Benzocyclobutenone enolate: an anion with an antiaromatic resonance structure †

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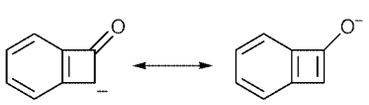
Received (in Cambridge, UK) 20th July 1999, Accepted 24th August 1999

Benzocyclobutenone enolate (**1a**) was synthesized by deprotonating its conjugate acid with fluoride ion in the gas phase using a Fourier transform mass spectrometer. Reactions of **1a** were explored and *C*-alkylation was found to be greatly preferred over oxygen attack. Thermodynamic properties ($\Delta H°_{acid}$(**1**) = 360.3 ± 2.1 kcal mol^{-1}, EA(benzocyclobutenyl radical) = 1.90 ± 0.10 eV, and BDE(C–H) = 90.5 ± 3.1 kcal mol^{-1}) also were measured. The results are contrasted to *ab initio* calculations on cyclobutanone, benzocyclobutenone, and cyclobutenone enolates. Natural bond orbital and Bader analyses are reported too. Given our gas phase and computational results, we were able to devise conditions for the generation and trapping of **1a** in tetrahydrofuran despite previous failings reported in the literature.

Introduction

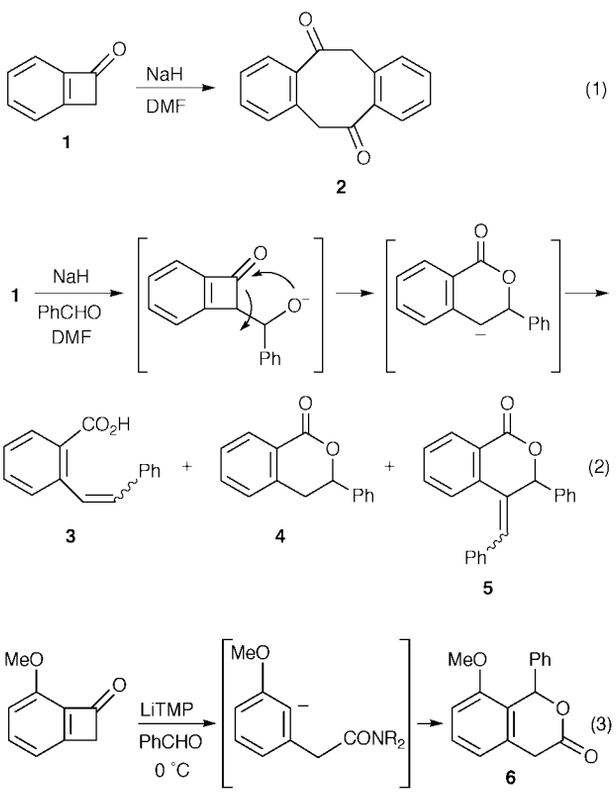
Enolates are important nucleophiles for forming carbon–carbon bonds in synthetic and biochemical transformations.[1,2] These ions also pose interesting questions in regard to their charge distributions and reactivities. For a typical enolate, the major resonance contributor represents a structure in which the charge resides on oxygen. The conjugate base of benzocyclobutenone (**1a**) is unusual in that this resonance form is a derivative of cyclobutadiene, an antiaromatic cyclic 4π electron system. The destabilizing character of this resonance structure is expected to influence the overall structure, reactivity and thermochemistry of **1a**.



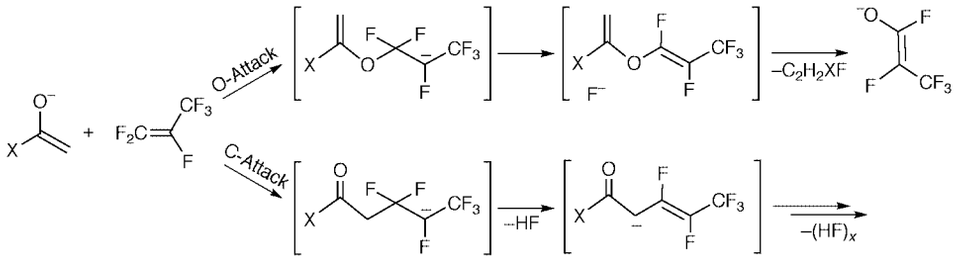
1a

Several years following the first reported synthesis of benzocyclobutenone (**1**),[3] evidence for its enolate was obtained when the dimer **2** was isolated upon treatment of **1** with sodium hydride [eqn. (1)].[4–6] Carrying out this reaction in the presence of one equivalent of benzaldehyde led to the recovery of acid **3** in a 50% yield. This product was postulated to arise from initial trapping of benzocyclobutenone enolate (**1a**) followed by subsequent cyclization and ring opening steps [eqn. (2)]. Detection of trace amounts of lactones **4** and **5** is consistent with the mechanism. Renewed efforts to trap benzocyclobutenone enolate derivatives were reported almost thirty years later.[7] *In situ* trapping experiments with lithium tetramethylpiperidide (LiTMP) and benzaldehyde at 0 °C afforded lactone **6** [eqn. (3)]. Formation of this product was proposed to go through a phenide intermediate which was intercepted by quenching with deuterium oxide. Furthermore, 2,2-dimethylbenzocyclobutenone undergoes this reaction suggesting that the intermediate is not a benzocyclobutenone enolate.

While an enormous amount of enolate chemistry has been studied in solution, gas-phase experiments have advantages in that one can probe the intrinsic reactivity and thermochemistry of a species. Unfortunately, mass spectrometry does not allow one to easily address the intriguing question of carbon *versus* oxygen reactivity for any given electrophile because the ionic products (which are what is detected) have the same mass-to-charge ratio. Collection of the neutral products of an ion–molecule reaction requires a tremendous effort;[8] consequently, a series of reagents which yield unique ionic products with oxy anions and carbanions have been developed.[9–14] Perfluorobenzene, perfluoropropylene and perfluorinated toluene are three such examples. These reagents react in a similar manner and differ only slightly in the percentage of carbon *versus* oxygen attack (Scheme 1). In the former case formation of an adduct followed by the loss of one or more molecules of hydrogen fluoride typically takes place whereas the latter pathway leads to O^-/F exchange. Thermodynamic (*i.e.*, the keto *vs.* enol energy difference) and frontier molecular orbital arguments have been offered to account for the observed product ratios



† In memory of Robert R. Squires.



