quantum yield of disappearance of 1 was 0.037.

Quantum Yield of 1 with Added Propanethiol. Propanethiol (2.4 mL) was added to an identical solution of 1 that was degassed for 30 min, irradiated for ~2h on the optical bench, and analyzed by HPLC. The solution absorbed 0.001 88 mE, and 0.0449 mmol of 1 was reacted. The quantum yield of disappearance of 1 was 0.024.

Quantum Yield with 3. A solution of 3 (65 mg) in MeOH/$CHCl_3$ (80 mL) was degassed for 45 min, irradiated on the optical bench, and analyzed by HPLC at approximately 1-h intervals.

Quantum Yield of 3 with Added Propanethiol. Propanethiol (2.4 mL) was added to an analogous solution of 3 (91.9 mg) in MeOH/$CHCl_3$ (78 mL). The solution was degassed for 30 min, irradiated on the optical bench, and aliquots were removed for HPLC analysis at ~30-min intervals.

Registry No. 1, 38048-32-7; 2, 574-25-4; 3, 6165-03-3; 4, 130948-35-5; 5, 1972-28-7; 6, 143330-50-1; 7, 143330-48-7; 14, 143330-49-8; propanethiol, 107-03-9; 4-[*N*-(propylsulfonyl)amino]benzyl alcohol, 143330-51-2; 4-aminobenzyl alcohol, 623-04-1; propanesulfonyl chloride, 10147-36-1; 4-(*N*-acetyl-*N*-(propylsulfonyl)amino)benzyl alcohol, 143330-52-3; 2′,3′,5′-tri-*o*-acetyl-6-thioinosine, 3021-21-4.

Gas-Phase Ambident Reactivity of Monohydrated Enolate Anions

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The gas-phase reactions between a series of monohydrated enolate anions and unsaturated perfluorocarbon compounds have been studied using Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometry. The influence of selective solvation at the oxygen atom on the ambident reactivity of enolate anions in the gas phase is investigated through comparison of the observed product distributions with previously obtained data for the corresponding unsolvated anions. This analysis indicates that probably in order to make the nucleophilic addition reactions energetically accessible the water molecule is vaporized from the reaction complex prior to the addition reaction step. This evaporation of a water molecule from the reaction complex is considered to recover the intrinsic chemical reactivity of the enolate anions which is confirmed by the agreement between the observed ambident chemical behavior of the monohydrated and unsolvated enolate anions.

Introduction

Ambident ions can be characterized as ions in which reactive sites are connected through mesomerism.[1,2] The competition between the reactive sites is generally rationalized in terms of orbital versus charge control[3] or by the hard and soft acid/base concept.[4-6]

It is known from studies in the condensed phase that the reaction selectivity of ambident enolate anions is strongly influenced by temperature, counterion, and solvent. Variation of the solvent, for example, may drastically change the reaction selectivity.[1,7,8] From experimental studies it follows that the atom accommodating most of the charge[9-11] is selectively solvated in protic media.[12] It is generally believed that in protic polar media the solvent molecules preferentially associate with the hard oxygen atom (which carries the larger part of the charge) of enolate anions, thereby shielding the oxygen nucleophilic center. This promotes reaction via the carbon nucleophilic center of the ambident anion.[7,8,13,14]

Occasionally, however, the influence of the solvent is cancelled or even overruled by the counterion. In nonpolar aprotic solvents, for example, ion pairs of alkali enolates are strongly associated, which again promotes reaction via the carbon nucleophilic center.[1,12] The reaction via the oxygen nucleophilic center gains importance if the polarity and basicity of the solvent are increased. This effect can be accounted for by the enhanced solvation of the counterion. Clearly, the intrinsic ambident chemical behavior of enolate anions can be masked by solvent and counterion association effects.

In order to tackle this problem, the intrinsic behavior of ambident ions has also been studied in the gas phase, typically making use of mass spectrometric techniques. Among the substrates which have been used to probe the ambident reactivity of anions in the gas phase,[15-23] un-

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saturated polyfluorinated compounds seem to be the most versatile and generally applicable because the product ion distribution can easily be associated with the reaction selectivity.[19–21]

Systematic studies on the reactivity of enolate anions toward unsaturated polyfluorocarbon compounds show that the relative yields of ionic products formed reveal the whole spectrum of ambident reactivity from 100% addition via the carbon nucleophilic center up to 99% addition via the oxygen nucleophilic center, depending on the nature of both the enolate anion and the polyfluorocarbon compound.[20–22]

