Competing bromination and oxidation pathways in acid bromate solutions: an experimental and theoretical study †

Gadi Rothenberg,‡ Richard M. H. Beadnall, John E. McGrady and James H. Clark *

Chemistry Department, University of York, Heslington, York, UK YO10 5DD.
E-mail: jhc1@york.ac.uk

Received (in Cambridge, UK) 5th September 2001, Accepted 12th December 2001
First published as an Advance Article on the web 22nd January 2002

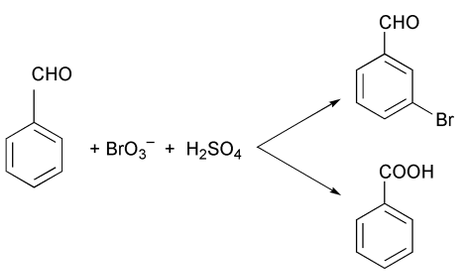
The qualities that render concentrated H_2SO_4–BrO_3 mixtures as powerful bromination and oxidation reagents are examined by following the reactions of acetophenone, cyclohexanol and benzaldehyde, and by using density functional theory (DFT) to study the dissociation of bromic acid ($HBrO_3$) and of bromate ions. The experimental results indicate that acid concentration and substrate type dictate the selectivity between the bromination and oxidation pathways. Supporting this, the computational studies show that the $HBrO_3$ molecule is metastable, its exothermic dissociation to {HOBr + O_2} being opposed by a significant barrier, higher than what is expected for intersystem crossing. The energetics of this dissociation are compared with O-atom transfer in the oxidation of methanol to formaldehyde, and the similar values ($\Delta H^\circ = -40.2$ and -44.6 kcal mol^{-1}, respectively) are consistent with the mixture of bromination and oxidation products observed in some of the experiments (*e.g.* with benzaldehyde). In the case of acetophenone, ring bromination is superseded by bromination of the side chain and debromination of the ring. The hypothesis that this is a rearrangement reaction induced by bromate is examined using substituted bromo- and chloroacetophenones as substrates. The general tendency of organic substrates to undergo fast oxidation and/or bromination in the presence of acid bromate is discussed.

Introduction

Oxidation and bromination processes are omnipresent in laboratory and industrial chemistry, from bulk chemical processing to pharmaceutical synthesis.[1] Although a multitude of reagents and methods are known, there are still cases where high yields are elusive and harsh and/or wasteful protocols are used. For example, the *meta*-bromination of aromatics containing electron-withdrawing groups (PhCHO, $PhNO_2$, *etc.*) is a sluggish process, which requires high temperatures and incurs large amounts of hazardous waste. Several studies have targeted the development of efficient *meta*-bromination protocols, reporting, *e.g.*, the use of HOBr in conjunction with silver or mercury salts,[2] the application of saturated zinc halides as solvents,[3] or the utilisation of acid bromate mixtures.[4,5]

The third option is especially worthy of study, as the combination bromate + acid features some unique chemical properties.[6] Under neutral conditions, alkali metal bromate salts are stable and can be safely kept on the shelf. In the presence of a Brønsted acid, however, they become strong brominating agents that can be used for difficult transformations, such as the bromination of benzaldehyde to 3-bromobenzaldehyde (Scheme 1). Remarkably, the addition of an acid also enhances the oxidative properties of the bromate ion, so much so that mixing bromate and acid with an oxidisable substrate can cause runaway reactions.

This high reactivity generates interest in acid bromate as a cheap and powerful oxidation and bromination reagent. However, the co-existence of two distinct reaction pathways, plus the fact that these fast chemical transformations involve complex equilibria between various species, has precluded the experimental determination of the active species responsible for the oxidation or bromination reactions. In such cases, computational tools may be advantageous.[7]



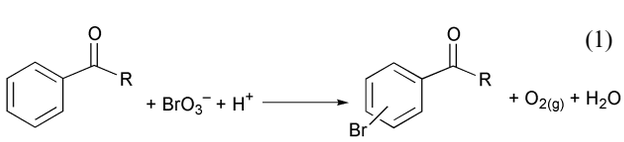
Scheme 1 Oxidation and bromination of PhCHO using acid bromate.

As part of our efforts to develop eco-efficient oxidative halogenation methods,[8] we investigated the application of acid bromate as an oxidation and bromination reagent. In this report, we combine experimental and theoretical methods to demonstrate that the selectivity towards oxidation or bromination when using acid bromate may depend on the specific dissociation pathways of bromic acid, $HBrO_3$.