Scheme 1 General reaction of an enolate with perfluoropropylene.

with cyclic and acyclic enolates.[11,13,14] Regrettably, the perfluorinated hydrocarbons react predominantly through carbon. An analogous reagent which differentiates between the two pathways and displays higher oxygen reactivity has not been developed.[15,16]

In order to gain an understanding of benzocyclobutenone enolate, we have carried out gas-phase experiments to explore its thermochemistry and reactivity. *Ab initio* calculations have been used to examine structural changes and charge redistribution upon anion formation in comparison to the enolates of cyclobutanone (**7**) and cyclobutenone (**8**). We also report successful trapping of benzocyclobutenone enolate in solution.

Experimental

Benzocyclobutenone, cyclobutanone and 1-phenylpropan-2-one were prepared by published methods.[17–19] Gas-phase experiments were carried out in a dual cell model 2001 Finnigan Fourier transform mass spectrometer (FTMS) equipped with a 3.0 T superconducting magnet. Benzocyclobutenone was deprotonated upon reaction with fluoride, which was generated by electron ionization of carbon tetrafluoride at 6 eV. The resulting enolate was isolated by ejecting undesired ions using a SWIFT waveform,[20] transferred to the second cell and cooled with an argon pulse (2×10^{-5} Torr). Neutral reagents were introduced into the second cell through slow leak valves, and the reactions of interest were monitored as a function of time.

Ab initio calculations were carried out using GAUSSIAN94[21] on Unix-based workstations or Cray supercomputers. All structures were optimized at the HF and MP2 levels of theory with the 6-31+G(d) basis set. Vibrational analysis at the HF and MP2 levels was performed to ensure that energy minima structures were found. Zero-point energy corrections were made using an empirical scaling factor of 0.9135 (HF) and 0.9646 (MP2).[22] Temperature corrections from 0 to 298 K were carried out by scaling the harmonic frequencies by 0.8929 (HF) and 0.9427 (MP2).[22] The B3LYP functional was also employed for certain species and the frequencies were used without adjustment. Natural bond orbital (NBO) and Bader's topological analyses were carried out to examine charge and structural changes.[23–25]

2-(Trimethylsilyl)benzocyclobutenone (9)

A solution of lithium tetramethylpiperidide was freshly prepared by reacting tetramethylpiperidine (1.7 ml, 10 mmol) and *n*-butyllithium (4 ml, 2.5 M, 10 mmol) in 150 ml of THF at 0 °C for 30 minutes. The solution was then cooled to −78 °C and chlorotrimethylsilane (20 ml, 0.16 mol) was added followed by benzocyclobutenone (1.0 g, 8.2 mmol). After three hours of stirring at −78 °C, the solution was allowed to slowly warm to room temperature. The reaction was quenched with 1 M HCl and diluted with hexanes after a period of 18 h. The organic layer was washed excessively with water to remove THF, dried with $MgSO_4$ and concentrated by rotary evaporation. The trapped product, **9**, (0.32 g, 21%) was obtained after separation from **1** (1 (**9**):1.5 (**1**)) by MPLC using 10% ethyl acetate in hexanes. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.20 (m, 4H), 3.84 (s, 1H), 0.07 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.2, 153.5, 146.6, 134.9, 127.2, 122.1, 120.1, 59.3, −2.7; IR (neat) 3065, 2956, 2896, 1757, 1579, 1460, 1438, 1251, 1146, 1087, 959, 868, 845, 753 cm^{-1}; HRMS-EI M$^{\cdot+}$ calcd for $C_{11}H_{14}OSi$ 190.0814, found 190.0802.

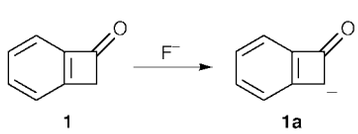
Table 1 Summary of bracketing studies for benzocyclobutenone enolate (**1a**)

Ref. acid	$\Delta H°_{acid}$/ kcal mol^{-1} [a]	Proton transfer	H/D Exchange
D_2O	392.9 ± 0.1	No	No
MeOD	383.5 ± 0.7	No	No
t-BuOD	374.6 ± 2.1	No	No
$(CH_3)_2C$=NOD	366.1 ± 2.2	No	Yes (1)
o-$FC_6H_4NH_2$	362.2 ± 2.2	No	N.a.
CF_3CH_2OD	361.8 ± 2.5	Yes [b]	No
$CF_3C(CH_3)_2OH$	360.1 ± 2.1	Yes [b]	N.a.
Pyrrole	358.7 ± 2.2	Yes	N.a.

[a] Acidity values taken from refs. 26 and 27. MeOD value from S. E. Barlow, T. T. Dang and V. M. Bierbaum, *J. Am. Chem. Soc.*, 1990, **112**, 6832. [b] Proton transfer is observed in both the forward and reverse directions.

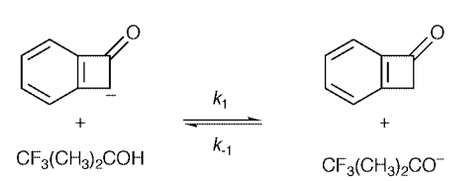
Results and discussion

Benzocyclobutenone enolate is readily generated in the gas phase by the reaction of **1** with fluoride ion [eqn. (4)]. The



(4)

thermodynamic stability of this species can be assessed by measuring its proton affinity and the electron affinity of the corresponding radical. The former value was initially bracketed by observing the occurrence or nonoccurrence of proton transfer with a series of standard reference acids (Table 1).[26,27] In particular, benzocyclobutenone enolate was found to deprotonate trifluoroethanol, 2-(trifluoromethyl)propan-2-ol, and pyrrole, but not less acidic compounds. In addition, upon reaction with dimethyl oxime-OD ($(CH_3)_2C$=NOD), **1a** undergoes a single hydrogen/deuterium exchange. Equilibrium measurements with 2-(trifluoromethyl)propan-2-ol enabled us to obtain a refined acidity value for **1** [eqn. (5)]. The bimolecular reaction



