7,14-Dichloro[1.1]metacyclophane: A Highly Strained Aromatic Intermediate

Maurice J. van Eis, Franciscus J. J. de Kanter, Willem H. de Wolf, and Friedrich Bickelhaupt*

Scheikundig Laboratorium, Vrije Universiteit, De Boelelaan 1083, NL-1081 HV, Amsterdam, The Netherlands

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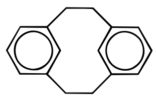
During the last four decades, [2.2]metacyclophane (**1**) and its derivatives have received considerable interest because of their unusual structure, reactivity, and spectroscopic properties. Although the parent compound was synthesized as early as 1899 by Pellegrin[1] and rediscovered by Baker[2] in 1950, the lower homologue, [1.1]-metacyclophane (**2**), has eluded synthesis. Both the difficult accessibility, resulting from its high strain, and its undoubtedly rich chemistry make **2** an interesting target. In particular, the close proximity of the 7,14-positions is expected to cause a strong interaction between the aromatic rings. In this communication we wish to report several indications for the intermediacy of a dichloro derivative of **2**, together with supporting PM3 calculations.



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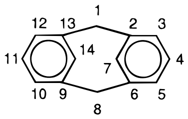

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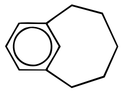

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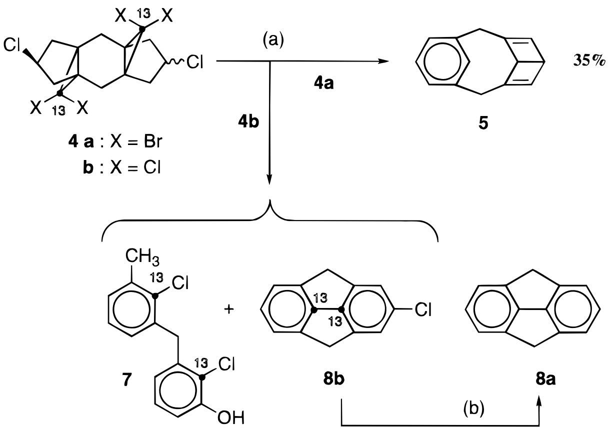
One can envision **2** to be a "double" [5]metacyclophane (**3**), and as [5]metacyclophanes can be easily generated from propellane precursors,[3] a similar synthetic approach to **2** was envisaged. In 1993, we reported that treatment of the hexahalobispropellane **4a** with *t*-BuOK in DMSO led to the formation of **5**, the mono-Dewar benzene analogue of **2** (Scheme 1).[3d]

In order to increase the thermal stability of the highly strained system of **2**, we have now attempted the synthesis of its dichloro derivative, 7,14-dichloro[1.1]-metacyclophane (**6**), by elimination reactions starting from **4b** in analogy to earlier metacyclophane syntheses.[3] Surprisingly, the reaction of **4b** with *t*-BuOK yielded, besides much polymeric material, two compounds **7** and **8b** in 9 and 10% yield, respectively (Scheme 1).[4,5] In particular the formation of the strained **8b** is intriguing. The structure of **8b** was corroborated by its reductive transformation to the parent hydrocarbon **8a**;[6] the latter was first synthesized by Trost *et al.*[7a] The formation of both compounds can be rationalized by invoking the intermediacy of **6** (Scheme 2).

The formation of phenol **7** gives strong support for the intermediacy of **6**. First, nucleophilic addition of a hydroxide ion[8] at a bridgehead position of **6** yields **9a**; this reaction, which is unfavorable in unactivated benzene derivatives, is facilitated by considerable release of strain and has precedent in [5]metacyclophane chemistry.[9] Next, protonation at C3 and deprotonation of the hydroxyl function furnishes **10**. Ring opening of **10** is again accompanied by release of strain and gives **11** which upon proton reshuffling leads to **12** and, after workup, to **7**. The yield of **7** increased to 40% when 4 equiv of water were purposely added; in this case **8b** was absent.