Results

Bromination of acetophenone

The experiments with acetophenone **1** [eqn. (1)] were carried out at 40–50 °C using equimolar amounts of either potassium or sodium bromate (Table 1). The reaction was fast, with



(1)

R = H, Me

† Electronic supplementary information (ESI) available: details of continuous flow EPR experiments; compound characterisation data (^{1}H NMR, MS) for the bromination of benzaldehyde. See http://www.rsc.org/suppdata/p2/b1/b108009a/

‡ *Current address*: Chemical Engineering Department, Universiteit van Amsterdam, Nieuwe Achtergracht 166, 1018 WV Amsterdam, The Netherlands. E-mail: gadi@science.uva.nl

 DOI: 10.1039/b108009a

Table 1 Bromination of PhCHO and PhCOMe[a]

Substrate	Cation	Conv. (%)	Selectivity (%)[b]		
			ortho	*meta*	*para*
PhCHO	K^+	20	10	85	*tr*
PhCHO	Na^+	30	20	76	1
PhCOMe	K^+	55	16	80	2
PhCOMe	Na^+	75	13	81	1

[a] Reaction conditions: 10 mmol substrate, 130 mmol 50% w/w H_2SO_4, 10 mmol bromate (added in 10 equal portions over 1 h), 1000 rpm magnetic stirring, 40–50 °C. [b] Yields are based on GC area, averaged over three samples for each point. *tr* = trace amount.

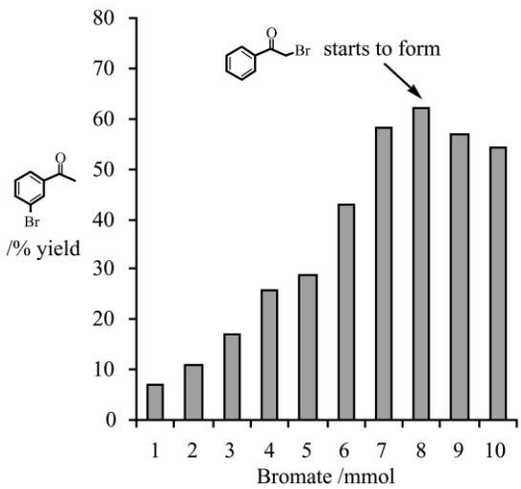


Fig. 1 Yield of *m*-bromoacetophenone **3** *vs.* bromate added to 10 mmol of **1**.

immediate evolution of gas after each bromate addition. Initially, the system became biphasic, with a dark brown organic layer forming on top of the lower aqueous layer. With continuous stirring the system returned to a monophasic solution in less than two minutes. A typical reaction profile is shown in Fig. 1. Note the decrease in the amount of *m*-bromoacetophenone **3** after 8 mmol of bromate has been added. This is due to the formation of phenacyl bromide **5** at the expense of **3**. If an excess of sodium bromate is used in the system, the consumption of **3** can be forced to progress further, yielding larger quantities of **5** together with di- and tri-brominated heavy compounds in the reaction mixture.[9] A reaction profile using two equivalents of sodium bromate with respect to substrate is shown in Fig. 2. Using a threefold excess of bromate did not affect the product distribution (after 2 equiv. of bromate were added, further bromate additions resulted in the nonproductive exothermic decomposition of the bromate to molecular bromine). Note, too, that similar results were observed when the *para*-isomer **4** was used instead of **3**.

Previous studies have demonstrated the crucial role played by the acid concentration in the bromination of deactivated aromatics using bromate salts.[4] In a series of experiments at various acid concentrations, a sharp increase in conversion was observed for the runs using 7 M acid and 10 M acid between 1–2 mmol bromate and 5–6 mmol bromate added, respectively. This similarity may indicate that the acid is consumed during the reaction and that for the bromination of acetophenone the optimal acid concentration is about 6 M.

Reactions of bromoacetophenones with acid bromate

The consumption of bromoacetophenone in this system to give phenacyl bromide is of interest, especially since the latter is not observed before a substantial amount of bromoacetophenone

