Pergamon

Tetrahedron Letters, Vol. 37, No. 48, pp. 8779-8782, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)02030-8

A Fragmentation-Photocyclization Approach Towards Homosecohexaprismane Skeleton.

Teh-Chang Chou,* Yu-Lin Yeh, and Gerng-Horng Lin

Department of Chemistry, National Chung Cheng University, Ming Hsiung, Chia Yi, 621, TAIWAN

Abstract: Birdcaged bicyclo[2.2.2]octene-1,4-diol **15** was prepared from Diels-Alder adduct of 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene in five steps. This diol underwent DIB-promoted fragmentation to give tetracyclic dienes **16** and **17**. Intramolecular [2+2]photocyclization of **16** and **17** furnished hexacyclic cage compounds **18** and **19** having homosecohexaprismane skeleton.

Hexaprismane ([6]-prismane) (**1**) is the heptacyclic, saturated hydrocarbon $(CH)_{12}$ in which the methine units are disposed equally at the corners of a regular hexagonal prism. The compound is a member of the enchanting prismane family made up of even number of methine units of general formula $(CH)_{2n}$ and possessing D_{nh} symmetry. For more than three decades, efforts to synthesize members of this prismane family have resulted in the conquest of [4]-prismane (cubane) in 1964,[1] [3]-prismane (triprismane) in 1973,[2] and [5]-prismane (pentaprismane, housane) in 1981.[3] Since then endeavor has been shifted to focus on [n]-prismanes of higher order,[4,5] particularly the next higher homolog, hexaprismane (**1**). Many diverse synthetic strategies and significant progress towards the synthesis of hexaprismane thereby surfaced with the successful syntheses of bissecohexaprismane (**2**) in 1978,[6] secohexaprismane (**3**)[7] and 1,4-bishomohexaprismane (garudane, **4**)[8] in 1987, and 1,4-bishomohexaprismanedione (**5**) in 1996.[9] Despite this, hexaprismane remains synthetically elusive.

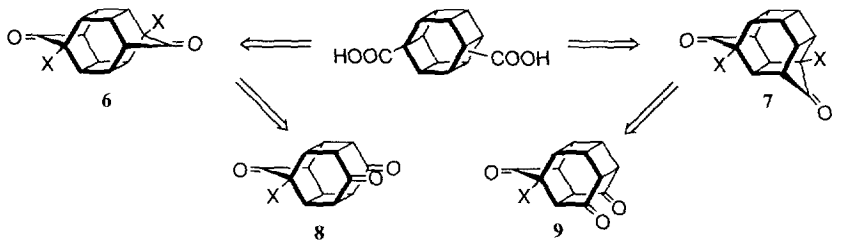
1 **2** **3** **4** **5**

Structurally, hexaprismane can be envisioned as a face-to-face dimer of benzene, in which two identical 6-membered rings are held together by six C-C bonds between them leading to a prismatic framework containing six 4-membered rings. Consequently, the major strategic concern in the synthesis of hexaprismane is the findings of methodology for proper assembly of two cyclohexane rings into a sterically more crowded and hence thermodynamically less favorable *syn*-arrangement, and for efficient construction of multiple cyclobutane rings in-between.

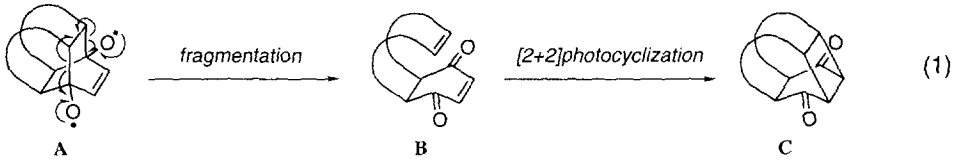
Given previous experience[1,3,6,7,8] and the thermochemical restrictions imposed upon intramolecular photocyclization of *cis*-divinylcyclobutane hydrocarbons,[10] we selected bishomohexaprismanediones **6** and **7** as eminently serviceable candidates for elaboration of hexaprismane, in the expectation of the Favorskii ring contractions[11] shown in Scheme I. Towards the heptacyclic ring skeleton of **6/7**, we contemplate on antithetic dissections to the hexacyclic systems **8/9** by removing one carbonyl group and with it two carbon-carbon bonds and one ring (Scheme I), and intend in the real synthesis to "repair" the hypothetical undoings of the antithetic process by the documented methods of introducing properly functionalized bridge between spatially

proximate carbonyl groups.[12]

