Direct Synthesis of Stable Adamantylideneadamantane Bromonium Salts

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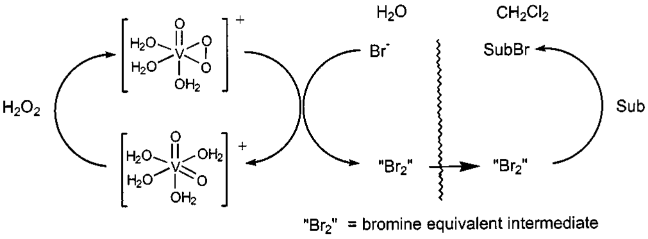
By using a V^V- or Mo^{VI}-catalyzed two-phase procedure for oxybromination of organic substrates, adamantylideneadamantane bromonium salts ($ADABr^+X^-$; X^- = V^V- and Mo^{VI}-containing anions) have been isolated and characterized. These salts proved to be significantly more stable relative to the corresponding tribromide derivative.

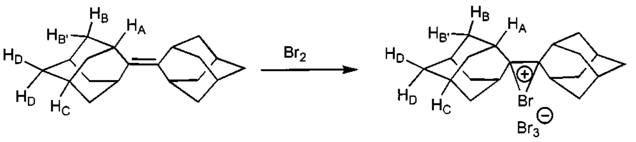
We have recently reported a two-phase procedure (see Scheme 1) which is a simple and efficient synthetic method for bromination and oxybromination of arenes and alkenes.[1] In the acidic aqueous phase the peroxometal derivative oxidizes the bromide ion to a species (probably a metal-bound hypobromite derivative) which then brominates the substrate dissolved in the organic phase. In the context of studies[2] aimed at elucidating the mechanistic details of this process, we analyzed the behavior of adamantylideneadamantane (ADA) in the V^V- and Mo^{VI}-catalyzed bromination in a two-phase system.[1]



Scheme 1. Two-phase system for vanadium-catalyzed bromination

ADA is a hindered substrate whose reactivity to electrophilic bromination ends at the stage of the bromonium ion[3][4] – the addition of a nucleophile being prevented for steric reasons. The ADA bromonium ion is also able to rapidly transfer Br^+ to acceptor olefins through a spiro intermediate.[5] The reactivity of the ADA system suggests that suitably constructed ADA bromonium ions could be used as chiral Br^+ sources. However, the difficulties in preparing chiral ADA derivatives and the instability of the halonium ions have raised doubts about the synthetic utility of the method.[6] The stability of the bromonium ions is also often affected by the nature of the counteranion.[7] Although the tribromide anion, formed by addition of Br_2 to the olefin in chlorinated solvents, can be replaced with almost nonnucleophilic species, the procedure, relatively easy with ADA,[5][8] can become more difficult when the instability of the bromonium ion prevents its isolation. Therefore, the synthesis of bromonium ions having unreactive counteranions may bypass some of the difficulties related to their use as chiral inducers.

When bromine reacts with ADA a yellowish precipitate is formed whose empirical formula and properties are consistent with it being the bromonium-tribromide molecule[9] shown in Scheme 2. The X-ray crystal structure of this salt has been solved.[9]



Scheme 2. Schematic formation of ADA bromonium ion; for clarity, in the substrate only selected hydrogen position are indicated, see text and ref.[9]

In order to detect the formation of the bromonium-tribromide ion in a two-phase reaction, ADA was reacted with $KBr/KBrO_3$ in an $H_2O/CHCl_3$ mixture (pH ca.1). As expected, after the formation of bromine, indicated by the development of the typical yellowish color, the slow formation of a precipitate in the organic phase was observed. This precipitate was separated from the organic phase and its ^1H NMR spectrum was recorded (Figure 1 spectrum A).

The NMR spectra of the tribromide salt, recorded at room temperature, are characterized by values of the chemical shifts of some protons lower than those previously reported in the literature[9] {H_A $\delta = 3.00$ [s, 4 H ($\delta = 3.11$[3][9])]; H_B $\delta = 2.21$ [d, 8 H, $J = 13$ Hz ($\delta = 2.51$[3] 2.53[9])]; $H_{B'}$ $\delta = 1.98$ [d, 8 H, $J = 13$ Hz ($\delta = 2.23$[3][9])]; H_C $\delta = 2.06$ [s, 4 H, ($\delta = 2.19$[9] 2.20[3])]; H_D $\delta = 1.94$ [s, 4 H, ($\delta = 2.04$[3][9])]} The differences observed are consistent with a degenerate transfer of Br^+ from the bromonium salt to ADA, thus suggesting the presence of free olefin in solution. On the other hand, it has previously been shown from UV measurements that an equilibrium between the salt, the $ADA\text{-}Br_2$ charge transfer complex and free olefin is rapidly established when the precipitated bromonium-tribromide salt is dissolved in 1,2-dichloroethane (DCE).[10] In fact, if the $ADABr^+Br_3^-$ sample dissolved in deuterated

