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Pentacyclo[5.1.0.$0^{2,4}$.$0^{3,5}$.$0^{6,8}$]octane (Octabisvalene)†

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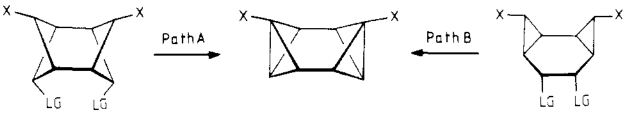
The title compound **4**, the third and last hitherto unknown formally saturated member of the $(CH)_8$ family,[1] should be intermediate in strain energy between cubane and cuneane, as Eaton noticed in 1970.[2] An MM2 calculation performed recently resulted in 154 kcal/mol of strain energy for **4** compared with 166 kcal/mol for cubane and 137 kcal/mol for cuneane.[3] This unusual polycyclic framework, potentially highly reactive as well as aesthetically appealing (D_{2h} symmetry), has resisted several previous attempts at synthesis. Thus twofold photochemical cyclobutene → bicyclobutane isomerization in a tricyclic precursor proved impossible,[4] while carbenoid intermediates derived from tetracyclo[5.1.0.$0^{2,4}$.$0^{3,5}$]octane did not undergo the expected insertion into a CH bond to form the missing lateral bicyclo[1.1.0]butane bond of **4**, instead either skeletal rearrangement[5] or polymerization[6] occurred. These failures were ascribed to the close spatial proximity of two highly reactive moieties, the intermediate carbene center and the bicyclobutane fragment.[7] We reasoned that it should be possible to build the octabisvalene carbon framework in a controlled manner by using tamed intermediates ("carbanions") and/or substitutively stabilized bicyclo[1.1.0]butane units, closing either two central bicyclobutane bonds (path A) or two lateral bicyclobutane bonds (path B) in the last steps (Scheme I). Path A suffered from inaccessibility of appropriately substituted diasteranes (the hydrocarbon being elusive until 1987[8]); path B, however, was recently used by us to prepare (*Z*)-3,7-bis(phenylsulfonyl)octabisvalene (**3**)[3] and octabisvalene-3-carbonitrile (**6**).[9,10] Here we report on the successful completion of the synthesis of parent compound **4** from either one of these precursors.

Disulfone **3**, obtained earlier in an eight-step sequence from *cis*-benzene trioxide **1** (overall yield 14%),[3] is now prepared in a two-step process (overall yield 24%), due to the finding that (i) the trisbenzenesulfonate **2** can be obtained in 84% yield in a one-flask procedure from **1** and 3 equiv of $PhSO_2CH_2Li$, followed by esterification with $PhSO_2Cl$ and (ii) triple cyclization to **3** is achieved again in a single operation (29%) by treatment of **2** with either $PhSO_2CH_2Li$ in THF or H_3CSOCH_2K in DMSO as the base (Scheme II).

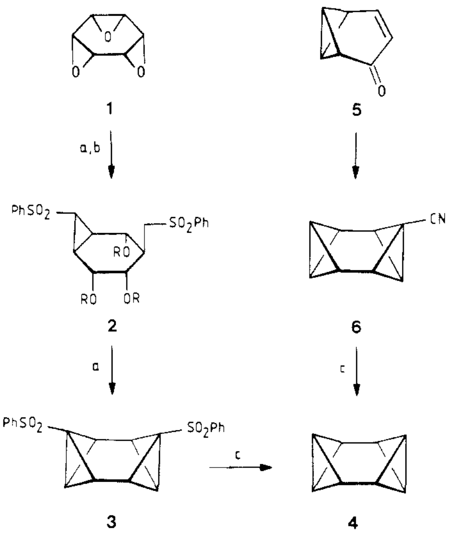
To obtain the hydrocarbon **4** from **3** twofold reductive scission of a C–S bond at a bicyclobutane bridgehead is required. Such a process necessarily involving radical and/or anionoid intermediates must not result in cleavage of the central bicyclobutane bond.[7] The 1-bicyclobutyl radical, though not known to the best of our knowledge,[11] should be regarded as presumably very reactive,[12] thus the generation and in situ protonation of such species should desirably be performed at low temperature.

