# Stereospecificity in the Gas Phase. Formation and Characterization of Configurationally Stable Cyclopropyl Anions

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**Abstract:** We report the gas-phase preparation of *cis*- and *trans*-β-formylcyclopropyl anion (**4c** and **4t**) via the room temperature fluorodesilylation of their corresponding trimethylsilyl derivatives. These homoenolates do not interconvert or undergo ring-opening isomerization at 25 °C, and can readily be differentiated with several chemical probes. The proton affinities of both **4c** and **4t** have been measured, and the results are compared to ab initio computations. Cyclization to a 2-bicyclobutoxide ion (**8**) has been considered, and although the process is calculated to have a small activation barrier, it is found to be thermodynamically unfavorable.

The ability to form a carbanion center at any position in a molecule (regiospecificity) with spatial control (stereospecificity) is a major objective in synthetic organic chemistry. Considerable progress has been made in this regard and a number of carbanions including vinyl,[1] cyclopropyl,[2] and α-heterosubstituted derivatives[3] are known to be capable of maintaining their configuration under the appropriate reaction conditions. Recent studies have also revealed that under special circumstances alkyl anions can be configurationally stable.[4] In the gas phase analogous developments would open up new avenues of exploration and would enable important condensed phase problems to be addressed in a solvent-free and counterion-free environment. Progress in this area has been limited, however, by a lack of stereospecific synthetic procedures.[5]

Electron ionization, chemical ionization, and collision-induced dissociation are three methods which have been used in the gas phase to prepare numerous carbanions.[6] One particularly versatile procedure is the fluorodesilylation of trialkylsilyl derivatives.[7] For example, deprotonation of methanethiol affords methyl thiolate (eq 1), whereas (trimethylsilyl)methanethiol reacts with fluoride ion to give thiomethyl anion (eq 2).[7e] This method, which was originally developed by DePuy and co-workers, takes advantage of the tremendous strength of the silicon–fluorine bond (~144 kcal mol$^{-1}$)[8] to selectively afford a carbanion at the site where the trialkylsilyl substituent is attached. It not only is regiospecific but recently was used to afford (*E*)- and (*Z*)-vinyl anions in the first stereospecific synthesis in the gas phase.[5]

$$CH_3SH \xrightarrow[-BH]{B^-} CH_3S^- \quad (1)$$

$$TMSCH_2SH \xrightarrow[-TMSF]{F^-} {}^-CH_2SH \quad (2)$$

Cyclopropyl anions have been the subject of several gas-phase investigations.[9] They are structurally stable with respect to ring-opening isomerization, but they can be induced to rearrange upon heating. Their configurational stability has not been examined, but it is calculated to be less than that for vinyl anions. This is in accord with the known behavior of these ions in solution and represents a potential difficulty in their gas-phase synthesis. Fortunately, this turns out not to be a significant obstacle, and we now report on the room temperature production and characterization of a cis and trans substituted cyclopropyl anion.

## Experimental Section

All of the gas-phase experiments were carried out at room temperature in a variable temperature flowing afterglow device which has previously been described.[7e] Typical operating conditions, $P_{He}$ = 0.35–0.40 Torr and $F_{He}$ = 150–175 atm cm$^3$ s$^{-1}$, were employed. Fluoride was generated by electron ionization of $NF_3$, and medium-pressure liquid chromatography (MPLC) purified samples of *cis*- and *trans*-2-(trimethylsilyl)-cyclopropanecarboxaldehyde (**1c** and **1t**) were used. All of the other neutral reagents were commercially available and used as supplied. Reported product distributions, unless otherwise noted, were obtained by extrapolating to zero reaction time so as to avoid contributions from secondary products and attain the primary branching ratio.

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**General Methods.** Nuclear magnetic resonance spectra were obtained in $CDCl_3$ on IBM NR/200, IBM NR/300, or Varian VXR-500S spectrometers and are reported in ppm ($\delta$). Infrared spectra were recorded on a Perkin-Elmer 1600 Series FT-IR spectrometer and are reported in wave numbers ($cm^{-1}$). Mass spectra were obtained on an AEI MS-30 and/or Finnigan MAT 95 mass spectrometer. Preparative gas–liquid chromatography (GLC) was carried out on a Varian Aerograph gas chromatograph with a helium flow of 60 mL $min^{-1}$.

**1,1-Dibromo-2-(trimethylsilyl)cyclopropane (2).**[10] A 2-L, three-necked, round-bottomed flask equipped with a reflux condenser, mechanical stirrer, and an addition funnel was charged with 51.6 g (0.51 mol) of vinyltrimethylsilane, 262 g (1.03 mol) of bromoform, and 4.8 g (0.026 mol) of tributylamine. A 50% wt/wt aqueous solution of sodium hydroxide (270 g of NaOH in 270 mL of $H_2O$) was slowly added with vigorous stirring, and the reaction mixture was maintained at room temperature for 3 days. Water (600 mL) and pentane (400 mL) were subsequently added, and the resulting solution was filtered. The aqueous layer was washed with pentane, and the combined organic material was dried over anhydrous magnesium sulfate. Removal of the solvent and simple distillation of the residue, all at aspirator pressure, afforded 44.1 g (32%) of **2**: $^1H$ NMR (200 MHz, $CDCl_3$) $\delta$ 1.82 (dd, 1H, $J$ = 6.0 and 12.6 Hz), 1.49 (dd, 1H, $J$ = 6.0 and 10.0 Hz), 0.93 (dd, 1H, $J$ = 10.0 and 12.5 Hz), 0.15 (s, 9H).

