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Enolates in 3-D: An Experimental and Computational Study of Deprotonated 2-Adamantanone

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Deprotonation of 2-adamantanone (1) in the gas phase affords the corresponding β -enolate anion. This ion was independently prepared by the fluoride-induced desilylation of 4-trimethylsilyl-2-adamantanone, and its reactivity and thermodynamic properties were measured ($\Delta H^{\circ}_{acid} = 394.7 \pm 1.4$, EA = 16.8 ± 1.6, and BDE = 97.9 ± 2.1 kcal mol⁻¹). Density functional theory calculations with B3LYP and M06-2X, and G3 energies are also reported. The computed relative stabilities of the conjugate bases of 1 are as follows: $\beta > \gamma > \alpha > \delta$. An attempt to prepare the γ -anion, however, resulted in the formation of its ring-opened isomer (i.e., deprotonated 7-methylenebicyclo[3.3.1]nonan-2-one).

Introduction

Deprotonation of carbonyl-containing compounds is a widely used method for generating stabilized anions and subsequently forming carbon-carbon bonds.1 Proton abstraction at the α -position often can be carried out with relatively weak bases because the charge in the resulting enolate anion is stabilized via delocalization due to resonance, inductive, field, and polarization effects. The acidity of polycyclic systems is greatly reduced when the α -hydrogens are located at a bridgehead position and the resulting carboncarbon double bond of the enolate ion corresponds to an anti-Bredt olefin.² In such cases, deprotonation can occur at positions further from the carbonyl group, but stabilization of the conjugate base is not as great as for an α -enolate.³ The resulting homoenolates are stabilized by several mechanisms (e.g., charge-dipole and orbital interactions) and have been a subject of long-standing interest both from a synthetic and a theoretical perspective.

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Acyclic ketones and larger more flexible bridged species where the α -position is blocked can be readily deprotonated by strong bases such as lithium diisopropylamide (LDA) or lithium tetramethylpiperidide (LTMP) to afford homoenolate ions.² These anionic intermediates typically can be trapped in good yields with a variety of electrophiles. More rigid species such as 2-adamantanone (1) are not deprotonated by strong bases, and their enolates are not synthetically accessible.⁵ They would be useful, however, since 1 is a pharmaceutical intermediate and a number of drugs are adamantane derivatives.⁶ Insights into nonenolizable ketones have been obtained by investigating their hydrogendeuterium (H/D) exchange behavior.



For example, three different sites undergo H/D exchange when 1 is reacted with *t*-BuOK in *t*-BuOD at 185 $^{\circ}$ C for

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FIGURE 1. Computed M06-2X/aug-cc-pVDZ geometries of the α - and β -enolate anions of 2-adamantanone. Bond lengths are in angstroms.

400 h.⁷ The β -axial hydrogens are replaced by deuterium 15 times more rapidly than the β -equatorial hydrogens and twice as fast as those at the α -position. This suggests that the β -axial hydrogens are the most acidic ones in 2-adamantanone, but 1 undergoes H/D exchange 100 times more slowly than camphenilone (**2**) and is not very acidic. To investigate the enolates of 2-adamantanone further, we report on the gas-phase deprotonation of **1**, the regiospecific generation of its β -enolate anion, and an attempt to form the γ -enolate anion. The reactivity of these ions and the acidity of 2-adamantanone are also reported, and the experimental results are supplemented with density functional theory and Gaussian-3 (G3)⁸ calculations on all five deprotonation sites of **1** (α , β_{ax} , β_{eq} , γ , and δ).

Results/Discussion

Deprotonation of 2-adamantanone was experimentally investigated with a Fourier transform mass spectrometer (FTMS) by reacting **1** with a series of anions of known basicity. If an efficient proton transfer is observed, then this indicates that 2-adamantanone is a stronger acid than the conjugate acid of the base (HB). A slow process or no proton transfer at all suggests just the opposite (i.e., $\Delta H^{\circ}_{acid}(HB) < \Delta H^{\circ}_{acid}(1)$). Strong bases such as amide and ethylamide ($\Delta H^{\circ}_{acid}(NH_3) = 403.4 \pm 0.1$ kcal mol⁻¹ and $\Delta H^{\circ}_{acid}(EtNH_2) = 399.3 \pm 1.1$ kcal mol⁻¹) rapidly deprotonate **1**, but additional products corresponding to nucleophilic attack at the carbonyl carbon followed by the loss of water were also observed (eqs 1 and 2).⁹ These

