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The Electron as a Protecting Group. 2. Generation of Benzocyclobutadiene Radical Anion in the Gas Phase and an Experimental Determination of the Heat of Formation of Benzocyclobutadiene

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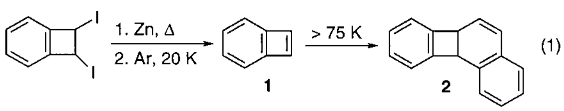
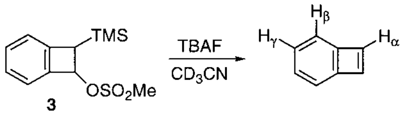
Abstract: Benzocyclobutadiene radical anion (**5**) was synthesized in the gas phase by three independent approaches: collision-induced dissociation (CID) of 1,2-benzocyclobutenedicarboxylate, reaction of 2-trimethylsilyl-1-benzocyclobutenyl anion with neopentyl nitrite followed by CID of the resulting β-nitroso carbanion intermediate, and reaction of the same β-silyl carbanion with molecular fluorine. The proton affinity and electron binding energy of **5** were measured (0.32 ± 0.05 eV and 368 ± 2 kcal mol^{-1}, respectively) and combined in a thermodynamic cycle to obtain the heat of hydrogenation (49 ± 4 kcal mol^{-1}) and the heat of formation (97 ± 4 kcal mol^{-1}) of benzocyclobutadiene (**1**). These results were compared to model compounds as well as MP2 and B3LYP calculations in order to assess the antiaromatic destabilization energy of **1**. Based upon our data, a predicted heat of formation for cyclobutadiene (102 kcal mol^{-1}) was obtained. This work demonstrates the utility of dicarboxylates as radical anion precursors and the electron as a protecting group.

Cyclobutadiene is one of the smallest cyclic 4 π electron systems, and its apparent simplicity coupled with its elusive nature has piqued the curiosity and sparked the imagination of generations of chemists. Numerous studies have been carried out on the parent compound and a wide variety of substituted derivatives.[1−4] Benzocyclobutadiene (**1**) is a particularly interesting example as it exhibits unstable behavior despite possessing an annelated aromatic fragment.[5−8] For many years, the existence of **1** could only be inferred from trapping experiments or recovery of the postulated Diels−Alder dimer **2**.[9,10] In 1976, Chapman and co-workers succeeded in isolating **1** in an argon matrix cooled to 20 K.[11] Benzocyclobutadiene was prepared in this instance by reacting 1,2-diiodobenzocyclobutene with zinc powder heated to 230 °C (eq 1). Upon warming, the matrix-isolated product was found to dimerize readily to **2**. These experiments provided the first spectroscopic data (UV and IR) of **1**.



(1)

More recently, a clever fast-flow NMR experiment produced further data to characterize **1**.[12] Benzocyclobutadiene was generated as a transient intermediate in solution by fluoride-induced elimination of **3** with tetra-*n*-butylammonium fluoride (TBAF) (eq 2). The reaction mixture was flowed through a NMR spectrometer and the following ^{1}H NMR resonances were assigned: δ 6.36 (H_α), 6.26 (H_β), and 5.78 ppm (H_γ). These data reflect the expected paratropic shift for antiaromatic compounds and closely resembles the spectrum of 1,2-bis(trimethylsilyl)benzocyclobutadiene (**4**).



(2)

Various derivatives of **1** that contain bulky substituents on the cyclobutadiene ring have been synthesized. Analogues with either hydrogen, simple alkyl groups, or a single phenyl group are unstable and have been recovered only as dimers or trapped products.[5,7] 1,2-Bis(trimethylsilyl)benzocyclobutadiene (**4**) represents the simplest derivative that has been isolated. This compound was prepared by electrocyclic ring closure of the appropriate dienediyne precursor and was found to be thermally stable, but extremely air sensitive (eq 3).[13]

Given the reactive nature of benzocyclobutadiene, we wanted to obtain thermochemical data to assess its stability and comment on any antiaromatic destabilization energy. To this end, we have

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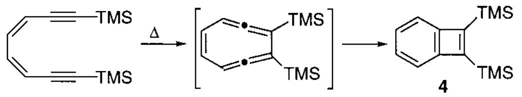
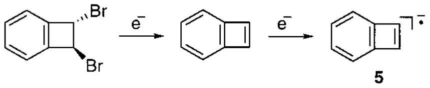


(3)

measured the heat of hydrogenation of **1** using a thermodynamic cycle and obtained its heat of formation. The key to our approach was the generation of benzocyclobutadiene radical anion (**5**) since *an electron can serve as a protecting group!*[14] This ion has been previously observed in an EPR spectrometer by reacting the requisite 1,2-dihalide precursor with solvated electrons at −60 °C (eq 4).[15,16]



(4)

In our study, benzocyclobutadiene radical anion was generated in the gas phase by two novel approaches: collision-induced dissociation (CID) of a dicarboxylate dianion and by reaction of a bis(trimethylsilyl) precursor first with fluoride ion and then with neopentyl nitrite followed by CID of the resulting β-nitroso carbanion intermediate. We were able to isolate the resulting radical anion **5** in our Fourier transform mass spectrometer (FTMS) and explore its thermochemistry. Experimental energetics have been compared with density functional theory calculations and are evaluated relative to cyclobutene and cyclobutadiene.

Experimental Section

Synthesis. Benzenediazonium-2-carboxylate,[17] 1,2-bis(trimethylsilyl)ethylene,[18] neopentyl nitrite,[19] and benzocyclobutenone oxime[20] were prepared according to literature procedures. All other reagents were purchased and used without further purification. NMR spectra were collected on a Varian VXR-300 spectrometer and are reported in ppm (δ). Infrared data were recorded on a Perkin-Elmer 1600 series FTIR, and the output is given in wavenumbers (cm^{-1}). High-resolution mass spectra were obtained on a Finnigan 2001 FTMS or MAT 95.

