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Chemical Properties of Dodecahedrane. Monofunctionalization Reactions

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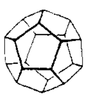
The I_h symmetry of the pentagonal dodecahedrane (**1**) qualifies it as the most highly symmetric of all organic molecules. One end result of this aesthetically appealing feature is the identity of all 20 constituent methine units. Since disclosure was made of the first synthesis of this spherical $C_{20}H_{20}$ system,[2,3] significant improvements have been realized in the Paquette approach[4,5] such that the compound can currently be obtained in 25-50-mg lots if desired. Since differently substituted dodecahedranes are of interest in their own right and as precursors to a host of interesting molecules, a systematic investigation of the chemical reactivity of **1** has been undertaken. Reported herein are key observations concerning the direct monofunctionalization of this unusual hydrocarbon.

The geometry[6,7] and rigid conformational characteristics[8] of **1** are recognized to require almost ideal sp^3 hybridization at carbon. Development of positive charge at any site is not expected to be met with ready accommodation of planarity. Moreover, the dodecahedryl cation (DDH^+) clearly lacks the normal stabilizing effect of alkyl substitution,[9] since no C–C (or C–H) bond can be oriented trans to the vacant orbital that is strongly directed to the molecular exterior. For these reasons, the generation of DDH^+ was expected to be akin to the behavior exhibited by the perhydrotriquinacene system, whose spectacular deviation from the norm[10] (10^9-fold rate retardation in solvolysis of the 10-tosylate)[11] has been documented. The situation is quite unlike that available in adamantane,[12] and indeed very significant differences have been found between adamantane and **1**.[13]

Stirring **1** in neat bromine *at room temperature*[14] overnight led quantitatively to monobromide **2a**. Although **2a** was unreactive toward K_2CO_3 or $AgNO_3$ in refluxing aqueous tetrahydrofuran,[15]



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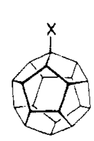
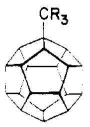
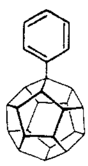


2a, X = Br
b, X = Cl
c, X = F



3a, CR_3 = COOH
b, CR_3 = COOMe
c, CR_3 = CH_2OH
3d, CR_3 = CHO
e, CR_3 = $CONH_2$
f, CR_3 = CH_3



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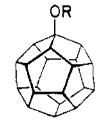
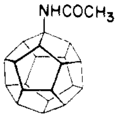


5a, R = $COCF_3$
b, R = H
5c, R = CH_3
d, R = NO_2



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conversion to chloride **2b** (91%) and fluoride **2c** (89%) proved possible with appropriate Lewis acid catalysis ($FeCl_3$, CH_2Cl_2, room temperature, 4 h; $AgBF_4$, CH_2Cl_2, Et_2O, room temperature, 20 h).[16] The sluggish response of DDH–Br to ionization was also encountered in our inability to achieve Koch–Haaf carboxylation under standard conditions.[14,17] However, when recourse was made instead to bubbling CO into magic acid solutions of **2a**,[18] access was successfully gained to **3a**. Direct treatment with CH_2N_2 gave in 60% yield the methyl ester **3b**, the structural features of which were corroborated by X-ray crystallographic analysis.[19] Alcohol **3c** and aldehyde **3d** were derived conventionally from **3b**. Exposure of the methyl ester to a large excess of Me_2AlNH_2 according to Weinreb,[20] but with gentle warming, provided amide **3e** in quantitative yield after 24 h.

Still more varied carbon functionalization was achieved by other avenues. For example, warming a mixture of **2a** and $FeCl_3$ in benzene for 3 h furnished the phenyl derivative **4** (94%). Direct methylation was most conveniently realized by exposure of **2a** to Me_3Al in hexane[21] (room temperature 24 h, 90%). The identity of **3f** with material prepared by total synthesis[22] was accomplished spectroscopically.