Scheme 1[a]



[a] (a) *t*-BuOK, DMSO, 8h, rt; (b) Et_3N, CH_3CN, irradiation (254 nm); (c) ^{13}C-labeling in **4b**, **7**, and **8**, is indicated by a dot.

The formation of **8b** is more difficult to rationalize and involves more deepseated rearrangements, in particular, of the chlorine function. In order to investigate whether or not this is a consequence of a rearrangement of the carbon skeleton, a ^{13}C-labeling experiment was performed (Scheme 1). The ^{13}C NMR spectrum of 7,14-[$^{13}C_2$] **8b** revealed the presence of an AB-system ($^1J_{CC} = 47.5$ Hz), which clearly indicates that the labeled carbon atoms end up connected to each other at the expected position.[6] This implies the occurrence of a transannular 1,4-chlorine shift. Here, we will not attempt to give a detailed explanation for the formation of **8b**, but one might assume a reaction path as outlined in Scheme 2. After the initial attack of a nucleophile, Nu, (e.g. Cl^- or *t*-BuO^-) on **6** to form **9b**, an intramolecular nucleophilic attack from C7 on C14 occurs under formation of a transannular bond, followed immediately by expulsion of Cl^- to give

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(1) Pellegrin, M. *Recl. Trav. Chim.* **1899**, *18*, 457.

(2) Baker, J.; McOmie, J. F.; Norman, J. M. *Chem. Ind.* **1950**, *77*.

(3) (a) In the case of [5]- and [6]metacyclophanes the thermal stability increases upon chlorine substitution. (b) Tobe, Y. *Top. Curr. Chem.* **1994**, *172*, 1. (c) Bickelhaupt, F.; De Wolf, W. H. In *Advances in Strain in Organic Chemistry*; Halton, B., Ed.; JAI Press Ltd: London, 1993; Vol. 3, p 185. (d) Wijsman, G. W.; Van Es, D. S.; De Wolf, W. H.; Bickelhaupt, F. *Angew. Chem.* **1993**, *105*, 739. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 726.

(4) Both new compounds were fully characterized by ^1H, ^{13}C NMR and mass spectroscopic methods.

(5) 2-Chloro-3-(2-chloro-3-methylbenzyl)phenol (**7**): ^1H NMR (400.1 MHz, $CDCl_3$, 298 K): δ 7.13 (dd, $J = 7.5$ Hz, 1.8 Hz, 1H), 7.08 (t, $J = 7.9$ Hz, 1H), 7.06 (t, $J = 7.5$ Hz, 1H), 6.92 (dd, $J = 8.2$ Hz, 1.6 Hz, 1H), 6.83 (dd, $J = 7.5$ Hz, 1.8 Hz, 1H), 6.59 (dd, $J = 7.6$ Hz, 1.6 Hz, 1H), 5.62 (s, 1H), 4.18 (s, 2H), 2.41 (s, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 151.42 (s), 137.84 (s), 136.76 (s), 136.54 (s), 134.42 (s), 129.08 (d), 127.82 (d), 127.43 (d), 126.06 (d), 122.16 (d), 120.42 (s), 114.06 (d), 37.31 (t), 20.68 (q); MS (70 eV) *m/z* 266 (M^+ ($C_{14}H_{12}{}^{35}Cl_2$), 80), 231 (85), 196 (100), 181 (24), 165 (20), 152 (17); HRMS: Calcd for $C_{14}H_{12}{}^{35}Cl_2$ 266.0265, Found 266.0270 ± 0.0006. 2-Chloro-4,8-dihydrocyclopenta-[*d,e,f*]fluorene (**8b**): ^1H NMR (400.1 MHz, $CDCl_3$, 298 K): δ 7.28 (s, 2H), 7.27 (d, $J = 7.1$ Hz, 2H), 7.10 (t, $J = 7.1$ Hz, 1H), 4.24 (s, 4H); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 154.07 (s), 153.16 (s), 137.90 (s), 137.24 (s), 132.73 (s), 128.02 (d), 125.55 (d), 124.65 (d), 44.60 (t); MS (70 eV) *m/z* 212 (M^+ ($C_{14}H_9{}^{35}Cl$), 100), 177 (34), 151 (8), 106 (5), 88 (12), 75 (5); HRMS: Calcd for $C_{14}H_9{}^{37}Cl$ 214.0367, Found 214.0369 ± 0.0006.

