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The Gas-Phase Cannizzaro Disproportionation Reactions of Benzaldehyde and Pivaldehyde

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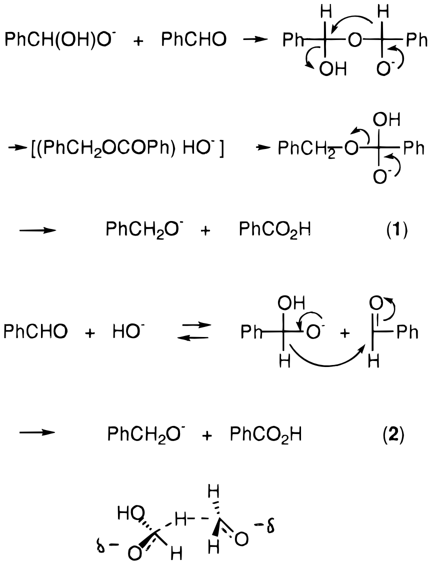
The Cannizzaro disproportionation reaction [$RCHO + HO^- \rightarrow RCH_2O^- + RCO_2H$ (R = *t*-Bu and Ph)] has been studied in the gas phase (i.e. in the absence of solvent) using ion cyclotron resonance (icr), flowing afterglow (FA), and conventional reverse sector mass spectrometers. In addition, the prototypical system HO^-/CH_2O has been studied using *ab initio* calculations at the MP3SDQ/6-311++G(d,p)//RHF/6-311++G(d,p) level of theory. Product ions RCH_2O^- are observed in the icr spectrometer following inefficient reactions, but are not formed from thermalized reactant ions in the FA instrument. The gas-phase Cannizzaro reaction has an effective internal constraint, even though the overall reaction is exothermic. In the reverse sector mass spectrometer, competitive processes form (i) the "Cannizzaro" ions $RCH(OH)O^-$, RCH_2O^-, and RCO_2^-, and (ii) $RCH(OH)OCH(R)O^-$, produced by nucleophilic addition of $RCH(OH)O^-$ to RCHO. The ion $RCH(OH)OCH(R)O^-$ is not an intermediate in the gas-phase Cannizzaro reaction since it does not decompose to form either RCH_2O^- or RCO_2^-. The experimental and theoretical data are consistent with the operation of an inefficient stepwise mechanism in which the first-formed species $RCH(OH)O^-$ transfers a hydride ion to RCHO.

Introduction

The Cannizzaro disproportionation reaction in its simplest form involves the reaction of HO^- with aromatic aldehydes, or aliphatic aldehydes with no α-hydrogen (like formaldehyde and pivaldehyde), to form RCH_2OH and RCO_2H as the major products.[1] The reaction is solvent dependent and requires heating in the presence of base, usually using concentrated aqueous sodium hydroxide. In the case of benzaldehyde, the rate is concentration dependent, i.e., $[PhCHO]^2[OH^-]$.[2] The first mechanistic proposal for this reaction is shown in sequence **1** (Scheme 1),[3] i.e., addition of HO^- to benzaldehyde to yield a tetrahedral adduct which then undergoes nucleophilic addition with a second molecule of benzaldehyde. Hydroxyl transfer following hydride migration within this intermediate initiates disproportionation to form benzyl alcohol and benzoic acid. The isolation of benzyl benzoate as a minor product added credence to this proposal.[4] This mechanistic proposal is both of historical significance and of special relevance to the present investigation.

Scheme 1



(A)

It is now considered that the mechanism of the Cannizzaro reaction is that shown in sequence **2** of Scheme 1.[5] The reaction must be inefficient because of the unfavorable orientiation required in order to effect the intermolecular hydride transfer. Some evidence in support of this mechanistic proposal follows. A Hammett plot for the reactions of HO^- with substituted benzaldehydes [in $MeOH/H_2O$ (1:1)] gives a straight line with a high ρ value (+3.76) indicating that (i) the reaction rate is enhanced for electron-withdrawing substituents and (ii) the rate-determining step does not change as the electronic effect of the substituent is altered.[6] The hydride transfer is involved in the rate-determining step since a primary kinetic isotope effect ($k_H/k_D = 1.8$) has been measured for the comparative reactions of aqueous sodium hydroxide with PhCHO and PhCDO.[7] *Ab initio* calculations (RMP4/6-31+G level) for the prototypical

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[1] Cannizzaro, S. *Ann.* **1853**, 88, 129.

[2] Molt, E. L. *Recl. Trav. Chim. Pays Bas* **1937**, *56*, 233. Eitel, A.; Lock, G. *Monatsch. Chem.* **1939**, *72*, 392. Tommila, E. *Ann. Acad. Sci. Fenn. Ser. A* **1942**, *59*, 3; *Chem. Abstr.* **1944**, *38*, 6175.

[3] Fredenhager, H.; Bonhoeffer K. F. *Z. Phys. Chem.* **1938**, *A181*, 379. Geissman, T. A. *Org. React.* **1944**, *2*, 94.

[4] Lachman, A. *J. Am. Chem. Soc.* **1923**, *45*, 2356.

[5] Swain, C. G.; Powell, A. L.; Sheppard, W. A.; Morgan, C. R. *J. Am. Chem. Soc.* **1979**, *101*, 3576. Swain, C. G.; Powell, A. L.; Lynch, T. J.; Alpha, S. R.;Dunlap, R. P. *J. Am. Chem. Soc.* **1979**, *101*, 3584.

[6] Jaffe, H. H. *Chem. Rev.* **1953**, *53*, 209.

[7] Wiberg, K. B. *J. Am. Chem. Soc.* **1954**, *76*, 5371. Luther, D.; Koch, H. *Chem. Ber.* **1966**, *99*, 2227.