1,2-Diethoxycarbonyl Benzocyclobutene (6). Diethyl fumarate (200 g, 1.2 mol) and 1,2-dichloroethane (400 mL) were placed in a three-necked 1-L round-bottomed flask fitted with a condenser. Benzenediazonium-2-carboxylate freshly prepared from 15 g (0.11 mol) of anthranilic acid was then added to the reaction flask as a solution in 30 mL of 1,2-dichloroethane (Caution: This benzyne precursor must be kept “solvent wet” as it is explosive when dry.). The resulting mixture was refluxed for 25 min, and then the solvent was removed by rotary evaporation. Residual diethyl fumarate was collected by simple distillation under reduced pressure (bp = 100−102 °C at 0.7 Torr) and the crude, tarlike residue was dissolved in methylene chloride. A small amount of silica gel was added to the mixture, and after the solvent had evaporated, the doped silica gel was placed on top of a packed flash chromatography column. The product was eluted with 2.5−5% ethyl acetate in hexanes. If necessary, **6** was further purified from residual diethyl fumarate by MPLC using 10% ethyl acetate in hexanes. Overall, 3.3 g of the diester was isolated as an orange oil (12% yield from anthranilic acid): ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.18−7.29 (m, 4H), 4.62 (s, 2H), 4.21 (q, J = 7.2 Hz, 4H), 1.29 (t, J = 7.2 Hz, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 170.6, 142.1, 128.7, 122.8, 61.3, 49.7, 14.3; IR (neat) 2982, 1740, 1728, 1457, 1368, 1288, 1186, 1031, 738 cm^{-1}; HRMS-EI M$^{\bullet+}$ calcd for $C_{14}H_{16}O_4$ 248.1049, obsd 248.1033.

1,2-Benzocyclobutenedicarboxylic Acid (7). 1,2-Diethoxycarbonyl benzocyclobutene (**6**; 0.5 g, 2 mmol) was dissolved in 8 mL of methanol and a solution of potassium hydroxide (0.09 g, 16 mmol) in 10 mL of methanol was added. The mixture was refluxed for 21 h and then concentrated by rotary evaporation. The crude salt was dissolved in water and washed twice with ether. The aqueous layer was then acidified with 2 M HCl. The product was extracted with ether, dried with MgSO$_4$, and concentrated by rotary evaporation to afford 0.25 g (65%) of the desired product: ^{1}H NMR (300 MHz, CD$_3$OD) δ 7.82 (m, 2H), 7.19 (m, 2H), 4.51 (s, 2H). There is a small amount of what we presume is the *cis*-diacid based upon its resonance at δ 4.57 (s). ^{13}C NMR (75 MHz, CD$_3$OD) δ 172.7, 141.9, 128.1, 122.4, 49.6; IR (KBr) 3070 (br), 2889, 1719, 1702, 1420, 1237, 1220, 843, 752 cm^{-1}; HRMS-CI (ammonia) $[M + H]^+$ calcd for $C_{10}H_9O_4$ 193.0501, obsd 193.0498; $[M + NH_4]^+$ calcd for $C_{10}H_{12}NO_4$ 210.0766, obsd 210.0770.

1,2-Bis(trimethylsilyl)benzocyclobutene (8). 1,2-Bis(trimethylsilyl)ethylene (2.0 g, 12 mmol) and 1,2-dichloroethane (100 mL) were placed in a three-necked 250-mL round-bottomed flask fitted with a condenser. Benzenediazonium-2-carboxylate prepared from 5 g (0.04 mol) of anthranilic acid was then added to the flask as a solution in 5 mL of 1,2-dichloroethane. The mixture was refluxed for 25 min, cooled, and passed through a short column of neutral alumina. The solvent and ethylene derivative were collected as a mixture by bulb-to-bulb distillation (0.1 Torr) and recycled. The crude product was purified by column chromatography with hexanes to give **8** as a colorless liquid in 6% yield (0.6 g) from anthranilic acid. For the gas-phase experiments, **8** was further purified by preparative gas chromatography using a 12 ft × 0.25 in. 10% SE 30 column at 150 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.07−7.05 (m, 2H), 6.90−6.87 (m, 2H), 2.73 (s, 2H), −0.034 (s, 18H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 146.8, 125.2, 120.9, 34.9, −3.0; IR (neat) 3013, 2953, 1450, 1248, 1188, 866, 860, 847, 837 cm^{-1}; HRMS-EI M$^{\bullet+}$ calcd for $C_{14}H_{24}Si_2$ 248.1417, obsd 248.1417.

Gas-Phase Experiments. All work was carried out in a dual cell Finnigan FTMS interfaced with a custom-built Analytica electrospray ionization (ESI) source. In general, all ions of interest were isolated by ejecting unwanted species with a SWIFT waveform or a chirp broadband excitation for low masses.[21,22] Ions were vibrationally cooled with pulses of argon (10^{-5} Torr), neutral reagents were introduced via slow leak or pulsed valves, and all reactions were monitored as a function of time.

Ions generated by ESI were formed in the following manner. A 500 μM solution of the dicesium salt of benzocyclobutenedicarboxylic acid was prepared by adding equimolar amounts of the diacid **7** and cesium hydroxide and diluting appropriately with a 35:65 (v/v) methanol−water mixture. The pH of the solution was measured to be 9; it was found that more basic solutions, pH 11−12, lead to a dramatically reduced dianion signal. The solution was sprayed at a rate of 5−8 μL min^{-1} with the aid of a syringe pump and coaxial flow of nitrogen gas (backing pressure 80 psi). The basic design of the Analytica-Finnigan source involves a grounded needle enclosed in a charged metal cylinder. Sprayed ions travel through a 14-in. glass capillary which has voltages applied at each end and is fitted with a focusing end plate at the entrance. The capillary region is maintained at ∼1.5 Torr and dried with a counterflow of heated (200 °C) nitrogen. Upon exiting the capillary, the ions pass through a skimmer cone to an adjustable amplitude hexapole where they are accumulated and collisionally cooled for ∼1−2 s. This region is pumped with an Edwards Diffstak model 160M diffusion pump and is maintained at $\sim 1 \times 10^{-6}$ Torr. After the ions are released from the hexapole, they are guided by horizontal and vertical deflectors to a series of acceleration and deceleration lenses and then ultimately trapped in the FTMS cell at $\sim 1 \times 10^{-8}$ Torr. The dianion, m/z 95, was fragmented by sustained off-resonance irradiation

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(SORI).[23] Low molecular weight multiply charged ions are not common ESI species, and the following typical source voltages were used to obtain optimal dianion signal: cylinder 2.6 kV, end plate 3.0 kV, capillary 5.5 kV (front) -88 V (back), skimmer cone -28 V, acceleration lenses 330 V, deceleration lenses 19.0 V, and high voltage 1.5 kV. The hexapole is set with a frequency of 5.2 MHz and was operated with the amplitude offset and end cap tuned to 1 and -3 V, respectively, during the accumulation period.