***cis*- and *trans*-1-Bromo-2-(trimethylsilyl)cyclopropane (3c and 3t).** A 1-L, two-necked, round-bottomed flask was equipped with a condenser and an addition funnel. Lithium aluminum hydride (6.1 g, 0.16 mol) and 100 mL of dry ether were placed in the flask and stirred with a magnetic stir bar under a nitrogen atmosphere. An ethereal solution of the dibromide (43.9 g (0.16 mol) of **2** and 300 mL of $Et_2O$) was slowly added, and the resulting mixture was heated to reflux for 14–18 h. Gas chromatography proved to be a convenient means for monitoring this reaction as one can readily separate the starting material and the two products with a 10% Carbowax 20M column at 120 °C. The reaction was quenched with water, and the organic material was washed several times with $H_2O$. The resulting ethereal solution was dried with anhydrous $MgSO_4$ and concentrated under reduced pressure. Simple distillation of the product at aspirator pressure afforded 12.9 g (42%) of an approximately 3:1 mixture of **3c** and **3t**. This mixture was used in the next step and was only separated for characterization purposes. **3c**: $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 3.27 (ddd, 1H, $J$ = 3.8, 6.9, and 8.1 Hz), 1.21 (ddd, 1H, $J$ = 5.1, 6.9, and 11.4 Hz), 0.81 (ddd, 1H, $J$ = 3.9, 5.2, and 9.1 Hz), 0.083 (s, 10H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 23.0 (CHBr), 12.4 ($CH_2$), 6.2 (*C*HTMS), –0.7 (TMS); HRMS-EI calcd for $C_6H_{13}BrSi$ ($^{79}Br$) 191.9970 found 191.9961 ($M^+$), calcd for $C_6H_{13}BrSi$ ($^{81}Br$) 193.9950 found 193.9927 ($M^+$). **3t**: $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 2.77 (ddd, 1H, $J$ = 3.3, 4.9, and 6.5 Hz), 1.05 (m, 1H), 0.83 (ddd, 1H, $J$ = 5.3, 6.5, and 8.4 Hz), 0.25 (m, 1H), –0.03 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 18.5 (CHBr), 12.5 ($CH_2$), 10.1 (*C*HTMS), –2.6 (TMS); HRMS-EI calcd for $C_6H_{13}BrSi$ ($^{79}Br$) 191.9970 found 191.9953 ($M^+$), calcd for $C_6H_{13}BrSi$ ($^{81}Br$) 193.9950 found 193.9924 ($M^+$).

***cis*- and *trans*-2-(Trimethylsilyl)cyclopropanecarboxaldehyde (1c and 1t).** A 250-mL, three-necked, round-bottomed flask equipped with a condenser, addition funnel, and septum was filled with 32.3 mL of 1.7 M *t*-BuLi (0.055 mol) and cooled to –78 °C under a nitrogen atmosphere. A mixture of 5.30 g (0.027 mol) of *cis*- and *trans*-1-bromo-2-(trimethylsilyl)cyclopropane (**3c** and **3t**), and 100 mL of dry ether was slowly added over 45 min with continuous stirring. The reaction was maintained at –78 °C for an additional 10–15 min and then was quenched with 2.01 g (0.027 mol) of freshly distilled (over BaO) DMF. The resulting solution was allowed to warm to room temperature and was stirred for an additional hour. It was subsequently poured into a separatory funnel containing 12 g of concentrated HCl and 50 mL of ice water. The resulting mixture was shaken vigorously for ~1 min, and then the two layers were separated. The aqueous portion was washed three times with $Et_2O$, and the combined organic material was extracted twice with $H_2O$ and once with brine. Anhydrous $Na_2SO_4$ was used to dry the solution, and the solvent was stripped off with a rotary evaporator to afford 3.38 g (88%) of a crude mixture of aldehydes. The product had a tendency to decompose upon exposure to air, but its lifetime could be extended considerably (weeks) by storing it in $Et_2O$ under a nitrogen atmosphere in the cold. Purification and separation of the two isomers was accomplished via MPLC on a silica gel column using a 50:1 hexane/ethyl acetate mixture. **1c**: $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.97 (d, 1H, $J$ = 6.9 Hz), 1.97 (m, 1H), 1.37 (ddd, 1H, $J$ = 4.1, 7.5, and 9.9 Hz), 1.13 (quint, 1H, $J$ = 4.4 Hz), 0.40 (q, 1H, $J$ = 9.4 Hz), 0.09 (s, 9H); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$ 201.8 (CHO), 28.6 (*C*HCHO), 11.8 ($CH_2$), 9.8 (*C*HTMS), –0.5 (TMS); HRMS-EI calcd for $C_7H_{14}OSi$ 142.0813 found 142.0823 ($M^+$, 0.07%), calcd for $C_6H_{11}OSi$ 127.0579 found 127.0587 ($M - CH_3^+$, 100%), calcd for $C_3H_9Si$ 73.0473 found 73.0453 ($M - C_4H_5O^+$, 26%). **1t**: $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 8.64 (d, 1H, $J$ = 6.6 Hz), 1.67 (m, 1H), 1.21 (m, 1H), 0.97 (ddd, 1H, $J$ = 4.3, 7.3, and 8.2 Hz), 0.45 (ddd, 1H, $J$ = 5.8, 8.3, and 10.8 Hz), –0.033 (s, 9H); $^{13}C$ NMR (50 MHz, $CDCl_3$) $\delta$ 201.0 (*C*HO), 26.7 (*C*HCHO), 10.3 ($CH_2$), 6.8 (*C*HTMS), –2.6 (TMS); HRMS-EI calcd for $C_7H_{14}OSi$ 142.0813, found 142.0824 ($M^+$, 3.3%), calcd for $C_6H_{11}OSi$ 127.0579, found 127.0581 ($M - CH_3^+$, 48%), calcd for $C_3H_9Si$ 73.0473, found 73.0451 ($M - C_4H_5O^+$, 100%), calcd for $C_4H_5O$ 69.0340, found 69.0368 ($M - TMS^+$, 1.2%).

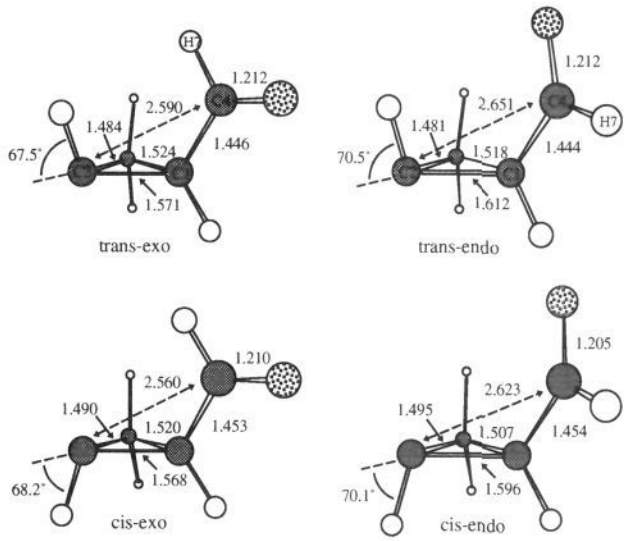



**Figure 1.** Calculated structures (6-31+G(d)) for *cis*- and *trans*-$\beta$-formylcyclopropyl anion (**4c** and **4t**). Bond lengths are in Å and angles are in deg.