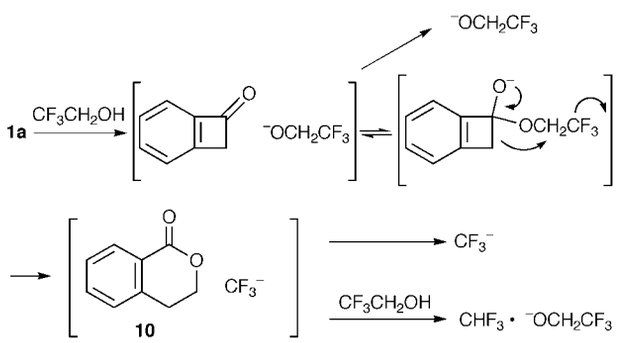
(5)

rates in both directions, k_1 and k_{-1}, were obtained using eqn. (6), where k_{obs} = the slope of a plot of ln [anion] *vs.* time (in

$$k_1 \text{ or } k_{-1} = \frac{k_{obs} R_x T}{9.66 \times 10^{18} [P]} \quad (6)$$

seconds), R_x = the pressure gauge correction for the neutral[28] (a function of the polarizability[29]), T = 300 K, and P = the pressure of the neutral compound (Torr). Data were collected over approximately two half-lives (3–10 s) following an argon pulse (10^{-5} Torr) and a 500 ms vibrational cooling delay. The values obtained, $k_1 = (2.50 \pm 0.16) \times 10^{-10}$ and $k_{-1} = (2.50 \pm 0.55) \times 10^{-9}$ cm^3 molecule^{-1} s^{-1}, represent the average (± standard deviation) of six and nine measurements, respectively, taken on three separate days. Given the uncertainty associated with accurate pressure readings, a 50% error in both rates has been assumed for further data analysis.[30] The value of $\Delta G°_{rxn}$ (−1.42 ± 0.15 kcal mol^{-1}) was combined with a calculated $\Delta S°_{rxn}$ (−3.70 e.u.),[31] and the reported acidity of 2-(trifluoromethyl)propan-2-ol (360.1 ± 2.1 kcal mol^{-1}) to give $\Delta H°_{acid}$ (**1**) = 360.3 ± 2.1 kcal mol^{-1}. This result is in good agreement with theory which predicts a value of 359.2 kcal mol^{-1} (MP2/6-31+G(d) at 298 K).

Based on the bracketing results, trifluoroethanol also appeared to be a reasonable acid for an equilibrium acidity measurement. However, we found that in addition to proton transfer, the reaction with this alcohol gives a trace of CF_3^- and an *m*/*z* 169 product. The last of these species was identified as a $CHF_3 \cdot CF_3CH_2O^-$ cluster based upon high resolution mass measurement and the observation of $CF_3CH_2O^-$ upon low energy fragmentation (SORI).[32] This cluster is not generated in the FTMS upon reaction of the alcohol with trifluoromethyl anion so benzocyclobutenone enolate appears to be involved in its formation. A mechanism is outlined in Scheme 2. Proton



Scheme 2 Proposed mechanism for the reaction of **1a** with trifluoroethanol.

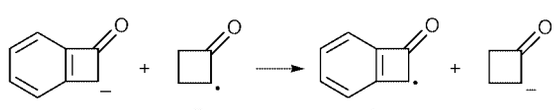
transfer leads to an ion–molecule complex which can dissociate or the newly formed trifluoroethoxide may attack the carbonyl carbon. Ring expansion *via* a tetrahedral intermediate (or transition state) with concomitant expulsion of trifluoromethyl anion leads to **10**. Subsequent separation of the two compounds gives CF_3^-, while a solvent switching reaction with trifluoroethanol affords the *m*/*z* 169 cluster. The driving force for this process is the relief of strain in benzocyclobutenone and it is facilitated by the fact that a benzylic carbon, which is capable of stabilizing a(n incipient) radical or charged center, is the migrating group. The generality of this reaction was briefly explored with the enolates of cyclobutanone, acetone, acetophenone and 1-phenylpropan-2-one. In each case no $CHF_3 \cdot$ $CF_3CH_2O^-$ was produced, and except for the last case, proton transfer was observed. 2-Fluoroethanol, however, reacts with **1a** in similar fashion to trifluoroethanol and affords $F^- \cdot HOCH_2CH_2F$ (Scheme 3). In this case ring expansion to a five- or seven-membered lactone can, in principle, take place (pathways a and b, respectively). Either way, this reaction is inefficient compared to the one with 2,2,2-trifluoroethanol, probably because the initial proton transfer is 11 kcal mol^{-1} endothermic in the former case and only 1.5 kcal mol^{-1} endothermic in the latter instance. 2-(Trifluoromethyl)propan-2-ol does not react in an analogous fashion, presumably because of steric hindrance.

Table 2 Electron affinity bracketing results for benzocyclobutenone radical

Ref. cmpd	EA/eV[a]	Electron transfer
Maleic anhydride	1.44 ± 0.10	No
p-$NO_2C_6H_4COCH_3$	1.57 ± 0.10	No
p-$NO_2C_6H_4CHO$	1.691 ± 0.087	No
3,5-di-$CF_3C_6H_3NO_2$	1.79 ± 0.10	No
3,5-di-*t*-Bu-*o*-quinone	1.804 ± 0.087	No
o-CH_3-*p*-quinone	1.852 ± 0.087	No
p-NCC_6F_4CN	1.89 ± 0.10	No
p-Quinone	1.91 ± 0.10	Yes
p-$NO_2C_6H_4NO_2$	2.00 ± 0.10	Yes

[a] Values taken from refs. 26 and 27.