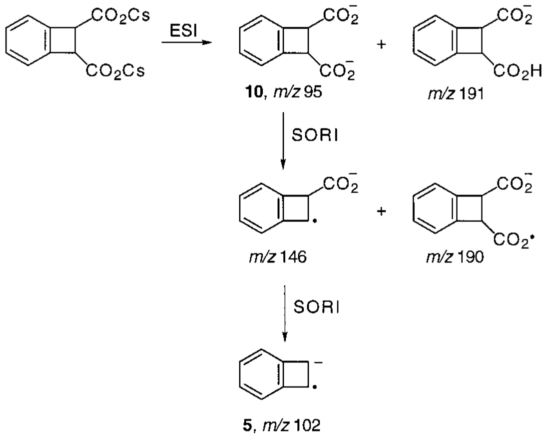
For the independent synthesis of benzocyclobutadiene radical anion via a nitroso intermediate, 1,2-bis(trimethylsilyl)benzocyclobutene (**8**) was introduced at static pressure through a direct inlet into the source cell which also contained freshly prepared neopentyl nitrite in a 3-fold excess. Carbon tetrafluoride was then pulsed into the cell at $\sim 10^{-6}$ Torr and ionized at 6 eV to produce fluoride ion. The mixture was allowed to react for 7 s, then the ions were transferred to the second cell, and the ion of interest (*m*/*z* 132) was isolated. It was subsequently excited off-resonance (SORI) to 1.5 eV in the presence of 10^{-5} Torr argon. The chemistry of the desired fragment ion was then studied.

Computations. All calculations were performed using Gaussian94[24] installed on IBM and SGI workstations. Geometries were optimized with the B3LYP functional and the 6-31+G(d) basis set. In the case of open shell species, an unrestricted wave function was used, and the spin contamination was found to be acceptable (i.e., $\langle S^2 \rangle < 0.78$). The nature of each stationary point was investigated by a full vibrational analysis and all minima were found to have positive frequencies. Some species were also optimized at the HF and MP2 levels of theory by employing the same basis set. Zero-point energy corrections were made using scaling factors of 1.00, 0.9135, and 0.9646 for B3LYP, HF, and MP2 results, respectively.[25] Computed acidities correspond to $\Delta H°_{\text{acid}}$ at 298 K while all other quantities are for $\Delta H°$ at 0 K. Temperature adjustments from 0 to 298 K were carried out by scaling the vibrational frequencies by 1.00 (B3LYP), 0.8929 (HF), and 0.9427 (MP2).[24] The reported charges are taken from natural population analyses obtained from the natural bond orbital (NBO) formalism.[26,27]

Results and Discussion

One approach to evaluating the extent to which a molecule is destabilized by antiaromaticity is to compare its thermochemistry with a reference compound in which the unfavorable interaction is removed. In this vein, we have measured the heat of formation of benzocyclobutadiene (**1**) relative to that of benzocyclobutene (i.e., the heat of hydrogenation of **1**). Obtaining these data by conventional means would be quite difficult due to benzocyclobutadiene's reactive nature; therefore, we have employed a thermodynamic cycle as outlined in eq 7a−7f (see below). This approach requires the proton affinities and electron binding energies of benzocyclobutadiene radical anion (**5**) and the conjugate base of benzocyclobutene (**9**), the known ionization potential (IP) of hydrogen atom, and the bond dissociation energy (BDE) of dihydrogen; the proton affinity of an anion is equivalent to the acidity ($\Delta H°_{\text{acid}}$) of its conjugate acid (HA) and the electron binding energy of A$^-$ is synonymous with the electron affinity (EA) of the corresponding radical. Synthesis of benzocyclobutadiene radical anion enabled these measurements to be made.

Scheme 1. Synthesis of Benzocyclobutadiene Radical Anion (**5**) via Collision-Induced Dissociation of Dicarboxylate Dianion **10**



Our group recently reported a regiospecific method for generating distonic radical anions in the gas phase.[14] This methodology involves collision-induced dissociation of a dicarboxylate dianion where the multiply charged precursor is produced by ESI. In this manner, benzocyclobutadiene radical anion (**5**) was prepared from dicarboxylate **10,** which was sprayed from a basic solution of benzocyclobutenedicarboxylic acid into our FTMS.[28] Ion **10** could be isolated and given sufficient energy (1.2 eV) by irradiating off-resonance (SORI) concurrent with a pulse of argon (10^{-5} Torr) to yield two products at *m*/*z* 146 and 190; energies reported for CID and SORI experiments have not been corrected for the ion's center of mass. These ions correspond to the loss of a molecule of carbon dioxide and an electron, and an electron, respectively (Scheme 1, Figure 1). Before the pulsed argon gas is pumped away, the *m*/*z* 146 ion is excited with 3.6 eV of energy (SORI) to yield the benzocyclobutadiene radical anion at *m*/*z* 102. This final product ion can be directly obtained from on- or off-resonance excitation of **10**, but the yield is not as good as in the two-step procedure. It is also worth noting that the observation of the distonic radical anion product at *m*/*z* 190 is an anomalous result in our experience with dicarboxylate fragmentation chemistry. Independent experiments revealed that the *m*/*z* 190 ion affords fragments at *m*/*z* 146 and 102 under consecutive SORI excitations.