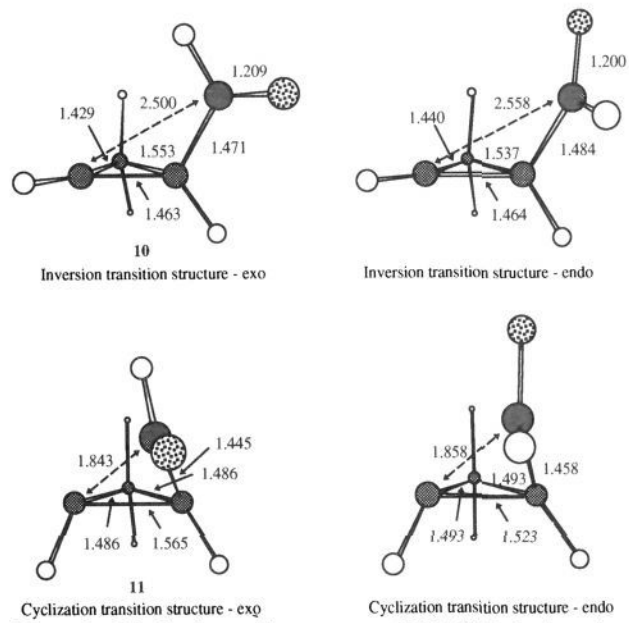



**Figure 2.** Calculated transition structures (6-31+G(d)) for inversion and cyclization of $\beta$-formylcyclopropyl anion (**10** and **11**, respectively). Bond lengths are in Å and angles are in deg.

**Calculations.** Ab initio molecular orbital computations were carried out using Gaussian 92[11] on a Cray X-MP, IBM RS/6000, or SGI Iris workstation. Geometries were optimized employing $C_1$ or $C_S$ symmetry and HF/6–31+G(d)[12] or MP2/6-31+G(d)[13] wave functions (Figures 1 and 2). Each structure was verified as a potential energy minimum or first-order saddle point by computing its Hessian matrix at the level of

(10) This compound has previously been reported and was prepared using an almost identical procedure. Weber, A.; Sabbioni, G.; Galli, R.; Stämpfli, U.; Neuenschwander, M. *Helv. Chim. Acta* **1988**, *71*, 2026.

**Table 1.** Calculated Energies (in hartrees) for Cyclopropanecarboxaldehyde (**7**), β-Formylcyclopropyl Anion (**4c** and **4t**) and Related Structures

| structure | HF[a] | MP2[a] | ZPE[b] | MP2[c] | MP2[d] | MP3[d] | QCISD(T)[d] |
|---|---|---|---|---|---|---|---|
| 7-endo | −229.793 936 | −230.487 785 | 54.72 | | | | |
| 7-exo | −229.794 176 | −230.487 248 | 54.68 | | | | |
| 4t-endo | −229.132 695 | −229.843 388 | 45.40 | | | | |
| 4t-exo | −229.140 193 | −229.851 494 | 45.49 | | | | |
| 4c-endo | −229.129 118 | −229.838 106 | 45.09 | | | | |
| 4c-exo | −229.139 433 | −229.847 116 | 45.35 | −229.849 591 | −229.977 441 | −229.993 428 | −230.042 581 |
| 8-endo | −229.116 292 | −229.841 584 | 45.92 | | | | |
| 8-exo | −229.124 833 | −229.849 610 | 45.85 | −229.851 753 | −229.975 733 | −229.987 242 | −230.035 807 |
| 9-endo | −229.731 659 | −230.435 328 | 54.92 | | | | |
| 9-exo | −229.729 515 | −230.431 709 | 54.62 | | | | |
| 10-endo | −229.092 311 | −229.807 978 | 43.72 | | | | |
| 10-exo | −229.107 942 | −229.824 126 | 44.23 | | | | |
| 11-endo | −229.108 317 | −229.832 833 | 45.07 | | | | |
| 11-exo | −229.118 398 | −229.840 857 | 45.23 | −229.841 087 | −229.968 490 | −229.980 654 | −230.031 349 |

[a] Energy for the HF/6-31+G(d) optimized geometry using the same basis set. [b] The HF/6-31+G(d) zero-point energies were scaled by 0.89. [c] MP2/6-31+G(d) optimized structures and energies. [d] Single point energies using the 6-311++G(d,p) basis set and MP2/6-31+G(d) optimized structures.

**Table 2.** Relative Energies for Isomeric Structures in kcal mol$^{-1}$ [a]

| structure | HF[b] | MP2[b] | MP2[c] | MP2[d] | MP3[d] | QCISD(T)[d] |
|---|---|---|---|---|---|---|
| 7-endo | 0.19 | 0 | | | | |
| 7-exo | 0 | −0.30 | | | | |
| 8-endo | 40.52 | 35.09 | | | | |
| 8-exo | 39.47 | 33.12 | | | | |
| 4t-endo | 4.62 | 5.00 | | | | |
| 4t-exo | 0 | 0 | | | | |
| 4c-endo | 6.55 | 8.01 | | | | |
| 4c-exo | 0.34 | 2.61 | 0 | 0 | 0 | 0 |
| 8-endo | 15.43 | 6.65 | | | | |
| 8-exo | 10.00 | 1.54 | −0.86 | 1.57 | 4.38 | 4.75 |
| 10-endo | 28.28 | 25.54 | | | | |
| 10-exo | 18.98 | 15.91 | | | | |
| 11-endo | 19.61 | 11.29 | | | | |
| 11-exo | 13.42 | 6.41 | 5.22 | 5.50 | 7.90 | 6.93 |

[a] All energies have been corrected for zero-point energy differences using scaled (0.89) Hartree–Fock frequencies. [b] HF/6-31+G(d) basis set and optimized geometries. [c] MP2/6-31+G(d) optimized structures and energies. [d] Single point energies using the 6-311++G(d,p) basis set and MP2/6-31+G(d) optimized structures.