To further examine the stability of benzocyclobutenone enolate, the electron affinity of the corresponding radical (**1r**) was investigated by examining electron transfer reactions between **1a** and a series of reference compounds.[33] These experiments were monitored as a function of time to ensure that any observed electron transfer was due to the reaction of **1a** with the given reagent. The results are given in Table 2 and enable us to assign EA(**1r**) = 1.90 ± 0.10 eV, which compares favorably with a directly calculated value of 1.76 eV at the UB3LYP/6-31+G(d) level. An isogyric reaction with cyclobutanone enolate (EA(**7r**) = 1.84 eV) at the same level of theory provides even better agreement with experiment [1.94 eV, eqn. (7)]. Our

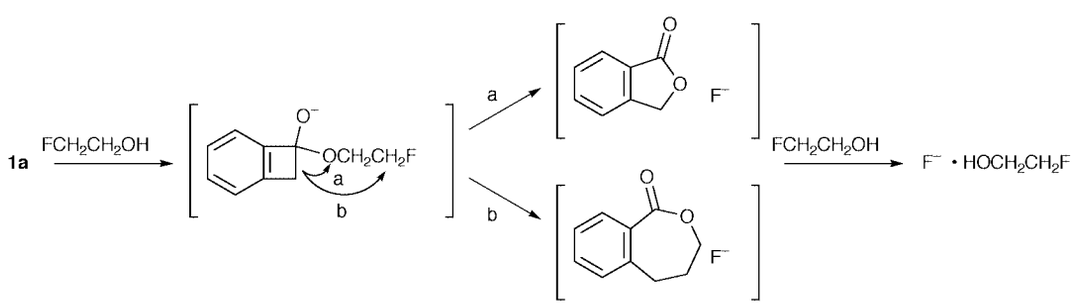


$$EA(\mathbf{1r}) = \Delta H°_{rxn}\,(UB3LYP/6\text{-}31+G(d)) + EA(\mathbf{7r}) \qquad (7)$$

electron affinity and acidity measurements can be combined to provide a value of 90.5 ± 3.1 kcal mol^{-1} for the C–H bond energy in benzocyclobutenone [eqn. (8), Table 3].

$$BDE(HX) = \Delta H°_{acid}(HX) - IP(H) + EA(X) \qquad (8)$$

The reactivity of benzocyclobutenone enolate was also examined and particular attention was paid to the nucleophilic site (*i.e.*, C- *vs.* O-attack). Perfluorobenzene reacts with **1a** solely through the carbon end of the ambident nucleophile to afford



Scheme 3 Reaction of benzocyclobutenone enolate with 2-fluoroethanol.

Table 3 Comparison of the thermochemical properties of benzocyclobutenone. Parenthetical values correspond to computational results. Acidities are at the MP2/6-31+G(d) (298 K) and electron affinities are at the UB3LYP/6-31+G(d) (0 K) levels of theory

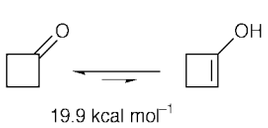
Cmpd	$\Delta H°_{acid}$/ kcal mol^{-1}	EA/eV	BDE/ kcal mol^{-1}
Benzocyclobutenone (**1**)	360.3 ± 2.1 (359.2)	1.90 ± 0.10 (1.76 and 1.94)[a]	90.5 ± 3.1
1-Phenylpropan-2-one	350.2 ± 2.5		
Cyclobutanone (**7**)	367.2 ± 4.1 (364.3)	1.84 ± 0.07 (1.66)	96.0 ± 4.4
Cyclobutenone (**8**)	(381.4)	(0.89)	
Benzocyclobutene	386.2 ± 2.4[b]	< 1.11	< 98
Ethylbenzene	379.8 ± 2.4	0.80 ± 0.13	84.6 ± 2

[a] See text for details. [b] Unpublished results, M. C. Hare and S. R. Kass.

an adduct − HF ion while perfluoropropylene gives 98.5% C- and 1.5% O-attack.[34] This difference is consistent with the higher percentage of carbon reactivity previously reported for hexafluorobenzene.[11,13] It is interesting to note that if **1a** is given excess kinetic energy *via* a chirp[35] excitation, a small amount of oxygen alkylation is observed with C_6F_6 (~2–5% upon excitation of **1a** with 15 eV for 100–300 ms concurrent with a 10^{-5} Torr pulse of argon) and the proportion of this reaction channel increases to approximately 10–20% with C_3F_6.

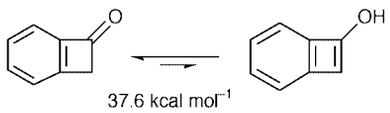
There are two general explanations in the literature for the observed regioselectivity of enolates with perfluorinated hydrocarbons.[11,13] Both correlate well with most of the reported data; however, there are some anomalous results. One explanation involves the energy difference between the keto and enol tautomers (ΔH_{KE}) of the carbonyl compound.[11] A thermodynamic argument works in this case because the kinetically controlled ratios have been shown to be a reflection of the initial reaction step energetics (*i.e.* carbanion *vs.* oxy anion attack). Moreover, alkylation and protonation are sufficiently similar energetically that this difference can be tolerated.[36,37] In general, carbon selectivity has been observed when ΔH_{KE} is large (~30–40 kcal mol^{-1}), whereas a smaller difference (ΔH_{KE} = 10–15 kcal mol^{-1}) results in oxygen reactivity. Alternatively, interactions of the enolate's highest occupied molecular orbital (HOMO) and the perfluorinated reagent's lowest unoccupied molecular orbital (LUMO) have been used to explain the carbon and oxygen regioselectivity.[13] The following trend has been observed for C_3F_6 (LUMO = −4.53 eV): higher HOMO energies (> −1.7 eV) lead to predominantly oxygen attack whereas enolates with lower HOMO energies (< −1.9 eV) display carbon reactivity. In the case of C_6F_6 (LUMO = −4.83 eV), the values are shifted up by 0.10 eV.