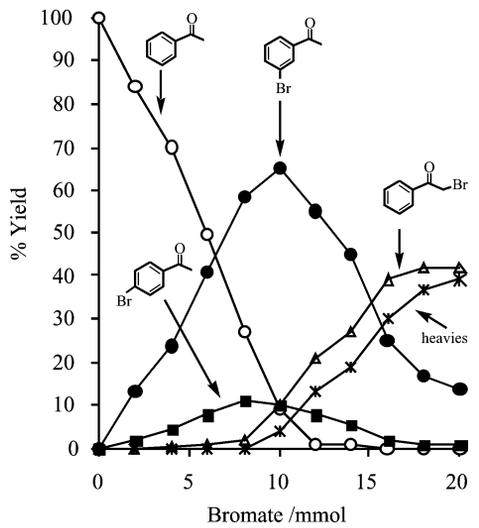
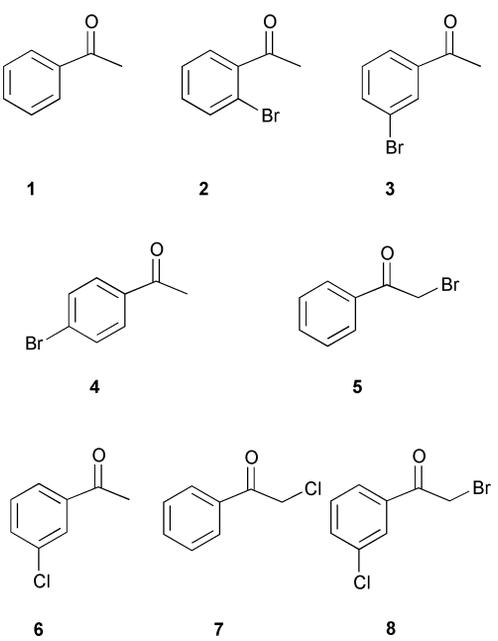


Fig. 2 PhCOMe conversion and product distribution as a function of added bromate.



has formed. We tested this reaction further, using pure **2**, **3**, and **4** as substrates. In all three cases, the same formation of **5** was observed as for the *m*-bromoacetophenone which was formed in the original reaction with **1**. Moreover, repeating this series of experiments using varied amounts of sodium bromate showed that *this reaction required a stoichiometric equivalent of bromate*.

The reaction profiles and product distribution using acetophenone and bromoacetophenone raise doubts about whether the alkyl bromine atom originates from the bromate ion. Moreover, the experiments using pure **2**, **3**, and **4** as substrates show that **5** may be formed through an intramolecular process, as neither acetophenone **1** nor any of the other monobrominated compounds was observed (*i.e.* when **2** was used as a substrate, **3** and **4** were not observed). Note that under the same reaction conditions the reactions using **2**, **3**, and **4** proceeded at similar rates.[10] This suggests that the formation of **5** from any bromoacetophenone is not a concerted process, because then different reaction rates could be expected for the different substrates.

Analogous experiments were run using *m*-chloroacetophenone **6**, reasoning that phenacyl chloride **7** may be obtained. Instead, there was exclusive ring bromination of the starting material, and further reaction yielding bromochlorophenacyl

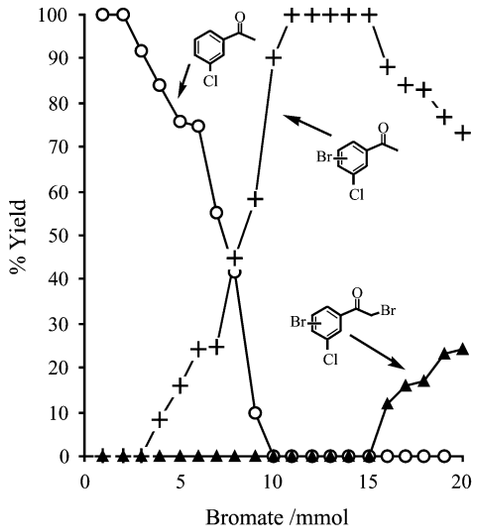


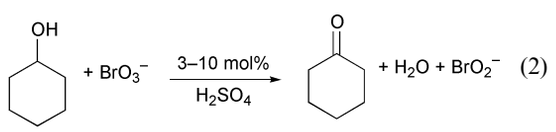
Fig. 3 Reaction of *m*-chloroacetophenone in the presence of acid bromate.

bromide occurred only when more than one and a half equivalents of bromate were added (Fig. 3). Remarkably, **7** and *m*-chlorophenacyl bromide **8** were not observed.

We also attempted to observe possible paramagnetic intermediates in the reaction **3**⟶**5** using electron paramagnetic resonance (EPR). Due to the fast reaction between **3** and acid bromate, pre-mixed samples did not show any EPR activity, but in continuous flow EPR experiments some free-radical species were observed. Unfortunately, the resolution was not high enough to assign their structure (see the supplementary material for full details of the EPR experiments).

Reactions of cyclohexanol and benzaldehyde with acid bromate

In a typical reaction [eqn. (2)] equimolar amounts of



cyclohexanol (CyOH) and $KBrO_3$ or $NaBrO_3$ were stirred for 2–3 min in refluxing CH_2Cl_2, after which a predetermined amount of concentrated H_2SO_4 was added to the mixture. Reaction progress was monitored by GC. The major product was cyclohexanone, plus small amounts (*ca.* 1–2%) of heavy compounds which were not characterised.

