encompasses an enormous range of activities, in which synthesis of the designed symmetric molecules is an aesthetically pleasing endeavour.[1] The elegant synthesis of tetracyclopropylmethane **1** by de Meijere and co-workers[2] that has remained elusive until now (although the corresponding hexacyclopropylethane **2** was made about three decades back)[3] illustrates the difficulties in attaining the designed symmetric molecules.[4] The inherent steric crowding in **1** affects its conformation in the solid state resulting in an unexpected S_4 symmetry (Fig. 1).[2] In this context, it will be interesting to see what one can expect when such a steric crowding is relaxed to a certain extent as in **3**, the homologue of **1**, and how the solid state structure of **3** will be influenced by the diminished steric crowding around the central quaternary carbon and by the directional preferences of the cyclopropyl group. This communication describes the synthesis of tetrakis(cyclopropylmethyl)methane (**3**) and its solid state structure. The planned synthesis of **3** consists of an exquisite application of our *gem*-diallylation approach[5] for the synthesis of the diallyl derivative **9**, and subsequent twofold cyclopropanation of **9**. The synthesis commenced from the dicyclopropyl acetone (**4**) which was made according to the known procedure.[6] The Wadsworth-Emmons-Horner olefination of **4** by treating with diethylethoxycarbonylmethyl phosphonate resulted in the α,β-unsaturated ester **5** (Scheme 1). The ester **5** was subsequently reduced to the allyl alcohol **6**, by treating with DIBAL-H at −78 °C. ^{1}H, ^{13}C-NMR and MS studies substantiated the assigned structure of **6**. Cyclopropanation of the allyl alcohol **6** was carried out by using Furukawa's modification[7] for Simmons-Smith cyclopropanation (Et_2Zn and CH_2I_2 in ether at −20 °C for 12 h) to obtain the cyclopropanated alcohol **7**. In the ^{1}H-NMR spectrum of **7**,[10a] the hydrogens of three cyclopropane rings appeared separately and in the high field region. In the ^{13}C-NMR spectrum, one of the methylene carbons bearing the cyclopropyl (cyclopropyl = Cp) group shielded strongly (*ca.* 6 ppm) compared to the other similar methylene carbon. This can be attributed to the γ-effect[8] resulting from the through space interaction between the hydrogens of *cis*-oriented cyclopropylmethylene Cp–CH_2, and of the H_2C–OH. The alcohol was converted to its xanthate derivative **8** by treatment with CS_2 and MeI in presence of NaH. The crucial reaction, *i.e.*, transformation of **8** to the diallyl compound **9** was achieved by treating it with allyltributylstannane, catalytic AIBN in refluxing benzene in an overall yield of 43%.[5] The ^{1}H- and ^{13}C-NMR spectra of the diallyl compound **9** were as expected and only half of the signals were seen.[10b] Following the similar protocol of de Meijere and co-workers that has been used in the synthesis of **1**,[2] cyclopropanation of the diallyl compound **9** was succesfully achieved by treating **9** with an excess ethereal solution of diazomethane in the presence of catalytic $Pd(OAc)_2$,[9] and the tetracyclopropyl derivative **3** was obtained in good yield.

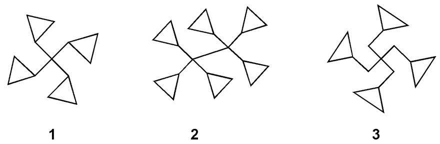
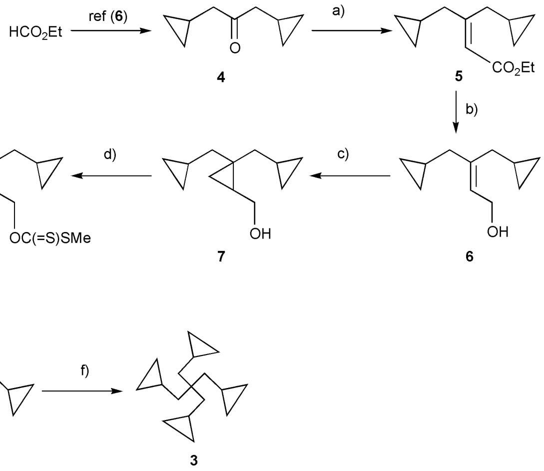