The small amount of oxy anion reactivity for **1a** under thermal conditions was not unexpected given that perfluoropropylene has been reported to react with cyclobutanone enolate entirely through carbon in an ICR and in a 96 (C):4 (O) ratio in the higher pressure regime of a flowing afterglow.[11,14] We repeated this measurement in our FTMS and observed ~5–10% *O*-alkylation. This preference for carbon attack can be accounted for by two main factors. First, the keto tautomer is favored by 19.9 kcal mol^{-1} [eqn. (9), MP2/6-31+G(d)] and



(9)

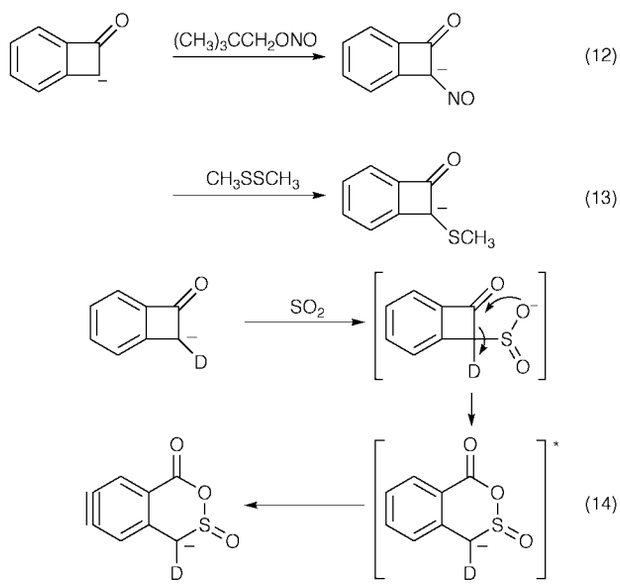
second, the HOMO energy of cyclobutanone enolate is a relatively low −1.84 eV.[38] The situation for benzocyclobutenone enolate is further biased towards carbon reactivity. The HOMO energy (−1.9 eV) is slightly lower and the keto form is much more favored [eqn. (10), ΔH_{KE} = 37.6 kcal mol^{-1} at the MP2/6-31+G(d) level], undoubtedly because of the antiaromatic nature of the enol form; in this regard it is interesting to note that at the same level of theory, ΔH_{KE} = 55.2 kcal mol^{-1} for cyclobutenone [eqn. (11)]. Given the small C/O selectivity difference between **1a** and **7a**, their similar HOMO energies and disparate keto-enol tautomerization energies, we conclude that the HOMO–LUMO interaction is the key factor in determining the regioselectivity in this system. This conclusion is in accord with a previous analysis of enolate ions by Zhong and Brauman.[16] Finally, it is worth mentioning that condensed-phase studies show parallel behavior for small cyclic enolates (*i.e.*, alkylation of four- to six-membered rings occurs preferentially at carbon).[39]



(10)

(11)

Additional reactivity studies with benzocyclobutenone enolate were carried out. The product ion obtained with neopentyl nitrite [eqn. (12)] is consistent with the behavior of other enolates.[40] Likewise, dimethyl disulfide reacts with **1a** to afford an α-thiomethyl enolate [eqn. (13)].[41] The transformation with sulfur dioxide is interesting in that it slowly leads to the formation of an adduct ion which has lost two hydrogen atoms. Experiments with **1a**-d_1, produced by hydrogen–deuterium exchange, suggest a benzyne-type product such as shown in eqn. (14). Carbonyl sulfide and carbon disulfide only give adduct ions upon reaction with **1a** and no products are detected with nitrous oxide.



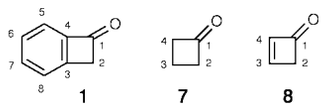
(12)

(13)

(14)

Given the stability of benzocyclobutenone enolate in the gas phase, the ability to generate the anion in solution seemed like a manageable task. Our gas-phase acidity measurement for **1** can be used to estimate a pK_a value in dimethyl sulfoxide (DMSO) if we assume that the difference between **1** and 1-phenylpropan-2-one is the same in both phases. This is not an unreasonable approximation for compounds that give delocalized ions since a linear correlation with unit slope has been found between $\Delta H°_{acid}$ (gas phase) and pK_a(DMSO).[42] Given that $\Delta\Delta H°_{acid}$(**1** − 1-phenylpropan-2-one) = 10.1 kcal mol^{-1} or 7.2 pK units and that

Table 4 Structural changes upon deprotonation for **1**, **7** and **8** at the MP2/6-31+G(d) level of theory

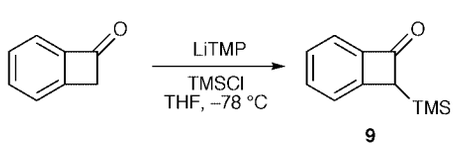


1 **7** **8**

Bond or angle[a]	**1** (C_s)	**1a** (C_s)	**7** (C_s)	**7a** (C_1)	**8** (C_s)	**8a** (C_2)
C=O	1.218	1.250	1.218	1.274	1.218	1.236
C1–C2	1.567	1.426	1.531	1.397	1.567	1.518
C2–C3	1.524	1.466	1.555	1.516	1.523	1.422
C3–C4	1.403	1.428	1.555	1.561	1.358	1.422
C1–C4	1.500	1.572	1.531	1.555	1.499	1.518
C4–C5	1.395	1.371				
C5–C6	1.400	1.436				
C6–C7	1.410	1.391				
C7–C8	1.405	1.428				
C3–C8	1.391	1.390				
C2–H	1.096	1.087	1.095	1.092	1.096	1.095
<C2–C1–C4	89.9	88.5	92.4	91.4	89.8	91.0
<C1–C2–C3	83.9	91.5	87.3	94.8	82.6	84.9
<C2–C3–C4	95.5	92.7	90.5	86.9	96.7	99.2
<C1–C4–C3	90.7	87.7	87.3	87.0	91.0	84.9
<C1–C2–H	114.1	133.6	116.0	133.2	114.1	128.2[b]

[a] Bond lengths and angles are in angstroms and degrees, respectively. [b] The hydrogen atom is bent 43° out of the plane of the ring.

the pK_a of the latter compound is 19.4,[43] we estimate that the pK_a of benzocyclobutenone is 27. In qualitative accord with this prediction, we found that **1** can be deprotonated with lithium tetramethylpiperidide and trapped *in situ* by chlorotrimethylsilane at −78 °C under dilute conditions [eqn. (15)].