Our efforts turned to examining the thermochemistry of the observed $C_8H_6^{\bullet-}$ (*m*/*z* 102) ion. The electron binding energy of this species was determined by reacting it with several reference compounds and observing the occurrence or nonoccurrence of electron transfer as a function of time. Upon reaction with acetophenone, benzaldehyde, molecular oxygen, carbon disulfide, and sulfur dioxide, ion **5** undergoes electron transfer (Table 1). This process does not occur with nitric oxide or phenanthrene. These observations lead to a bracketed electron affinity of 0.32 ± 0.05 eV for C_8H_6.[29] This result is in excellent agreement with theory (UB3LYP/6-31+G(d)), which predicts a value of 0.36 eV for benzocyclobutadiene. Moreover, these

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[28] 1,2,4,5,7-Cyclooctapentaene is a high-energy intermediate or transition structure and is less stable than benzocyclobutadiene. The relative energy difference between the corresponding radical anions also should be large, particularly since benzocyclobutadiene radical anion is not a 4 π electron system. In accord with this expectation, **5** is 63.3 kcal mol^{-1} more stable than 1,2,4,5,7-cyclooctapentaene radical anion at the AM1 level and initial attempts to locate the latter species at the B3LYP/6-31+G(d) level led back to the former ion.

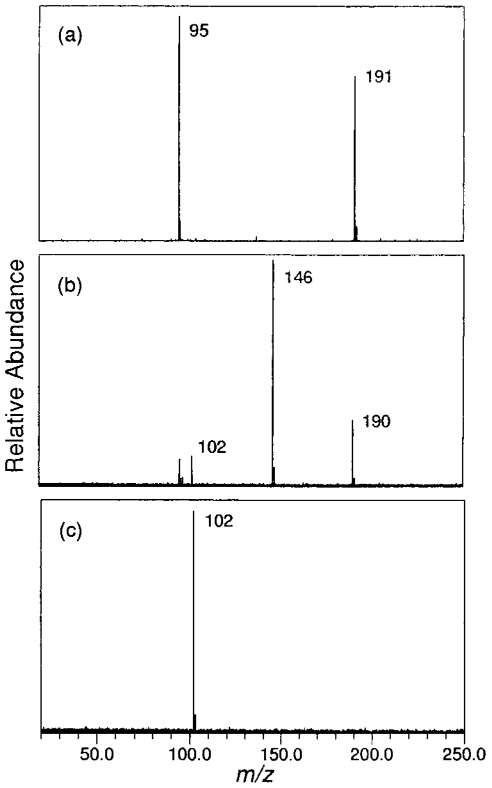


Figure 1. Sequence for generation of benzocyclobutadiene radical anion. (a) Initial mass spectrum (one scan) of the sprayed benzocyclobutenedicarboxylic acid: dianion **10**, *m/z* 95, and monodeprotonated diacid, *m/z* 191. (b) Results from isolation and excitation of *m/z* 95. See text for details. The spectrum represents an average of eight scans. (c) Isolation of **5**, *m/z* 102. The spectrum represents an average of 24 scans.

Table 1. Electron Affinity Bracketing Results for Benzocyclobutadiene (**1**)

compound	EA (eV)[a]	electron transfer
NO	0.026 ± 0.005	no
phenanthrene	0.307 ± 0.012	no
$PhCOCH_3$	0.334 ± 0.004	yes
PhCHO	0.429 ± 0.009	yes
O_2	0.451 ± 0.007	yes
CS_2	0.51 ± 0.10	yes
SO_2	1.107 ± 0.008	yes

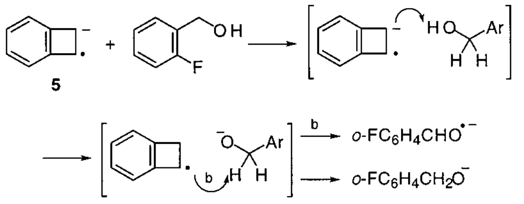
[a] Values taken from ref 31.

Table 2. Results for the Proton Affinity Measurement of Benzocyclobutadiene Radical Anion (**5**)

acid	ΔH°_{acid}[a] (kcal mol^{-1})	proton transfer
CH_3OD	383.5 ± 0.7	no
$CH_3CH_2CH_2C{\equiv}CH$	379.8 ± 2.5	no
$(CH_3)_3COD$	374.6 ± 2.1[b]	no
CD_3CN	372.9 ± 2.1[b]	no
FCH_2CH_2OH	371.2 ± 2.9	no
$PhC{\equiv}CH$	370.7 ± 2.3	no
$PhCH_2OH$	370.0 ± 2.1	no
$(CH_3)_2C{=}NOH$	366.0 ± 2.2	yes
CF_3CH_2OH	361.8 ± 2.5	yes

[a] Acidity values taken from ref 31. [b] Values for protio reagent are given.

Scheme 2. Reaction of Radical Anion **5** with *o*-Fluorobenzyl Alcohol



data allow us to address the question of ring opening of the $C_8H_6^{\bullet-}$ ion. If such a pathway did occur, a phenide or acetylide ion would be produced. Both of these ions would have electron binding energies in excess of 1 eV (i.e., EA($C_6H_5^\bullet$ = 1.096 eV and EA ($HC_2^\bullet$) = 2.956 eV)[30,31]

The proton affinity of **5** was investigated by titrating it with a variety of standard reference acids. In particular, benzocyclobutadiene radical anion was found to rapidly deprotonate dimethyl oxime and 2,2,2-trifluoroethanol ($k \sim 10^{-9}$ cm^3 molecule^{-1} s^{-1}) but not less acidic compounds (Table 2). These results allow us to assign ΔH°_{acid} (**11**) = 368 ± 2 kcal mol^{-1}, which is in good accord with the UB3LYP/6-31+G(d) value of 371.8 kcal mol^{-1}. We were unable to observe hydrogen−deuterium incorporation into **5** with *tert*-butyl alcohol-OD contrary to our expectation. Presumably, upon deuteron transfer, the lifetime of the resulting ion−molecule complex is too short for the alkoxide to move to the opposite side of the ring, and thus, the initial deuterium is reabstracted. Similar situations have been reported previously for acetylide and the conjugate bases of dihalobenzenes.[32−34]