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condensation reactions are analogous to the reactivity of ketones with amines in solution, and both $CH_2=N^-$ and 2-azaallyl anion have been previously generated in the gas phase.^{10,11} B3LYP/aug-cc-pVDZ¹² calculations on the alkoxide and amide ions shown in eq 1 (**10** and **1N**, respectively) and the four-centered transition structure for their interconversion were found to be 36.5, 24,0, and 11.4 kcal mol⁻¹ more stable than the sum of the energies of 2-adamantanone and amide ion, respectively. These results, consequently, are in accord with the proposed pathways illustrated in eqs 1 and 2.





Dimethylamide ($\Delta H^{\circ}_{acid}(Me_2NH) = 396.4 \pm 0.9 \text{ kcal mol}^{-1}$) does not possess an α -hydrogen because it is the conjugate base of a secondary amine, so it cannot lead to the formation of an imine. Therefore, it was not surprising that it only undergoes a rapid $(k = (1.90 \pm 0.13) \times 10^{-9} \text{ cm}^3 \text{ molecules}^{-1} \text{ s}^{-1})$ proton transfer. Hydroxide ion is a weaker base $(\Delta H^{\circ}_{acid}(H_2O) =$ 390.7 ± 0.1 kcal mol⁻¹) and does not abstract a proton from 1, but does react to give an adduct ion that presumably is the result of nucleophilic addition to the carbonyl group (eq 3). Fragmentation of this ion by collision-induced dissociation (CID) gives back the hydroxide ion. Taken together, these results indicate that 2-adamantanone is more acidic than dimethylamine but less acidic than water, which enables us to assign $\Delta H^{\circ}_{acid}(1) = 393.6 \pm 2.9$ kcal mol⁻¹. These experiments do not shed light on which position is the most acidic site in the molecule, especially since no H/D exchange was observed with D_2O or ND_3 .



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 TABLE 1.
 Relative Stabilities of the α -, β -, γ -, and δ -Enolate Anions of 2-Adamantanone Computed at the B3LYP, M06-2X, and G3 Levels^a

| anion | | M06-2X | | |
|------------------|--------------|-----------------|----------|-------|
| | B3LYP DZ^b | DZ^b | TZ^{c} | G3 |
| α | 6.33 | 4.27 | 4.25 | 5.60 |
| $\beta_{\rm ax}$ | 0.00 | 0.00 | 0.00 | 0.00 |
| β_{eq} | 5.08 | 4.46 | 4.60 | $-^d$ |
| $\beta_{\rm cv}$ | 2.46 | -1.58 | -2.08 | 0.56 |
| γ | 2.30 | 2.28 | 2.21 | 3.40 |
| δ | 8.16 | 6.17 | 6.45 | 7.55 |

^{*a*}All values are at 298 K and are in kcal mol⁻¹. ^{*b*}DZ = aug-cc-pVDZ. ^{*c*}TZ = maug-cc-pV(T+d)Z (see ref 14). ^{*d*}The $1\beta_{eq}$ anion cyclizes upon optimization at the MP2(full)/6-31G(d) level, which precludes a G3 energy determination.

To address this issue, DFT calculations were carried out on 2-adamantanone and its conjugate bases. B3LYP was employed because of its successful track record and popularity, but the more recent M06-2X functional developed by Truhlar et al.¹³ was also used because in its early testing it was found to be more accurate. All five deprotonation sites in 1 were examined and six different anions were located since the β -anion can cyclize to form a three-membered ring. The structures of the α - and β -enolates are given in Figure 1 and all of the computed geometries can be found in the Supporting Information. G3 energies were also computed since this model chemistry has been extensively benchmarked and is often accurate to within 2 kcal $mol^{-1.8}$ The relative energies of the six enolate anions are given in Table 1 and all three approaches indicate that the stability order is $\beta > \gamma > \alpha >$ δ . These predictions are in accord with the H/D exchange results of Stothers in *t*-BuOD in that the β_{ax} anion is found to be more stable than the α and β_{eq} anions. In addition, the M06-2X calculations (but not B3LYP) indicate that the α -position in 1 is more acidic than the β_{eq} hydrogens, which reproduces the observed $\beta_{ax} > \alpha > \hat{\beta}_{eq}$ H/D exchange behavior.⁷ All of the calculations indicate that the γ -anion is more stable than the α -anion, however, but the former site was not observed to undergo H/D exchange.