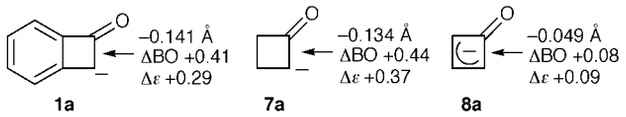


9 (15)

The worked up reaction mixture contained starting material, trapped product (**9**) and dimer **2** in an 11 : 8 : 1 ratio.[44] This result does not reflect optimized experimental conditions, but instead illustrates that benzocyclobutenone enolate can be trapped in solution at low temperatures (−78 °C) contrary to previous efforts carried out at higher temperatures (≥0 °C).[6,7] Moreover, this method offers a possible alternative synthesis for α-substituted benzocyclobutenones[45] which are of potential interest in the synthesis of anticancer agents and macromolecules.[46,47]

With our experimental knowledge of benzocyclobutenone enolate, we turned to theory to elucidate the pertinent factors contributing to its stability. Natural bond orbital (NBO)[23,24] and Bader[25] analyses were carried out on MP2/6-31+G(d) optimized structures of **1**, cyclobutanone (**7**), cyclobutenone (**8**) and their corresponding enolates. These formalisms furnish atomic charges as well as descriptive properties of the bonds such as hybridization, ellipticity, and electron density at the critical point (ρ_c) which was used to calculate bond orders.[48,49]

Initial examination of the structural differences of **1** and **1a** (Table 4) provides a platform for understanding the NBO and Bader results. Upon deprotonation of **1** (at C2), the remaining hydrogen moves into the plane of the bicyclic system allowing the resulting charge to be aligned with the π system of the carbonyl group and the benzene ring. To accommodate these changes, the C1–C2–C3 angle enlarges by 7.6° and the C1–C4, C3–C4 and C=O bonds elongate by 0.072, 0.025 and 0.032 Å.[50] The C1–C4 bond is less restricted and consequently increases more, this also helps alleviate the antiaromatic character in the system. These changes are further reflected in the NBO hybridization which shows diminished s-character in the bonds (Table 5). In contrast, the bonds emanating from the anionic site show substantially increased s-character (C1–C2: 32.4%-21.8% (**1**) *vs.* 38.7%-32.7% (**1a**); C2–C3: 24.7%-31.0% (**1**) *vs.* 30.6%-33.2% (**1a**) and undergo large bond contractions [0.141 (C1–C2) and 0.058 Å (C2–C3)]. Overall, Bader's analysis of the bond order, and ellipticity changes provide a consistent theme upon going from **1** to **1a**: the C1–C2 and C2–C3 bonds become stronger and the C1–C4, C3–C4, and C=O bonds weaken (Table 5).



1a **7a** **8a**

Fig. 1 Changes in the C1–C2 bond upon deprotonation in benzocyclobutenone (**1**), cyclobutanone (**7**), and cyclobutenone (**8**).

The bond localization index ($L(d_{cc})$) can be used to assess the distortion in the benzene moiety.[51] This parameter is a simple summation of absolute deviations of the individual bond lengths from the average bond length. For example, $L(d_{cc})$ equals zero for D_{6h} benzene and 0.36 for a hypothetical cyclohexatriene. The aromatic ring in benzocyclobutenone is almost entirely delocalized ($L(d_{cc}) = 0.03$) but undergoes some fixation upon deprotonation to **1a** ($L(d_{cc}) = 0.14$). This results in bond alternation (C5–C6 and C7–C8 lengthen while C4–C5, C6–C7, and C3–C8 shorten) and accompanying changes in the bond order and ellipticity. The alternation in the benzene moiety, however, is less significant than in the four-membered ring.

Comparable structural changes occur in the four-membered ring of cyclobutanone (**7**) upon anion formation. The bonds emanating from the anionic center (C2) contract and are strengthened, while the C3–C4, C1–C4, and C=O bonds expand and are weakened, although not to as large an extent; the C1–C2–C3 angle opens up as well. In contrast, deprotonation of cyclobutenone leads to a C_2 anion in which the C2–C3 bond contracts by 0.101 Å, the C3–C4 expands by 0.064 Å, and the C2 and C4 hydrogens lie on the opposite side and 43° out of the C2–C3–C4 plane. Smaller changes are found in the C1–C2 and C=O bond lengths (and in comparison to **1a** and **7a**) such that **8a** clearly resembles an allylic anion rather than an enolate. Consistent with this view, the HOMO of cyclobutenone enolate is that of an allyl anion and not an enolate.

Fig. 1 summarizes the C1–C2 bond in **1a**, **7a**, and **8a**, which is the most critical one in assessing the cyclobutadiene character in **1a** and **8a**. In the former species there clearly is double bond character between C1 and C2 in that the changes upon deprotonation of its conjugate acid are virtually the same as in cyclobutanone enolate (*i.e.*, the bond lengths decrease by 0.13–0.14 Å, the bond orders increase by 0.41–0.44, and the ellipticities increase by 0.29–0.37). Cyclobutenone enolate, on the other hand, is anomalous. Deprotonation of its conjugate acid leads to relatively little change in the C1–C2 bond.

Additional insight can be obtained by examining the NBO and Bader charges on the individual atoms (Fig. 2 and Table 6). The absolute values are quite different for the two methods but the relative electron populations are in good accord and provide a coherent picture. Deprotonation of cyclobutanone leads to a build up of charge at the acidic site and delocalization on to the more electronegative oxygen atom. The carbonyl carbon also is less electron deficient in the electron rich enolate. Similar results are seen for **1a**, but less charge is delocalized on to the carbonyl group because it is further spread out over the benzene ring. Perhaps the most unexpected result is the charge at C5 and C7. None of the canonical resonance structures support a build up of electron density at these positions and thus changes in the σ-framework contribute to the overall charge distribution.