Signal loss was a common observation for many of the alcohols studied for which proton transfer is not thermodynamically favored. Similar observations were made by Guo and Grabowski during their investigation of *o*-benzyne radical anion.[35] They attributed loss of the starting ion to a reaction pathway that involves proton transfer followed by hydrogen atom abstraction from an adjacent CH_x group. For example, with methanol, the resulting ionic product by this mechanism would be formaldehyde radical anion, which is unstable with regard to electron loss and thus is not detected. To observe this type of reaction with **5**, we used an alcohol whose corresponding aldehyde radical anion has a positive electron affinity. *o*-Fluorobenzyl alcohol proved to be a suitable precursor, and both the alkoxide (o-$FC_6H_4CH_2O^-$) and the aldehyde (o-$FC_6H_4CHO^{\bullet-}$, EA = 0.637 eV) were detected in a 6:1 ratio (Scheme 2).

To further ensure we had synthesized the radical anion of benzocyclobutadiene, we sought to prepare it by an independent route. Atomic oxygen anion ($O^{\bullet-}$) has been shown to yield distonic radical anions and water by abstraction of both a proton and a hydrogen atom from many compounds.[36] A labeling experiment with 1,1-dideuteriobenzocyclobutene, unfortunately,

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(29) The statistical error using the phenanthrene and acetophenone data is 0.01 eV, but a more realistic estimate is 0.05 eV. This is based upon the fact that the latter reaction is fast ($\sim 10^{-9}$ cm^3 molecule^{-1} s^{-1}) but still could be endothermic by 1 kcal mol^{-1}.

(30) Gunion, R. F.; Gilles, M. K.; Polak, M. L.; Lineberger, W. C. *Int. J. Mass Spectrom.* **1992**, *117*, 601−620.

(31) Bartmess, J. E. *NIST Chemistry WebBook, NIST Standard Reference Database Number 69*; Mallard, W. G., Linstrom, P. J., Eds.; National Institute of Standards and Technology: Gaithersburg, MD 20899 (http://webbook.nist.gov), February 2000.

(32) Kato, S.; DePuy, C. H.; Gronert, S.; Bierbaum, V. M. *J. Am. Soc. Mass Spectrom.* **1999**, *10*, 840−847.

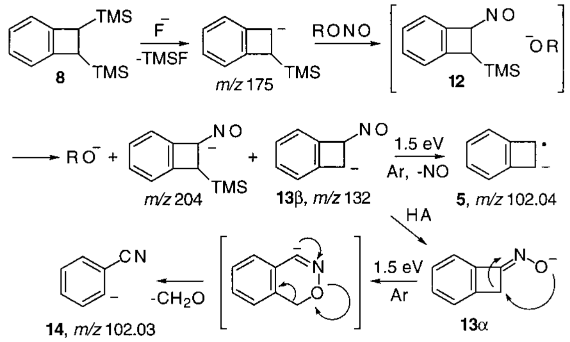
(33) Chan, S.; Enke, C. G. *J. Am. Soc. Mass Spectrom.* **1994**, *5*, 282−291.

(34) Grabowski, J. J.; DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1983**, *105*, 2565−2751.

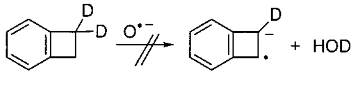
(35) Guo, Y.; Grabowski, J. J. *J. Am. Chem. Soc.* **1991**, *113*, 5923−5931.

(36) Lee, J.; Grabowski, J. J. *Chem. Rev.* **1992**, *92*, 1611−1647.

Scheme 3. Alternative Synthesis of **5** via a *β*-Nitroso Carbanion Intermediate



did not support abstraction of a vicinal hydrogen and deuterium from the four-membered ring as the dominant reaction pathway (eq 5).[37]



(5)

Squires and co-workers developed a regiospecific radical anion synthesis which involves treating an appropriate bistrimethylsilyl-substituted substrate first with fluoride ion and then with molecular fluorine.[38] We attempted this reaction with 1,2-bis(trimethylsilyl)benzocyclobutene (**8**) but were initially unsuccessful in generating the desired product because of the extreme reactivity of F_2 (see below). However, we did discover that alkyl nitrites can be used in a similar fashion to ultimately afford benzocyclobutadiene radical anion (Scheme 3). Specifically, the $[M - TMS]^-$ ion (*m*/*z* 175) produced upon fluorodesilylation of **8** reacts by a substitution pathway with neopentyl nitrite to give the complex **12**.[39] This intermediate can dissociate to give $(CH_3)_3CH_2O^-$, the alkoxide can deprotonate the newly formed nitroso derivative (minor pathway), or it can cleave of the trimethylsilyl group to yield a *β*-nitroso carbanion. The species of interest, **13*β***, can be isolated in the FTMS cell and subsequently excited under SORI conditions (1.5 eV) to produce a mixture of CN^-, NCO^-, and ions corresponding to the loss of a hydrogen atom (*m*/*z* 131), formaldehyde (*m*/*z* 102.03), and nitric oxide (*m*/*z* 102.04). Optimal conditions for the generation of the *m*/*z* 102 ions gave the following relative product distribution: CN^-, 58%; *m*/*z* 131, 19%; NCO^-, 15%; and *m*/*z* 102, 8%. This process was also investigated using isoamyl nitrite; however, NO_2^- was formed as the major product at the expense of **13*β***.