In one of the above studies[21] we have found a correlation between the reaction selectivity and the energy of the HOMO of the enolate anions, as determined by their experimental photoelectron detachment threshold energies.[24–26] The nature of this correlation strongly suggests that the competition between the reaction via oxygen and carbon is controlled by specific frontier orbital interactions of the reactants rather than by the charge distribution in the enolate anions alone. For enolate anions with a relatively low energetic HOMO, the reaction path seems to be dominated by interaction of the LUMO of the substrate with the HOMO of the enolate anion. The orbital coefficient in this MO is largest on the less electronegative carbon atom, and consequently reaction preferentially takes place via the carbon end of the enolate anion. For enolate anions with a relatively high energetic HOMO, the reaction path seems to be dominated by the interaction with the HOMO-1 of the enolate anion. The orbital coefficient in this MO is largest on the more electronegative oxygen atom, and consequently reaction preferentially takes place via the oxygen nucleophilic center.

In the last decade there is an increasing interest in the reactivity of partially solvated anions in the gas phase. Several theoretical studies on the influence of solvation on the reactivity of anions have been reported[27–33] together with studies of acid–base reactions,[34,35] nucleophilic additions,[36–38] ligand or solvent switching,[34,39–43] and substitutions[34,44–49] of partially solvated anions. It is generally accepted that the chemistry of partially solvated anions in the gas phase can be extrapolated to the chemistry in the condensed phase,[34,50,51] although there is some doubt whether this is always justified.[44] Therefore, in an attempt to bridge the gap between the gas- and condensed-phase studies, the gas-phase reactivity of monohydrated enolate anions has been investigated in order to examine the influence of specific solvation on the ambident chemical behavior of enolate anions.

Table I. Oxygen versus Carbon Addition in the Reactions between Monohydrated/Unsolvated Enolate Anions and C_XF_6

reactant ion	substrate	unsolvated anion %O	unsolvated anion %C	monohydrated anion %O	monohydrated anion %C
$H(CO)CH_2^-$	C_6F_6	81[a]	19[a]	97	3
	C_3F_6	94[a]	6[a]	95	5
$CH_3(CO)CH_2^-$	C_6F_6	19[a]	81[a]	35	65
	C_3F_6	84[a]	16[a]	80	20
$CD_3(CO)CD_2^-$	C_6F_6	22	78	43	57
	C_3F_6	85	15	84	16
cyclo $C_5H_7O^-$	C_6F_6	0[b]	100[b]	6	94
	C_3F_6	0[b]	100[b]	0	100

[a] Data taken from ref 21. [b] Data taken from ref 22.

Experimental Section

Experiments were carried out with a FT-ICR mass spectrometer, built at the University of Amsterdam and equipped with a Bruker 1.4 T electromagnet and a cubic inch cell. General operating and experimental procedures have been described previously.[52] The monohydrated enolate anions were made in situ via a reaction with monohydrated ethoxide. This monohydrated ethoxide was formed via an elimination reaction between primarily formed hydroxide ions and diethyl ether.[52,53,54] As an example, the formation of a monohydrated acetone enolate anion is given in eqs 1 and 2:

$$OH^- + C_2H_5OC_2H_5 \rightarrow C_2H_4 + [^-OC_2H_5, H_2O] \tag{1}$$

$$[^-OC_2H_5, H_2O] + CH_3COCH_3 \rightarrow HOC_2H_5 + [^-CH_2(CO)CH_3, H_2O] \tag{2}$$

The total pressure was kept typically around 2.4×10^{-4} Pa. The partial pressures of the unsaturated perfluorocarbon compound

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and the neutral ketone were kept typically around 2.5×10^{-5} Pa. To eliminate the remote possibility of a contribution to the product ion mixture from the reaction between desolvated enolate anions and unsaturated perfluorocarbon compounds, the possibly formed unsolvated enolate anions were ejected continuously from the FT-ICR cell during the experiments.

Reactions between hexafluorobenzene and translationally excited acetone enolate anions were performed by exciting the enolate anion with an on-resonance single frequency excitation field with a duration of 2 ms and varying field strength from 0 to 50 V/m which corresponds to a translational energy of 0–100 eV.

The temperature of the FT-ICR cell was around 330 K as measured by a thermocouple on the trapping plate opposite the filament. The segmented Fourier transform (SEFT) procedure,[55] developed in our laboratory, was used to determine relative ion abundances with an accuracy of ±10%. The lower accuracy of the relative ion abundances in comparison with previous studies (1%[21,55]) are due to the relatively high pressures used in this study.

Materials. All chemicals employed were commercially available and were used without further purification.