Once again cyclobutenone enolate is quite different from benzocyclobutenone and cyclobutanone enolates. In this case

Table 5 Natural bond orbital hybridizations and Bader's topological parameters (ρ_c, $\nabla^2 p_c$, and ε) for **1**, **7**, **8** and their corresponding enolates

			Baders topological parameters			
Cmpd	Bond	NBO s-character	ρ_c	$\nabla^2 p_c$	ε	BO
1 (**1a**)	C=O	33.7–41.6 (33.8–40.0)	0.397 (0.371)	0.273 (−0.347)	0.082 (0.073)	2.55 (2.16)
	C1–C2	32.4–21.8 (38.7–32.7)	0.235 (0.294)	−0.518 (−0.735)	0.040 (0.333)	0.90 (1.31)
	C2–C3	24.7–31.0 (30.6–33.2)	0.244 (0.266)	−0.548 (−0.612)	0.007 (0.166)	0.95 (1.09)
	C3–C4	30.1–30.0 (27.7–29.0)	0.315 (0.300)	−0.853 (−0.793)	0.197 (0.122)	1.50 (1.36)
	C1–C4	34.2–30.1 (27.6–29.6)	0.261 (0.225)	−0.617 (−0.463)	0.090 (0.050)	1.06 (0.84)
	C4–C5	39.8–33.6 (41.3–35.4)	0.308 (0.318)	−0.840 (−0.864)	0.172 (0.254)	1.44 (1.53)
	C5–C6	34.8–35.0 (34.3–3.43)	0.306 (0.286)	−0.822 (−0.727)	0.210 (0.177)	1.42 (1.25)
	C6–C7	34.9–35.0 (36.1–36.2)	0.302 (0.310)	−0.806 (−0.825)	0.194 (0.275)	1.38 (1.45)
	C7–C8	35.0–34.6 (34.9–34.6)	0.305 (0.289)	−0.815 (−0.741)	0.207 (0.225)	1.41 (1.27)
	C3–C8	38.7–34.2 (38.9–35.1)	0.310 (0.308)	−0.846 (−0.820)	0.190 (0.225)	1.45 (1.44)
	C2–H	26.7–100 (36.5–100)	0.267 (0.260)	−0.904 (−0.888)	0.014 (0.054)	1.10 (1.05)
7(**7a**)	C=O	33.2–41.9 (33.4–38.4)	0.396 (0.353)	0.295 (−0.224)	0.066 (0.054)	2.53 (1.92)
	C1–C2	33.6–23.1 (38.7–35.4)	0.252 (0.308)	−0.593 (−0.788)	0.046 (0.420)	1.00 (1.44)
	C2–C3	24.6–24.2 (29.6–27.4)	0.234 (0.245)	−0.509 (−0.536)	0.009 (0.098)	0.89 (0.96)
	C3–C4	24.2–24.6 (23.4–24.3)	0.234 (0.229)	−0.509 (−0.487)	0.009 (0.036)	0.89 (0.86)
	C1–C4	33.6–23.1 (28.0–25.5)	0.252 (0.236)	−0.593 (−0.514)	0.046 (0.067)	1.00 (0.90)
	C2–H	27.1–100 (34.9–100)	0.267 (0.260)	−0.908 (−0.848)	0.017 (0.061)	1.10 (1.05)
8(**8a**)	C=O	33.7–41.7 (32.2–42.1)	0.397 (0.380)	0.273 (0.176)	0.078 (0.041)	2.55 (2.29)
	C1–C2	33.4–22.1 (34.1–28.9)	0.238 (0.250)	−0.528 (−0.552)	0.030 (0.124)	0.91 (0.99)
	C2–C3	24.2–29.6 (33.9–34.2)	0.248 (0.291)	−0.561 (−0.722)	0.170 (0.233)	0.97 (1.29)
	C3–C4	35.4–34.3 (34.3–34.2)	0.333 (0.291)	−0.923 (−0.772)	0.327 (0.233)	1.69 (1.29)
	C1–C4	34.2–28.7 (34.1–29.5)	0.266 (0.250)	−0.642 (−0.552)	0.112 (0.124)	1.09 (0.99)
	C2–H	26.8–100 (35.7–100)	0.268 (0.258)	−0.909 (−0.831)	0.012 (0.053)	1.11 (1.04)

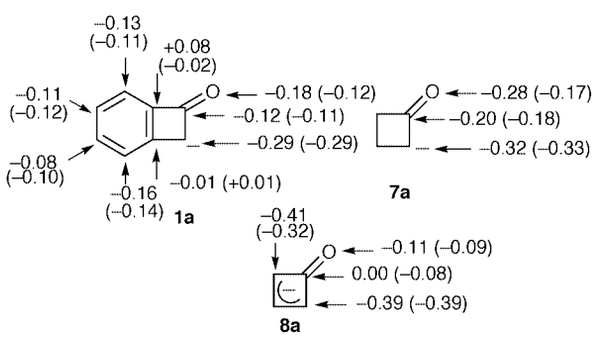
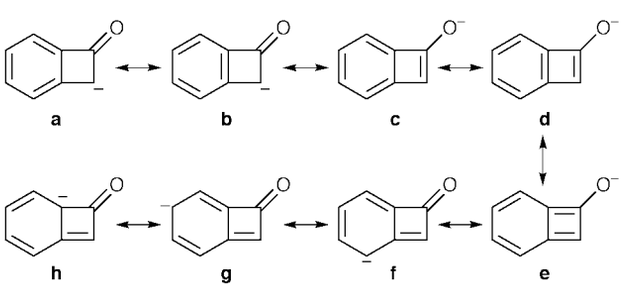


Fig. 2 Charge redistribution upon deprotonation of benzocyclobutenone (**1**), cyclobutanone (**7**), and cyclobutenone (**8**). Both the NBO and Bader charges (parenthetical values) represent the difference between the enolate and neutral and have the contributions from the hydrogens added into the carbon atoms to which they are attached. MP2/6-31+G(d) structures and wave functions were employed.



only 10–15% of the charge is delocalized on to the carbonyl group as opposed to 45–50% in **7a** and 23–30% in **1a**. The two α carbons (C2 and C4) are equivalent in the anion and bear 70–80% of the charge, exactly what one would expect for an allylic ion.