Investigation of the controlled oxygenation of **1** was successful from several directions. Dodecahedranol (**5b**) was obtained in 76% yield by treatment of **1** with $Pb(OAc)_4$ in a CF_3COOH–CH_2Cl_2 solvent system containing LiCl[23] followed directly by saponification of the trifluoroacetate **5a**. Alternatively, **5a** is available by reaction of **2b** with $AgOCOCF_3$ in CF_3COOH (room temperature, 18 h, 96%). A related protocol (AgOTf, CH_3OH–CH_2Cl_2 (1:1), room temperature, 18 h) was utilized to prepare methyl ether **5c** (71% from **2b**). Dissolution of **2a** into magic acid at −78 °C and quenching of the cation solution in cold methanol[24] delivered **5c** with almost equal efficiency (61%). Treatment of **1** with commercial $NO_2{}^+BF_4{}^-$ in $CHCl_3$[25] gave rise to nitrate ester **5d** (84%) rather than the nitro compound.

Finally, formation of a nitrogen derivative was achieved by again making recourse to the triflate.[26] Suspension of **2a** and AgOTf

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[1] The Ohio State University Postdoctoral Fellow, 1986-1988.

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[3] An alternative route to **1** from pagodane has recently been described: Fessner, W.-D.; Murty, B. A. R. C.; Worth, J.; Hunkler, D.; Fritz, H.; Prinzbach, H.; Roth, W. D.; Schleyer, P. v. R.; McEwen, A. B.; Maier, W. F. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 452.

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[13] Space limitations preclude substantive discussion of these issues here. However, detailed comparison will be made later in a full paper.

[14] The bromination of adamantane is reported to require heating at the reflux temperature for 4.5 h: Stetter, H.; Schwarz, M.; Hirschhorn, A. *Chem. Ber.* **1959**, *92*, 1629.

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Table I. Monosubstituted Dodecahedranes

substituent	mp, °C	^{13}C δ (quart C)	m/z (M^+) calcd	m/z (M^+) obsd
Br	>240	96.98	340.0650	340.0628
Cl	>280	104.39	294.1175	294.1140
F	>260	137.64	278.1487	278.1476
COOH	>250	b	304.1463	304.1449
COOMe	192-193	84.54	319[c]	319
CH_2OH	>250	81.86	290.1681	290.1659
CHO	>250	90.00	288.1514	288.1519
$CONH_2$	>250	85.61	303.1623	303.1640
C_6H_5	200-201	84.42	336.1870	336.1874
$OCOCF_3$	183-185[a]	126.47	258.1408[d]	258.1407
OH	>250	115.99	276.1515	276.1482
ONO_2	220	129.89	259[e]	259
$NHCOCH_3$	>250	95.77	317.1780	317.1772

[a] Dec 220 °C. [b] Very low solubility. [c] CI (M + 1). [d] ($M^+ - CF_3COOH$). [e] ($M^+ - ONO_2$).

in hot acetonitrile and subsequent hydration delivered **6** (100%).

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Chemical Properties of Dodecahedrane. The Dodecahedryl Cation and 1,16-Dodecahedryl Dication. Regioselective Difunctionalization of the Sphere[1a]

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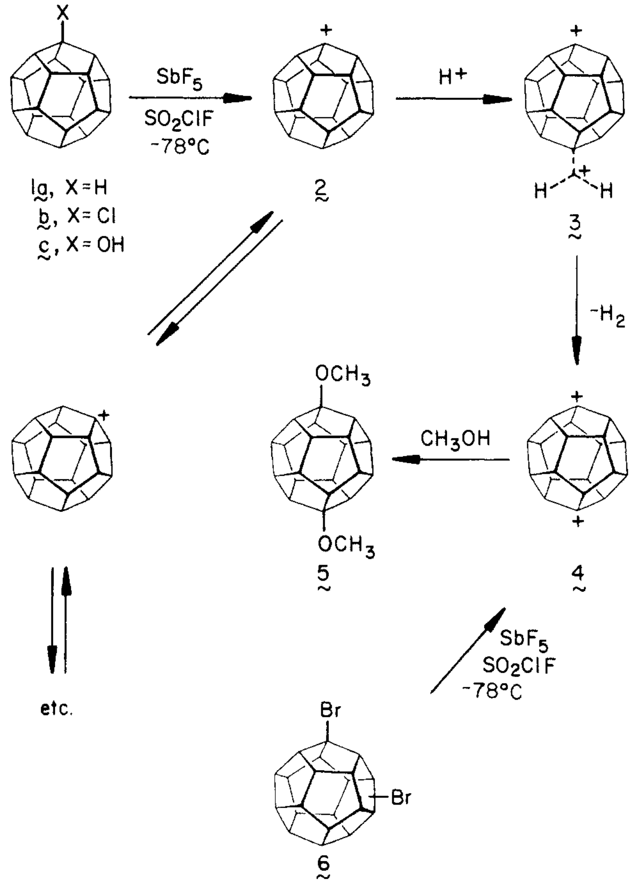
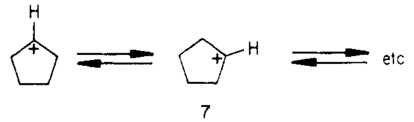
The challenge of defining practical synthetic routes for arrival at dodecahedrane (**1a**) has been met in two laboratories.[2,3] The preceding report defines for the first time various protocols capable of delivering a wide range of monofunctionalized dodecahedranes.[4] Practical exploitation of this chemistry rests heavily, although not exclusively, on *transient generation and efficient trapping* of the monocation. Several empirical observations made in the course of these studies implicated for $C_{20}H_{19}^+$ (**2**) a lability that was not at all expected.[5] For this reason, we sought to generate and examine **2** under long-life conditions. Herein is described the direct spectral observation of **2** in superacid solution, an analysis of its stability and capacity for degenerate isomerization, and the remarkable ease of its conversion to the 1,16-dication **4**.