Fig. 1



Scheme 1 *Reagents and conditions*: (a) $(EtO)_2P(O)CH_2CO_2Et$, NaH, THF, rt, 12 h, 62%; (b) DIBAL-H, THF, −78 °C, 6 h, 72%; (c) Et_2Zn, CH_2I_2, diethyl ether, −20 °C, 24 h, 90%; (d) CS_2, MeI, NaH, THF, rt, 1 h; (e) allyl$SnBu_3$, AIBN, benzene, reflux, 12 h, 42% from **7**; (f) $Pd(OAc)_2$, CH_2N_2, ether, rt, 1 h, 92%.

As shown in Fig. 2, in the solid state compound **3**[11] adopts a C_2-symmetric conformation showing diminished symmetry when compared to **1**, because of the flexibility around the central carbon. In the crystal lattice, four molecules of **3** were found having a dimeric structure and its 3-dimensional structure consists of an antiparallel orientation between two adjacent repeating dimeric units.

In conclusion, an expedient synthesis of the symmetric product 'tetrakis(cyclopropylmethyl)methane' has been described for the first time using a radical based diallylation reaction as the key step. A similar approach for the synthesis of

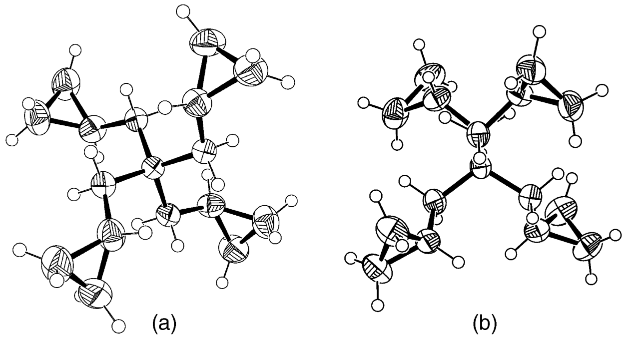

(a)
(b)

Fig. 2 *ORTEP* representation (a) of **3** and (b) of **3** in C_2-symmetric orientation.

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Cp-subsituted (aromatic) tetrakis(cyclopropylmethyl)methane derivatives and the dependence of their solid state structure on substituent is under the way.

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Notes and references

1 P. E. Eaton, *Synthesis of Non-Natural Products: Challenge and Reward*, (Tetrahedron Symposia-in-Print no. 26), Pergamon Press, Oxford, 1986; M. M. Haley and W. B. Wan in *Advances in Strained and Interesting Organic Molecules*, ed. B. Halton, Jai Press Inc, Stamford, 2000, **8**, p. 1; T.-L. Ho, *Symmetry: A Basis for Synthetic Design*, Wiley, New York, 1995.

2 S. I. Kozhushkov, R. R. Kostikov, A. P. Molchanov, R. Boese, J.-B. Buchholz, P. R. Schreiner, C. Rinderspacher, I. Ghiviriga and A. de Meijere, *Angew. Chem.*, 2001, **113**, 179; *Angew. Chem., Int. Ed.*, 2001, **40**, 180.

3 For the synthesis of **2** see: J. C. Martin and J. W. Timberlake, *J. Am. Chem. Soc.*, 1970, **92**, 978; For crystal structure of **2** see W. Bernlohr, H.-D. Beckhaus, K. Peters, H. G. von Schnering and C. Ruchardt, *Chem. Ber.*, 1984, **117**, 1013.

4 For recent reviews on multiple cyclopropyl systems see: A. de Meijere and S. I. Kozhushkov, *Chem. Rev.*, 2000, **100**, 93; R. Faust, *Angew. Chem.*, 2001, **113**, 2312; *Angew. Chem., Int. Ed.*, 2001, **40**, 2251.

5 M. K. Gurjar, S. V. Ravindhranath and S. Karmakar, *Chem. Commun.*, 2001, 241.

6 R. C. Kerber and C.-M. Hsu, *J. Am. Chem. Soc.*, 1973, **95**, 3239.

7 J. Furukawa, N. Kawabata and J. Nishimura, *Tetrahedron*, 1968, **24**, 53; N. Kawabata, T. Nakagawa, T. Nakao and S. Yamashita, *J. Org. Chem.*, 1977, **42**, 3031.