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HO^-/CH_2O system indicate that in the absence of solvent the hydride transfer is not linear [the CHC angle is 162° in the transition state (see **A**, Scheme 1)].[8]

This is an interesting reaction to study in the gas phase (i.e., in the absence of solvent), since there are several matters to resolve; viz. (i) does the Cannizzaro reaction occur in the gas phase for benzaldehyde and pivaldehyde and (ii) if it does, is the mechanism one of those shown in Scheme 1? This investigation probes the reactions of HO^- with benzaldehyde and pivaldehyde in the gas phase and uses *ab initio* calculations with the prototypical system HO^-/CH_2O to assist with the interpretation of the experimental results.[9]

Results and Discussion

We will later provide experimental evidence that excludes sequence **1** (Scheme 1) from being the mechanism of the Cannizzaro reaction. Thus, we describe first *ab initio* calculations concerning the mechanism summarized in sequence **2**.

(A) *Ab initio* calculations for the Cannizzaro Reaction and a Competing Process for the Model System HO^-/CH_2O. A reaction coordinate diagram depicting Cannizzaro mechanism **2** (Scheme 1) for the model system HO^-/CH_2O is shown in Figure 1. Also included in Figure 1 are data for the reaction between $HOCH_2O^-$ and CH_2O to yield $HOCH_2OCH_2O^-$. We consider this system prototypical for the pivaldehyde and benzaldehyde systems studied experimentally in the present investigation (cf. ref 9). *Ab initio* calculations were carried at the MP3SDQ/6-311++G(d,p)//RHF/6-311++G(d,p) level of theory.

The initial reaction between HO^- and CH_2O has been studied in greater depth using a potential energy map constructed from 200 individual points computed at the QCISD/6-311++G(d,p)//HF/6-311++G(d,p) level of theory. The varied coordinates of the map were the position of the hydroxide oxygen relative to the CO bond of formaldehyde. All other coordinates were fully optimized without constraints. The reaction between HO^- and CH_2O proceeds directly to the tetrahedral species $HOCH_2O^-$ which lies 35.3 kcal mol^{-1} below reactants. The potential surface shows that no association complex (or cluster) corresponding to $[HO^-(CH_2O)]$ is involved in this reaction: indeed, there is no discrete species corresponding to $[HO^-(CH_2O)]$ on the surface. In contrast, the ion $HOCH_2O^-$ is a discrete species lying in a deep potential well.

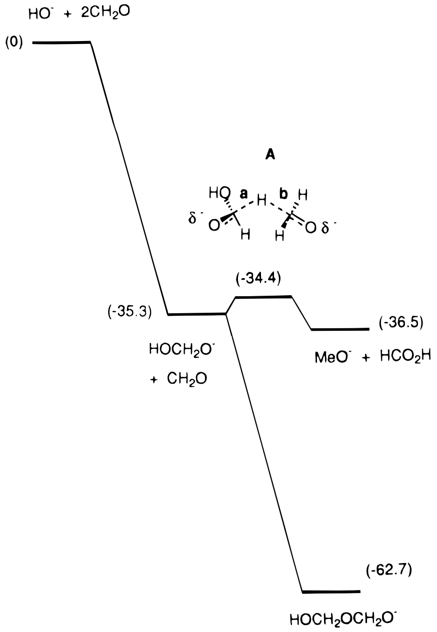

Figure 1. Energy [kcal mol^{-1}] profile of the Cannizzaro reaction for the HO^-/CH_2O system together with the formation of $HOCH_2OCH_2O^-$ (from $HOCH_2O^-$ plus CH_2O). (i) Calculations carried out using Gaussian 92[10] at the MP3SDTQ/6-311++ G(d,p)//RHF/6-311++G(d,p) level of theory. (ii) Full geometries of $HOCH_2O^-$ and **A** are are available as Supporting Information. (iii) The *ab initio* computed exothermicity of the overall process (−36.5 kcal mol^{-1}) should be compared with that of −36.4 kcal mol^{-1}, calculated using experimental figures (ΔH°_f values of neutrals and radicals;[11] electron affinities, HO[12] and MeO[13]). (iv) The overall reaction $2CH_2O + HO^- \rightarrow CH_3OH + HCO_2^-$ (cf. section on chemical ionization mass spectrometry) is exothermic by 77.0 kcal mol^{-1} (calculations at level of theory indicated above). (v) We have investigated a number of conformations of $HOCH_2OCH_2O^-$. The lowest energy conformer is that of the cyclic structure formed by H bonding between the two terminal oxygens (−62.7 kcal mol^{-1}). A linear conformer with all the bonds staggered is less stable by 19.8 kcal mol^{-1}.

When energized $HOCH_2O^-$ approaches formaldehyde it may undergo the two competitive reactions shown in Figure 1. The first reaction involves the nucleophilic attack of the alkoxide center of $HOCH_2O^-$ at the electrophilic carbon of formaldehyde. This reaction proceeds without barrier and via a deep channel to form $HOCH_2OCH_2O^-$. This product is highly energized [−62.7 kcal mol^{-1} (see Figure 1)], so the reaction is reversible unless $HOCH_2OCH_2O^-$ is thermalized. The second reaction between $HOCH_2O^-$ and CH_2O is the Cannizzaro process: this process is essentially irreversible.[14] The hydride transfer of the Cannizzaro process is not linear: this is shown in transition state **A** (Figure 1), in which the relevant geometric features are a = 1.329 Å, b =

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[8] Rajyaguru, I. H.; Rzepa, H. S. *J. Chem. Soc., Chem. Commun.* **1987**, 998.

[9] (i) The reactions between HO^- and CH_2O in the gas phase have a complication which does not pertain for the analogous benzaldehyde and pivaldehyde systems. Although the Cannizzaro process may, in principle, occur to yield MeO^-, this ion is also formed by a competitive process from $[H^-(H_2O)]$ as follows: (i) $HO^- + CH_2O \rightarrow [(H_2O)^-CHO] \rightarrow [H^-(H_2O)] + CO$ and (ii) $[H^-(H_2O)] + CH_2O \rightarrow MeO^- + H_2O$. Miller, T. M.; Viggiano, A. A.; Miller, A. E. S.; Morris, R. A.; Henchman, M.; Paulson, J. F.; VanDoren, J. M. *J. Chem. Phys.* **1994**, *100*, 5706 and references cited therein. (ii) The Cannizzaro reaction of formaldehyde does occur in the gas phase as evidenced by the reaction between $H^{18}O^-$ with $CH_2{}^{16}O$ in the chemical ionization source of the VG ZAB 2HF mass spectrometer to form the adduct ion of empirical formula $CH_3{}^{16}O^{18}O^-$, together with product ions $CH_3{}^{16}O^-$ and $HC^{18}O^{16}O^-$ (these results are similar to data shown in Tables 1 and 2 for the analogous reactions with benzaldehyde and pivaldehyde).