**Table 3.** Calculated Acidities (MP2/6-31+G(d)//6-31+G(d) + ZPE) in kcal mol$^{-1}$ [a]

| acid | 7 | 7 | 9-exo | 9-endo | 7 | 7 | 9-exo | 9-endo |
|---|---|---|---|---|---|---|---|---|
| conjugate base | 4c | 4t | 8-exo | 8-endo | 8-exo | 8-endo | 4c | 4c |
| acidity ($\Delta H_{acid}$) | 392.7 | 390.0 | 356.5 | 363.6 | 391.6 | 396.7 | 357.6 | 359.5 |

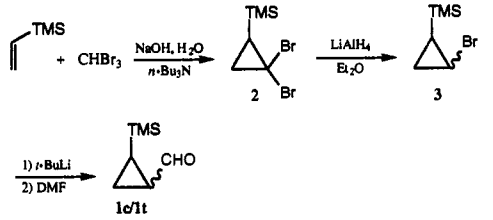
[a] The most stable conformation for any given structure was used.

theory which was used for the optimization. As required, all minima had positive force constants while transition structures had one imaginary frequency and one negative eigenvalue. Single point energy calculations were carried out with a more flexible basis set (6–311++G(d,p)) and at a higher level of theory in order to obtain more accurate results (Tables 1–3).

## Results and Discussion

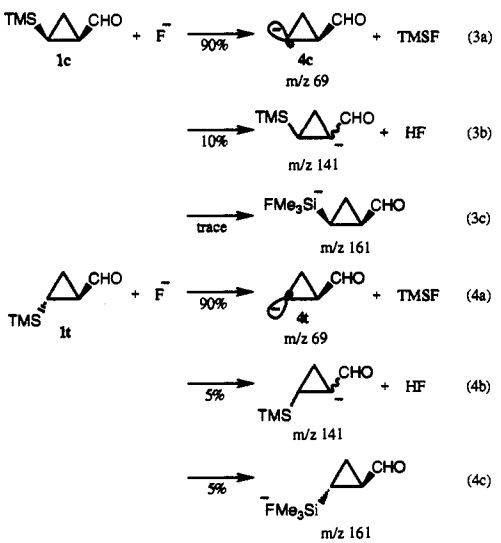
*cis*- and *trans*-2-(Trimethylsilyl)cyclopropanecarboxaldehyde (**1c** and **1t**) were synthesized in a three-step procedure illustrated in Scheme 1. Dibromocarbene, generated under phase-transfer conditions, adds to vinyltrimethylsilane to afford 1,1-dibromo-2-(trimethylsilyl)cyclopropane (**2**). Reduction of one of the

**Scheme 1**




bromines can be accomplished with tri-*n*-butyltin hydride, but lithium aluminum hydride was found to be more convenient. A ~3:1 cis to trans mixture of monobromides **3** results, and both isomers were separated by gas–liquid chromatography for characterization purposes. The mixture of geometric isomers was carried on to the desired aldehydes. Metal–halogen exchange with *tert*-butyllithium at −78 °C followed by a dimethylformamide quench gives a cis/trans mixture of 2-(trimethylsilyl)cyclopropanecarboxaldehyde in the same proportions as the starting bromide. Separation of the two epimers by preparative gas chromatography was unsuccessful using several different columns but can be accomplished via medium-pressure liquid chromatography using a 50:1 hexanes to ethyl acetate solution. Both aldehydes are somewhat air-sensitive and are best stored under an inert environment. If the proper precautions are taken, these compounds can be stored in a freezer for weeks at a time.

Fluoride ion generated by electron impact on nitrogen trifluoride reacts with **1c** and **1t** at room temperature in our variable temperature flowing afterglow device to afford two distinct *m/z* 69 (M-TMS) ions (eqs 3 and 4). These stereoisomeric β-sub-




(11) Gaussian 92, Revision C; Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A.

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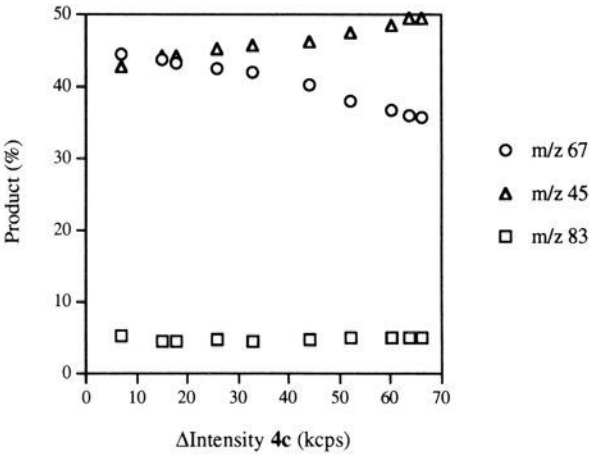



**Figure 3.** A typical branching ratio determination of the initial product distribution for the reaction of **4c** with nitrous oxide. Note, kcps stands for kilocounts per second.

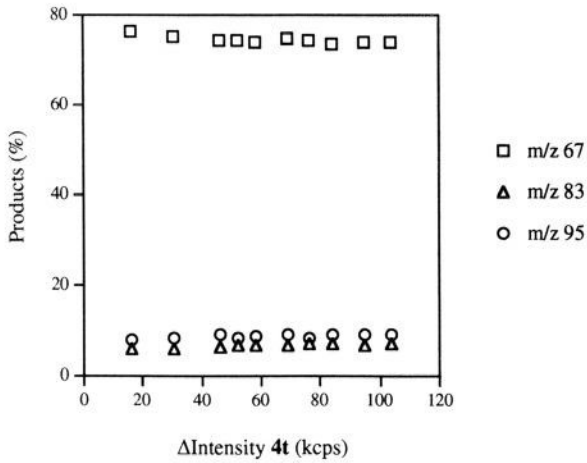
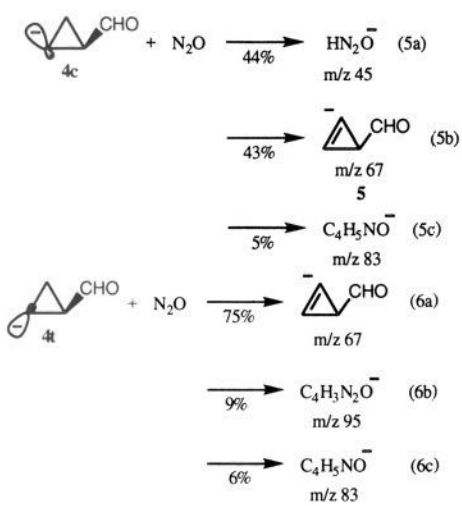



**Figure 4.** A typical branching ratio determination for the reaction of **4t** with nitrous oxide, where kcps stands for kilocounts per second.

stituted cyclopropyl anions (**4c** and **4t**) can be differentiated with several chemical probe reagents. For example, nitrous oxide reacts with the cis isomer (**4c**) to afford $HN_2O^-$ ($m/z$ 45) as a major product ion, whereas it is not formed from the trans species (**4t**) in significant amounts (Figures 3 and 4). Both reactions produce additional products (Table 4), and those which are formed in a relative abundance of at least 5% are illustrated in eqs 5 and 6.[14]