No conversion (<1%) of the alcohol was observed in the absence of either BrO_3^- or H_2SO_4 (even when 100 mol% of H_2SO_4 was used). In the presence of BrO_3^-, however, 10 mol% of acid was sufficient to effect >95% conversion of the alcohol to the ketone. These results are in good agreement with the acid-catalysed bromate oxidation observed for aromatic aldehydes[11] and benzylic alcohols.[12] Note that in oxidation reaction with acid bromate the bromous acid can also react further or disproportionate under the reaction conditions.

The bromination of benzaldehyde was carried out in a similar manner to the reactions with acetophenone [see eqn. (1) and Table 1 above]. Benzaldehyde can react with acid bromate either as a reductant (to form benzoic acid) or as a "Br^+" acceptor, to give ring-bromination (chiefly to *m*-bromobenzaldehyde). Previously, it was hypothesised[11] that the oxidation of benzaldehyde using acid bromate proceeds through the formation of an intermediate compound, which was postulated to be an organic bromate ester. This ester could form through the reaction of benzaldehyde with either BrO_3^- or $HBrO_3$ (Scheme 2). Although the ester intermediate could not be isolated or observed using the tools available at that time, Sen Gupta and co-workers[11] deduced its existence from rigorous kinetic experiments.

Using attenuated total reflection (ATR) spectroscopy, we have now observed direct interactions between BrO_3^- and benzaldehyde. Thus, 50 mM solutions of BrO_3^- and benzaldehyde in DMSO showed upon mixing three main spectral changes pointing to an interaction between the bromate ion and the carbonyl group: a shift in the C=O stretch from 1723 to 1706 cm^{-1}, and two new peaks, at 1359 and at 1219 cm^{-1}, respectively. This weakening of the C=O bond would be expected when an organic-inorganic ester forms.

Table 2 Absolute energies

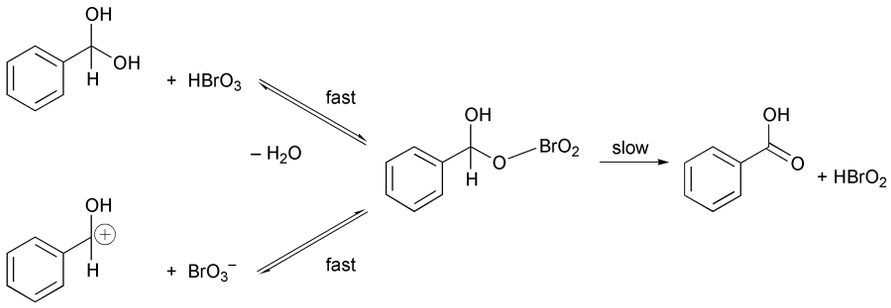
Species	Energy/kcal mol^{-1}
$HBrO_3$	−416.0
BrO_3^-	−378.2
$HBrO_2$	−319.0
BrO_2^-	−262.2
HOBr	−234.8
OBr^-	−161.5
O_2 (triplet)	−221.4
O_2 (singlet)	−193.7
O (^3P)	−37.8
H_2O	−322.4
CH_3OH	−685.2
CH_2O	−504.4

Computational studies

Here, we used density functional theory to complement the experimental results presented above. It has previously been suggested that bromination occurs *via* decomposition of $HBrO_3$ to HOBr and O_2, with subsequent protonation of the hypobromous acid generating Br^+ *in situ*.[13] The oxidation, in contrast, was thought to proceed by oxygen atom transfer, *via* a bromate ester, resulting in the formation of $HBrO_2$. We have investigated the principal electronic features and energetics of both these pathways. The total energies of the optimized structures of all calculated species are collected in Table 2.

Bromination: dissociation of $HBrO_3$ into HOBr and O_2

As noted above, solutions of the bromate ion, BrO_3^-, are found to be stable, while addition of acid results in decomposition. Our initial goal was therefore to compare the energetics of the two reactions, $BrO_3^- \longrightarrow \{OBr^- + O_2\}$ and $HBrO_3 \longrightarrow \{HOBr + O_2\}$. The optimized structure of the bromate anion has C_{3v} symmetry, with Br–O bond lengths of 1.77 Å. Protonation of one of the three oxygen atoms reduces the symmetry to C_s, and optimisation (starting from the structure of the anion) results in an increase of the protonated Br–O bond length to 2.02 Å, while the other two contract somewhat to 1.71 Å. In contrast, the structures of the hypobromous acid and its anion are very similar, with Br–O bond lengths of 1.92 and 1.91 Å, respectively. A comparison of the energetics of the anionic and protonated species reveals that the release of O_2 is exothermic in both cases, by 40.2 kcal mol^{-1} for $HBrO_3$ (Fig. 4), but by only 4.7 kcal mol^{-1} for the anion. Thus, on purely thermodynamic grounds, both BrO_3^- and $HBrO_3$ should decompose spontaneously with evolution of O_2. The origin of their stability can be traced, at least in part, to the triplet ground state of the oxygen molecule, which necessitates an intersystem crossing along the reaction pathway (the $^3A'$ state in Fig. 4). Such a change in spin state is, however, likely to be rapid in the presence of a heavy atom such as bromine, so that the intersystem crossing barrier is unlikely to be solely responsible for the kinetic stability. Indeed, for the protonated species, the decomposition into $\{HOBr + O_2\}$ in its excited



Scheme 2 Formation of bromate ester intermediate in the case of the hydrated form (top) or the protonated form (bottom) of benzaldehyde. In both cases, the resulting $HBrO_2$ species can oxidise another two aldehyde molecules.