Benzocyclobutenone is a stronger acid than cyclobutanone by 6.9 ± 5 kcal mol^{-1} and this difference is well reproduced by *ab initio* calculations at the MP2/6-31+G(d) level [eqn. (16), Table 3]. On the other hand, 1-phenylpropan-2-one, an acyclic model, is more acidic than **1** by 10.1 ± 3 kcal mol^{-1} [eqn. (17)]. This latter difference is not surprising given that benzocyclobutene (cyclic) is less acidic than ethylbenzene (acyclic) by 6 ± 3 kcal mol^{-1}, and suggests that there is little, if any,

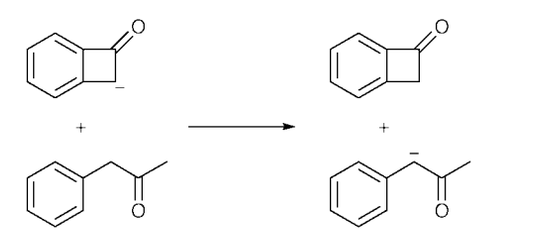
Table 6 Natural population analysis and Bader charges (parenthetical values) for **1**, **7**, **8** and their corresponding enolates

Atom[a]	**1**	**1a**	**7**	**7a**	**8**	**8a**
O	−0.49 (−1.14)	−0.67 (−1.26)	−0.50 (−1.15)	−0.78 (−1.32)	−0.50 (−1.15)	−0.61 (−1.24)
C1	0.56 (1.08)	0.44 (0.97)	0.57 (1.06)	0.37 (0.88)	0.52 (1.08)	0.52 (1.00)
C2	−0.02 (0.06)	−0.31 (−0.23)	−0.04 (0.03)	−0.36 (−0.30)	−0.06 (0.06)	−0.45 (−0.33)
C3	−0.02 (−0.04)	−0.03 (−0.03)	0.02 (0.04)	−0.10 (−0.12)	0.10 (0.02)	0.00 (−0.11)
C4	−0.15 (−0.07)	−0.07 (−0.09)	−0.01 (0.03)	−0.11 (−0.13)	−0.06 (−0.01)	−0.45 (−0.33)
C5	0.05 (0.04)	−0.08 (−0.07)				
C6	0.02 (0.02)	−0.09 (−0.10)				
C7	0.02 (0.02)	−0.06 (−0.08)				
C8	0.03 (0.03)	−0.13 (−0.11)				

[a] Charges on hydrogen atoms have been summed in to the carbons to which they are attached.

(16)

$\Delta H°_{rxn}$ = −6.9 ± 5 kcal mol^{-1}
= −5.1 kcal mol^{-1} MP2/6-31+G(d)

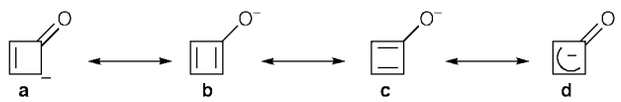


(17)

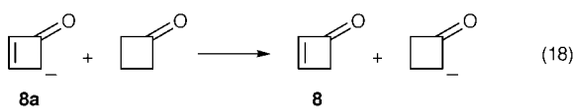
$\Delta H°_{rxn}$ = −10.1 ± 3 kcal mol^{-1}

destabilization in **1a** as a result of cyclobutadiene character in the anion. This view is consistent with the structure of **1a**, its charge distribution, and Bader parameters such as the bond critical point, bond order, and ellipticity. It also is interesting to note that while resonance delocalization accounts for about two thirds of the stabilization in acetaldehyde enolate (*i.e.*, the rotational barrier is 36 kcal mol^{-1} at the MP2/6-31+G(d)//HF/6-31+G(d) level[52] but $\Delta\Delta H°_{acid}$(ethane − acetaldehyde) = 54 kcal mol^{-1}) the contribution in **11a**, and presumably **1a**, is much larger (i.e., the rotational barrier about the Ph**CH**$^{-}$**–CH**O bond is 26.7 kcal mol^{-1} compared to $\Delta\Delta H°_{acid}$(ethylbenzene − phenylacetaldehyde) = 31 kcal mol^{-1}).[53]

The conjugate base of cyclobutenone (**8a**) is the simplest

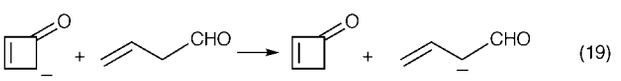


enolate which can have cyclobutadiene character.[54] In contrast to benzoannelation of cyclobutanone enolate, introduction of a double bond is highly disfavored [eqn. (18) and (19)]. At the



(18)

$\Delta H°_{rxn}$ = −17.1 kcal mol^{-1} (MP2/6-31+G(d))



(19)

$\Delta H°_{rxn}$ = −26.7 kcal mol^{-1} (MP2/6-31+G(d)//HF/6-31+G(d))

MP2/6-31+G(d) level of theory, benzocyclobutenone is computed to be 22 kcal mol^{-1} more acidic than cyclobutenone and the corresponding radical also is substantially more stabilized (*i.e.*, ΔEA(**1r** − **8r**) = 0.9 eV). The former difference is considerably smaller than that between benzocyclopropene and cyclopropene (34.5 kcal mol^{-1}) at the same level of theory.[55] This represents a leveling effect and is not surprising since cyclobutenone is much more acidic than cyclopropene ($\Delta\Delta H°_{acid}$ = 38.7 kcal mol^{-1}). As for the relative lack of stability of **8a**, this is due to its inability to distribute the charge on to oxygen *via* resonance structures **b** and **c** and the resulting distortion to an allylic-type ion (resonance structure **d**).

Conclusion

Benzocyclobutenone enolate was generated in the gas phase by deprotonation of **1**. The measured thermochemistry ($\Delta H°_{acid}$ = 360.3 ± 2.1 kcal mol^{-1}, EA = 1.90 ± 0.10 eV and BDE = 90.5 ± 3.1 kcal mol^{-1}) suggests that there is little, if any, antiaromatic destabilization of **1a** as a result of a resonance structure with cyclobutadiene character. In fact, an analysis of the ion's structure using NBO and Bader's parameters reveals that **1a**'s overall stability is a result of its ability to distort and alleviate the 4π electron interaction, and to distribute the charge over the benzene ring and the electronegative oxygen atom. Anion **1a** displays carbon reactivity with perfluorinated reagents under thermal conditions, but can be induced to react through oxygen upon excitation. Despite previous reported failures, benzocyclobutenone enolate was trapped *in situ* with an electrophile in the liquid phase.

Acknowledgements

Support from the National Science Foundation, the donors of the Petroleum Research Foundation, as administered by the American Chemical Society, the Minnesota Supercomputer Institute, and the University of Minnesota – IBM Shared Research Project is gratefully acknowledged.

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Paper 9/05868K