Careful dissolution of 5 mg of chlorododecahedrane (**1b**)[4] in 1 mL of SO_2ClF containing ~250 mg of SbF_5 at −78 °C in a 5-mm NMR tube gave a pale yellow-colored solution. The 200 MHz ^1H NMR spectrum[6a] of this solution at −70 °C revealed a set of three absorptions at δ 4.64 (br, 3 H), 3.05 (br, 7 H), and 2.59 (br, 9 H) as seen in Figure 1A.[6b] The peaks did not split further at 500 MHz. The 50 MHz ^{13}C spectrum consisted of six absorptions at 363.9 (s), 81.1 (d), 64.4 (d), 64.1 (d), 63.0 (d), and 60.9 (d) ppm, clearly indicating formation of the static dodecahedryl cation (**2**). Ion **2** was similarly obtained from dodecahedranol (**1c**),[4] although more slowly. The limited solubility of dodecahedrane necessitated that the superacidic medium be warmed to 0 °C for dissolution to occur. Under these conditions, smooth conversion to **2** also materialized.



We considered that the dodecahedryl cation could undergo rapid hydrogen scrambling (through 1,2-hydride shifts) similar to that observed in cyclopentenyl cation **7**, a process that would render



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all the carbon and hydrogen atoms equivalent. However, no such degenerate process was observed as indicated by the lack of change in the ^1H NMR line shapes, even when solutions of **2** were allowed to warm to 0 °C. Thus, the lower barrier for such degenerate rearrangement is approximately 15 kcal/mol. The findings presented below suggest that the actual barrier is not apt to be much higher however.

Upon standing in the superacidic solution for 6-7 h at −50 °C, monocation **2** is slowly and irreversibly transformed into a new species displaying much simplified NMR spectra. Only two absorptions are seen at δ 4.74 (br, 6 H) and 3.23 (br, 12 H) in

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(1) (a) Considered as Stable Carbocations, Part 271 at the University of Southern California. (b) The Ohio State University Postdoctoral Fellow, 1986-1988.

(2) (a) Ternansky, R. J.; Balogh, D. W.; Paquette, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 4503. (b) Paquette, L. A.; Ternansky, R. J.; Balogh, D. W.; Kentgen, G. *Ibid.* **1983**, *104*, 5446.

(3) Fessner, W.-D.; Murty, B. A. R. C.; Worth, J.; Hunkler, D.; Fritz, H.; Prinzbach, H.; Roth, W. D.; Schleyer, P. v. R.; McEwen, A. B.; Maier. W. F. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 452.

(4) Paquette, L. A.; Weber, J. C.; Kobayashi, T., preceding paper in this issue.

(5) Unpublished observations of J. C. Weber and T. Kobayashi at The Ohio State University.

(6) (a) The NMR spectra were recorded on a Varian Associates Model VXR-200 NMR spectrometer equipped with a variable temperature broad band probe. (b) The observed relative intergral area of the three absorptions of 3:7:9 in **2** indicates that the apical hydrogen atom at the 16-position which is farthest from the positive charge experiences more deshielding (δ = 3.05) than the other belt hydrogens (δ = 2.59) which are much closer to the positive charge. This may be due to a unique cage effect in the dodecahedrane skeleton.

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