The relative instability of the α -enolate of **1** is due to its inability to delocalize the charge via resonance, and the resulting electron–electron repulsion between the lone pairs of electrons on the carbon at the carbanion center and the oxygen atom. The latter interaction results in the anion breaking symmetry ($C_S \rightarrow C_1$) to diminish this repulsion. Since H/D exchange is observed at the α -position in solution, this presumably is due to the interaction of the carbonyl oxygen atom with the cation associated with the base.

As for the preferred structure of the β -anion, it may well be the cyclized species as predicted with the M06-2X functional, but the energy difference between the β_{cy} and β_{ax} ions is small and their relative stability is reversed by B3LYP and G3 calculations. Our computations do not lead to a clear prediction for the preferred structure of the β -enolate anion, consequently, but they do indicate that the β -position is the most acidic site in 2-adamantanone. Additional calculations at the M06-2X/aug-cc-pVDZ level also indicate that the interconversion of the β_{eq} anion to its axial and cyclic counterparts should occur readily since the isomerization barriers are small (i.e., 0.3 and 10.4 kcal mol⁻¹, respectively).

To further examine the deprotonation site of 2-adamantanone, the β -anion (**1** β) was selectively generated via the fluoride-induced desilylation of an ~1:1 mixture of axial and equatorial 4-trimethylsilyl-2-adamantanone (eq 4).¹⁵ The resulting anion (which presumably consists of a



rapidly interconverting mixture of $1\beta_{ax}$ and $1\beta_{cy}$) was transferred to the second reaction cell in the FTMS where it was collisionally cooled with a pulse of argon and then allowed to react with a variety of neutral reagents. Water rapidly protonated 1β , dimethylamine reacted slowly (k = $(3.14 \pm 0.14) \times 10^{-10}$ cm³ molecules⁻¹ s⁻¹), and ethylamine and ammonia did not undergo proton transfer at all, but the addition – H₂O products shown in eqs 1b and 2b were produced. These results are qualitatively the same as for deprotonated 2-adamantanone, which indicates that depronation takes place primarily, if not exclusively, at the β -position. In addition, the rate constants for the deprotonation of 1 with Me₂N⁻ and the protonation of 1β with Me₂NH can be combined to derive an equilibrium constant since $K = k_1/k_{-1}$ as illustrated in eq 5.

$$\int \int \int e^{-k_1} + Me_2 N + Me$$

The resulting value for K is 6.05 ± 0.49 , which leads to $\Delta G^{\circ}_{acid}(1 - Me_2NH) = -1.1 \pm 0.6 \text{ kcal mol}^{-1}$ if a conservative uncertainty of $\pm 100\%$ for K is used in the error analysis. This free energy acidity difference can be combined with the literature value for dimethylamine $(\Delta G^{\circ}_{acid}(Me_2NH) = 388.2 \pm 0.9 \text{ kcal mol}^{-1})$ to afford $\Delta G^{\circ}_{acid}(\mathbf{1}) = 387.1 \pm 1.1 \text{ kcal mol}^{-1}$. To obtain the deprotonation enthalpy, the entropies for 1 and 1β are needed. These quantities were computed by using unscaled B3LYP and M06-2X vibrational frequencies with the aug-ccpVDZ basis set. Both methods provide $T\Delta S^{\circ}_{acid}(1)$ terms that differ by only 0.4 kcal mol⁻¹ for the β_{ax} and β_{cy} anions, and only 0.1 kcal mol⁻¹ when the same ion is used. If one assumes uncertainties of ± 2 eu for the individual entropies, then M06-2X leads to $T\Delta S^{\circ}_{acid}(1) = 7.6 \pm$ $0.9 \text{ kcal mol}^{-1}$ for the cyclic ion. This enables us to assign $\Delta H^{\circ}_{\text{acid}}(1) = 394.7 \pm 1.4 \text{ kcal mol}^{-1}$, which is in good accord with the bracketing results. It also is well-reproduced by B3LYP/aug-cc-pVDZ, M06-2X/aug-cc-pVDZ, M06-2X/maug-cc-pV(T+d)Z,¹⁴ and G3 calculations which give deprotonation enthalpies of 394.0, 393.8, 394.1, and 396.8 kcal mol⁻¹, respectively. Our equilibrium acidity for 1 indicates that it is a

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much weaker acid than a typical ketone (e.g., ΔH°_{acid} (cyclohexanone) = 366.4 ± 2.0 kcal mol⁻¹), but a stronger acid than an alkane (e.g., ΔH°_{acid} (CH₄) = 416.7 ± 0.7 kcal mol⁻¹).