[10] Frisch, M. L.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. J.; 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. Gaussian 92, Revision G3, Gaussian Inc., Pittsburg, PA, 1992.

[11] Primary data from (i) Bartmess, J. E. *The 1987 Gas Phase Acidity Scale*, University of Tennessee, **1987**; and also (ii) Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. Gas Phase Ion and Neutral Thermochemistry. *J. Phys. Chem. Ref. Data* **1988**, *17*, Suppl. 1. The computer-based version was used.

[12] Schultz, P. A.; Mead, R. D.; Jones, P. L.; Lineberger, W. C. *J. Chem. Phys.* **1982**, *77*, 1153.

[13] Engelking, P. C.; Ellison, G. B.; Lineberger, W. C. *J. Chem. Phys.* **1978**, *69*, 1826.

[14] The reaction is essentially irreversible because (i) the reverse reaction must have a small Arrhenius factor because of the unfavorable orientation required for the transfer of a hydride ion from MeO^- to HCO_2H and (ii) if separated MeO^- and HCO_2H are able to approach, the more likely reaction would be $MeO^- + HCO_2H \rightarrow MeOH$ and HCO_2^- [$\Delta H = -46$ kcal mol^{-1} (cf. also footnote 22)].

1.371 Å and angle C−H−C = 151.0°.[15] There is an impediment to the Cannizzaro process. Even though the activation barrier is low [0.9 kcal mol^{-1} (Figure 1)], the reaction channel is very narrow. The unfavorable orientation of $HOCH_2O^-$ with CH_2O required to allow passage over saddle point **A** makes the probability of the Cannizzaro reaction low (relative to that of the efficient reaction forming $HOCH_2OCH_2O^-$), leading to a small Arrhenius factor.[16]

(B) The Experimental Evidence Based on (i) Ion Cyclotron Resonance and (ii) Flowing Afterglow Experiments. We first investigated the reaction of HO^- with pivaldehyde and benzaldehyde in our Dynaspec ICR 9 spectrometer. The reactant ion HO^- was formed by electron impact on water at 7.1 eV and a pressure of 1×10^{-5} Torr. The cell voltages were adjusted so the transit time of HO^- in the cell was 1×10^{-3} s, the neutral aldehyde was then added, and the product anions were monitored within the total pressure range $(2-4) \times 10^{-5}$ Torr. The alkoxide ion RCH_2O^- was formed in each case (i.e., t-$BuCH_2O^-$ and $PhCH_2O^-$ from pivaldehyde and benzaldehyde, respectively): neither the adduct $RCH(OH)O^-$ nor the carboxylate anion RCO_2^- were detected [cf. sequence **2** (Scheme 1)].

The HO^-/pivaldehyde system is typical. On admission of pivaldehyde to initially give a total cell pressure of 2×10^{-5} Torr, deprotonation was effected to form m/z 85[17] as the sole anionic product. Increasing the amount of pivaldehyde to a total pressure of 3×10^{-5} Torr resulted in the formation of t-$BuCH_2O^-$ (m/z 87), and at a total pressure of 4×10^{-5} Torr, the abundance of the Cannizzaro product was three times that of m/z 85. Cyclotron ejection experiments show strong coupling of m/z 85 to m/z 17 (HO^- is the direct precursor of the deprotonated species), whereas m/z 87 is only weakly coupled to m/z 17 (in line with formation of m/z 87 via a stepwise process from HO^-). Finally, the reaction between HO^- and t-BuCDO yielded t-$BuCD_2O^-$ (m/z 89), as required by both mechanisms shown in Scheme 1.

A qualitative indication of the rate of the reaction forming t-$BuCH_2O^-$ is provided by the following experiment. The experimental conditions are set to give the highest yield of t-$BuCH_2O^-$ (total cell pressure, 4×10^{-5} Torr—see above), and then acetone (ca. 1×10^{-7} Torr) is added to the cell. Deprotonation of acetone instantly yields m/z 57 $(CH_2COMe)^-$ [the reaction between HO^- and acetone proceeds for every collision between reactants[18]], and the Cannizzaro product is not observed. Thus the Cannizzaro reaction is of low efficiency under the conditions of the icr experiment.

The above results are in accord with the *ab initio* data (Figure 1) depicting Cannizzaro mechanism **2**. The reaction of HO^- with RCHO gives an energized adduct which then reacts with another molecule of RCHO to form RCH_2O^- anion plus RCO_2H in an exothermic reaction. The RCH_2O^- ion is the only detectable ionic product of this Cannizzaro reaction under the conditions of the icr experiment. Energized species $RCH(OH)OCH(R)O^-$ are not detected in icr experiments.

The Cannizzaro reaction observed under icr conditions is very inefficient, even though the process, overall, is significantly exothermic. Experimentally, there is an impediment for the hydride transfer process, in accord with the computational data for the prototypical system described above. Thus, under the conditions of the icr experiment the $RCH(OH)O^-$ ions are formed with excess energy and either revert to reactants or effect the Cannizzaro reaction. Any energized $RCH(OH)OCH(R)O^-$ reverts to reactants.

If we could carry out reactions of HO^- with benzaldehyde and pivaldehyde where both reactant and product ions can be efficiently thermalized, and if the scenario shown in Figure 1 is correct, $RCH(OH)O^-$ [and perhaps $RCH(OH)OCH(R)O^-$] ions might be observed directly, but the Cannizzaro process should be inoperative because of the impediment to hydride transfer. In order to test this hypothesis, we have carried out the reactions of HO^- with benzaldehyde and pivaldehyde in a flowing afterglow instrument, where reactant (and product) anions are thermalized by collisions with both the helium carrier gas and the other neutrals that are present in the flow tube. The reaction between HO^- and benzaldehyde yields deprotonated benzaldehyde and a species m/z 123 ($PhCHO + HO^-$), with the latter species reacting with a second molecule of benzaldehyde to yield m/z 229 ($2PhCHO + HO^-$).[20] No $PhCH_2O^-$ ion is observed. Exactly the same scenario pertains for pivaldehyde (cf. also ref 19). These results are reproducible: the reactions have been repeated on several occasions.