(6) See Supporting Information.

(7) (a) Trost, B. M.; Kinson, P. L. *J. Am. Chem. Soc.* **1970**, *92*, 2591. (b) Trost, B. M.; Kinson, P. L.; Maier, C. A.; Paul, I. C. *J. Am. Chem. Soc.* **1971**, *93*, 7275. (c) Wentrup, C.; Becker, J. *J. Am. Chem. Soc.* **1984**, *106*, 3705.

(8) Hydroxide ions are derived from small amounts of water present in the reaction mixture, which in small scale reactions is unavoidable due to the hygroscopic nature of DMSO and *t*-BuOK.

(9) Kraakman, P. A.; Valk, J. M.; Niederländer, H. A. G.; Brouwer, D. B. E.; Bickelhaupt, F. M.; De Wolf, W. H.; Bickelhaupt, F.; Stam, C. H. *J. Am. Chem. Soc.* **1990**, *112*, 6638.

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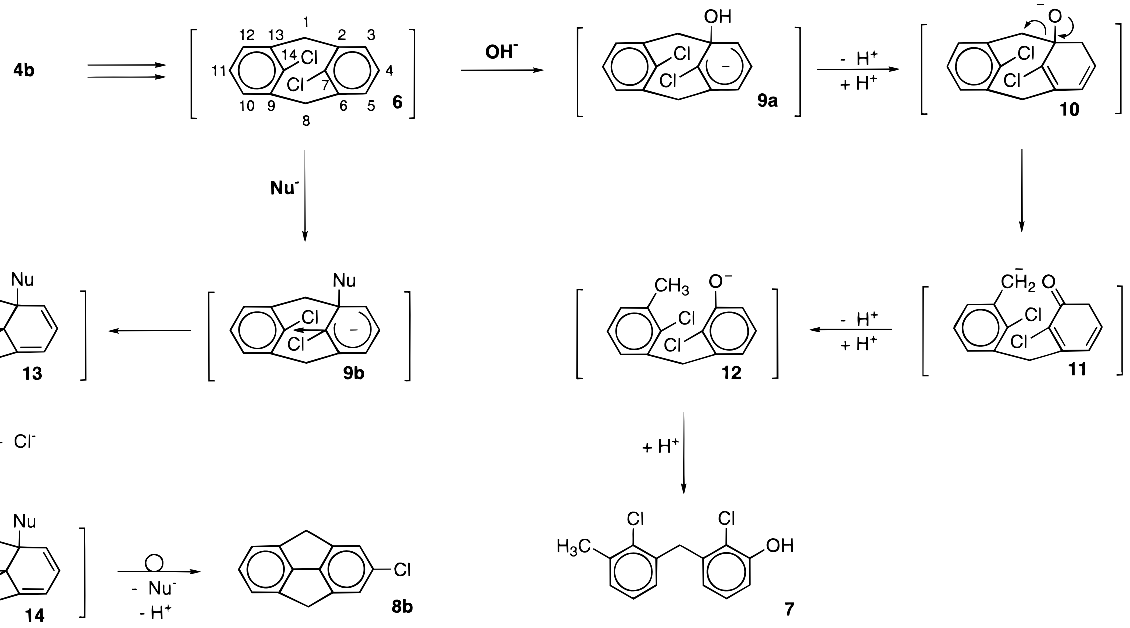
Scheme 2[a]



[a] Nu^-: nucleophile (Cl^-, *t*-BuO^-).

