Ion pair formation in the addition of protic reagents to alkynes

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The reaction of oct-4-yne with 20% trifluoroacetic acid and a variety of relatively weak nucleophiles in methylene chloride was found to produce a mixture of anion incorporated and solvent incorporated products. The rates of these reactions with a range of salt concentrations were found to be proportional to the rates of reaction of simple alkenes under similar conditions. The results are explained by the formation of an intermediate ion pair in contrast to the reactions of alkynes with bromide or iodide which proceeded by a concerted mechanism.

Introduction

In earlier papers, we reported the results of kinetic and product studies of the addition of HBr to unconjugated alkenes[1] and alkynes.[2] These reactions were performed using 20% trifluoroacetic acid in methylene chloride with a wide concentration range of tetrabutylammonium bromide. The acidities of these solutions were found to be greatly affected by the salt concentrations, becoming more acidic as the salt concentration increased from 0.01 M to 0.2 M but becoming less acidic as the bromide concentration was increased further. The acidities of these solutions were measured by their ability to protonate a neutral Hammett base leading to a value of $H_o - pK_a$. Similar product results had been found earlier in the reaction of alkenes with HCl[3] and HBr[4] in acetic acid with added halide ion and those results were interpreted in terms of competing second and third order mechanisms. Our kinetic results over a wide range of bromide concentrations excluded that possibility in our system.

In all of these solutions, alkenes were found to produce a variety of unrearranged and rearranged bromides and trifluoroacetate esters as well as some isomerized starting material. The rates of these reactions were found to be linearly dependent upon the alkene concentration and $H_o - pK_a$. These results suggested an Ad_E2 mechanism proceeding through an ion pair. At the higher salt concentrations, the weakened acidity of the solutions required greater bromide participation in the transition state leading to a tighter ion pair. The result of this was to find more unrearranged, Markovnikov alkyl bromide but the reaction rate remained independent of bromide concentration up to 1.0 M salt.

In contrast to this behavior, unconjugated alkynes were found to undergo exclusive *anti* addition of HBr at a rate dependent upon the alkyne concentration, $H_o - pK_a$ *and bromide concentration*. These results suggested an Ad_E3 mechanism involving attack of the bromide ion on a preformed alkyne–acid complex. In the more acidic solutions, the vinyl bromide product was vulnerable to further protonation but the weakened acidity of the concentrated salt solutions precluded any further reaction. The alkyne was still reactive in these solutions, however, because its rate of reaction was promoted by the high bromide ion concentration. Thus, the addition of one equivalent of HBr was easily achieved.

Alkyne reactions using tetrabutylammonium iodide gave the corresponding iodide products, however, the chloride salt produced stereochemically diverse vinyl chlorides and trifluoroacetates. This paper reports a more complete study of the reaction of oct-4-yne with chloride ion and some other weakly nucleophilic anions under the same conditions as in our previous study.

Table 1 Half lives and relative product yields for the reaction of oct-4-yne with 20% TFA in CH_2Cl_2 with 0.20 M tetrabutylammonium salts

Anion used (Y)	$t_{1/2}$/min	R-Y/ROTFAc	Z/E (R-Y)
None	20000	0	—
PF_6^-	5600	0	—
BF_4^-	2600	0	—
$CF_3SO_3^-$	248	4.6	0.7
$CH_3SO_3^-$	2600	1.5[a]	1.7
Cl^-	1600	14	9
Br^-	46	>200	32
I^-	8	>200	>200

[a] This value decreases with time.

Results

Effect of nucleophile strength on rates and product ratios

To screen a variety of nucleophiles, we performed kinetic and product studies on the reaction of oct-4-yne in 20% trifluoroacetic acid in methylene chloride with a 0.2 molar concentration of some tetra-*n*-butylammonium salts. Table 1 gives the results of these reactions.

These data show that a 0.2 M concentration of any salt increases the rate of reaction over the salt free solution, presumably by stabilizing the developing cation as it presumably stabilizes the protonated Hammett base. Only the bromide and iodide ions show the enhanced effect of their nucleophilic involvement in the rate determining step. Similarly, only these stronger nucleophiles produce the highly chemoselective and stereoselective product ratios throughout a full range of anion concentrations. Somewhat surprisingly, the triflate ion was more reactive than the mesylate ion and the addition products were less prone to further reaction (isomerization, solvolysis and ketone formation).

