Acknowledgment. These investigations were supported by the NSF (Presidential Young Investigator Award), the Alfred P. Sloan Foundation, and the Dreyfus Foundation (Teacher-Scholar Award, 1984-1989). Matching funds for the PYI were generously provided by Stuart Pharmaceuticals and Pfizer, Inc. We thank Dr. Terrence W. Doyle (Bristol-Myers Co.) for several stimulating discussions on this topic and Dr. Glen Spears for many helpful suggestions.

Supplementary Material Available: Spectral data and experimental procedures for **8-13** and **15-17** (10 pages). Ordering information is given on any current masthead page.

1,2:3,4:5,6-Tris(bicyclo[2.2.2]octeno)tropylium Ion: An All-Hydrocarbon Carbocation with Extraordinary Stability

Koichi Komatsu,* Hidekazu Akamatsu, Yasuhisa Jinbu, and Kunio Okamoto†

Department of Hydrocarbon Chemistry
Faculty of Engineering, Kyoto University
Sakyo-ku, Kyoto, 606 Japan

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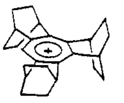
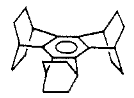
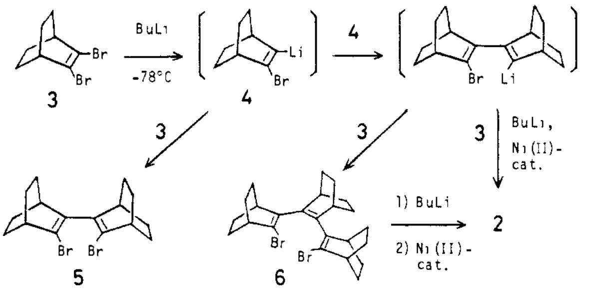
How much stability can be attained by a carbocation composed of only carbon and hydrogen? Here we report the synthesis of a new tropylium ion annelated with three bicyclo[2.2.2]octene units **1**, which shows a pK_{R^+} of 13.0, the highest value ever recorded. Also described is a possible reaction pathway for the formation of its precursor, the highly symmetrical benzene **2**.


1


2

Continuous efforts have been made for the search of new carbocations possessing enhanced thermodynamic stability. So far, the cyclopropenylium ion substituted with guaiazulenyl[1] or cyclopropyl groups[2] is ranked as the most stable with a pK_{R^+} value around 10.0. In the tropylium ion series, σ-conjugative stabilization by poly(cyclopropyl) groups seems to be limited due to the saturation effect.[3] Nevertheless, it is more effective than π-conjugation,[4] inductive electron donation,[3] or intramolecular charge-transfer interaction.[5] In this connection, it has been shown that the annelation with a bicyclo[2.2.2]octene unit is more effective in stabilizing the tropylium ion than that with a highly strained bicyclo[2.1.1]hexene unit.[6] Thus, substantial stabilization is expected for the trisannelated cation **1**.

For the synthesis of the precursor benzene **2**, trimerization of bicyclo[2.2.2]octyne or its equivalent seemed feasible. Following the Gassman's method for generation of norbornyne,[7] the dibromide **3**[8] was lithiated with n-butyllithium at -78 °C in THF and was treated with 10 mol % of nickelocene (or $NiBr_2(PPh_3)_2$). After completion of the reaction by slowly warming to room temperature, there were isolated the expected benzene **2**[8] and the trimeric dibromide **6**[8] in yields of 33% and 18%, respectively. The rest of the products were a mixture of relatively low molecular weight bromides containing one to three bicyclooctene units, rather than high polymers. When 0.5 equiv of n-butyllithium was used, the dimeric dibromide **5**[8] was obtained in 34% yield in place of any appreciable amount of **2**. These results suggest that **2** is formed not necessarily by trimerization of bicyclo[2.2.2]octyne but by way of consecutive coupling of the bicyclo[2.2.2]octene unit. This is supported also by the fact that **6** is quantitatively cyclized to **2** by the same procedure.



The CuBr-catalyzed ring expansion of **2** proceeded only by the use of a large excess (25 molar equiv) of diazomethane in refluxing 1,2-dichloroethane. The resulting cycloheptatriene,[8] which was isolated in 15% yield (92% based on consumed **2**) by chromatography over SiO_2(93%)-$AgNO_3$(7%), was treated with $Ph_3C^+SbF_6^-$ to give the salt **1**·SbF_6^-[8] in 91% yield.