Another measure of the stability of an anion is the electron affinity of the corresponding radical, which provides the energy difference between the anion and the radical. This quantity was measured by reacting 1β (generated via eq 4) with a series of electron transfer reagents with known electron affinities. Electron transfer was not observed with 2-fluorobenzaldehyde (EA = 0.64 ± 0.11 eV) or 2-fluorobenzonitrile (EA = 0.70 ± 0.10 eV), but readily occurred with 4-trifluoromethylbenzonitrile (EA = $0.76 \pm 0.09 \text{ eV}$), perfluorotoluene (EA = 0.86 ± 0.11 eV), and stronger oxidants. This enables us to assign EA = 0.73 ± 0.07 eV $(16.8 \pm 1.6 \text{ kcal mol}^{-1})$ to the radical corresponding to 1β , and this is in excellent accord with B3LYP/aug-cc-pVDZ, M06-2X/aug-cc-pVDZ, M06-2X/maug-cc-pV(T+d)Z, and G3 predictions of 0.70, 0.69, 0.72, and 0.75 eV, respectively. In this instance, the experimental value is between that for an alkyl radical (EA(CH₃) = 1.8 \pm 0.7 kcal mol⁻¹) and an α -radical derived from an enolizable ketone such as cyclohexanone (e.g., EA = $35.2 \pm$ $0.2 \text{ kcal mol}^{-1}$).

The homolytic bond dissociation energy (BDE) for 2-adamantanone at the β -position can be derived from the acidity and electron affinity measurements by using the thermodynamic cycle shown in eq 6, where the ionization energy (IE) of hydrogen is well-known to be 313.6 kcal mol^{-1} . This leads to BDE(1 β) = 97.9 ± 2.1 kcal mol⁻¹, which is well-reproduced by B3LYP/aug-cc-pVDZ, M06-2X/aug-cc-pVDZ, M06-2X/maug-cc-pV(T+d)Z, and G3 calculated energies of 95.3, 97.3, 98.2, and 99.9 kcal mol^{-1} , respectively. It is also the same as the secondary C–H bond dissociation energy of propane $(98.6 \pm 0.4 \text{ kcal mol}^{-1})^{16}$ indicating that the β -anion is stabilized by the remote carbonyl group whereas there is little, if any, effect on the radical. The thermodynamic properties at the other positions in 2-adamantanone were explored computationally and are given in Table S1 in the Supporting Information.

$$BDE(HX) = \Delta H^{\circ}_{acid}(HX) - IE(H^{\bullet}) + EA(X^{\bullet})$$
 (6)

Enolates are commonly employed in solution to make C–C bonds by reacting them with a wide variety of electrophiles. The reactivity of 1β , consequently, was explored in the gas phase with a number of different electrophiles. Hexafluorobenzene, which has been used to differentiate *C*- vs *O*-reactivity in α -enolates,¹⁷ somewhat surprisingly was found to give telltale products for both reaction pathways. That is, an (adduct – HF) ion was formed (75%, *C*-alkylation) as was pentafluorophenoxide (25%, *O*-alkylation; eq 7). Carbon protonation of 1β is favored by 25.9 kcal mol⁻¹ over that at oxygen based upon M06-2X/maugcc-pV(T+d)Z calculations, and this thermodynamic preference is unlikely to be reversed in the alkylation reaction with hexafluorobenzene. The formation of the new C–C

or C–O σ -bond provides a sufficiently large driving force to enable both reaction pathways to occur. This behavior contrasts with the α -enolate of cyclohexanone, which was found to give 98% *C*-alkylation with hexafluorobenzene.^{17a}