The proposed structures and molecular formulas are consistent with isotopic labeling studies carried out with $^{15}N$-labeled nitrous oxide ($^{15}NNO$)[15] and $d_1$-$\beta$-formylcyclopropyl anion produced from a ~4:1 cis:trans mixture of 2-(trimethylsilyl)cyclopropanecarboxaldehyde (**1**) in which the aldehydic hydrogen has been replaced by a deuterium atom.[16] In particular, the $m/z$ 45 ion increased in mass by 1 amu when $^{15}NNO$ was used enabling us to rule out the isobaric formate ($HCO_2^-$) ion. The $m/z$ 45, 67, 83, and 113 ions were also found to gain 1 mass unit when the $d_1$-anion was reacted with unlabeled nitrous oxide. These changes indicate that *it is the aldehydic hydrogen which is transferred to nitrous oxide to afford $HN_2O^-$* (Scheme 2). This clarifies why **4c** reduces $N_2O$ but **4t** does not. Initial addition of $N_2O$ to the $\beta$-formylcyclopropyl anion affords a cis adduct in which proton transfer can take place from the aldehydic site to the terminal nitrogen via a five-membered ring transition state. In the analogous trans species the two groups are too far apart, and the requisite proton transfer cannot occur.

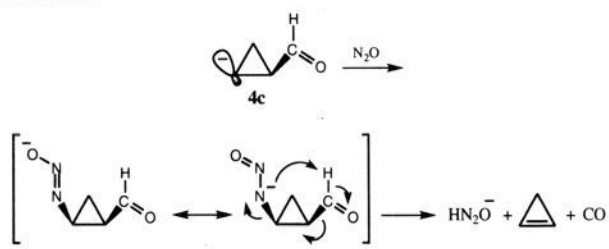
Another reagent which is useful for distinguishing between **4c** and **4t** is carbon disulfide (eqs 7 and 8). In both reactions four product ions are formed, but with the former the $HS^-$:$HCS_2^-$ ratio is approximately 2:1 (42:19), whereas it is 1:6 (8:47) with the latter species (Figures 5 and 6).[17] This result along with the $N_2O$ data clearly indicates that **4c** and **4t** do not interconvert at

**Table 4.** Initial Product Distributions for the Reactions of **4c** and **4t** with $N_2O$, $CS_2$, COS, and $O_2$[a]

| reactant | reagent | products |
|---|---|---|
| **4c** | $N_2O$ | $HO^-$ (17, 1%), $HCN_2^-$ (41, 2%), $HN_2O^-$ (45, 44%), **5** (67, 43%), $C_4H_5NO^-/C_3H_3N_2O^-$ (83, 5%), $C_4H_3N_2O^-$ (95, 4%), adduct (113, 1%) |
| | $CS_2$ | $HS^-$ (33, 42%), $HCS_2^-$ (77, 19%), SAT (101, 37%), adduct (145, 2%) |
| | COS | $HS^-$ (33, trace), $HC{\equiv}CCH{=}CHS^-$ (83, 5%), SAT (101, 88%), adduct (129, 7%) |
| | $O_2$ | $HO^-$ (17, 30%), $HC_2^-$ (25, 10%), $HO_2^-$ (33, 10%), $^-CH_2CHO$ (43, 15%), $HCO_2^-$ (45, 25%), $C_3H_3O^-$ (55, 10%) |
| **4t** | $N_2O$ | $HO^-$ (17, 2%), $HCN_2^-$ (41, 4%), $HN_2O^-$ (45, 2%), **5** (67, 75%), $C_4H_5NO^-/C_3H_3N_2O^-$ (83, 6%), $C_4H_3N_2O^-$ (95, 9%), adduct (113, 3%) |
| | $CS_2$ | $HS^-$ (33, 8%), $HCS_2^-$ (77, 47%), SAT (101, 44%), adduct (145, 1%) |
| | COS | $HS^-$ (33, 4%), $HC{\equiv}CCH{=}CHS^-$ (83, 7%), SAT (101, 79%), adduct (129, 10%) |
| | $O_2$ | $HO^-$ (17, 33%), $HC_2^-$ (25, 9%), $HO_2^-$ (33, 10%), $^-CH_2CHO$ (43, 17%), $HCO_2^-$ (45, 22%), $C_3H_3O^-$ (55, 9%) |

[a] The values in parentheses are mass-to-charge ratios and relative amounts, respectively. Product distributions for the reactions with COS and $O_2$ are approximate. [b] SAT, sulfur-atom transfer.

**Scheme 2**




(14) Another possible structure for the $m/z$ 67 ion (eqs 5b and 6a) is a vinyl anion in which the double bond is conjugated to the formyl group. This isomer is calculated to be less stable at the MP2/6-31+G(d)//6-31+G(d) level by 5.1 kcal mol$^{-1}$, so we favor the structure shown in the text (**5**).

(15) Nitrous oxide-2-$^{15}N$ ($^{15}N$, 99%) was obtained from Cambridge Isotope Laboratories.

(16) The deuterium-labeled compound was prepared simply by using $d_7$-DMF instead of the protio reagent.

(17) We have also looked at the reaction of a **4c**/**4t** mixture in which the aldehydic hydrogen has been replaced by a deuterium atom. Deuterium was not incorporated into $HS^-$ or $HCS_2^-$ but was found in the other two products.

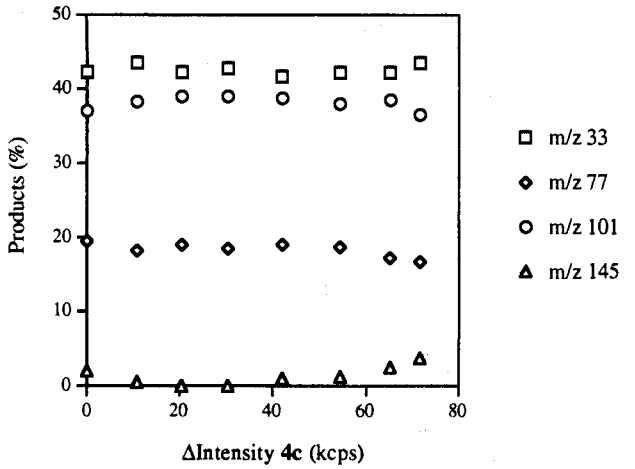



**Figure 5.** A typical branching ratio measurement for the reaction of **4c** with carbon disulfide, where kcps stands for kilocounts per second.