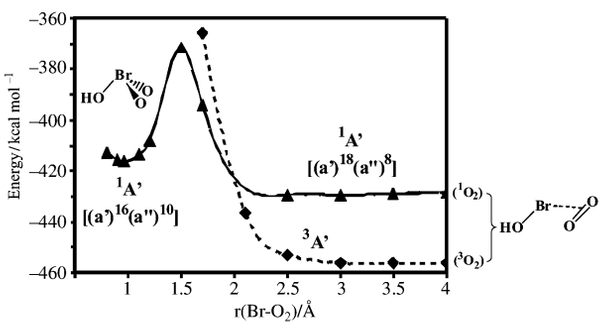


Fig. 4 Potential energy curves for the dissociation of $HBrO_3$ to {HOBr + O_2} on the singlet and triplet surfaces. The abscissa represents the distance from the Br atom to the midpoint between two oxygen atoms.

singlet state is still found to be strongly exothermic (−12.5 kcal mol^{-1}, Fig. 4), suggesting that the change of spin state is not the dominant factor.

The potential energy curve for the singlet state, $^1A'$ (shown in Fig. 4) reveals an alternative explanation for the stability of BrO_3^- salts and for the apparent metastability of $HBrO_3$. There is a significant barrier between $HBrO_3$ and {HOBr + O_2}, rising as a result of a change in electronic configuration from $(a')^{16}(a'')^{10}$ {$HBrO_3/BrO_3^-$} to $(a')^{18}(a'')^8$ {$HOBr/OBr^-$ + $^1O_2$}. This barrier is sufficient to prevent the spontaneous decomposition of $HBrO_3$. For the bromate anion, the lower exothermicity of the decomposition reaction will lead to an even larger barrier, consistent with the stability of BrO_3^- salts.

Oxidation: oxygen atom transfer leading to {$HBrO_2$ + O}

In contrast to the decomposition into {HOBr + O_2}, the oxygen atom transfer is rather more difficult to model computationally, as the free oxygen atom is not a chemically reasonable species. As a result, the dissociation of $HBrO_3$ into {$HBrO_2$ + O (^3P)} is highly endothermic (59.2 kcal mol^{-1}). The oxidation reaction pathway can, however, be modeled more realistically by supplying a substrate, in this case MeOH, to act as an O atom acceptor. The resulting isodesmic reaction [eqn. (3)] is

$$CH_3OH + HBrO_3 \longrightarrow H_2C{=}O + H_2O + HBrO_2 \quad (3)$$
$$\Delta H^\circ = -44.6 \text{ kcal mol}^{-1}$$

exothermic by −44.6 kcal mol^{-1}, which is very close to the value for O_2 dissociation. Moreover, the energetics of O atom transfer will necessarily depend on the substrate. In certain cases, the two reactions, oxygen-atom transfer (leading to oxidation) and O_2 loss (leading to bromination) may be competitive, giving rise to the product mixtures observed, for example, in the case of benzaldehyde.

The calculations illustrate a number of important points that relate to the experimental observation. First, both BrO_3^- and $HBrO_3$ are thermodynamically unstable with respect to decomposition to O_2 and HOBr. A change in electronic configuration along the dissociation pathway, however, renders both species kinetically stable, albeit to a lesser extent for the protonated species. This metastability allows the bimolecular oxygen-atom transfer reaction to compete with O_2 loss, leading to a mixture of products. Note that although our calculations pertain to the gas phase and some discrepancies with the experimental liquid phase system could be expected, significant differences between the bromate ion and bromic acid are observed, which are in good agreement with the experimental results.