2-Fluorobenzaldehyde undergoes an interesting acyl transfer reaction with $\mathbf{1\beta}$ (eq 8). The major product is due to proton transfer (60%), but nucleophilic addition to the carbonyl group leads to a tertiary alkoxide that is also observed (20%). Addition reactions of this sort are disfavored at low pressures because the resulting adduct ion has enough energy to revert back to the starting materials. It is not surprising, therefore, that the resulting alkoxide ion undergoes a subsequent fragmentation. Since the best anionic leaving group is fluorophenide and the resulting 4-acyl-2-adamantanone has an acidic α -hydrogen to the formyl group, we propose that **3** is the structure of the resulting product ion. This behavior is analogous to the previously reported fragmentation behavior of alkoxides.¹⁸



Basic carbanions react with carbonyl sulfide via a number of interesting pathways,¹⁹ so its reactivity with 1β was also explored. In this case, two product ions were observed (eq 9). The major (80%) ion formed is due to

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sulfur-atom transfer while the minor species is a thiocarboxylate anion.



Proton abstraction at the γ -position of 2-adamantanone is predicted to be the second most favorable site in the molecule. To try and generate this anion and probe the long-range stabilization responsible for its stability, we synthesized 5-carboxy-2-adamantanone (4) in one step from 5-hydroxy-2-adamantanone as described in the literature.²⁰ Electrospray ionization of the acid readily afforded the carboxylate anion, and as anticipated it lost carbon dioxide upon collisioninduced dissociation (eq 10). The resulting ion did not react with background water suggesting that the γ -enolate (1γ) was not formed. Proton abstraction did not occur with acetone ($\Delta H^{\circ}_{acid} = 369.1 \pm 2.1 \text{ kcal mol}^{-1}$) either, but readily took place with 2,2,2-trifluoroethanol (ΔH°_{acid} = 361.7 ± 2.5 kcal mol⁻¹). These results suggest that the proton affinity of the decarboxylated anion is 365.1 ± 4.0 kcal mol⁻¹, and this indicates that an isomerization to a more stable anion took place. An E1cB elimination of the γ -enolate would afford a stabilized α -enolate (5), and we suggest that this is the product ion that is formed upon decarboxylation of the conjugate base of 4. In accord with this hypothesis, M06-2X/ aug-cc-pVDZ calculations give $PA(5) = 363.3 \text{ kcal mol}^{-1}$, which is in excellent agreement with the experimental data. A small ring-opening barrier of 6.3 kcal mol⁻¹ was also computed, and this value decreases to 5.2 kcal mol^{-1} with the larger maug-cc-pV(T+d)Z basis set. B3LYP/aug-cc-pVDZ calculations give a barrier height of 4.5 kcal mol^{-1} , so both functionals indicate that the γ -anion is a labile species prone to rearrangement.



Conclusions

Deprotonation of 2-adamantanone in the gas phase affords the corresponding β -enolate anion, which was independently prepared by the fluoride-induced desilylation of 4-trimethylsilyl-2-adamantanone. Proton abstraction does not take place at the α -position to the carbonyl group as is commonly the case for most ketones. This is because the requisite orbitals which would enable resonance stabilization are perpendicular to each other, and the α -enolate anion

resonance structure with a C-C double bond corresponds to an anti-Bredt olefin. The axial anion at the β -position is predicted to be \sim 5 kcal mol⁻¹ more stable than its equatorial epimer, but it is unclear if carbon-carbon bond formation leading to a ring-closed cyclopropoxide ion is the lowest energy β -anion structure. In any case, there is a significant long-range stabilization of the anion as it is more stable than alkyl anions and no more basic than 2-naphthyl anion (i.e., $\Delta H^{\circ}_{acid}(1 - naphthalene) = 394.7 \pm 1.4 - 394.2 \pm 1.2$ or 0.5 ± 1.8 kcal mol⁻¹). The other conjugate bases of **1** are also stabilized by the carbonyl group and their relative predicted stability order is $\beta > \gamma > \alpha > \delta$. An attempt to generate the γ -enolate anion from its corresponding carboxylate anion resulted in the formation of the conjugate base of 7-methylenebicyclo[3.3.1]nonan-2-one (i.e., a ring-opened α -enolate ion).