The rate of quenching of the HO^- signal for the benzaldehyde reaction is 1.0×10^{-9} cm^3 molecule^{-1} s^{-1}. The two primary product ions are $(PhCHO - H)^-$ and $(PhCHO + HO^-)$. The branching ratio for the formation of $(PhCHO + HO^-)$ is 0.1. Thus the rate for the formation of $(PhCHO + HO^-)$ is 1.0×10^{-10} cm^3 molecule^{-1} s^{-1}, which corresponds to an efficiency of 0.025 [the theoretical ADO (collision) rate for this system is 4.0×10^{-9} cm^3 molecule^{-1} s^{-1} [21]]. Thus only one in forty collisions between HO^- and PhCHO leads to a detectable $(PhCHO + HO^-)$ species: the adduct is presumably stabilized in a three-body reaction with helium.

The data to date suggest that there is an impediment to Cannizzaro hydride transfer in the gas phase for both the benzaldehyde and pivaldehyde systems. The further observation that $(2RCHO + HO^-)$ ions[21] are observed in the FA but not in the icr experiment confirms that such ions can only be detected under conditions where collisional deactivation removes the excess energy of formation of the product anion.

Unfortunately, these FA experiments do not allow us to determine the structures of the key $(RCHO + HO^-)$

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(15) The bond angle of 151.0° and the energy (relative to reactants) of −34.4 kcal mol^{-1} for **A** are different from those calculated earlier [viz. 162° and −20.2 kcal mol^{-1} (at RMP4/6-31+G level)].[8]

(16) A similar scenario has been described for the reaction $NH_3 + CH_3OCH_2^+ \rightarrow CH_3NH_3^+ + CH_2O$. Okada, S.; Abe, Y.; Tanaguchi, S.; Yamabe, S. *J. Am.Chem. Soc.* **1987**, *109*, 295.

(17) Noest, A. J.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1980**, *102*, 6427. Peerboom, R.; Ingermann, S.; Nibbering, N. M. M. *Recl. Trav. Chim. Pays Bas* **1985**, *104*, 74.

(18) Bowie, J. H.; Hayes, R. N.; Sheldon, J. C.; DePuy, C. H. *Aust. J. Chem.* **1986**, *39*, 1951.

(19) It has already been mentioned that the adduct t-BuCH(OH)-O^- is formed in a three-body reaction [HO^-/He/t-BuCHO] in the FA and that this process is more efficient than deprotonation of pivaldehyde to form the homoenolate anion. DePuy C. H. Unpublished observations, cited in DePuy, C. H.; Grabowski, J. J.; Bierbaum, V. M.; Ingemann, S.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1985**, *107*, 1093.

(20) The $(2PhCHO + HO^-)$ ion is a secondary product, since its abundance extrapolates to zero at zero flow rate.

(21) Su,T.; Bowers, M. T. *Int.J. Mass Spectrom. Ion Phys.* **1973**, *12*, 347.

(22) Raftery, M. J.; Bowie, J. H.; Sheldon, J. C. *J. Chem. Soc., Perkin Trans. 2* **1988**, 563.

(23) Eichinger, P. C. H.; Bowie, J. H.; Blumenthal, T. *J. Org. Chem.* **1986**, *51*, 5078.

and ($2RCHO + HO^-$) species. From the data shown in Figure 1, we would expect the ions to correspond to the tetrahedral species $RCH(OH)O^-$ and $RCH(OH)OCH(R)O^-$, but the FA data do not differentiate between tetrahedral species and association complexes (in which the components are held together by hydrogen bonding or other forces). If we could form these ions in the chemical ionization source of a conventional mass spectrometer, we could identify their structures from a study of their fragmentation behavior. In addition, some of the $RCH(OH)O^-$ ions formed in such a high-pressure source should have sufficient energy to react with RCHO and initiate the Cannizzaro reaction (as was observed in the icr experiments). The structures of the Cannizzaro product anions could be confirmed from a comparison of their fragmentation behavior with those of authentic anions formed by independent syntheses. In order to probe these possibilities, we now describe the ionic products for the respective reactions of HO^- with benzaldehyde and pivaldehyde in the chemical ionization source of a VG ZAB 2HF mass spectrometer.

(C) The Evidence Based on Chemical Ionization Mass Spectrometry. The reactions of HO^- with pivaldehyde and benzaldehyde are similar: we describe the benzaldehyde system in detail.

(i) The Reaction between HO^- and Benzaldehyde. The reaction between HO^- and PhCHO, at an estimated pressure of 10^{-1} Torr in the chemical ionization source of the VG ZAB 2HF instrument, results in a number of pronounced peaks which we attribute to the Cannizzaro reaction. The resultant conventional negative-ion chemical ionization (NICI) spectrum is recorded in Table 1.

We propose that the product ions listed in Table 1 for the HO^-/PhCHO system [with the exception of *m/z* 105 $(PhCHO - H)^-$] are formed by either the Cannizzaro reaction or a related process. The peaks at *m/z* 107 and 121 are produced by the Cannizzaro product ions $PhCH_2O^-$ and $PhCO_2^-$, respectively.[24] These ions were identified by comparison of their collision-induced mass spectra (CID MS/MS) with those of authentic ions formed respectively by deprotonation of benzyl alcohol and benzoic acid. These spectra are recorded in Table 2. The following labeling data (see Table 2) are consistent with the formation of *m/z* 107 and 121 by a Cannizzaro process (Scheme 1), i.e., the reactions between (i) HO^- and PhCDO give *m/z* 109 ($PhCD_2O^-$) and 121 ($PhCO_2^-$) and (ii) $H^{18}O^-$ and PhCHO give *m/z* 107 ($PhCH_2O^-$) and 123 ($PhC^{16}O^{18}O^-$).[25]