Discussion

When evaluating the oxidation and bromination mechanisms using acid bromate it is important to remember that the system is very sensitive to changes in substrates and/or conditions. This is a result of the presence of three simultaneous processes (oxidation, bromination, and violent decomposition of bromate to bromine and oxygen at high acid concentrations). Since the energetics of these three processes are comparable, changing the substrate or slightly changing the reaction conditions may result in dramatic effects.[14]

As mentioned above, it has previously been suggested that in bromination reactions using acidic solutions of bromate, decomposition to HOBr and O_2 occurs and the bromination is due to the reaction of the "bromonium" ion which is formed in the equilibrium $HOBr + H^+ \rightleftharpoons [H_2OBr]^+ \rightleftharpoons \{H_2O + \text{“}Br^+\text{”}\}$.[12] These earlier studies were performed in dilute acidic solutions, and any extrapolation of the results to concentrated systems should be done cautiously.[15] We suggest that the two dissociation pathways of $HBrO_3$ may be responsible for the bromination and the oxidation reactions, respectively. Which of the two pathways dominates will depend on the substrate and on the acidity of the medium. Thus, for substrates such as CyOH or benzaldehyde, the facile formation of the bromate ester would result in the oxidation pathway dominating, while for $PhNO_2$, according to Harrison *et al.*,[4a] only bromination occurs. At high acid concentrations (>75% w/w H_2SO_4) bromate decomposes to molecular bromine. A summary of the possible reactions for various substrate types is given in Table 3.

Regarding the transformation of the bromoacetophenones **2**, **3**, and **4** to **5**: this reaction consumes 1 molar equivalent of bromate, and the experimental results indicate that it is not a concerted process. The bromination of the aromatic ring is reversible, and depends on the relative concentrations of Br_2 and Br^-, as was demonstrated recently by Choi and Chi.[16] In the presence of acid bromate the equilibrium (4) would

$$BrO_3^- + 5Br^- + 6H^+ \rightleftharpoons 3H_2O + 3Br_2 \quad (4)$$

favour the product side, so that only small amounts of debromination would be expected. Moreover, bromination–debromination equilibria do not explain why **5** does not

Table 3 Summary of reactions in acid bromate systems

Substrate type	Acid conc.	Intermediate	Result
Oxidation only *e.g.* CyOH	Low	Bromate ester	Oxidation
	Medium	Bromate ester	Oxidation
	High	Bromine	Decomposition
Bromination only *e.g.* $PhNO_2$[a]	Low	—	No reaction
	Medium	$[H_2OBr]^+$	Bromination
	High	Bromine	Decomposition
Oxidation and bromination *e.g.* PhCHO	Low	Bromate ester	Oxidation
	Medium	$[H_2OBr]^+$	Bromination
	High	Bromine	Decomposition

[a] See ref. 4*a*.

form directly from **1** or why a bromate ion is needed for the formation of **5**. Apparently there are two different mechanisms, one for ring bromination (*vide supra*) and one for side-chain bromination. The latter could be a free-radical reaction, in which a $Br^{\bullet}$ radical, formed from a reaction between $HBrO_3$ and "Br^+", undergoes Markownikoff addition[17] to the enol tautomer of the substrate.

The fast reactions of acetophenone and bromoacetophenones in this system preclude the derivation of precise kinetic constants, but from the analogous reaction of **6** we may infer that in this case the "rearrangement" of a Cl atom is much slower than the bromination of the ring. Indeed, the scission of the Ar–Cl bond would be expected to be much slower than that of its Ar–Br equivalent.[18] Furthermore, the absence of the intermediate **8** in the reaction that forms bromochlorophenacyl bromide is significant, as it indicates that **8** is brominated even faster than **6**. It is unlikely that direct attack of the bromate Br atom on the side-chain occurs, as no side-chain bromination is observed before all of the substrate has undergone ring bromination.

In conclusion, we propose that the mixture of products obtained in the reaction of organic substrates with acid bromate mixtures stems from the metastable nature of bromic acid, $HBrO_3$. Decomposition of the latter to {HOBr + O_2}, followed by protonation of HOBr leads to bromination, while oxygen-atom transfer (to an appropriate oxygen acceptor) results in oxidation *via* a bromate ester. The harnessing of this chemically reactive system for effective synthesis is a two-sided issue, as the exothermicity can be a problem, but the stability of the bromate salt and the fact that acid bromate mixtures can be more reactive than molecular bromine may lead to more applications of this reagent combination in the future.

Experimental

^{1}H NMR spectra were measured on a JEOL 270 instrument at 270 MHz in $CDCl_3$. δ_H values are reported in ppm relative to Me_4Si. GC analysis was performed on a Varian 3800 instrument fitted with a DB-5 capillary column. Low-resolution EI GCMS was performed on a Micromass Autospec instrument connected to a HP 5980 GC with a Supelco MN5 column (30 m × 0.25 mm).

EPR spectra were recorded on a Bruker ESP-300 spectrometer equipped with an X-band klystron and 100 kHz modulation. All solutions were deoxygenated both prior to and during use by purging with oxygen-free nitrogen. Deionised water was used for all experiments. ATR measurements were performed using a Nicolet Magna IR 760 spectrometer with a SpectraTech variable-angle ATR attachment.[19] All chemicals were purchased from commercial firms (>98% pure) and used without further purification. All products are known compounds and were identified by comparison of their ^{1}H NMR, spectra, MS data and GC retention times to standard samples. Reactions were performed in glass apparatus in thermoregulated oil baths in a fume hood.