The structures of the *m*/*z* 102 ions generated in this process are assigned as benzocyclobutadiene radical anion (*m*/*z* 102.04) and the conjugate base of benzonitrile (**14**, *m*/*z* 102.03) based on their reactivity. The ions were not separated for chemical studies since the small mass difference would have made it difficult to eject one without significantly exciting the remaining ion (Figure 2). Their reactivities were assessed based on the product intensity relative to that of the starting ions in the mixture and the independent synthesis of **14**. In particular, the $C_8H_6^{\bullet-}$ ion undergoes electron transfer with benzaldehyde and carbon disulfide, but not with nitric oxide, which is identical to the behavior of benzocyclobutadiene radical anion. Ion **14** does not react in this manner with these reagents and abstracts a sulfur and an oxygen atom from carbon disulfide and sulfur dioxide, respectively. It also undergoes four hydrogen−deuterium exchanges with deuterium oxide and both H/D exchange and proton transfer with methanol-OD, which is consistent with the known proton affinity (383.2 ± 2.5 kcal mol^{-1}) of **14**.[31]

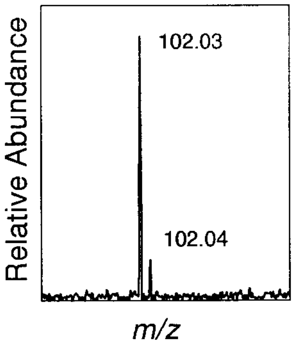


Figure 2. Resolution of benzocyclobutadiene radical anion, *m*/*z* 102.04 and the conjugate base of benzonitrile, *m*/*z* 102.03.

A pathway for the formation of the conjugate base of benzonitrile is given in Scheme 3. The nitroso product (**13*β***) can readily isomerize to **13α** in the presence of proton sources such as water, which is consistent with the exothermicity for this process (36.5 kcal mol^{-1} at the MP2/6-31+G(d)//HF/6-31+G(d) level). Evidence for the rearranged ion was demonstrated by reacting **13*β*** with D_2O and observing that the label in the resulting d_1 species could not be washed out with H_2O. During excitation of the *m*/*z* 132 ion (13α/**13*β***), **13α** loses formaldehyde to yield the conjugate base of benzonitrile (**14**). Independent experiments confirm this reaction pathway; deprotonation of benzocyclobutenone oxime gives authentic **13α**, which fragments under the same reaction conditions to afford **14** but not **5**. It should be noted that the ratio of ions **5** and **14** generated in this reaction is not necessarily a reflection of the amount of **13α** and **13*β*** present since the CID efficiencies for both species need to be considered. The amount of α and *β* isomers was estimated to be 1.2:1.0 based on the assumption that all of the **13*β*** would isomerize to **13α** and incorporate one deuterium with methanol-OD.

Although the yield of benzocyclobutadiene radical anion was low by the above route, the nitrite chemistry offers an attractive alternative to molecular fluorine and excellent promise for systems in which an acid-catalyzed isomerization of the nitroso intermediate is not feasible. The reaction of the $[M - TMS]^-$ ion of **8** with fluorine was reinvestigated after building a special inlet system for F_2 to minimize its resonance time in the tubing leading to the FTMS cell,[40] and we were able to generate **5**. The reaction of the $[M - TMS]^-$ ion of **8** with F_2 was found to afford a range of products, and the yield of the $C_8H_6^{\bullet-}$ ion was low (worse than the nitrite route). Nevertheless, we were able to explore the ion's reactivity; it transfers an electron to carbon disulfide and deprotonates dimethyl oxime, but not *tert*-butyl alcohol. This behavior is identical to our previous observations for **5**. Overall, we have prepared the radical anion of benzocyclobutadiene by three independent routes.

It is worth further addressing the possibility of isomerization of this ion. As mentioned earlier, the low electron affinity observed argues against ring opening of **5** to a phenide or

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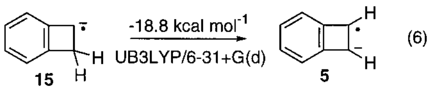
[37] Ions at *m*/*z* 102, 103, 104, and 105 were observed in a 1.0:1.0:6.5:3.4 ratio and correspond to $M - D_2$, $M - HD$, $M - H_2$, and/or $M - D$, and $M - H$, respectively. Subtracting out the $M - H/M - D$ contribution in the absence of an isotope effect affords a d_0:d_1:d_2 ratio of 1.0:1.0:3.1, which can be fit by 1, 1, and 1,*n* abstraction; the 1,2 pathway need not be taking place.

[38] Wenthold, P. G.; Hu, J.; Squires, R. R. *J. Am. Chem. Soc.* **1994**, *116*, 6961−6962.

[39] King, G. K.; Maricq, M. M.; Bierbaum, V. M.; DePuy, C. H. *J. Am. Chem. Soc.* **1981**, *103*, 3, 7133−7140.

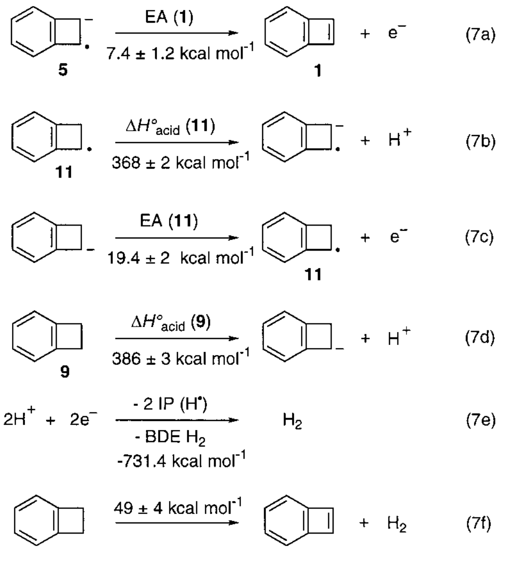
[40] Reed, D. R.; Kass, S. R., unpublished results.

acetylide ion. Calculations (UB3LYP/6-31+G(d)) also predict the 1,2 radical anion **5** to be more stable than the 1,1-isomer **15** by 18.8 kcal mol^{-1}. Moreover, isomerization to the 1,α- 1,*β*-, 1,*γ*-, and 1,*δ*-isomers is calculated to be 23.5, 26.5, 25.5, and 22.8 kcal mol^{-1} endothermic, respectively, with α, *β*, etc., denoting positions of the fused aromatic ring. The energetics of eq 6 suggested that **5** could be synthesized by an acid-induced rearrangement of **15**. 1,1-Benzocyclobutene radical anion (**15**) was thus prepared by electron impact (3.6 eV, 60 *μ*A) of the requisite diazirine.[41] Unfortunately, we were unable to carry out the isomerization as deuterium incorporation was not observed upon reaction with ammonia-*d*$_3$, dimethylamime-*d*$_1$, deuterium oxide, or methanol-OD. With the last two reagents, significant signal loss was observed, and the occurrence of proton transfer was not detected until reaction with *tert*-butyl alcohol despite the fact that the calculated proton affinity of **15** is 390.1 kcal mol^{-1} (UB3LYP/6-31+G(d)). The 1,1 radical anion also reacts with carbon disulfide by abstraction of a sulfur atom and with sulfur dioxide by electron transfer, which is in accord with a calculated electron affinity of 1.14 eV for the singlet benzocyclobutene carbene. Overall, these data distinguishes **15** from **5**.