Results

Reactions between monohydrated enolate anions $[E, H_2O]^-$ and the unsaturated perfluorocarbon compounds hexafluorobenzene, C_6F_6, and hexafluoropropene, C_3F_6, have been found to result in the formation of product ions of the type $C_xF_5O^-$ and $[E + C_xF_6 - nHF]^-$ (n = 1–2 for C_6F_6, n = 1–4 for C_3F_6).

Similar to the analysis of the reactions of unsolvated enolate anions,[19-21] the summed yield of $[E + C_xF_6 - nHF]^-$ ions has been related to the proportion of the studied reaction course proceeding via addition of the carbon nucleophilic center (eq 3a), whereas the yield of $C_xF_5O^-$ ions has been related to the proportion of the reaction taking place via the oxygen nucleophilic center (eq 3b). The results of this analysis for the reactions of a series of monohydrated enolate anions are listed in Table I.

$$[E, H_2O]^- + C_xF_6 \xrightarrow{\text{via C}} [E + C_xF_6 - nHF]^- + nHF + H_2O \qquad (3a)$$

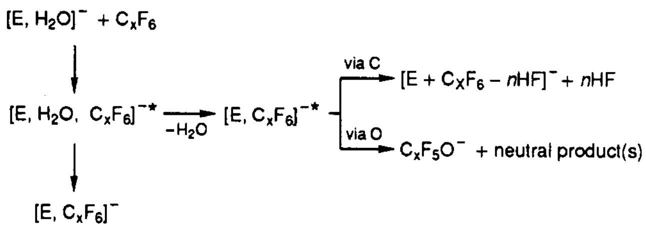
$$[E, H_2O]^- + C_xF_6 \xrightarrow{\text{via O}} C_xF_5O^- + \text{neutral products} \qquad (3b)$$

In addition to the common product ions $C_xF_5O^-$ and $[E + C_xF_6 - nHF]^-$ a small contribution (<12%) of $[E + C_3F_6]^-$ product ions has been found in the reactions between the monohydrated enolate anions and hexafluoropropene. Formally, formation of this product ion can be regarded as a solvent switching process where the water molecule is exchanged for the hexafluoropropene molecule (eq 4). However, the results do not show whether this product ion is still a solvated enolate anion or a nucleophilic addition product.

$$[E, H_2O]^- + C_3F_6 \rightarrow [E + C_3F_6]^- + H_2O \qquad (4)$$

Yet, it has been shown that collisional activation of these adduct ions formed by association of the unsolvated enolate anions and hexafluoropropene under a relatively high pressure in a flowing afterglow apparatus[20] exhibits product ion distributions which are identical to those obtained for the thermal reactions between the enolate anions and hexafluoropropene. Therefore, neglect of the minor contribution of the $[E + C_3F_6]^-$ product ion in the analysis of the product ion distribution in terms of ambident reactivity of the enolate anions in their reaction with hexafluoropropene is not expected to influence seriously the conclusions to be drawn.

Scheme I



Unexpectedly, in none of the reactions studied have hydrated product ions been detected, which reveals that the solvent molecule escapes the ion/molecule reaction complex somewhere along the reaction coordinate.

Discussion

The results in Table I show the ambident chemical behavior of monohydrated enolate anions in their reaction with unsaturated perfluorocarbon compounds. If this behavior is compared with the ambident chemical behavior of the corresponding unsolvated enolate anions (included in Table I) it appears that solvation of an enolate anion with a single water molecule does not drastically change the gas-phase ambident chemical behavior of the enolate anions. In the reactions between the series of enolate anions studied and hexafluoropropene no significant changes are encountered (see Table I). For the reactions with hexafluorobenzene it seems that association with a single water molecule slightly enhances the proportion of the reaction course which proceeds via the oxygen nucleophilic center (see Table I). These results are highly unexpected since it was anticipated that solvation would selectively shield the oxygen nucleophilic center and consequently would promote strongly the proportion of the reaction proceeding via the carbon nucleophilic center of the enolate anions.

This expectation is based on results of both theoretical[56] and experimental studies,[57] which indicate that in gaseous monohydrated enolate anions the water molecule is specifically associated with the oxygen atom in the enolate anion via a relatively strong hydrogen bond. The unexpected behavior of monohydrated enolate anions elicits the conclusion that the water molecule is not involved in the addition step of the reaction which implies that the water molecule has vaporized from the reaction complex prior to this addition step as suggested in Scheme I. This is compatible with the observation of solvent switching product ions in the reactions with hexafluoropropene and with the remarkable result that in none of the reactions studied could hydrated product ions be detected (see above).