Derivatives of 2-adamantanone are of interest as medicines. The synthesis of these compounds is hindered by the fact that strong bases have proven to be ineffective at deprotonating 2-adamantanone. Our results suggest that the fluoride-induced desilylation of trimethylsilyl-2-adamantanones in the presence of electrophiles may prove to be useful for making derivatives of these compounds.

Experimental Section

Gas-Phase Experiments. A dual cell model 2001 Finnigan FTMS was used with a 3 T superconducting magnet. This instrument has been updated with IonSpec electronics and is controlled by a PC running the Omega 8.0 data system. The vacuum inlet also has been extensively modified by adding pulse valves, slow leak valves, and a gas ballast. These changes facilitate kinetic measurements, and enable a wide variety of neutral reagents to be conveniently employed. 2-Adamantanone and 4-trimethylsilyl-2-adamantanone, which was prepared as described in the literature,¹⁵ were introduced into one of the FTMS cells at static pressures via a direct inlet metered with a Granville-Philips (model 203) variable leak valve. Electron ionization (7.5 eV) of a pulse of ethylamine afforded ethylamide (CH₃CH₂NH⁻), which was subsequently isolated and allowed to react with 1. The resulting $(M - 1)^{-}$ anion was transferred to the second FTMS cell where it was cooled with a pulse of argon and isolated before monitoring its reactivity with a static pressure of selected neutral reagents. Alternatively, electron ionization of NF₃ produced fluoride ion, which was allowed to react with 4-trimethylsilyl-2-adamantanone. The resulting $(M - Si(CH_3)_3)^-$ anion was transferred to the second reaction region and cooled with a pulse of argon. It was then isolated and allowed to react with different neutral compounds as a function of time. Electron ionization (7.5 eV) of a pulse of ammonia afforded amide ion, which was allowed to react with ethylamine, dimethylamine, or water to afford their conjugate bases. The resulting ions (NH₂⁻, CH₃CH₂NH⁻, (CH₃)₂N⁻, and OH⁻) were transferred to the second FTMS cell where they were isolated, cooled with an argon pulse, and allowed to react with the 2-adamantanone.

Electrospray experiments were carried out with an IonSpec ESI FTMS equipped with a 3 T magnet and a modified inlet system similar to the one noted above. Data acquisition and processing was carried out with a PC running the Omega software package. The $(M - 1)^-$ anion of 5-carboxy-2-adamantanone was generated by spraying the acid²⁰ into the instrument from a 30 mM aqueous methanol solution (3:1 (v/v) CH₃OH/H₂O). Fragmentation of the resulting carboxylate anion via collision-induced dissociation (CID) with argon was carried out by using

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an off-resonance excitation pulse. The resulting decarboxylated ion $((M - CO_2)^-)$ was cooled with a pulse of argon, isolated, and allowed to react with static pressures of Bronsted acids.

Computations. All of the computed structures were fully optimized by using the B3LYP¹² and M06-2X¹³ density functionals with the aug-cc-pVDZ basis set. In the latter case, optimized geometries were also calculated by using the minimally augmented triple- ζ + d basis set (i.e., maug-cc-pV(T+d)Z) recently reported by Papajak and Truhlar.¹⁴ Vibrational frequencies were computed for each structure to ensure that energy minima on the potential energy surface were located, and to enable thermal corrections to the enthalpy to be calculated. Unscaled frequencies were used for this purpose and small vibrational modes which contribute more than 0.30 kcal mol⁻¹ were replaced by $1/_2 RT$. G3 energies are also reported and were computed as described in the literature.⁸ In this instance, scaled frequencies (0.8929) were used to correct the zero-point energies

and make the thermal energy corrections. All of the resulting energetic quantities reported herein are room temperature enthalpies. The computations were carried out at the Minnesota Supercomputer Institute for Advanced Computational Research with Gaussian 03^{21} (B3LYP) or Gaussian 09 (M06-2X and G3).²²

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Supporting Information Available: Computed structures, energies, and a table of the predicted thermodynamic properties of the different deprotonated 2-adamantanone ions are provided along with complete citations to refs 21 and 22. This material is available free of charge via the Internet at http:// pubs.acs.org.

⁽²¹⁾ Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A., et al. *Gaussian 03*; Gaussian, Inc., Wallingford, CT, 2004.

⁽²²⁾ Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A., et al. *Gaussian 09*; Gaussian, Inc., Wallingford, CT, 2009.