Scheme I[a]



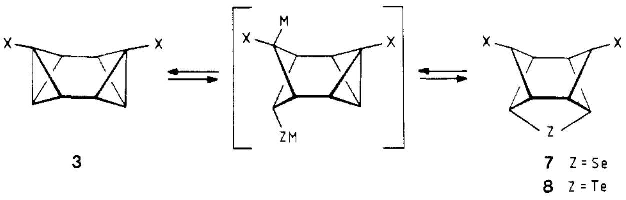
[a] X = acidifying substituent; LG = leaving group.

Scheme II[a,b]



[a] R = SO_2Ph. [b] (a) $PhSO_2CH_2Li$ (3 equiv), (b) $PhSO_2Cl$ (3 equiv), (c) Na/liquid NH_3.

Scheme III[a]



[a] X = SO_2Ph; M = Li, Na.

Although contradictory reports exist on the reactivity of alkyl aryl sulfones toward Na in liquid NH_3,[13,14] this mild reagent seemed attractive in that it is known not to affect bicyclo[1.1.0]butanes[5a,15] (in contrast to Na/Hg[3]) and since its use will make unnecessary the separation of volatile **4** from any organic solvent. In fact, treatment of a suspension of **3** in liquid NH_3 with 8 equiv of Na at -78 °C for a few minutes and quenching with solid NH_4Cl results in ca. 20% yield of **4**[16] along with benzene. After evaporation of the NH_3 **4** is separated from NH_4Cl and sulfur-containing byproducts by distillation in vacuo into a cold trap (liquid N_2).

Cyano-substituted octabisvalene **6** (obtained from tricyclo[4.1.0.$0^{2,7}$]hept-4-en-3-one (**5**) in five steps, 10% overall)[9] as a precursor to **4** poses the problem of cleavage of the exocyclic C–C bond without affecting the molecular skeleton. Fortunately, the C–CN bond is prone to reductive cleavage by a variety of reag-

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† This paper is dedicated to Prof. E. J. Corey on the occasion of his 60th birthday.

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ents,[17] one of them again being Na in liquid NH_3.[18] In fact treatment of **6** with this reagent furnishes **4** in 32% yield.[16]

Hydrocarbon **4**, isolated as a colorless solid (mp 27-30 °C) by preparative GLC on SE 30 at 50 °C, is characterized by its mass spectrum (very similar to that of cubane[19]) [*m/e* 104 (15), 103 (43), 102 (10), 78 (100), 77 (44), 63 (18), 52 (45), 51 (67), 50 (51), 39 (83), 38 (23)], by its simple IR spectrum [3088, 3016, 1434, 1411, 1120 cm^{-1} (in CCl_4)], and by its unique NMR spectra: ^1H NMR ($CDCl_3$, 250 MHz) $\delta = 2.19$ and 1.87 (multiplets of 4 H each); coupling constants obtained by simulation: $J_{1,2} = 4.9$, $J_{1,3} = 0.1$, $J_{1,5} = -0.6$, $J_{1,6} = 5.4$, $J_{1,7} = 2.8$, $J_{3,4} = 11.3$, $J_{3,7} = 0.0$, $J_{3,8} = 0.0$; ^{13}C NMR ($CDCl_3$) $\delta = 35.09$ (d, $^1J = 160$ Hz, C-1) and 9.58 (d, $^1J = 206$ Hz, C-3). **4** is thermally inert up to 140 °C (in pyridine-d_5). A study on reactivity and properties of **4** in relation to bicyclo[1.1.0]butane and to other $(CH)_8$ isomers is in progress.