Scheme I *Construction of hexaprismane skeleton by Favorskii ring contraction*



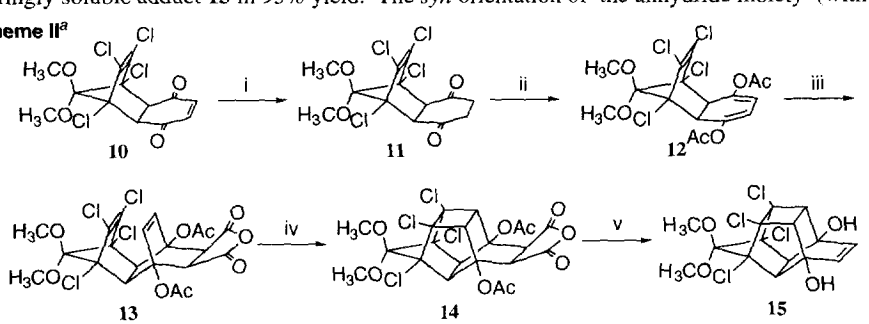
As part of a continuing program which is concerned with the synthesis and chemistry of polycyclic cage compounds,[13] we have developed a tactic for the construction of hexacyclic carbon framework of **8/9** from a caged bicyclo[2.2.2]octen-1,4-dioxy radical (**A**) by a fragmentation-photocyclization approach as depicted in eq 1. This approach is of merits for at least three reasons: (i) the progenitor of 1,4-dioxy radical **A** is easily accessible,[14] (ii) both carbon frameworks of **8** and **9** could be conceivably obtained from **A** by this process, and (iii) most importantly the required *syn*-stereochemistry of fragmentation product with proximately located C=C double bonds for effecting intramolecular [2+2]photocyclization could be inherited from cage skeleton of progenitor and well controlled by the mechanistic nature of this fragmentation. This idea has been successfully implemented and is the subject of this paper.



(1)

The preparation of the required birdcaged 1,4-diols is outlined in Scheme II, starting from the readily available Diels-Alder adduct **10**[15] of 1,4-benzoquinone and 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene. Enedione **10** was first reduced with 15% aq $TiCl_3$ in acetone[16] to provide the known dione **11**[17] which was converted to the dienol diacetate **12** by the reaction of **11** with acetic anhydride in the presence of amine bases. Diels-Alder reaction of diene **12** with an acetylene equivalent (maleic anhydride) in benzene under reflux furnished sparingly soluble adduct **13** in 95% yield. The *syn* orientation of the anhydride moiety (with respect

Scheme II[a]

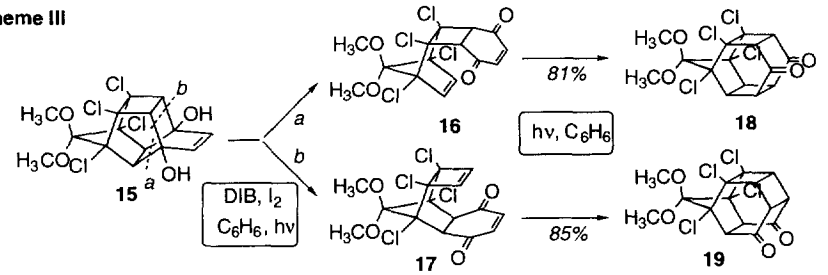


[a] (i) 15% aq $TiCl_3$, acetone, rt, 2 h, *97%*; (ii) Ac_2O, Et_3N, 4-DMAP, rt, 6 h, *72%*; (iii) maleic anhydride, benzene, N_2, reflux, *95%*; (iv) acetone, light, 2 - 3 h, *99%*; (v) Cu_2O, 2,2'-bipyridine, quinoline, H_2O, 120-130 °C, 12 h, then 190-200 °C, 24 h, *55%*.