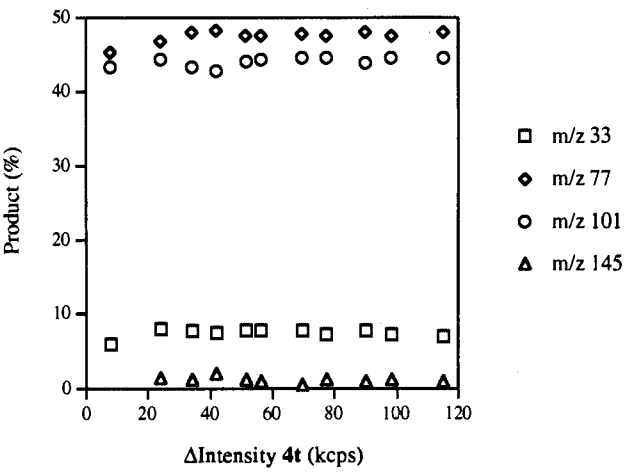
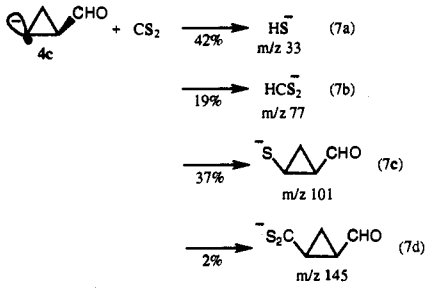
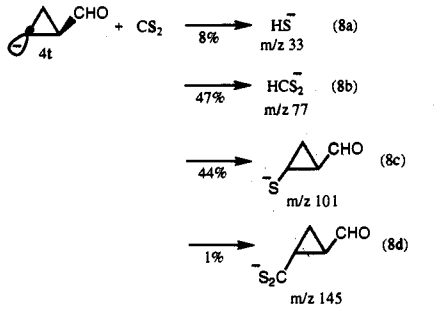


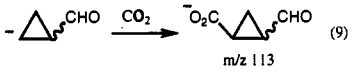

**Figure 6.** A typical branching ratio measurement for the reaction of **4t** with carbon disulfide, where kcps stands for kilocounts per second.

room temperature. Moreover, since the 1-formylallyl anion does not react with nitrous oxide and only gives an adduct and a small amount of sulfur-atom transfer with carbon disulfide it also is apparent that neither **4c** or **4t** undergoes a ring-opening isomerization at 25 °C.[9b]

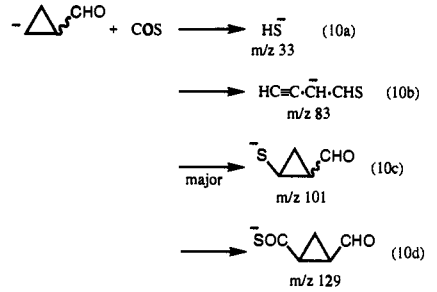


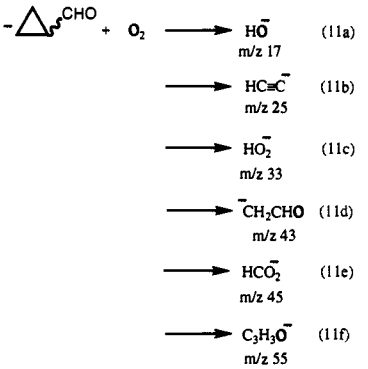




Additional reactions of **4c** and **4t** were examined with $CO_2$, COS, and $O_2$, but the product distributions are very similar for both species (Table 4). Carbon dioxide affords an adduct ion upon reaction with **4c** or **4t** (eq 9), carbonyl sulfide's behavior




is similar to that of carbon disulfide and leads to four product ions (eq 10),[18] while molecular oxygen reacts extremely inefficiently to produce a number of oxidation products (eq 11). Collision-induced dissociation of **4c** and **4t** was also briefly




investigated using argon as the collision gas.[19] Both ions fragment predominately to give $m/z$ 41 ($C_3H_5^-$, M − CO) along with smaller amounts of $m/z$ 51 ($CH_2{=}CH\text{-}C{\equiv}C^-$, M − $H_2O$) and $m/z$ 67 ($C_4H_3O^-$, M − $H_2$). Trace ions at $m/z$ 17 ($OH^-$), 39 ($C_3H_3^-$), and 43 ($C_2H_3O^-$) were also observed under some conditions. Dissociation of the $d_1$-anion led to a shift in the $m/z$ 41 and 43 ions to 42 and 44, respectively. The mass of the other fragments were unaffected. These results are in accord with the given structures and molecular formulas and were helpful in ruling out other possibilities, e.g., $HC{\equiv}CO^-$ (M − $C_2H_4$, $m/z$ 41) would be expected to have the same mass when the $d_1$-labeled substrate is used, and thus is an unlikely possibility.

The proton affinity of both β-formylcyclopropyl anions (**4c** and **4t**) or equivalently, the acidity of cyclopropanecarboxaldehyde at the β-position were measured by adding reference acids of known strength to each ion and looking for the occurrence or nonoccurrence of proton transfer. Fluorobenzene ($\Delta H_{acid}$ = 387.2 kcal mol$^{-1}$), methanol-OD ($\Delta H_{acid}$ = 383.5 kcal mol$^{-1}$), and stronger acids protonate **4c** and **4t**, whereas deuterium oxide ($\Delta H_{acid}$ = 392.0 kcal mol$^{-1}$) leads to only a trace of $OD^-$ and dimethylamine ($\Delta H_{acid}$ = 396.2 kcal mol$^{-1}$) undergoes no apparent

(18) A **4c**/**4t** mixture in which the aldehydic hydrogen was replaced by a deuterium atom was also allowed to react with COS. Due to the presence of an impurity and the minor amounts of $HS^-$ which are produced in this reaction, we were unable to determine whether this ion incorporates deuterium. The other three products all increase in mass by 1 amu; $m/z$ 83 → 84, 101 → 102, 129 → 130.

(19) These experiments were carried out with our recently retrofitted variable temperature flowing afterglow triple quadrupole apparatus.