The pronounced peak at *m/z* 123 is the result of addition of HO^- to benzaldehyde and could, in principle, correspond either to the cluster ion [$(PhCHO)HO^-$] and/or the tetrahedral adduct [$PhCH(OH)(O^-)$]. If the cluster ion is the initial product of this reaction, its collision-induced spectrum would show only loss of water, and that loss of water would exclusively involve the oxygen from the initial HO^- species. The spectrum of *m/z* 123 is

Table 1. Negative Ion Mass Spectra of Cannizzaro Systems[a]

system	$(RCHO - H)^-$	$(RCDO - H)^-$	RCH_2O^-	RCD_2O^-	RCO_2^-	RC^{16}-$O^{18}O^-$	RCH-$(OH)O^-$	RCD-$(OH)O^-$	$RCH(^{18}OH)O^-$	RCO_2^-CHR	RCO_2^-CDR	$RC(^{18}O)$-O^-CHR	RCH(OH)-$OCH(O^-)R$	RCD(OH)-$OCD(O^-)R$	$RCH(^{18}OH)$-$OCH(O^-)R$
$PhCHO/HO^-$	10		15		15		30			100			8		
$PhCDO/HO^-$															
$PhCHO/H^{18}O^-$															
t-$BuCHO/HO^-$	25		40^b		52		62			100			2		
t-$BuCDO/HO^-$		35		15	100			58			20			2	
t-$BuCHO/H^{18}O^-$	30		22			35			65			100			3
CH_2O/HO^-			100		78		10						10		

[a] The spectra are very dependent on source pressure. Small variations in pressure give significant differences in the relative abundances of peaks. [b] There is also a peak at *m/z* 105 (8%) in this spectrum corresponding to [*t*-$BuCH_2O^-(H_2O)$]. The analogous peak from *t*-$BuCHO/H^{18}O^-$ is [*t*-$BuCH_2O^-(H_2{}^{18}O)$] (*m/z* 107) confirmed by CID MS/MS data, viz. 87 ($H_2{}^{18}O$) 100, 19 ($H^{18}O^-$) 8.

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[24] The ΔH values for the reactions (i) $HO^- + 2PhCHO \rightarrow PhCH_2O^- + PhCO_2H$ and (ii) $HO^- + 2PhCHO \rightarrow PhCH_2OH + PhCO_2^-$ are −38 and −86 kcal mol^{-1} respectively (primary data from ref 11).

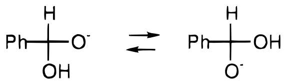
[25] (i) The possibility that some of *m/z* 121 comes from *m/z* 123 by loss of H_2 can be excluded, since a B^2/E-linked scan of source-formed *m/z* 121 shows no formation of this ion from *m/z* 123. (ii) The alternative scenario that *m/z* 121 comes, even partially, from a benzoic acid impurity in the benzaldehyde can be excluded since $H^{18}O^-$ and PhCHO gives $PhC^{16}O^{18}O^-$: no $PhCO_2^-$ (*m/z* 121) is observed. (iii) Product peaks arising from the reaction between $H^{18}O^-$ and PhCHO are monitored within 30 s of admission of $H_2{}^{18}O$ into the ion source. This is necessary to minimize the formation of products arising from the reaction of $H^{18}O^-$ with $PhCH^{18}O$ (see Table 2 for full details).

Table 2. Collisional Activation MS/MS Data for Product Ions from $PhCHO/HO^-$ and Labeled Systems

system	mass	spectrum [*m/z* (loss) relative abundance]
$PhCHO/HO^-$	107	106 ($H^\bullet$) 81, 105 (H_2) 52, 77 (CH_2O) 100, 29 (C_6H_6) 1
$PhCH_2O^-$ 22	107	106 ($H^\bullet$) 71, 105 (H_2) 44, 77 (CH_2O) 100, 29 (C_6H_6) 2
$PhCDO/HO^-$	109	108 ($H^\bullet$) 50, 107 ($H_2,D^\bullet$) 7, 106 (HD) 9, 78 (CHDO) 22, 77 (CD_2O) 100
$PhCD_2O^-$ 22	109	108 ($H^\bullet$) 55, 107 ($H_2,D^\bullet$) 6, 106 (HD) 8, 78 (CHDO) 26, 77 (CD_2O) 100
$PhCHO/HO^-$	121	120 ($H^\bullet$) 85, 77 (CO_2) 100
$PhCO_2^-$	121	120 ($H^\bullet$) 80, 77 (CO_2) 100
$PhCHO/H^{18}O^-$	123[a]	122 ($H^\bullet$) 78, 77 ($C^{16}O^{18}O$) 100
$PhCHO/HO^-$	123	122 ($H^\bullet$) 100, 121 (H_2) 88, 105 (H_2O) 98, 77 (HCO_2H) 5
$PhCDO/HO^-$	124	123 ($H^\bullet$) 100, 121 (HD) 48, 106 (H_2O) 88, 105 (HOD) 92, 77 (DCO_2H) 8
$PhCHO/H^{18}O^-$	125	124 ($H^\bullet$) 100, 123 (H_2) 78, 107 (H_2O) 88, 105 ($H_2{}^{18}O$) 77, 77 ($HCO^{18}OH$) 7
$PhCHO/HO^-$	183	182 ($H^\bullet$) 100, 181 (H_2) 30, 155 (CO) 4, 153 (CH_2O) 6, 105 (C_6H_6) 97, 77 (C_7H_6O) 18
$Ph_2CHO^{-(23)}$	183	182 ($H^\bullet$) 100, 181 (H_2) 28, 155 (CO) 2, 153 (CH_2O) 16, 105 (C_6H_6) 80, 77 (C_7H_6O) 27
$PhCHO/HO^-$	211	210 ($H^\bullet$) 82, 183 (CO) 100, 165 (CO_2) 1, 153 ($C_2H_2O_2$) 1, 133 (C_6H_6) 15, 105 (PhCHO) 44, 77 ($C_6H_5^-$) 2
$PhCO_2^-CHPh$	211	210 ($H^\bullet$) 85, 183 (CO) 100, 165 (CO_2) 1, 153 ($C_2H_2O_2$) 0.5, 133 (C_6H_6) 12, 105 (PhCHO) 42, 77 ($C_6H_5^-$) 2
$PhCDO/HO^-$	212	211 ($H^\bullet$) 68, 184 (CO) 100, 134 (C_6H_6) 15, 133 (C_6H_5D) 18, 106 (PhCHO) 30, 105 (PhCDO) 35, 78 ($C_6H_5D^-$) 2, 77 ($C_6H_5^-$) 7
$PhCHO/H^{18}O$	213[a]	212 ($H^\bullet$) 95, 185 (CO) 79, 183 ($C^{18}O$) 100, 135 (PhH) 28, 107 (PhCHO) 56, 105 ($PhCH^{18}O$) 48, 77 ($C_6H_5^-$) 12
	215[a]	214 ($H^\bullet$) 80, 185 ($C^{18}O$) 100, 137 (PhH) 14, 107 ($PhCH^{18}O$) 53, 77 ($C_6H_5^-$) 6
$PhCHO/HO^-$	229	228/227[b] ($H^\bullet,H_2$) 45, 211 (H_2O) 100, 123 (PhCHO) 5, 105[$PhCH(OH)_2$]2
$PhCHO/H^{18}O^-$	231, 233, 235[a,c]	