to the C = C double bond) in the adduct **13** is assigned by expectation of an endo-type addition in accordancewith the Alder rule. Irradiation of **13** in acetone for 2-3 h produced a quantitative yield of hexacyclic photoadduct **14**. This photoclosure confirmed that the two C = C double bonds in **13** were in close proximity and thus the dienophile approached **12** from the less hindered "outside" face in the Diels-Alder reaction leading to the formation of **13**. When **14** was subjected to oxidative degradation with complexed Cu_2O in hot quinoline in the presence of a small amount of water,[18] the reaction effected degradation and the concomitant removal of acetyl groups to provide the desired birdcaged enediol **15** in 55% yield.[19]

With the acquisition of birdcaged **15**, we now shifted our efforts to effect the fragmentation reaction; the key reaction that "unlocks" the birdcaged hexacyclic framework to tetracyclic skeleton (**15→16/17**, Scheme III). As the initial attempts to effect the fragmentation reaction using HgO/I_2 and $Pd(OAc)_4/I_2$ were unsuccessful, recourse was taken to DIB/I_2 [20] as an oxidant. Thus, when a benzene solution of **15** in the presence of DIB and iodine was irradiated under nitrogen atmosphere with a 500-W tungsten filament lamp for 3 h, a mixture of two isomeric products, **16** and **17** (1:1 ratio *via* ^1H NMR spectral analysis), was obtained in 91% yield (Scheme III). Compounds **16** and **17** could not be separated by column chromatography, but were isolated in pure form by repeated recrystallization. The ^1H NMR spectrum of **16** shows two methoxy singlets (δ 3.55/3.52), two singlets (δ 6.74/6.00) for olefinic protons, and one singlet (δ 4.03) for methine protons. Taken into account with the nine-line ^{13}C NMR spectrum, **16** had to be C_s symmetrical as its precursor **15**. However, these spectral data would also be consistent with another product **17**, formed *via* fragmentation route b (Scheme III). In addition to the absorption (δ 3.73) for accidentally equivalent methoxy groups, the ^1H NMR spectrum of **17** also displays two singlets (δ 6.73/5.94) for olefinic protons, and one singlet (δ 3.95) for methine protons. A clue which might differentiate the structures of these two isomeric products came from NOE measurements. Irradiation of methine protons of **17** at δ 3.95 enhanced methoxy protons at δ 3.73 by 0.9%, but such enhancement was not observed at all in the corresponding NOE experiment on **16**.

Scheme III

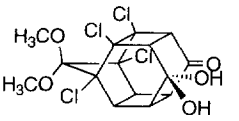


With the successful attainment of the key tetracyclic dienes **16/17**, the next operation was to call for an intramolecular photoclosure to acquire the homosecohexaprismane framework (e.g. **8/9**). Irradiation of **16/17** in benzene did take the expected course with olefinic protons being gradually and completely disappeared in 5 h, and the desired photoadducts **18/19** were obtained in 81%/85% yields, respectively (Scheme III). Hygroscopic nature of diketones **18/19** made recording their ^1H and ^{13}CNMR spectra difficult, particularly the former one whose structure was thus established as its monohydrates **18a**.[19] Unequivocal evidence for the structure **18** was obtained *via* X-ray crystallographic analysis for the corresponding monohydrate **18a** as shown in Figure 1.[21]

In short, we have disclosed a novel approach to properly functionalized homosecohexaprismane framework from a readily available caged bicyclo[2.2.2]octen-1,4-diol **15** by "cage enlargement" *via* a fragmentation-photocyclization process (eq 1 and Scheme III). The strategy delineated here offers opportunity

for amplification to hexaprismane itself as well as its related systems and will be reported in due course.