The definite upfield shifts observed for both the ^{13}C and ^1H NMR signals of the tropylium ring in **1** as compared with those in the bicyclo[2.2.2]octenotropylium ion **7**[9] are indicative of decreased charge density on the cationic ring in **1** and its enhanced thermodynamic stability. The pK_{R^+} value was then determined spectrophotometrically at 25 °C in a glycine (0.1 M)-NaOH (0.1 M) buffer prepared in 50% aqueous MeCN (pH 10). By further alkalification with 20% NaOH, *the half-neutralization point, which corresponds to the pK_{R^+} value, was attained at pH 13.0.*[10] In accord with this, **1** undergoes no reaction with such nucleophiles as PhS^- (pK_a of the conjugate acid, 8.3), PhO^- (9.9), CO_3^{2-} (10.3), and Et_3N (11.0). The enhanced stability of **1** is also demonstrated by its highly negative reduction potential (E_{pc} = -1.120 V versus Ag/Ag^+ in MeCN by cyclic voltammetry with a scan rate of 0.1

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† Present address: Meisei Chemical Works, Ltd., 1 Nakazawacho, Nishikyogoku, Ukyo-ku, Kyoto, 615 Japan.

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(8) All new compounds were characterized by their IR, UV, ^1H NMR, and ^{13}C NMR spectral data and elemental analyses and/or mass spectroscopy. Selected spectral data for the important compounds are given below. For the full description of spectral data, see Supplementary Material. **1**·SbF_6^-: mp 290-292 °C dec; UV (MeCN) λ_{max} 256 (log ϵ 4.71), 308 nm (4.01); ^1H NMR (300 MHz, CD_3CN) δ 8.55 (1 H, s), 4.13 (2 H, s), 4.07 (2 H, s), 3.56 (2 H, s), 2.05 (12 H, d), 1.44 (12 H, d); ^{13}C NMR (25 MHz, CD_3CN) δ 168.3 (s), 166.0 (s), 163.9 (s), 144.2 (d), 42.7 (d), 36.6 (d), 36.1 (d), 25.0 (t), 24.8 (t), 24.7 (t). **2**: mp 277-279 °C (sealed tube); UV (MeCN) λ_{max} 222 sh (log ϵ 3.62), 260 nm (2.47); ^1H NMR ($CDCl_3$) δ 3.29 (6 H, s), 1.75 (12 H, d), 1.35 (12 H, d); ^{13}C NMR ($CDCl_3$) δ 134.2 (s), 28.7 (d), 26.5 (t). **5**: mp 118-125 °C; ^1H NMR ($CDCl_3$) δ 2.76 (4 H, s), 1.53 (16 H, s); ^{13}C NMR ($CDCl_3$) δ 143.9 (s), 119.4 (s), 42.2 (d), 38.1 (d), 26.4 (t), 26.3 (t). 6: mp 156.0-158.0 °C; ^1H NMR ($CDCl_3$) δ 2.79 (2 H, s), 2.60 (4 H, s), 1.50 (24 H, br s); ^{13}C NMR ($CDCl_3$) δ 143.9 (s), 139.7 (s), 118.9 (s), 42.4 (d), 39.3 (d), 34.8 (d), 26.8 (t), 26.7 (t), 26.4 (t). **8**·SbF_6^-: mp >300 °C; UV (MeCN) λ_{max} 262 (log ϵ 4.73), 317 (3.93), 330 nm (3.91); ^1H NMR (CD_3CN) δ 3.96 (6 H, s), 2.82 (3 H, s), 2.02 (12 H, d), 1.42 (12 H, d); ^{13}C NMR (CD_3CN) δ 164.9 (s), 162.6 (s), 162.4 (s), 162.3 (s), 36.6 (d), 36.0 (d), 35.8 (d), 24.8 (t), 24.7 (t), 24.6 (q), 24.55 (t).

(9) ^1H NMR (300 MHz, CD_3CN) δ 8.98 (5 H, s), 3.76 (2 H, s), 2.11 (4 H, d), 1.46 (4 H, d); ^{13}C NMR (CD_3CN) δ 176.5 (s), 152.2 (d), 151.5 (d), 151.2 (d), 42.5 (d), 24.5 (t) (Nakazawa, T.; Niimoto, Y.; Kubo, K.; Murata, I. *Angew. Chem.* **1980**, *92*, 566; *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 545 and ref 6).