8 K. Seidman and G. E. Maciel, *J. Am. Chem. Soc.*, 1977, **99**, 659.

9 R. Paulissen, A. J. Hubert and P. Teyssie, *Tetrahedron Lett.*, 1972, 1465; J. Kottwitz and H. Vorbruggen, *Synthesis*, 1975, 636.

10 (*a*) *Spectral Data of Compound* **7**: ^{1}H-NMR (300 MHz, $CDCl_3$): 0.04–0.07 (m, 4 H); 0.19 (t, J = 5.2 Hz, 1 H); 0.38–0.51 (m, 4 H); 0.60 (dd, J = 8.8, 4.9 Hz, 1 H); 0.67–0.80 (m, 2 H); 1.03 (ddt, J = 8.7, 6.9, 5.4 Hz, 1 H); 1.15–1.30 (m, 2 H); 1.45–1.63 (m, 2 H); 3.56 (dd, J = 11. 2, 8.3 Hz, 1 H); 3.68 (dd, J = 11.2, 6.9 Hz, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 4.1, 4.5, 4.7, 4.8 (4 t, 4 C); 8.3, 8.9 (2 d, 2 C); 16.1 (t, 1 C); 25.6 (d, 1 C); 36.3, 42.2 (2 t, 2 C); 63.5 (t, 1 C). (*b*) *Spectral Data of Compound* **9**: ^{1}H-NMR (300 MHz, $CDCl_3$): 0.01–0.06 (m, 4 H); 0.40–0.49 (m, 4 H); 0.58–0.74 (m, 2 H); 1.27 (d, J = 6.3 Hz, 4 H); 2.8 (d, J = 7.3 Hz, 4 H); 5.00–5.08 (m, 4 H); 5.74–5.94 (ddt, J = 16.5, 9.2, 7.5 Hz, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 5.1 (t, 4 C); 5.9 (d, 2 C); 41.0 (s, 1 C); 41.8 (t, 4 C); 117.0 (t, 2 C); 135.4 (d, 2 C). (*c*) *Spectral Data of Compound* **3**: ^{1}H-NMR (500 MHz, $CDCl_3$): 0.01–0.06 (m, 8 H); 0.39–0.44 (m, 8 H); 0.64 (br.septet, J = 6.4, 4 H); 1.42 (d, J = 6.3 Hz, 8 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 5.26 (t, 8 C); 6.18 (d, 4 C); 29.76 (s, 1 C); 42.69 (t, 4 C). Elemental analysis Calc. for $C_{17}H_{28}$ (Mol. Wt.: 232.39) C, 87.86; H, 12.14; found C, 87.62; H, 12.27%.

11 Single crystals of **3** were recrystallised from hexane and data were collected on a Bruker SMART APEX CCD diffractometer. *Crystal data*: $C_{17}H_{28}$, M = 232.39, crystal dimensions 0.07 × 0.23 × 0.77 mm, monoclinic, space group $P2_1/n$, a = 8.8129(7) , b = 10.3361(8) , c = 16.6850(13) Å, β = 100.858(1)°, V = 1493(2) Å^3, Z = 4, D_c = 1.034 g cm^{-3}, μ (Mo-K_α) = 0.057 mm^{-1}, T = 293(2) K, 7607 reflections measured, 2620 unique [$I > 2\sigma(I)$], R value 0.0615, $wR2$ = 0.1451 (all data R = 0.0785, $wR2$ = 0.1551). All the data were corrected for Lorentzian, polarisation and absorption effects. SHELX-97[12] was used for structure solution and full matrix least squares refinement on F^2. Hydrogen atoms were included in the refinement as per the riding model. CCDC 174509. See http://www.rsc.org/suppdata/cc/b1/b110246j/ for crystallographic files in .cif format.

12 G. M. Sheldrick, SHELX-97 program for crystal structure solution and refinement, University of Gottingen, Germany, 1997.