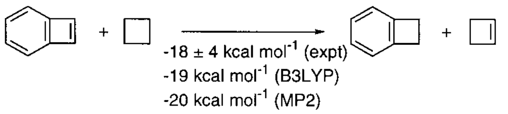


(6)

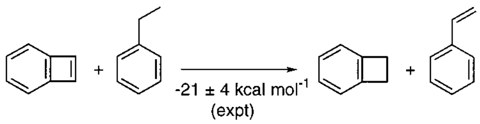
The thermochemistry of benzocyclobutadiene radical anion can now be used to derive the heat of formation of **1**. The electron binding energy (EBE = 7.4 ± 0.3 kcal mol^{-1}) and proton affinity (PA = 368 ± 2 kcal mol^{-1}) of **5** can be combined with the same quantities for the conjugate base of benzocyclobutene (EBE = 19.4 ± 2 kcal mol^{-1}, PA = 386 ± 3 kcal mol^{-1}),[42] along with the ionization potential of the hydrogen atom (IP = 313.6 kcal mol^{-1}) and the bond dissociation energy of molecular hydrogen (104.2 kcal mol^{-1}) in a thermodynamic cycle (eq 7) to yield a value of 49 ± 4 kcal mol^{-1} for the heat of hydrogenation of benzocyclobutadiene. This result is in good accord with calculated values for this quantity of 55 kcal mol^{-1} (UB3LYP/6-31+G(d)) and 52 kcal mol^{-1} [43] and leads to $\Delta H°_f$ (**1**) = 97 ± 4 kcal mol^{-1} given the known heat of formation of **9** (47.7 ± 0.2 kcal mol^{-1}).[44] One can also derive the first and second C−H bond dissociation energies for **9** (92 ± 4 and 62 ± 2 kcal mol^{-1}, respectively), which indicates that the *π* bond is only worth 30 ± 4 kcal mol^{-1} compared to a typical value of 65 and 58 kcal mol^{-1} for cyclobutene.[45]



The heat of hydrogenation of **1** is expected to be large due to its strain energy (SE) and antiaromatic destabilization. The extent of the former contribution (40 kcal mol^{-1}) was estimated to be equal to the SE of **9** (33.2 kcal mol^{-1})[46] plus the difference in strain energy between 3,4-dimethylenecyclobutene (SE = 36.6 kcal mol^{-1})[47] and cyclobutene (SE = 29.8 kcal mol^{-1}), the latter term accounting for the two additional sp^2-hybridized centers in **1** relative to **9**. The antiaromatic destabilization energy (19 kcal mol^{-1}) of **1** was determined to be equal to the energy remaining after subtraction of its SE and the energy of strain-free components (Benson's group equivalents) from its experimental heat of formation. Isodesmic reactions with cyclobutene, styrene, and cyclobutadiene also provide a context for the above results (eqs 8−10). Hydrogenation of **1** is 18 ± 4 kcal mol^{-1} more exothermic than cyclobutene (eq 8), and this can be taken as the antiaromatic destabilization energy of **1** in the same way that the difference between cyclobutadiene and cyclobutene (31 kcal mol^{-1})[48] is used to assess the stability of cyclobutadiene. In a similar fashion, benzocyclobutadiene can be compared with its linear analogue, styrene (eq 9).

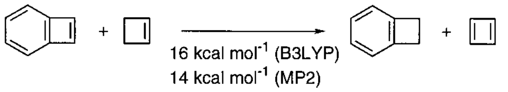


(8)



(9)

In this case, the latter compound is favored by 21 ± 4 kcal mol^{-1}.[49] Both ab initio and density functional theory reproduce the experimental energetics of eq 8, which provides credence for the calculated energy difference with cyclobutadiene (eq 10).



(10)

We find that the 4 *π* electron interaction is disfavored by an additional 15 kcal mol^{-1} in the parent versus the benzoannelated derivative. This computed reaction enthalpy, in conjunction with

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[41] Broadus, K. M.; Kass, S. R. *J. Org. Chem. Soc.* **2000**, *65*, 6566−6571.

[42] Glasovac, Z.; Eckert-Maksic, M.; Broadus, K. M.; Hare, M. C.; Kass, S. R. *J. Org. Chem.* **2000**, *65*, 1818−1824.

[43] Schulman, J. M.; Disch, R. L. *J. Am. Chem. Soc.* **1993**, *115*, 11153−11157.

[44] Roth, W. R.; Biermann, M.; H., D.; Jochems, R.; Mosselman, C.; Hermann, H. *Chem. Ber.* **1978**, *111*, 3892−3903.

[45] This value was derived from the known heats of formation of cyclobutane (6.78 ± 1.4 kcal mol^{-1}) and cyclobutene (37.45 ± 0.37 kcal mol^{-1}) and the known C−H bond dissociation energy of the former compound (96.5 ± 1 kcal mol^{-1}). See: (a) Cox, J. D., Pilcher, G. *Thermochemistry of Organic and Organometallic Compounds*; Academic Press: New York, 1970. (b) Lide, D. L., Ed. *CRC Handbook of Chemistry and Physics*, 77th ed.; CRC Press: Boca Raton, FL, 1996.