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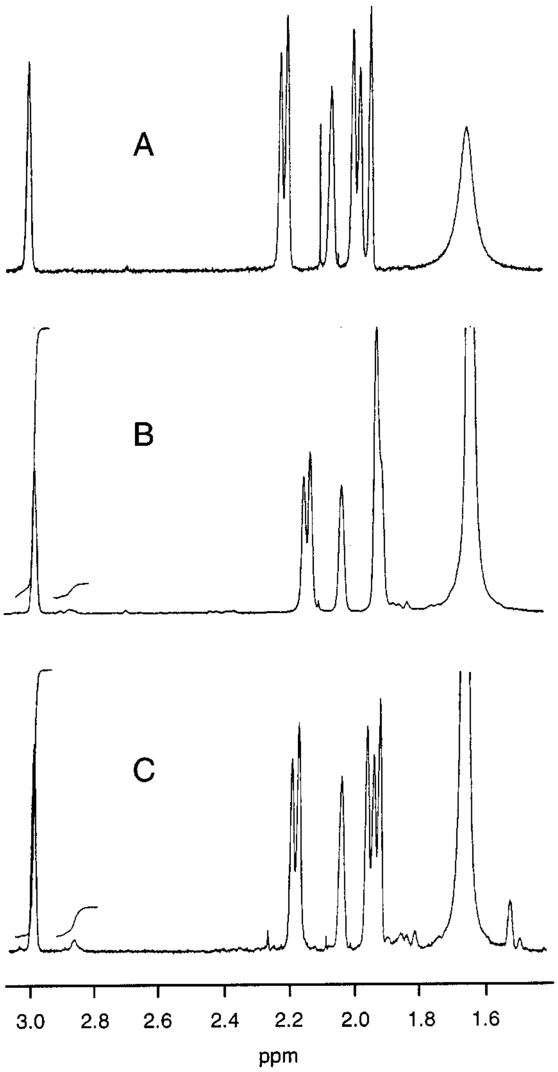

Figure 1. ^{1}H NMR spectra at 600 MHz in deuterated DCE of the precipitates obtained from ADA in the presence of: **A**. KBr/KBrO$_3$; **B**. KBr/NH$_4$VO$_3$/H$_2$O$_2$; **C**. KBr/Na$_2$MoO$_4$/H$_2$O$_2$; in the two-phase system

DCE is not maintained in the dark at low temperature, a rapid evolution of bromine, indicated by the fading of the yellowish color, is observed.

ADA bromination was also carried out in the two-phase system,[1] containing hydrogen peroxide and potassium bromide in the acidic aqueous phase in the presence of NH$_4$VO$_3$ or Na$_2$MoO$_4$ respectively (see Experimental Section for details). In both cases formation of a precipitate in the organic layer was observed. Contrary to the behavior reported above, these products when isolated and dissolved in deuterated DCE appear to be fairly stable and only decompose after a few days. The ^{1}H NMR spectra at 600 MHz of the two products isolated from these metal-catalyzed reactions are reported in Figure 1, spectra B and C respectively. All three salts present similar spectroscopic behavior thus suggesting that, in the presence of VO$_3^-$ or HMoO$_4^-$ as counteranion, the bromonium ion can also transfer Br$^+$ to free ADA. The presence of ADA most likely arises from co-precipitation of the olefin during the formation of the bromonium salt, although attack of the counteranion on the Br$^+$, by a reversible formation of the bromonium salt, cannot be excluded.

The molecular mass of the organic cations of the three products has been determined by GC/MS, and corresponds to that of ADA plus Br. We therefore propose that the stability of the salts isolated from the metal-catalyzed reaction mixture is due to the presence of a different counter-ion X$^-$, i.e. a V^{V}- or Mo^{VI}-containing species.

In order to confirm this proposal we have analyzed solutions of the three salts by Electrospray Ionization Mass Spectrometry (ESI-MS)[11][12] both in positive and negative ion mode. With this technique we have observed for the three samples, in positive ion mode, a peak at $m/z = 347$, with the expected isotopic pattern due to the presence of one bromine atom, corresponding to the C$_{20}$H$_{28}$Br$^+$ species, see Figure 2. It should be noted that the theoretical m/z values reported are those of the most abundant peak.