Acknowledgment. We thank the National Science Council of the ROC for financial support (NSC85-2113-M-194-001).



18a

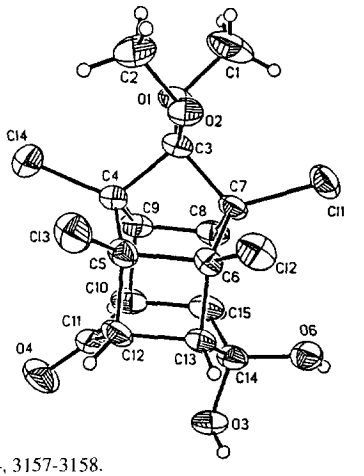


Figure 1. X-ray structure for **18a.**

*Compound **18** crystallized from acetone as a monohydrate **18a** with solvent trapped between two molecules of the unit cell.*

References and Notes

(1) Eaton, P. E.; Cole, Jr., T. W. *J. Am. Chem. Soc.* **1964**, *86*, 962-964, 3157-3158.

(2) Katz, T. J.; Acton, N. J. *J. Am. Chem. Soc.* **1973**, *95*, 2738.

(3) (a) Eaton, P. E.; Or, Y.-S.; Branca, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 2134-2136. (b) Eaton, P. E.; Or, Y.-S.; Branca, S. J.; Shankar, B. K. R. *Tetrahedron* **1986**, *42*, 1621-1631.

(4) For recent reviews on [n]-prismanes, see: (a) Mehta, G. in *Strain and Its Implications in Organic Chemistry* de Meijere, A.; Blechert, S., Eds. Kluwer Academic Publishers: Dordrecht, 1989, pp 269-281. (b) Mehta, G.; Padma, S. in *Carbocyclic Cage Compounds: Chemistry and Applications*, Osawa, E.; Yonemitsu, O., Eds. VCH: Weinheim, Germany, 1992, pp 183-215. (c) Forman, M. A.; Dailey, W. P. *Org. Prep. & Proc. Int.* **1994**, *26*, 291-320.

(5) (a) Mehta, G.; Padma, S.; Jemmis, E. D.; Leela, G.; Osawa, E.; Barbiric, D. A. *Tetrahedron Lett.* **1988**, *29*, 1613-1616. (b) Mehta, G.; Padma, S. *J. Org. Chem.* **1991**, *56*, 1298-1299. (c) Mehta, G.; Reddy, S. H. K.; Padma, S. *Tetrahedron* **1991**, *47*, 7821-7836. (d) Mehta, G.; Padma, S.; Venkatesan, K.; Begum, N. S.; Moorthy, J. N. *Indian J. Chem.* **1992**, *31B*, 473-482. (e) Forman, M. A.; Dailey, W. P. *J. Org. Chem.* **1993**, *58*, 1501-1507.

(6) Eaton, P. E.; Chakraborty, U. R. *J. Am. Chem. Soc.* **1978**, *100*, 3634-3635.

(7) (a) Mehta, G.; Padma, S. *J. Am. Chem. Soc.* **1987**, *109*, 2212-2213. (b) Mehta, G.; Padma, S. *Tetrahedron* **1991**, *47*, 7783-7786.

(8) (a) Mehta, G.; Padma, S. *J. Am. Chem. Soc.* **1987**, *109*, 7230-7232. (b) Mehta, G.; Padma, S. *Tetrahedron* **1991**, *47*, 7807-7820.

(9) Golobish, T. D.; Dailey, W. P. *Tetrahedron Lett.* **1996**, *37*, 3239-3242.

(10) (a) Osawa, E.; Aigami, K.; Inamoto, Y. *J. Org. Chem.* **1977**, *42*, 2621-2626. (b) Mehta, G.; Padma, S.; Osawa, E.; Barbiric, D. A.; Mochizuki, Y. *Tetrahedron Lett.* **1987**, *28*, 1295-1298. (c) Schmidt, W.; Wilkins, B. T. *Tetrahedron* **1972**, *28*, 5649-5654.