[a] The situation with the ^{18}O labeling experiment is complex because of ^{18}O label incorporation into benzaldehyde [i.e., the initially formed $PhCH(^{18}OH)O^-$ equilibrates to $PhCH(OH)^{18}O^-$ and this mixture can revert to PhCHO and $PhCH^{18}O$ as well as reacting further via the competing Cannizzaro and nucleophilic addition processes]. The incorporation of label into benzaldehyde is facile as shown by the following experiments. When the spectrum of the $PhCHO/H^{18}O^-$ system is measured within thirty seconds of admission of the mixture to the source, the peaks observed for the nucleophilic addition reactions appear predominantly at *m/z* 125, 213, and 231 (each ion contains one ^{18}O atom), with smaller accompanying peaks (<25%) at *m/z* 127, 215, and 233 (each ion contains two ^{18}O atoms). Within 10 min of the introduction of $H_2{}^{18}O$, an equilibrium situation is reached with a complex pattern of peaks appearing at *m/z* 125 and 127, 213, and 215 and 231, 233, and 235. [b] Peaks are not fully resolved. [c] These peaks are of small abundance: MS/MS data were not meaningful in these cases.

Scheme 2



listed in Table 2, together with those of the analogous *m/z* 124 (formed from HO^- and PhCDO) and 125 (from $H^{18}O^-$ and PhCHO). The CID MS/MS data for *m/z* 123 and its two labeled analogues are as follows: (i) *m/z* 123 loses HCO_2H and H_2O, (ii) *m/z* 124 loses DCO_2H and H_2O, and (iii) *m/z* 125 loses $HC^{16}O^{18}OH$ together with $H_2{}^{16}O$ and $H_2{}^{18}O$ (10:9). These data, particularly those which indicate the equilibration of the two oxygens (see, e.g., Scheme 2), are consistent with *m/z* 123 being the tetrahedral adduct.[26]

$[PhCH(OH)O^-\ (PhCHO)]$ **(3)**

$PhCH(OH)OCH(O^-)Ph$ **(4)**

The ion at highest mass in the $HO^-/PhCHO$ mass spectrum shown in Table 1 is *m/z* 229. This species shifts to *m/z* 231 for both of the systems $HO^-/PhCDO$ and $H^{18}O^-/PhCHO$. The ion is either the association complex (cluster) **3** or product **4**, formed by nucleophilic addition of the tetrahedral adduct (*m/z* 123) with benzaldehyde [and the key intermediate in the Cannizzaro mechanism shown in sequence **1** (Scheme 1)]. If *m/z* 123 corresponds to **4**, and if **4** is the key Cannizzaro intermediate shown in sequence **1**, then **4** should form $PhCH_2O^-$ and $PhCO_2^-$ on collisional activation. No peaks corresponding to $PhCH_2O^-$ or $PhCO_2^-$ are present in the spectrum of *m/z* 229; thus this ion is not an intermediate in the Cannizzaro reaction. Instead, the ion fragments by loss of water (Table 2). The corresponding losses from the labeled analogues are (i) $HO^-/PhCDO$ − loss of HOD from *m/z* 231 and (ii) $H^{18}O^-/PhCHO$ − losses of H_2O and $H_2{}^{18}O$ from *m/z* 231.

The labeling data (above, and see Tables 1 and 2) together with the following product ion studies indicate the structure of *m/z* 229 to be **4**. Since **4** is not an intermediate in the Cannizzaro reaction, the mechanism outlined in sequence **1** (Scheme 1) is not operative in the gas phase. The loss of water from *m/z* 229 forms *m/z* 211 which is identified as deprotonated benzyl benzoate (Scheme 3) [benzyl benzoate is a byproduct in the condensed-phase reaction of HO^- with benzaldehyde[4] (see Introduction)]. The ion *m/z* 211 is formed both in field-free regions and in the ion source of the mass spectrometer, and a B^2/E-linked scan spectrum of source-formed *m/z* 211 confirms that it, like the corresponding ion in the CID spectrum (Table 2), is formed exclusively from *m/z* 229.

The CID spectrum of source-formed *m/z* 211 is recorded in Table 2 and is identical with that of deprotonated benzyl benzoate. There are two mechanisms which can account for the loss of water from **4**. The first involves the hydride transfer process shown in sequence **1** (Scheme 1) to form an anion complex in which HO^- deprotonates benzyl benzoate to form the product anion. The second is outlined in Scheme 3, and involves a cyclization/deprotonation and ring-opening mechanism. We are unable to differentiate between these proposals on currently available evidence, but of the two, we prefer the latter.