Effect of anion concentration on rates and product ratios

Because chloride and triflate ions gave relatively stable products, we decided to investigate their behavior more fully. Although the ionization state of chloride in trifluoroacetic acid was not clear, we decided to study this reaction as a comparison to our earlier work with halide ions and the previous studies by Fahey[5] on the addition of HCl to alkynes in acetic acid.

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Table 2 Half lives, relative product yields and relative acidities for the reaction of oct-4-yne with 20% TFA in CH_2Cl_2 with added tetrabutylammonium chloride

[Cl$^-$] used/M	$t_{1/2}$/min	% *Z*-RCl	% *E*-RCl	% ROTFAc	log [In]/[HIn]
0.01	7830	38.9	32.5	28.6	
0.05	3780	58.6	24.7	16.7	−1.20
0.10	2260	71.9	17.1	11.0	−1.40
0.20	1600	84.1	9.2	6.7	−1.64
0.40	1540	94.8	3.1	2.1	−1.70
0.60	3090	99.3	0	0.7	−1.29
0.80	20100	100	0	0	−0.61
1.00	204500	100	0	0	+0.29

Table 3 Half lives and relative product yields for the reaction of oct-4-yne with 20% TFA in CH_2Cl_2 with added tetrabutylammonium trifluoromethanesulfonate (triflate)

[Tf$^-$] used/M	$t_{1/2}$/min	% *Z*-Trif	% *E*-Trif	% ROTFAc
0.01	318	9.9	68.0	17.9
0.05	506	20.0	54.5	24.6
0.10	289	24.4	56.7	15.8
0.20	248	33.6	47.3	17.5
0.40	420	49.8	37.9	11.4
0.60	3480	67.4	26.8	4.78
0.80	42500	79.0	18.4	3.05
1.00	210000	80.9	18.0	0.08

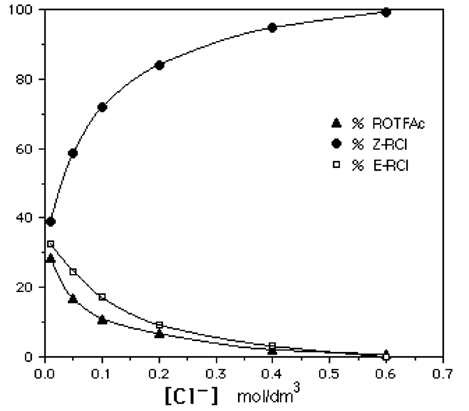

Fig. 1 Relative product yields as a function of the chloride ion concentration.

Table 2 shows the half lives and product yields resulting from varying the chloride ion concentration and these data are also shown graphically in Fig. 1. The product ratios and stereoselectivity increased with the increasing concentration of the salt. The remaining product is octan-4-one.

The tetrabutylammonium trifluoromethanesulfonate initially produced erratic results; rapid early reaction followed by a significant decrease in the rate. This was attributed to the presence of triflic acid and, therefore, the salt was neutralized prior to its use in all subsequent reactions.

Table 3 shows the half-lives and product yields resulting from varying the triflate ion concentration. Again, the product ratios and stereoselectivity increased with the increasing concentration of the salt. The sulfonate products showed some tendency toward solvolysis, especially noticeable with the longer reaction times. These product ratios were therefore extrapolated back to the original values and exhibit some uncertainty.

Discussion

The acidities of solutions of bromide, chloride and triflate were found to be equal within our experimental methods and were used interchangeably.

The dependence of the rate of disappearance of the octyne in the chloride reaction was found to be linearly dependent upon the $H_o - pK_a$ values of the solutions with a slope of 1.1. This relationship may be seen in Fig. 2 showing the dependence of log *k* on the $H_o - pK_a$ of the solutions and its independence from chloride ion. This excellent fit suggests that the rate of this reaction is dependent upon H_o and otherwise independent of chloride ion. The product composition, however, suggests a concerted mechanism at the highest concentrations of salt. It should be noted that the kinetic dependence of chloride ion might not be detected at a chloride concentration near one molar.

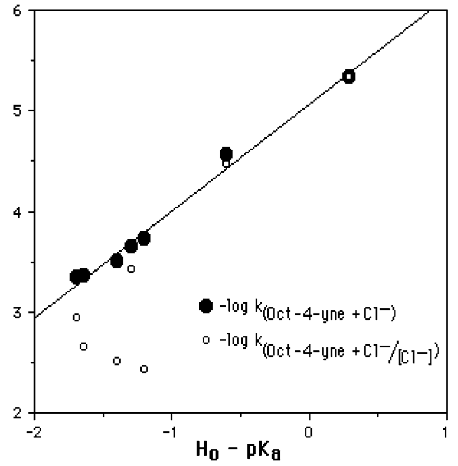

Fig. 2 (Negative) Logarithm of pseudo first order rate constant for chloride addition to oct-4-yne against $H_o - pK_a$ of reaction solution.