(11) For an overview, see: Chenier, P. J. *J. Chem. Ed.* **1978**, *55*, 286-291.

(12) (a) Dauben, W. G.; Cunningham, Jr., A. F. *J. Org. Chem.* **1983**, *48*, 2842-2847. (b) Marchand, A. P.; Deshpande, M. N. *J. Org. Chem.* **1989**, *54*, 3226-3229. (c) Marchand, A. P.; Rajapaksa, D. *Tetrahedron Lett.* **1993**, *34*, 1463-1466. (d) Aleksandrov, A. M.; Pehk, T. J.; Petrenko, A. E.; Watson, W. H. *J. Org. Chem.* **1994**, *59*, 3709-3711.

(13) Studies on Cage Compounds. 7. Part 6: Chou, T.-C.; Hong P.-C; Wu, Y.-F.; Chang, W.-Y.; Lin, C.-T.; Lin, K.-J. *Tetrahedron* **1996**, *52*, 6325-6338.

(14) (a) Chou, T.-C.; Chuang, K.-S.; Lin, C.-T. *J. Org. Chem.* **1988**, *53*, 5186-5170. (b) Lin, C.-T.; Hwang, B.-P.; Chou, T.-C. *J. Chin. Chem. Soc.* **1993**, *40*, 159-167. (c) Chou, T.-C.; Jiang, T.-S.; Hwang J.-T.; Lin, C.-T. *Tetrahedron Lett.* **1994**, *35*, 4165-4168. (d) Lin, C.-T.; Wang N.-J.; Yeh, Y.-L.; Chou, T.-C. *Tetrahedron* **1995**, *51*, 2907-2928.

(15) Marchand, A. P.; Chou, T.-C. *J. Chem. Soc. Perkin Trans. I* **1973**, 1948-1951.

(16) Blaszczak, L. C.; McMurry, J. E. *J. Org. Chem.* **1974**, *39*, 258-259.

(17) Chou, T.-C.; Hong, F.-T.; Chuang, K.-S. *Tunghai J.* **1987**, *28*, 659-668.

(18) (a) Snow, R. A.; Degenhardt, C. R.; Paquette, L. A. *Tetrahedron Lett.* **1976**, *17*, 4447-4450. (b) Fessner, W.-D.; Sedelmeier, G.; Spurr, P. R.; Rihs, G.; Prinzbach, H. *J. Am. Chem. Soc.* **1987**, *109*, 4626-4642.

(19) All new compounds (**12** - **19**) exhibited spectroscopic data consistent with the assigned structure and gave satisfactory elemental analysis. **18** was hygroscopic and thus analyzed as its monohydrates **18a**. Selected spectral data: **16** ^{13}C NMR (50 MHz, $CDCl_3$) δ 193.4 (s), 142.7 (d), 139.0 (d), 117.6 (s), 78.7 (s), 76.6 (s), 55.4 (d), 52.9 (q), 52.7 (q). **18a** ^1H NMR (200 MHz, acetone-d_6) δ 5.51 (s, 1H, -OH), 5.23 (s, 1H, -OH), 3.67 (s, 3H), 3.60 (s, 3H), 3.41-3.46 (m, 2H), 3.27 (br d, J = 2.5 Hz,1H), 3.23 (br d, J = 2.5 Hz, 1H), 3.04-3.29 (m, 2H). **19** ^1H NMR (200 MHz, $CDCl_3$) δ 3.77-3.82 (m, 2H), 3.68 (br s, 6H), 3.55 (br s, 2H), 3.46-3.50 (m, 2H).

(20) Boto, A.; Betancor, C.; Prange, T.; Suárez, E. *J. Org. Chem.* **1994**, *59*, 4393-4401, and references cited therein.

(21) We thank Dr. K.-J. Lin, Institute of Chemistry, Academia Sinica, Taipei, for having performed the X-ray structure analysis. The crystal data will be reported in a full account of this research, but until then is available from the author upon request.

(*Received in Japan* 13 *September* 1996; *accepted* 14 *October* 1996)