(10) Averaged from triplicate values: 13.15, 12.95, and 12.88. This value was reproduced by using the phosphate-glycine-NaOH buffer and also for the perchlorate salt, **1**·ClO_4^-. The neutralization was completely reversible, regenerating **1** after acidification. This value does not seem to be due to destabilization of the neutral precursor, since the steric constraint between the neighboring bicyclic units is even more severe in the planar cationic form than in the boat-shaped precursor cycloheptatriene.

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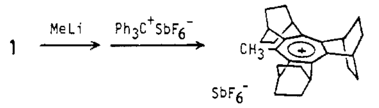
V/s) as compared with **7** (−0.765 V) or the unsubstituted tropylium ion (−0.510 V).

In pursuit of further possible stabilization, **1** was converted to the fully substituted cation **8**.[8] However, **8** was found to be somewhat less stable than **1** as is shown by its pK_{R^+} (12.4) and reduction potential (−1.094 V). This is ascribed to the decreased planarity of the seven-membered ring due to the steric repulsion between overcrowding substituents.[11]



8

A single straight line (slope 0.870, correlation coefficient 0.9988) is obtained when pK_{R^+} is plotted against E_{pc} for **1**, **7**, **8**, and a series of cyclopropyltropylium ions (c-$Pr_nC_7H_{7-n}^+$, n = 0–3). From this plot, stabilization by annelation with one bicyclo[2.2.2]octene unit is shown to be almost twice as effective as that by substitution with one cyclopropyl group. Thus, the cyclic 6π/7C system in **1** is strongly stabilized by the inductive effect plus σ–π conjugation of the tropylium 2p orbitals with the σ-bonds, which are rigidly fixed in the position nearly parallel to the vacant 2p orbitals.[12]

Acknowledgment. We thank the Ministry of Education, Science and Culture for a Grant-in-Aid for Scientific Research (no. 61134038).

Supplementary Material Available: Spectral and analytical data, UV spectra of **1** at different pH's, a plot of pK_{R^+} against E_{pc}, and results of INDO MO calculations (5 pages). Ordering information is given on any current masthead page.

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(12) This is supported by the results of INDO MO calculations on the cation **7** as a model, in comparison with the tropylium ions annelated with bicyclo[2.1.1]hexene and with cyclopentene. The results show that **7** has the lowest charge density on the cationic ring and the highest π-bond order between the tropylium ring and the σ-framework: see Supplementary Material.

Polar Host–Guest Interaction. Binding of Nonionic Polar Compounds with a Resorcinol–Aldehyde Cyclooligomer as a Lipophilic Polar Host[†1]

Yasuhiro Aoyama,* Yasutaka Tanaka, Hiroo Toi, and Hisanobu Ogoshi

Department of Materials Science and Technology
Technological University of Nagaoka
Kamitomioka, Nagaoka, Niigata 940-21, Japan

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Recognition of nonionic polar moieties through the hydrogen-bonding interaction constitutes an important challenge in molecular recognition but still remains largely unexplored.[2,3] Especially important are the hydroxyl and amide groups and nitrogen heterocycles since they are constituents of such important biomolecules as sugars, peptides, nucleosides and nucleotides, vitamins, and coenzymes. We wish to report here that a lipophilic resorcinol–aldehyde cyclooligomer provides effective binding sites in apolar media for a variety of polar compounds of biological origin.

The acid-catalyzed reaction of resorcinol with dodecanal in ethanol under conditions similar to those for the reaction with CH_3CHO or C_6H_5CHO to give **1b**[4] or **1c**[5] afforded the cyclooligomer **1a** as a monohydrate having good solubilities in apolar solvents.[6] Acetylation of **1a** gave octaacetate **2a**.[6] The ^1H NMR spectra of **1a** and **2a**[6] in light of structures[4,5,7] of octaacyl derivatives **2b** and **2c** suggested that **1a** has a crown[5] or bowl-shaped[3a,3b,8] conformation with alkyl chains in an all-axial and all-cis configuration and OH groups which are hydrogen-bonded. Vapor pressure osmometry (VPO) indicated that **1a** is aggregated in $CHCl_3$ or C_6H_6, whereas **2a** is monomeric.[6] The polar substrates investigated are glycerol (**3**), D-glucose (**4**), D-ribose (**5**), riboflavin (vitamin B_2, **6a**), vitamin B_{12} (cyanocobalamin, **7a**), and hemin (**8**). They are all insoluble in CCl_4 and C_6H_6.