CAUTION! Mixing of BrO_3^- salts and H_2SO_4 results in a strong exothermic reaction. A bucket of crushed ice should be kept handy to quench possible runaway reactions. Extreme caution should be taken if scaling up these procedures.

General procedure for bromination using acid bromate

Example: bromination of acetophenone 1 with H_2SO_4 and $NaBrO_3$. 8.0 mL (440 mmol) water were poured into a two-necked, round-bottomed flask fitted with a reflux condenser and a magnetic stirring bar. Then, 8.0 mL (130 mmol) of 98% w/w sulfuric acid were added dropwise to the flask while stirring. 1.2 mL (10 mmol) of acetophenone were added and the stirring rate was increased to >1000 rpm. Sodium bromate was added in 1 mmol portions at regular time intervals until 1.49 g (10 mmol) had been added (typically 1 h). Samples were taken after each addition of bromate, extracted in 2 mL ether, washed with 2 mL 30% aq $Na_2S_2O_3$, and analysed by GC [ramp at 15 °C min^{-1} from 50 °C to 250 °C, t_R (min) **1** 2.8; **2** 5.9; **3** 6.3; **4** 7.0; **5** 8.3]. Reaction profiles were based on the average of three separate measurements. Spectral data: **1** M^+ 120; *m*/*z* = 105 (100%), 77 (82), 51 (34), 120 (25), 43 (16), 74 (7), 39 (6); δ_H 8.0 (d), 7.6–7.4 (m), 2.6 (s). 2-Bromoacetophenone **2** δ_H 7.6 (d), 7.4–7.2 (m), 2.6 (s). 3-Bromoacetophenone **3** M^+ 198; *m*/*z* = 183 (100%), 155 (49), 43 (38), 76 (37), 198 (35), 50 (32), 38 (6); δ_H 8.1 (s), 7.9 (d), 7.7 (d), 7.3 (t), 2.6 (s). Phenacyl bromide **5** M^+ 200; *m*/*z* = 105 (100%), 77 (41), 200 (21), 51 (20), 120 (12), 91 (12); δ_H 8.1 (s), 7.9 (d), 7.7 (d), 7.3 (t), 2.6 (s).

Oxidation of cyclohexanol

1.0 g (10 mmol) CyOH was added to a flask as above containing 10 mL water and 10 mL CH_2Cl_2. The mixture was heated to reflux and after 2–3 min 1.67 g (10 mmol) $KBrO_3$ and predetermined quantities of conc. H_2SO_4 were added. The reaction was stirred for 5 h, quenched with 30% aq $Na_2S_2O_3$ and analysed by GC [t_R (min) CyOH 8.6; Cy=O 9.3].

Computational methods

All calculations described in this work were performed using the Amsterdam Density Functional (ADF) program developed by Baerends *et al.*[20] The local density approximation to the exchange potential was used, along with the correlation potential of Vosko *et al.*[21] Gradient corrections to exchange (Becke[22]) and correlation (Perdew[23]) were also included. A double-ζ Slater-type orbital basis set extended with a single d-type polarization function was used to describe all elements. Electrons in orbitals up to and including 1s {O, C} and 4d {Br} were considered to be part of the core and treated in accordance with the frozen core approximation. All geometries were fully optimized using the algorithm of Versluis and Ziegler.[24] Potential energy curves were generated by fixing the distance from the Br atom to the midpoint between two oxygen atoms, and allowing all other independent parameters to optimize freely.

Acknowledgements

We thank Dr A. C. Whitwood and Dr R. Sayer (University of York) for performing the EPR and ATR measurements, the EPSRC and Contract Chemicals Ltd for financial support (to RMHB) and the European Commission for a Marie Curie Individual Research Fellowship (to GR).

References

1 For recent reviews on bromination, see (*a*) S. D. R. Christie, *J. Chem. Soc., Perkin Trans. 1*, 1999, 737; (*b*) R. S. Brown, *Acc. Chem. Res.*, 1997, **30**, 131. On oxidation (*c*) M. Besson and P. Gallezot, *Catal. Today*, 2000, **57**, 127; (*d*) S. Imamura, *Ind. Eng. Chem. Res.*, 1999, **38**, 1743; (*e*) For a monograph, see R. A. Sheldon and J. K. Kochi, *Metal Catalyzed Oxidations of Organic Compounds*, Academic Press, New York, 1981.