Appropriate starting materials for a path A access to the octabisvalene framework, functionalized tetracyclo[4.1.1.$0^{2,4}$.$0^{3,5}$]octanes or tricyclo[3.1.1.$1^{2,4}$]octanes, are now available by addition of nucleophiles to **3**.[3] Thus attack of the divalent nucleophiles Na_2Se and Na_2Te on **3** in MeOH/THF furnishes the selenide **7** and the telluride **8** (89% and 87% yield, respectively, Scheme III), which upon treatment with excess *n*-butyllithium in THF undergo metalation and double intramolecular ring-closing substitution to afford **3** (64% and 83%, respectively).[20]

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ClO_2 Oxidation of Amines: Synthetic Utility and a Biomimetic Synthesis of Elaeocarpidine[1]

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Chlorine dioxide (ClO_2)[2] is a gaseous free radical that is readily generated and stored in moderate concentrations (ca. 0.25 M at 0-5 °C) in either aqueous or selected organic solvents. ClO_2 reacts with tertiary amines to produce iminium ions which undergo hydrolysis in the presence of water (eq 1). Kinetic studies by

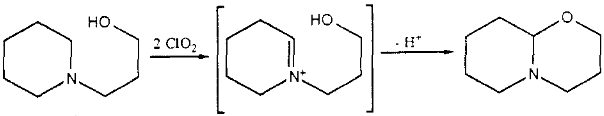
$$R_2\ddot{N}-CH_2R' \overset{\cdot ClO_2}{\rightleftharpoons} R_2\dot{N}^+-CH_2R' \xrightarrow{-H^+} R_2\overset{\cdot}{\overline{N=C}}HR'$$

$$\xrightarrow{\cdot ClO_2} R_2N^+{=}CHR' \xrightarrow{H_2O} R_2\ddot{N}H + R'CHO + H^+ \quad (1)$$

Rosenblatt and co-workers[3] have determined that the oxidation of tertiary amines by ClO_2 occurs via an electron abstraction route similar to that involved in the electrochemical oxidation of amines.[4]

Surprisingly, the synthetic utility of ClO_2 has hardly been explored.[2] We report here the use of ClO_2 to generate and trap iminium ions in situ with both internal and external nucleophiles, yielding a variety of α-substituted amines and nitrogen heterocycles.

Tertiary aminoalcohols react with ClO_2 in basic media to give moderate yields of bicyclic oxazolidines and tetrahydro-1,3-oxazines (Table I). Yield optimization studies using 1-piperidinepropanol (**1**) as a model substrate (eq 2) indicated that the



1 **2** (2)

maximum yield (62-67%) of the desired bicyclic product **2** was obtained in the range of pH 9-11. In a typical oxidative cyclization a solution of ClO_2 was slowly added to a solution of the amine; sodium borate buffer, along with simultaneous addition of aqueous NaOH, was used to maintain the pH in the range 9.0 ± 0.2. Cyclizations of 2-methyl-substituted 1-piperidinepropanol and 1-piperidineethanol (Table I) show that there is a distinctly greater regiochemical tendency for ring closure to take place at the less-substituted α-carbon of the piperidine moiety. On the other hand, the mechanistically different $Hg(OAc)_2$ oxidations of the same compounds[5] yield products resulting from oxidation and ring closure predominately at the more-substituted piperidine α-carbon.

Reaction of tertiary amines with ClO_2 in the presence of 5-7 mol-equiv of aqueous sodium cyanide as an external nucleophile affords 53-83% yields of α-cyano-substituted tertiary amines (Table II).[5,6]

In the case of oxidative α-cyanation of *N*-methylpyrrolidine a high ratio of ring cyanation to methyl cyanation (>8:1) was observed. This same observation in the electrochemical cyanation has been explained as an electrode effect.[4] However, a stereoelectronic requirement for periplanarity of an α C-H bond with the partially occupied orbital on the nitrogen of the intermediate aminium radical cation in the second step of the oxidation (loss of a proton from the 2-carbon), may, at least in part, offer a better explanation for the observed results.[7]

α-Cyano-substituted tertiary amines can provide masked carbonyl anion equivalents in basic media[8,9] and iminium ion salts through loss of cyanide ion in acidic media.[10] This versatility makes the N,N-disubstituted α-aminonitriles available directly from fully formed tertiary amines by ClO_2-mediated cyanation (as well as $Hg(OAc)_2$ oxidation[5,6] and the three-step "one-pot" modified Polonovski procedure[10]) excellent intermediates for synthetic purposes.[8]

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