Evidently, association with a water molecule reduces the reactivity of the enolate anion as a result of which the energy gained upon encounter with the perfluorocarbon compound is not sufficient to allow a fair competition between the addition reaction and the dissociation of the encounter complex back to the reactants or the "boil off" of a water molecule. This "boil off" of a water molecule recovers the intrinsic reactivity of the enolate anion in the reaction complex. This recovery of the intrinsic reactivity may result in a product ion distribution due to the competition between the oxygen and carbon nucleophilic centers which is similar to the product ion distribution for the reaction of the unsolvated enolate anion in agreement

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with the present results. The reduction of the reactivity of the enolate anion upon association with a water molecule may be the result of an enhancement of the diffuse character of the charge and of a drastic lowering of the HOMO energy of the enolate anion. Although the influence of hydration on the HOMO energy of an enolate anion is not known, it has been shown for several anions in the gas phase that solvation leads to a (0.5–1.3 eV)[58,59] higher energy required to remove an electron from the anion which can be associated with a lowering of HOMO energy.

"Boiling off" of water molecules during the gas-phase reactions of hydrated reactant ions is not an uncommon phenomenon, since it has been shown frequently that reactions of mono- and polyhydrated reactant ions may result in complete or partial desolvation of the ionic products.[34,37,38,44,45] Yet, it is not always clear if the evaporation of water molecules is fueled by the energy gained upon formation of the reaction encounter complex or by the energy released in the ion/molecule reaction which takes place in the solvated reaction complex.

Although the related phenomenon of ligand or solvent switching for solvated gaseous ions is well-known, the question remains if the exchange of the water molecule for a perfluorocarbon molecule which is assumed to precede the reaction between the presently studied enolate anions and the perfluorocarbon molecule is energetically accessible. The thermodynamics of this solvent switching process is not known. However, it has been shown in both theoretical[56,60] and experimental[40,61,62] studies that the electrostatic bonding between Cl^- and hexafluorobenzene is ca. 8 kJ mol^{-1} more favorable than the clustering of Cl^- with H_2O, which indicates that the assumed solvent switching step in the presently studied reactions is not energetically blocked. Yet, evaporation of the water molecule from the encounter complex can be expected to cool off the reaction complex as a result of which the excess internal energy may be lower than for the same complex formed upon encounter of the unsolvated enolate anion and the unsaturated fluorocarbon molecule. In spite of this anticipated difference in excess internal energy, only for the reactions with hexafluorobenzene a small shift in the reaction selectivity towards addition via the oxygen nucleophilic center has been detected upon association of the enolate anion with a water molecule. This seemingly insensitivity for variation of the excess internal energy of the reaction complex may be due to a relatively small or similar activation entropy of the two reaction channels. This is supported by the observation that translational excitation up to 100 eV of the unsolvated enolate anion from acetone showed no significant shift of the reaction selectivity in the reaction with hexafluorobenzene. Nevertheless, it would be much more conclusive to study the temperature dependence of the ambident chemical behavior of the unsolvated enolate anions.

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Total Synthesis of Some Marasmane and Lactarane Sesquiterpenes

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A general and efficient synthetic route to the marasmane sesquiterpenes (±)-isovelleral (**2**) and (±)-stearoylvelutinal (**1b**) is described. Total syntheses of two other naturally occurring sesquiterpenes, deconjugated anhydrolactarorufin A (**5**) and lactarorufin A (**6**), were achieved using an acid-catalyzed ring expansion of lactone **25**. All four syntheses are highly stereoselective and do not require the use of any protecting groups. Finally, the protic acid-catalyzed degradation of velutinal (**1a**) was investigated in an effort to chemically induce the biologically important conversion of velutinal (**1a**) to isovelleral (**2**). The experimental results thus obtained indicate that an enzymatic mechanism for the key transformation of velutinal (**1a**) into isovelleral (**2**) is more plausible than one that is acid-catalyzed.

Marasmane and lactarane sesquiterpenes, representative examples of which are shown below, have been isolated from basidiomycetes of several genera, including *Marasmius*, *Lactarius*, and *Russula*.[2] Some of these sesquiterpenes appear to be part of a complicated chemical defense mechanism in which fatty acid esters (**1b**,**c**) of the unstable hemiacetal velutinal (**1a**) serve as inactive forms of the ammunition.[3] For example, injury of a specimen of *Lactarius velereus* causes rapid enzymatic hydrolysis of ester **1b** to **1a**, which is further transformed by an unknown mechanism, enzymatic or chemical, into the strongly antifungal and antibacterial sesquiterpene dialdehydes isovelleral (**2**)[4] and velleral (**4**).[5] Compounds **2** and **4** impart a pungent taste to the fungi, and **2** is a potent insect and opossum antifeedant.[6] Furthermore, **2** shows significant mutagenic activity in the Ames *Salmonella*/microsome assay and may be a contributing

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