Vigorous stirring of a two-phase mixture of a solution of **1a** in CCl_4 or C_6D_6 (1–2 × 10^{-2} M, 4 vols) and **3** (neat) or H_2O (1 vol) at 20 °C for 24 h resulted in transfer of the latter into the former solution, the stoichiometries **3**:**1a** = H_2O:**1a** = 4:1 being established by ^1H NMR integration.[9] When a 50% (mol/mol) aqueous solution of **3** ([**3**] = [H_2O] = 11 M) was used, only ca. 4 mol of H_2O was incorporated with little extraction of **3**. Similar extraction studies using saturated or very concentrated aqueous solutions of **4** (3.1 M) and **5** (5.5 M) showed a striking difference in their affinities to **1a** in CCl_4; little extraction of **4**, while ready extraction of **5** (ca. 1 mol per mol of **1a**).[9] The selectivity may be explained in terms of directions of OH groups.[10] The formation of a stable complex between **1a** (3.6 × 10^{-4} M) and **6a** or **7a** in C_6H_6 was suggested by the extraction of **6a** or **7a** from a very dilute solution in water or even in 1 N aqueous HCl in which **6a** was protonated.[11] The distributions of **6a** or **7a** (G) between

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[†] This paper is dedicated to the late Professor Iwao Tabushi.

(1) Molecular Recognition. 1. Presented at the 12th International Symposium on Macrocyclic Chemistry, Hiroshima, Japan, 1987; Abstracts, p 89.

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(6) **1a**: yield 70% after thorough washing with water followed by recrystallization from methanol or ethanol: mp 270–271 °C dec; ^1H NMR ($CDCl_3$) δ 7.20 and 6.10 (each s, each 4 H, Ar-H), 4.28 (t, 4 H, Ar-CRH-Ar), 2.21 and 1.29 (CH_2, 80 H), 0.90 (t, 12 H, CH_3), 9.60 and 9.28 (each s, each 4 H, Ar-OH), 4.95 (br s, 2 H, H_2O). Anal. ($C_{72}H_{112}O_8 \cdot H_2O$) C, H. **2a**: yield 72% after recrystallization from petroleum ether; mp 132–132.5 °C; ^1H NMR ($CDCl_3$) 6.89 (s, 4 H, Ar-H), ca. 6 (very br, 4 H, Ar-H), 4.14 (t, 4 H, Ar-CRH-Ar), 2.16 (br s, 24 H, CH_3CO), 1.84 and 1.26 (80 H, CH_2), 0.88 (t, 12 H, CH_3). Anal. ($C_{88}H_{128}O_{16}$) C, H. Molecular weights by VPO for C_6H_6 or $CHCl_3$ solutions are as follows: **1a**, 7066 (C_6H_6) or ca. 5000 ($CHCl_3$) (calcd 1124); **2a**, 1445 (C_6H_6) or 1447 ($CHCl_3$) (calcd 1442).

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(9) Clear solutions containing **1a** were separated by centrifugation and filtration. The ^1H NMR spectra showed a broad singlet at δ 9.6–9.7 for OH protons (8 H) of **1a** and signals due to substrates, e.g., at δ 3.34 (CH, 20 H) and 4.98 (OH, 12 H) for **3** and 2.93 (8 H) for H_2O. The assignments were confirmed by use of the substrates deuteriated at OH groups, i.e., **3**-d_3, **5**-d_4, and D_2O. The substrates solubilized (**3** and **5**) could also be reextracted with D_2O and identified further by means of ^1H NMR spectroscopy.

(10) Three cis secondary and one primary OH groups in **5** can interact simultaneously with OH groups of **1a** (CPK model). This is, however, not the case for **4** which has OH groups in various directions. The observation of some highly shielded C–H proton resonances at 0.2 ppm for bound **5** may be consistent with multipoint **5**–**1a** interaction which places some C–H protons of **5** in the vicinity of benzene rings of **1a**.

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