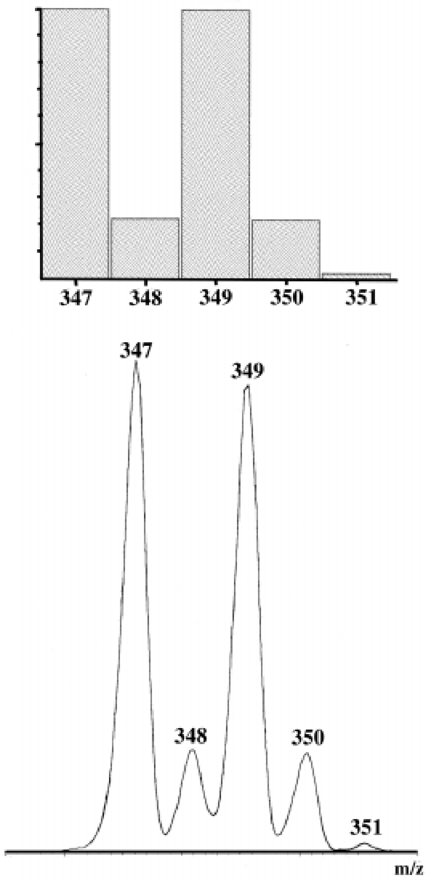

Figure 2. Observed (below) and calculated (above) isotopic distribution patterns of ions at $m/z = 347$

When the analysis was performed in negative ion mode we obtained spectra corresponding to solutions of Br$_3^-$, vanadate and molybdate. In the case of ADA/KBr/KBrO$_3$ the base peak of the mass spectrum corresponds to Br$_3^-$, as shown by the cluster of ions centered at $m/z = 239$ with the expected relative abundances. Peaks at $m/z = 295$ and 376, also present in the mass spectrum, can be assigned to [KHOBr$_3$]$^-$ and [KHOBr$_4$]$^{-\bullet}$ species, respectively, as confirmed by inspection of the experimental isotopic cluster, and are probably formed by clustering during the ESI process. Experiments conducted with the salt isolated from the V^V-catalyzed reaction confirmed the almost exclusive presence of the VO_3^- ion ($m/z = 99$), together with small amounts of an ionic species at $m/z = 117$ corresponding to $[VO_3H_2O]^-$.[13] Interestingly no ions at $m/z = 320$ corresponding to $[H_3V_{10}O_{28}]^{3-}$ were detected.[14]

The salt isolated from the Mo-catalyzed reaction shows a more complex behavior relative to the previous examples, probably due to the known tendency of molybdenum oxyanions to aggregate.[15] Together with the expected ions at $m/z = 163$ $[HMoO_4]^-$ and 207 $[HMoO_4, CH_3CN,H_2O]^-$, characterized by the expected isotopic pattern, formation of ionic species at $m/z = 224$, 296 and 440, corresponding to $[Mo_3O_{10}]^{2-}$, $[Mo_8O_{26}]^{4-}$ and $[Mo_6O_{19}]^{2-}$, respectively, is observed.

In conclusion, the data reported in this paper offer an elegant V^V- or Mo^{VI}-catalyzed method for the synthesis of ADA bromonium ions from hydrogen peroxide and potassium bromide. Further studies are warranted with the scope of improving the yields of pure salts. In particular, our methodology can be applied to the synthesis, from suitably constructed ADA derivatives, of chiral bromonium ions which might be used as chiral Br^+ sources. Our protocol compares well with the more difficult synthesis of the triflate derivatives.[5]

Experimental Section

All the inorganic salts were obtained from commercial sources and were used without further purification. H_2O_2 solutions were prepared by dilution in Milli-Q water of the appropriate amount of commercial (Carlo Erba) solution in water 70% (w/w). $CHCl_3$ was purified by using standard procedures. ADA was synthesized by a known method.[10][16]

Bromination reactions in the two-phase system were carried out in reactors kept at room temperature under magnetic stirring (900 rpm). ADA (0.1 mmol) was dissolved in 5 mL $CHCl_3$. and a solution of KBr (0.3 mmol) and $KBrO_3$ (0.06 mmol) in 5 mL of Milli-Q water at pH 1.1 ($HClO_4$) was added. The mixture was stirred for about two hours. The precipitate formed in the organic phase was collected by filtration at low temperature in the dark. In the metal-catalyzed reaction the aqueous phase contained 0.12 mmols of H_2O_2, 0.105 mmols of KBr at pH 1.1 and 0.12 mmols of NH_4VO_3 or 0.06 mmols of $(NH_4)_2MoO_4 \cdot 2H_2O$, respectively. The metal-catalyzed reactions were kept at room temperature whilst stirring for about 20 hours. All the bromonium salts were subsequently dissolved in the appropriate solvent for the analyses: GC-MS ($CHCl_3$), ^1H NMR(CD_2ClCD_2Cl), ESI-MS ($MeOH/H_2O$, CH_3CN/H_2O, 1:1). ESI conditions: solution flow rate 8μL min^{-1}, capillary temperature 145°C, spray voltage 2.4 kV, capillary voltage ±10−20 V, nebulizing gas N_2 (40 units flow rate).

GC-MS analysis were performed with an HP 5890 gas chromatograph linked to a HP 5970 mass selective detector. ^1H NMR spectra were recorded with a Bruker AC 250 instrument (250.18 MHz for ^1H) or a Bruker DMX-600 (600.13 MHz for ^1H). ESI-MS spectra were obtained with an LCQ instrument (Thermoquest).

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