The rate of disappearance of the octyne in the triflate reaction was found to give a poor linear fit with the $H_o - pK_a$ values of the solutions at low triflate concentrations. However, the Ad_E2 behavior may be seen by plotting the log of these rate constants against those for the addition of HBr to oct-1-ene (Fig. 3). The kinetic behavior of the alkene reactions has proved to be a more dependable indication of the Ad_E2 mechanism than our $H_o - pK_a$, especially at low ion concentrations. This may reflect the different abilities of ions to participate in an equilibrium *versus* a kinetic situation.

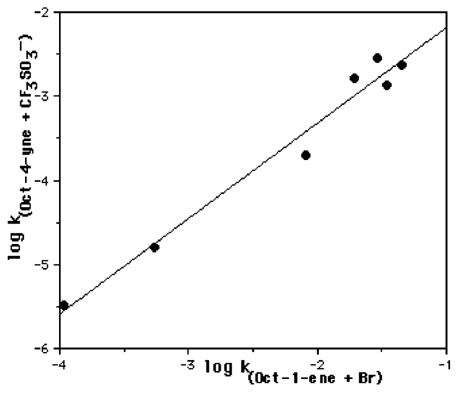

Fig. 3 Logarithm of pseudo first order rate constant for triflate addition to oct-4-yne *versus* logarithm of pseudo first order rate constant for bromide addition to oct-1-ene.

Conclusions

The rate of reaction of oct-4-yne with 20% trifluoroacetic acid in methylene chloride containing weakly nucleophilic anions shows a dependence upon H_o but no further dependence upon the anion concentration. This suggests that, under the conditions of these reactions, simple alkynes are protonated in the rate determining step. This result appears to remain consistent throughout the range of concentrations studied. Yet, the efficient capture of these anions at low concentrations suggests that the anions must be near the developing cation in the rate determining step. A similar environment may exist in the H_o determinations.

The increasing chemoselectivity and stereoselectivity seen at the higher salt concentrations is thought to arise from the weakened acidities in these solutions requiring a greater participation of the anion in the transition state leading to a tighter ion pair and an increased collapse to the selective product. This model parallels the picture described previously for the reaction of *alkenes*[1] with *all* of the anions tested in TFA–methylene chloride.

Experimental

The oct-4-yne, trifluoroacetic acid and solvents (HPLC grade) were obtained from Aldrich Chemical Co. and were used without further purification. The quaternary ammonium salts were obtained from Fluka Chemical and/or from Aldrich Chemical Co. and were kept in a desiccator prior to use. The tetrabutylammonium bromide was dried under vacuum at regular intervals.

Reactions were performed in glass-stoppered volumetric flasks by adding 1 or 2 drops of the preanalyzed alkyne–nonane mixture to 5 to 100 mL of the 20% trifluoroacetic acid in methylene chloride solution containing at least 10^{-3} moles of the quaternary ammonium salt. Results from 1 or 2 drops of alkyne (approximately 10^{-4} moles) are identical within experimental certainty. Aliquots (approximately 1/2 mL) were removed and quenched with 15 mL of water and 10 mL of hexanes. The hexanes layer was washed with another 10 mL of water and dried over anhydrous potassium carbonate prior to GC-MS analysis. Chromatographic peaks were identified by their mass spectrum as well as by relative retention times. Detector responses for the products were assumed to be equal. The vinyl halides were shown to be stable under the reaction conditions. Unless otherwise noted, all reactions were run at room temperature (20 ± 2 °C) and showed no evidence of exothermicity.

Mass spectra and chromatographic analyses were performed on a Hewlett Packard 5890 Chromatograph with a 12-m. HP-1 capillary column and a 5971A mass selective detector.

Neutralization of tetra-*n*-butylammonium trifluoromethanesulfonate

Twenty five grams of tetra-*n*-butylammonium trifluoromethanesulfonate (Aldrich) was stirred with 60 mL of distilled water at 65 °C. Three drops of a 0.1% alcoholic solution of phenolphthalein was added and this solution was neutralized by the dropwise addition of 40% aqueous tetra-*n*-butylammonium hydroxide (Aldrich). The resulting pink solution was extracted with two 25 mL portions of methylene chloride which were combined and rotary evaporated to produce a white solid which was further dried under a high vacuum.

Acknowledgements

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