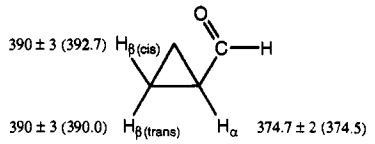
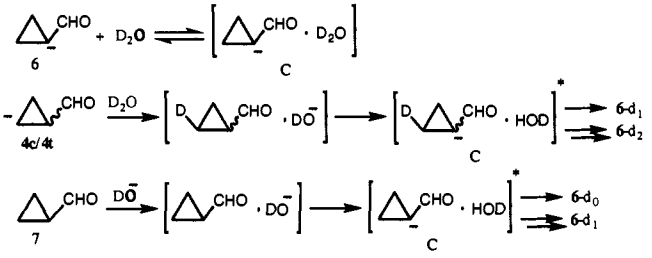


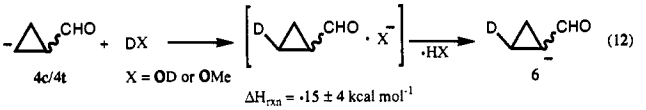

**Figure 7.** Experimental and calculated acidities (in kcal mol$^{-1}$) of the different sites in cyclopropanecarboxaldehyde (**7**). The latter values are in parentheses, and the results for the α-position come from ref 18.

**Scheme 3**



reaction.[20] This suggests that PA (**4c**) ≈ PA (**4t**) = 390 ± 3 kcal mol$^{-1}$ which is in good accord with a calculated value of 392.7 and 390.0 kcal mol$^{-1}$ for **4c** and **4t**, respectively, at the MP2/6-31+G(d)//6-31+G(d) level (Figure 7). The formyl group (X = CHO) acidifies the β-position relative to X = H by 22 ± 4 kcal mol$^{-1}$. If one uses computed values, the cis position is found to be enhanced by 20.1 kcal mol$^{-1}$, and the trans site is increased by 22.8 kcal mol$^{-1}$. This rather large substituent effect appears to be fairly typical[21] but is not well understood. Presumably, some combination of through bond and through space effects are responsible.

As one might anticipate, MeOD and $D_2O$ not only transfer a deuteron to **4c** and **4t** but they also induce an acid-catalyzed isomerization to the more stable α-formylcyclopropyl anion (**6**, eq 12). The latter reaction leads to the formation of a $d_1$-ion (**6**-$d_1$) and some $d_2$ species (**6**-$d_2$, ~4:1 $d_1/d_2$). The α-anion (**6**),




prepared simply by deprotonating cyclopropanecarboxaldehyde (**7**), does not undergo any hydrogen–deuterium exchange with deuterium oxide. It is well known, however, that $D_2O$ can induce H–D exchange at sites which are not the most acidic in a molecule and that the direction in which the exchange process is carried out can be important (Scheme 3).[22] In particular, ion–neutral complex **C** can be formed starting from **4c**/**4t** or **6**, but in the former case it will have more internal energy, the difference, PA(**6**)[9b] – PA(**4**), being 15 kcal mol$^{-1}$. The subsequent behavior of **C** can be different, and in this instance a second deuterium atom is incorporated into **6** when **4c**/**4t** is the starting ion. A qualitative potential energy surface for this process is illustrated in Figure 8 and indicates that the reaction of $DO^-$ with cyclopropanecarboxaldehyde should lead to **C** with approximately the same energy content as it has coming from **4c**/**4t**. The resulting α-formylcyclopropyl anion (**6**) would be expected to contain some deuterium, and this is exactly what is observed, i.e., the $d_0/d_1$ ratio is 3:1.

The structures and energies of the β-formylcyclopropyl anions (**4c** and **4t**) were examined via ab initio molecular orbital

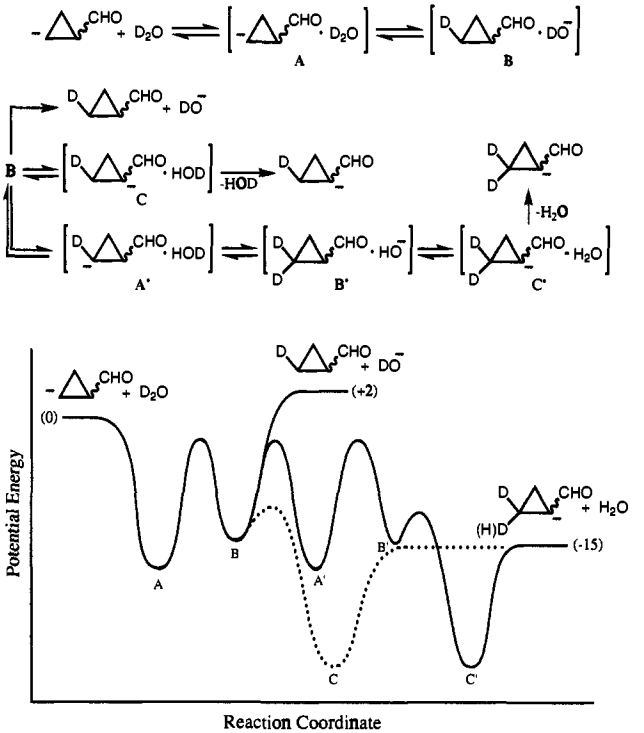



**Figure 8.** A qualitative potential energy surface for the reaction between β-formylcyclopropyl anion and deuterium oxide. Relative energies are given in kcal mol$^{-1}$ and are located in parentheses.

calculations. Optimizations were carried out at the Hartree–Fock (HF) level using the 6–31+G(d) basis set and electron correlation was accounted for by carrying out single point energy calculations using second-order Møller–Plesset perturbation theory (MP2/6-31+G(d)//6–31+G(d)).[12,13] Both the cis and trans ions are structurally similar and have a strong (5 kcal mol$^{-1}$) preference for the carbonyl oxygen atom to point away from the cyclopropane ring (exo) rather than toward it (endo, Figure 1). In contrast, there is virtually no energetic difference between the exo and endo conformers of cyclopropanecarboxaldehyde (**7**); both structures are oriented, however, so that the π bond of the carbonyl group overlaps with the Walsh orbitals of the cyclopropane.[9b] In the anions, the endo structures are disfavored presumably, because of electrostatic repulsion between the negative charge and the lone-pairs of electrons on the oxygen atom as well as dipolar destabilization. In order to minimize these influences the endo structures distort relative to the exo conformers so as to increase the distance between the charge bearing and aldehydic carbons (C2 and C4, respectively). In particular, the hydrogen attached to the carbanionic center bends 2–3° further out of the plane of the ring, the C1–C2 bond length increases 0.03–0.04 A°, both the C2–C1–C4 and C3–C1–C4 bond angles increase by a sum of 6°, and the carbonyl group twists further out of the H7–C1–C4 plane.