The fragmentations of $PhCO_2^-CHPh$ are summarized

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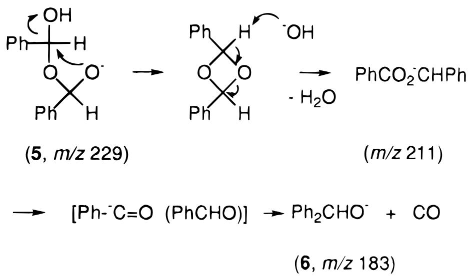
(26) An *ab initio* calculation [at MP3SDQ/6-311++G(d,p)//RHF/6-311 ++ G(d,p)] for the conversion $HOCH_2O^-$ to $^-OCH_2OH$ indicates a barrier of 21.6 kcal mol^{-1} for this process. Proton transfer should thus be facile, since $HOCH_2O^-$ is formed with an excess energy of 35.3 kcal mol^{-1}.

Table 3. Collisional Activation (CA MS/MS) and Charge Reversal [Positive Ion (CR MS/MS)][a] Data for Product Ions from the System *t*-BuCHO/HO^-

system	product mass	spectrum type	spectrum (CA [*m/z* (loss or formation) abundance], CR [*m/z* (abundance)])
t-BuCHO/HO^-	87	CA	85 (H_2)100, 29 (CHO^-)10
		CR	57 (43), 56 (14), 55 (14), 53 (9), 51 (8), 43 (14), 41 (85), 39 (100), 29 (16), 27 (4), 15 (2),14 (1)
t-$BuCH_2O^-$	87	CA	85 (H_2) 100, 29 (CHO^-) 11
		CR	57 (39), 56 (12), 55 (13), 53 (9), 51 (9), 43 (12), 41 (89), 39 (100), 29 (17), 27 (3), 15 (2), 14 (1)
t-BuCDO/HO^-	89	CA	86 (HD) 100, 30 (CDO^-)8
t-BuCHO/$H^{18}O^-$	87	CA	85 (H_2) 100, 29 (CHO^-) 12
t-BuCHO/HO^-	101	CA	100 ($H^\bullet$) 100
		CR	57 (51), 55 (12), 53 (14), 44 (39), 41 (86), 39 (100), 29 (6), 27 (13), 15 (1), 14 (2), 13 (1)
t-$BuCO_2^-$	101	CA	100 ($H^\bullet$) 100
		CR	57 (52), 55 (10), 53 (13), 44 (43), 41 (87), 39 (100), 29 (5), 27 (11), 15 (1), 14 (2), 13 (1)
t-BuCHO/HO^-	103	CA	102 ($H^\bullet$) 100, 101 (H_2) 4, 85 (H_2O) 88, 17 (HO^-) 15
t-BuCDO/HO^-	104	CA	103 ($H^\bullet$)100, 86 (H_2O) 78, 85 (HOD) 12, 17 (HO^-) 15
t-BuCHO/$H^{18}O^-$	105[b]	CA	104 ($H^\bullet$) 100, 103 (H_2)12, 87 (H_2O) 95, 85 ($H_2{}^{18}O$) 85, 19 ($H^{18}O^-$) 5, 17 (HO^-) 6
t-BuCHO/HO^-	171	CA	169 (H_2) 15, 114 ($C_4H_9^\bullet$) 65, 85 (*t*-BuCHO) 100

[a] Charge reversal (positive ion) spectra were obtained by charge stripping the appropriate negative ion to the corresponding positive ion (by collision with argon in the collision cell), reversing the electric sector voltage, and scanning the electric sector to obtain the mass spectrum of the parent positive ion.[25] [b] The exchange of ^{18}O into pivaldehyde is much less than that into benzaldehyde under the same experimental conditions. The incorporation of double ^{18}O label into these ions is minimal.

Scheme 3



in Scheme 3. The parent ion undergoes cleavage to form an ion complex which dissociates competitively to (i) form $[PhCO]^-$ (*m/z* 105) directly and (ii) lose CO following phenyl migration to yield deprotonated diphenyl methanol [**6** (Scheme 3), *m/z* 183]. The structure of the latter ion is confirmed by product ion studies (see Table 2 and cf. ref 23).

(ii) The Reactions of HO^- with Pivaldehyde. These reactions closely parallel those described above for the HO^-/PhCHO system. All data, including (i) labeling experiments and (ii) product ion studies (using both CID MS/MS and charge reversal (CR) MS/MS data[27]), are listed in Table 3.[28]

(C) Summary and Conclusions. (i) Ion cyclotron resonance experiments indicate that HO^- reacts with RCHO (R = *t*-Bu or Ph) to (a) effect deprotonation of RCHO and (b) produce RCH_2O^- ions by inefficient Cannizzaro reactions.

(ii) Similar reactions carried out with benzaldehyde and pivaldehyde under flowing afterglow (thermal) conditions do not yield the Cannizzaro product anions. Instead, $(RCHO - H)^-$, $(RCHO + HO^-)$, and $(2RCHO + HO^-)$ ions are detected.

(iii) Reactions carried out in the chemical ionization source of a VG ZAB 2HF instrument between HO^- and RCHO (R = *t*-Bu and Ph) form anions identified as RCH_2O^-, RCO_2^-, and $RCH(OH)O^-$, all of which are implicated in the Cannizzaro process. The formation of the carboxylate anion is rationalized by collision-induced stabilization of a transient complex $[RCH_2O^-(RCO_2H)]$ which may survive long enough to enable formation of RCO_2^- via the more stable complex $[(RCH_2OH)\ RCO_2^-]$.[29] The other product ion $[RCH(OH)OCH(R)(O^-)]$ is formed by a competitive reaction between $RCH(OH)O^-$ and RCHO. This ion is not involved in the Cannizzaro process.

The presented data are consistent with the studied HO^-/RCHO systems undergoing three reactions in the gas phase, viz. (i) deprotonation of RCHO, (ii) the formation of $RCH(OH)OCH(R)O^-$ [by an exothermic and reversible reaction between $RCH(OH)O^-$ and RCHO] which is only detected when the product anion is thermalized, and (iii) the gas-phase Cannizzaro reaction proceeding via the stepwise sequence shown in Figure 1, i.e., HO^- reacts with RCHO to yield $RCH(OH)O^-$, which if suitably energized, may transfer H^- inefficiently to RCHO to irreversibly yield RCH_2O^- and RCO_2H.