14. The subsequent reaction sequence, eventually resulting in the formation of **8b**, remains uncertain, but formally involves loss of the nucleophile, followed by a 1,4-migration of Cl^- and proton loss. It should be pointed out that analogous transannular reactions and rearrangements of substituents are not uncommon for [2.2]-metacyclophanes.[10] In those cases, transannular bond formation is induced by attack of an electrophile rather than by a nucleophile, and the mechanisms have not been elucidated.

In order to obtain support for the proposed mechanisms, the heats of formation and strain energies of **6**, **8b**, and several intermediates were calculated by the semiempirical PM3 method.[11] In analogy to [2.2]metacyclophane, the *anti*-conformation of **6** in which the aromatic rings point away from each other was found to be the most stable one ($\Delta\Delta H_f = 12$ kJ/mol). As anticipated, the strain energy (SE = 355 kJ/mol) by far exceeds that of *anti*-[2.2]metacyclophane (50−75 kJ/mol).[13,14] Therefore a strongly enhanced reactivity may be expected. In contrast to what one would expect intuitively, the SE of **6** is less than twice the SE of 11-chloro[5]-metacyclophane (**15**) (184 kJ/mol). This is probably due to the fact that the severe steric repulsion between the methylene groups in the bridge of **15** is partially absent in **6**. The structure of **6** showed some remarkable features, of which in particular the short transannular distance C7−C14 (2.563 Å) is worth mentioning; it is even shorter than the corresponding distance in [2.2]metacyclophane (2.633 Å).[15] Thus easy formation of a transannular bond in **6** is not surprising.

For the addition of OH^- to **6**, a large exothermic reaction enthalpy is calculated ($\Delta H_r = -294$ kJ/mol).[16,17] Moreover, the C1−C2 bond elongates to 1.626 Å upon OH^- addition, which is rather long for an sp^3-sp^3 bond. It is this bond which cleaves in the next steps (**9a** → **10** → **11**), causing a further relief of strain (ΔH_r (**9a** → **11**) = −187 kJ/mol). Furthermore, it is gratifying to find a gradual decrease of the system's energy throughout the proposed reaction sequence. For **8b** a considerable strain energy of 229 kJ/mol was estimated which is roughly in agreement with previously reported calculations for the parent compound.[7b] Attempts to intercept **6** with a dienophile such as hexafluorobutyne have thus far not been successful.

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Supporting Information Available: Experimental procedures and calculational details (6 pages).

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(10) (a) Sato, T.; Wakahayashi, M.; Okamura, T.; Amada, T.; Hata, K. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2363. (b) Tashiro, M.; Yamato, T. *J. Org. Chem.* **1981**, *46*, 1543. (c) Yamato, T.; Matsumoto, J.; Tokuhisa, K.; Shigekuni, M.; Suehiro, K.; Tashiro, M. *J. Org. Chem.* **1992**, *57*, 395. (d) Yamato, T.; Ide, S.; Tokuhisa, K.; Tashiro, M. *J. Org. Chem.* **1992**, *57*, 271.

(11) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209. The calculations were performed using MOPAC 93 (QCPE No. 445).

(12) Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; Wiley: New York, 1976.

(13) For [2.2]metacyclophane, an experimental strain energy of 50 kJ/mol has been reported;[14a] calculated values range from 54−75 kJ/mol.[14b,c]

(14) (a) Shieh, C.-F.; McNally, D.; Boyd, R. H. *Tetrahedron* **1969**, *25*, 3653. (b) Lindler, H. J. *Tetrahedron* **1976**, *32*, 753. (c) Fujise, Y.; Kakasto, Y.; Ito, S. *Tetrahedron Lett.* **1986**, *27*, 2907.

(15) Brown, C. J. *J. Chem. Soc.* **1953**, *3278.*

(16) ΔH_f (OH^-) = −73.2 kJ/mol (PM3).

(17) It should be noted that even for the addition of OH^- to 1-chloro-2,6-dimethylbenzene, a negative reaction enthalpy is calculated (ΔH_r = −171 kJ/mol), although the latter value is considerably smaller than that for the addition of OH^- to **6**.