The *cis*- and *trans*-exo-β-formylcyclopropyl anions differ by only 2.6 kcal mol$^{-1}$ (MP2/6-31+G(d)//6-31+G(d)) after their zero-point energies have been accounted for. Since the distance between the charge bearing carbon and the carbonyl carbon is similar in both species (2.56 A° (cis) and 2.59 A° (trans)), and rather long, there does not appear to be a direct interaction between these two sites. This suggests that the field effect (charge-dipole stabilization) which favors the trans ion and polarization which favors the cis ion ($P_{CHO} > P_H$)[23] are similar in magnitude. There is a significant inversion barrier (15.9 kcal mol$^{-1}$ for **4t**) which is similar to that for cyclopropyl anion at the same level of theory (16.3 kcal mol$^{-1}$, MP2/6-31+G(d)//6-31+G(d)).[9b] This prevents the interconversion of **4c** and **4t** at room temperature and accounts for our ability to differentiate these two species.

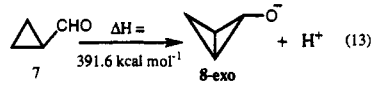
(20) All acidities, unless otherwise noted, come from ref 8. The deprotonation energy for MeOD comes from Barlow, S. E.; Dang, T. T.; Bierbaum, V. M. *J. Am. Chem. Soc.* **1990**, *112*, 6832.

(21) (a) Bartmess, J. E.; Burnham, R. D. *J. Org. Chem.* **1984**, *49*, 1382. (b) Chou, P. K., Ph.D. thesis, 1992. (c) Sachs, R. K. Ph.D. Thesis, 1993. (d) Dahlke, G. D.; Baschky, M. C., unpublished results.

(22) Squires, R. R.; Bierbaum, V. M.; Grabowski, J. J.; DePuy, C. H. *J. Am. Chem. Soc.* **1983**, *105*, 5185.

(23) Taft, R. W.; Topsom, R. D. *Prog. Phys. Org. Chem.* **1987**, *16*, 1.

The β-formylcyclopropyl anion is a homoenolate ion and as such there is the possibility of the cis structure cyclizing to either *exo*- or *endo*-2-bicyclobutoxide (**8**).[24,25] Since reactivity studies cannot necessarily differentiate between the two possibilities (both isomers could easily lead to the same products) we have examined **8** and its conjugate acid (2-bicyclobutanol, **9**) via high-level computations. The exo isomer of **8** is 5.11 kcal mol$^{-1}$ (MP2/6-31+G(d)//6-31+G(d)) more stable than the endo epimer. It also is more basic at carbon than oxygen (391.6 vs 356.5 kcal mol$^{-1}$, Table 3) and the former (eq 13) is in accord with our experimental measurement for **4c**. We therefore computed the



(13)

relative energy of **4c** and **8** at a variety of different levels (Table 2). Our best value, 4.75 kcal mol$^{-1}$ at the QCISD(T)/6-311++G(d,p)//MP2/6-31+G(d) level,[26] appears to be nearly converged and favors the open isomer (**4c**). This is in excellent accord with previous theoretical results on cyclopropoxide and β-formylethyl anion in which the cyclic structure was found to be favored by 4.43 kcal mol$^{-1}$ (QCISD(T)/6-311++G(d,p)//MP2/6-31+G(d))[27] given that there is a 8.9 kcal mol$^{-1}$ increase in strain energy in going from two cyclopropane rings (SE = 2 × 27.5 kcal mol$^{-1}$) to bicylobutane (SE = 63.9 kcal mol$^{-1}$),[28] i.e., 8.9 (ΔSE) + −4.43 (Δ*E* (acyclic model)) = 4.47 kcal mol$^{-1}$ as compared to our value of 4.75 kcal mol$^{-1}$. The cyclization barrier is found to be small at all levels of theory (5–13 kcal mol$^{-1}$, see Table 2) so equilibration between **4c** and **8** should be rapid and 2-bicyclobutoxide will only be present in trace quantities. It is worth adding that these results indicate that the C1 and C2 position in **4c** should rapidly interconvert.

(24) (a) Werstiuk, N. H. *Tetrahedron* **1983**, *39*, 205. (b) Nickon, A.; Lambert, J. L. *J. Am. Chem. Soc.* **1962**, *84*, 4604. (c) Nickon, A.; Lambert, J. L. *J. Am. Chem. Soc.* **1966**, *88*, 1905 and references therein.

(25) For previous work on homoenolates in the gas phase see: (a) Downard, K. M.; Hayes, R. N.; Bowie, J. H. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1815. (b) Waugh, R. J.; Hayes, R. N.; Eichinger, P. C. H.; Downard, K. M.; Bowie, J. H. *J. Am. Chem. Soc.* **1990**, *112*, 2537. (c) Peerboom, R.; Ingemann, S.; Nibbering, N. M. M. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 74. (d) Bartmess, J. E.; Caldwell, G.; Rozeboom, M. D. *J. Am. Chem. Soc.* **1983**, *105*, 340. (e) Noest, A. J.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1980**, *102*, 6427.

(26) Pople, J. A.; Head-Gordon, M.; Raghavachari, K. *J. Chem. Phys.* **1987**, *87*, 5968.

(27) Unpublished results.

(28) Wiberg, K. B. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 312.

## Conclusions

The fluorodesilylation of *cis*- and *trans*-2-(trimethylsilyl)-cyclopropanecarboxaldehye (**1c** and **1t**) affords the corresponding β-formylcyclopropyl anions (**4c** and **4t**) in a stereospecific manner. These ions do not interconvert or undergo ring-opening isomerization at 25 °C and can readily be distinguished with a number of chemical reagents. The formyl group imparts considerable stability on these anions relative to the parent ion, ΔΔPA = 22 kcal mol$^{-1}$, but they still are quite reactive species. Cyclization of these homoenolates to either the *endo*- or *exo*-2-bicyclobutoxide ion (**8**) is found to be thermochemically unfavorable by high-level ab initio calculations, which is in contrast to β-formylethyl anion, an acyclic analog. Most importantly, these results clearly demonstrate that stereochemistry can be successfully dealt with in the gas phase and that it will be possible to obtain mechanistic information and measure bond dissociation energies, acidities, and electron affinities with extraordinary specificity in future investigations.

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**Supplementary Material Available:** Energies and *xyz* coordinates for all of the structures reported in this work (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.