Experimental Section

Ab initio calculations of all species shown in Figure 1 were determined using Gaussian 92[10] with restricted Hartree−Fock wave functions [RHF/6-311++G(df,p)] and with initial force constants analytically computed. The final geometries were found to have no imaginary frequencies. The optimizations of transition states were computed with analytical force constants throughout. Final energies for all geometries of species shown in Figure 1 were determined at the MP3SDQ/6-311++G(d,p)//RHF/6-311++G(d,p) level. The potential surface which explores the initial reaction between HO^- and CH_2O to form $HOCH_2O^-$ was computed at the QCISD/6-311++G(d,p)//HF/6-311++G(d,p) level of theory.

Ion cyclotron resonance spectra were determined with an Dynaspec ICR 9 spectrometer equipped with a three-section cell. Experimental procedures have been reported previ-

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(27) Bowie, J. H.; Blumenthal, T. *J. Am. Chem. Soc.* **1975**, *97*, 2950. Szulejko, J. E.; Bowie, J. H.; Howe, I.; Beynon, J. H. *Int. J. Mass Spectrom. Ion Phys.* **1980**, *34*, 99.

(28) We have discounted the possibility that the pivaldehyde homoenolate anion[19] could transfer H^- to pivaldehyde yielding *t*-$BuCH_2O^-$ and 2,2-dimethylcyclopropanone, since this reaction cannot lead directly to the pivalate anion.

(29) A reviewer has indicated that if cluster $[RCH_2O^-(PhCO_2H]$ is formed then it will revert to the more stable cluster (by 30 kcal mol^{-1}) $[(RCH_2OH)PhCO_2^-]$. That is what we are saying as well; however if the initial cluster has even transient existence, it has some 35 kcal mol^{-1} of excess energy and should dissociate immediately to RCH_2O^- and RCO_2H, unless the transient species is deactivated and then converts to $[(RCH_2OH)RCO_2^-]$. An alternative and less likely explanation is that in the ZAB 2HF ion source the concentration of RCO_2H (formed in the Cannizzaro reaction) builds up with time so that deprotonation of RCO_2H with HO^- (or RCH_2O^-) causes deprotonation to RCO_2^-: the carboxylate anion is very stable as a consequence of the high electron affinity of $RCO_2^\bullet$.

ously.[30] In summary, the HO^- reactant ion was formed from water (cell pressure = 1×10^{-5} Torr) using an electron energy of 7.1 eV. Other reaction conditions: $\omega/2\pi = 153.7$ kHz, ion current in the 10^{-10} A range, emission current 0.2 μA, and ion transit time 1×10^{-3} s. Precursor ions in reaction sequences were determined by the cyclotron ejection technique (i.e., monitoring the change in product ion signal when the precursor ion is irradiated at its cyclotron frequency).

All FA experiments were carried out at 298 K using a recently modified FA reactor.[31] HO^- ions were prepared by electron impact (tungsten filament) on a mixture of N_2O (0.01 Torr) and CH_4 (0.02 Torr) in a stream of helium (0.45 Torr) flowing at a velocity of 204 cm^3 s^{-1} and confined in a 1 m × 7.6 cm stainless steel tube. After being thermally equilibrated by many collisions with the helium and precursor gases, the HO^- ions were allowed to react with the appropriate aldehyde (pivaldehyde or benzaldehyde) whose vapors were added to the flow tube through an inlet downstream of the ionizing region. The plasma was sampled at the end of the flow tube through a 0.5 mm orifice into a differentially pumped low-pressure region (1.3×10^{-7} Torr) where the ions were separated in an Extrel QC-50 quadrupole mass filter and detected by a channeltron electron multiplier (DeTec model 402). Rate constants were measured under pseudo-first-order conditions by monitoring the reactant HO^- ion density as a function of reaction distance using a measured flow of the neutral reagent.

Conventional HO^- negative ion chemical ionization mass spectra together with collisional activation (CID) mass spectra (MS/MS) were determined with a VG ZAB 2HF mass spectrometer.[32] Operating procedures, including linked scanning details (MS/MS and B^2/E), have been reported.[33] Specific details were as follows: the chemical ionization slit was used in the chemical ionization source, the ionizing energy was 70 eV, the ion source temperature was 100 °C, and the accelerating voltage was 7 kV. The liquid samples were introduced through the septum inlet with no heating (measured pressure of sample 1×10^{-6} Torr). The reacting anion was HO^- (from H_2O: measured pressure 1×10^{-5} Torr). The estimated total source pressure was 10^{-1} Torr. MS/MS data were obtained by using the magnet to focus those ions of particular mass, the ions were collision activated in the second collision cell [argon was used as collision gas (measured pressure, outside the cell, 2×10^{-7} Torr), giving a 10% reduction in the main beam, equivalent to single collision conditions], and the spectrum was produced by scanning the electric sector. Charge reversal (positive ion) mass spectra of negative ions[27] were measured under conditions similar to those of MS/MS experiments, except that the voltage of the electric sector was reversed to allow the transmission of the resulting positive ions.

Benzaldehyde and pivaldehyde were both commercial samples: each was carefully purified (no alcohol or acid impurities were present) and used immediately. Formaldehyde was produced by heating paraformaldehyde in the inlet system of the spectrometer. The gases used in the FA and MS instruments (N_2O, CH_4, He, and Ar) were of 99.99% purity. The labeled reactants used in the experiments using the VG ZAB 2HF instrument were DO^- (from D_2O, D_2 = 99.9%) and $H^{18}O^-$ (from $H_2{}^{18}O$, ^{18}O = 96%).

The deuterium-labeled aldehydes were prepared by reduction of methyl benzoate and methyl pivalate with lithium aluminum deuteride,[34] followed by oxidation[35] of the appropriate D_2 alcohol to the D_1 aldehyde (D_1 = 99%).

Acknowledgment. We thank the Australian Research Council for ongoing financial support of our negative ion program. One of us (S.D.) thanks the ARC for a research associate position.

Supporting Information Available: Geometries and energies of $HOCH_2O^-$ and transition state **A** (Figure 1) [MP3/6-311++G(d,p)//HF/6-311++G(d,p)] (1 page). This material is contained in 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.

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