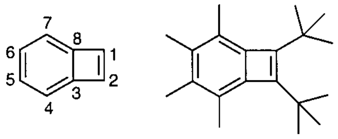
[46] This quantity was obtained from the heat of formation of **9** and strain-free group equivalents taken from: Benson, S. W. *Thermochemical Kinetics*, 2nd ed.; John Wiley and Sons: New York, 1976.

[47] The SE was derived from the heat of formation of 3,4-dimethylenecyclobutene (80.4 kcal mol^{-1}); see: Roth, W. R.; Lennartz, H.-W.; Vogel, E.; Leiendecker. M.; Oda, M. *Chem. Ber.* **1986**, *119*, 837−843.

[48] Glukhovtsev, M. N.; Laiter, S.; Pross, A. *J. Phys. Chem.* **1995**, *99*, 6828−6831.

[49] The heats of formation of styrene and ethylbenzene are 35.30 ± 0.25 and 7.15 ± 0.19 kcal mol^{-1}, respectively. See ref 45a.

Table 3. Optimized Bond Lengths for **1** (C_{2v}) and **5** (C_2) at the B3LYP/6-31+G(d) Level of Theory and Di-*tert*-Butyltetramethylbenzocyclobutadiene (**16**) from Experimental Data[a]



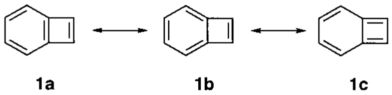
16

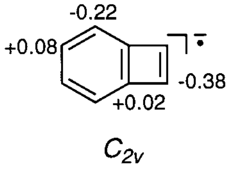
bond	**1**	**5**	**16**
C1−C2	1.354	1.427	1.357
C2−C3	1.525	1.469	1.533
C3−C4	1.363	1.382	1.366
C4−C5	1.438	1.431	1.440
C5−C6	1.381	1.401	1.370
C3−C8	1.425	1.468	1.401

[a] All bond lengths are in angstroms and the experimental data comes from Winter, W.; Straub, H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 127−128.

our measured heat of formation for **1** and the literature values for cyclobutene and **9**, enables us to predict ΔH°_f(cyclobutadiene) = 102 kcal mol^{-1}.[50] This result is in excellent accord with the G2 values (101 and 102 kcal mol^{-1}) reported by Rogers[51] and Glukhovtsev and Pross,[48] but is at the very lower end of the predicted value (114 ± 11 kcal mol^{-1}) of Peters and Synder.[52] This latter quantity was obtained by combining a photoacoustic measurement with computed AM1//MM3 heats for formation for three different compounds (two propellanes and phthalan), and thus, the claim that this work represents the first experimental determination of the heat of formation of cyclobutadiene is fallacious. It is also worth noting that simply by using MP2/6-31G(d)//HF/6-31G(d) or B3LYP/6-31G(d) calculations, the heat of formation of cyclobutadiene drops by 5.2 and 3.2 kcal mol^{-1}, respectively.[53] Clearly, a true experimental determination of this quantity would be of value.

It is not surprising that benzocyclobutadiene is stabilized relative to the parent as **1** is a larger system and the antiaromatic interaction can be alleviated by distortions in the molecular framework consistent with the resonance structures shown below. Computed geometries for **1** (B3LYP and MP2) are in reasonable accord with experimental data for 1,2-di-*tert*-butyl-3,4,5,6-tetramethylbenzocyclobutadiene (**16**) (Table 3), and both distort in a manner consistent with resonance structure **1b**. However, it has been noted that this bonding pattern fails to stabilize **1** to the extent it does 3,4-dimethylenecyclobutene since the latter compound can be isolated and is stable at room temperature.[6] Addition of an electron to **1** (i.e., formation of **5**) results in a more delocalized structure in the cyclobutadiene ring, which is consistent with an overall 9 π electron system (Table 3). It is interesting to note that the charge in **5** is calculated to be centralized in the cyclobutadiene ring and to some extent at C4 and C7. The charges shown below represent the difference between **5** and **1** and are taken from a natural population analysis of B3LYP structures with the hydrogen contributions summed into the heavy atoms. Additionally, a map of the spin density reveals the unpaired electron mainly resides in the π bonding orbitals of C1−C8 and C2−C3.





Conclusion

Benzocyclobutadiene radical anion (**5**) was generated in a Fourier transform mass spectrometer by collision-induced dissociation of an appropriate dicarboxylate dianion. The abundant ion signal for **5** and the clean nature of the preparative reaction sequence demonstrate the power of this methodology. We also discovered a new method for preparing distonic radical anions which is based on the dissociation of a β-nitroso carbanion intermediate. Specifically, benzocyclobutadiene radical anion was generated by reaction of a bis(trimethylsilyl) precursor with fluoride ion and then neopentyl nitrite followed by fragmentation of the resulting nitroso carbanion. The energetics of **5** were used in a thermodynamic cycle to afford the heat of hydrogenation of benzocyclobutadiene (49 ± 4 kcal mol^{-1}) and its heat of formation (97 ± 4 kcal mol^{-1}). The former value was found to be 18 kcal mol^{-1} larger than for cyclobutene and 15 kcal mol^{-1} smaller than for cyclobutadiene and indicates that there is significant antiaromatic destabilization of **1**.

Acknowledgment. We thank Prof. Mirjana Eckert-Maksic and Dr. Zoran Glasovac for providing 1,1-dideuteriobenzocyclobutene. Support from the National Science Foundation, the donors of the Petroleum Research Foundation, as administered by the American Chemical Society, and the Minnesota Supercomputer Institute are gratefully acknowledged.

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(50) The antiaromatic destabilization and strain energy contributions to the ΔH°_f of cyclobutadiene are predicted to be comparable (38 and 37 kcal mol^{-1}, respectively) using the G2 heat of formation (ref 48) and the same approach outlined for **1**.

(51) Rogers, D. W.; McLafferty, F. J.; Podosenin, A. V. *J. Phys. Chem.* **1996**, *100*, 17148−17151.

(52) Deniz, A. A.; Peters, K. S.; Synder, G. J. *Science* **1999**, *286*, 1119−1122.

(53) Glasovac, Z.; Eckert-Maksic, M.; Kass, S. R., unpublished results.