2 These salts are used to scavenge the bromide ions from the solution so that the formation of molecular bromine is minimised, see (*a*) T. J. Broxton, L. W. Deady, J. D. McCormack, L. C. Kam and S. H. Toh, *J. Chem. Soc., Perkin Trans. 2*, 1974, 1769; (*b*) C. S. Reddy and E. V. Sundaram, *Tetrahedron*, 1989, **45**, 2109.

3 A. Ewenson, D. Itzhak, M. Freiberg-Bergstein, A. Shushan, B. Croitoru, D. Beneish and N. Faza, WO 99/19275 (to Bromine Compounds Ltd).

4 (*a*) J. J. Harrison, J. P. Pellegrinia and C. M. Selwitz, *J. Org. Chem.*, 1981, **46**, 2169; (*b*) A. Groweiss, *Org. Process Res. Dev.*, 2000, **4**, 30.

5 Bromination using HOBr generated from bromate and an inorganic reducing agent such as $NaHSO_3$ was also reported, see (*a*) D. Kikuchi, S. Sakaguchi and Y. Ishii, *J. Org. Chem.*, 1998, **63**, 6023; (*b*) H. Ohta, Y. Sakata, T. Takeuchia and Y. Ishii, *Chem. Lett.*, 1990, 733.

6 Herein the term *acid bromate* refers to a solution or a mixture of a bromate salt and a strong concentrated Brønsted acid, *e.g.* $KBrO_3$ + 50% w/w H_2SO_4.

7 For example, numerical methods have been used to determine the equilibrium relationship between the various primary species in bromination reactions. See A. N. Shevelkova, Y. I. Sal'nikov, N. L. Kuz'mina and A. D. Ryabov, *FEBS Lett.*, 1996, **383**, 259.

8 (*a*) G. Rothenberg and J. H. Clark, *Green Chem.*, 2000, **2**, 248; (*b*) G. Rothenberg and J. H. Clark, *Org. Process Res. Dev.*, 2000, **4**, 270.

9 The identity of these products was determined by GCMS and ^{1}H NMR as (in descending order of quantity) dibromoacetophenone, tribromoacetophenone, bromophenacyl bromide and dibromophenacyl bromide.

10 A kinetic analysis could not be performed due to the high acid concentration and speed of the reaction. However, a rough estimation of the reaction rate was obtained from the comparison of end-of-reaction times.

11 K. K. Sen Gupta, H. Samaddar, P. K. Sen and A. Banerjee, *J. Org. Chem.*, 1982, **47**, 4511.

12 K. K. Sen Gupta, S. C. Kumar, P. K. Sen and A. Banerjee, *Tetrahedron*, 1988, **44**, 2225.

13 (*a*) C.-Z. Dong, M. Julia and J. Tang, *Eur. J. Org. Chem.*, 1998, 1689; (*b*) W. J. Wilson and F. G. Soper, *J. Chem. Soc.*, 1949, 3376.

14 To give two examples: in the bromination of nitrobenzene it was found that the yield of 3-bromonitrobenzene was nil below 50% w/w H_2SO_4, then rose sharply to 90% at 68% w/w H_2SO_4, and dropped to 15% at 70% w/w H_2SO_4 (all data from ref. 4*a*). In the case of benzaldehyde, which can undergo both oxidation and bromination reactions, it was found that 39% w/w H_2SO_4 was the optimal concentration to maximise 3-bromobenzaldehyde yield, provided that the temperature was kept at 90–100 °C, since under those reaction conditions $k_{oxidation} > k_{bromination}$ (see ref. 4*b*).

15 A specific study dealing with the kinetics of electrophilic aromatic bromination under dilute acidic conditions showed that it is unlikely that "Br^+" itself exists in solution, and that a better explanation would be the reaction of an {ArH + H_2OBr^+} complex in the rate-determining step. See H. M. Gilow and J. H. Ridd, *J. Chem. Soc., Perkin Trans. 2*, 1973, 1321.

16 H. Y. Choi and D. Y. Chi, *J. Am. Chem. Soc.*, 2001, **123**, 9202.

17 For a discussion, see N. S. Isaacs, *Physical Organic Chemistry*, Longman, Essex, 1987 pp. 740–743.

18 For recent studies on Ar–X bond scissions, see (*a*) L. Pause, M. Robert and J.-M. Savéant, *J. Am. Chem. Soc.*, 1999, **121**, 7158; (*b*) A. B. Pierini, J. S. Duca, Jr. and D. M. A. Vera, *J. Chem. Soc., Perkin Trans. 2*, 1999, 1003.

19 The spectra were recorded using a horizontally mounted trapezoid germanium internal reflection element (IRE) (81 × 11 × 4 mm, 60° bevel). Data acquisition of single-beam background spectrum of the bare IRE was accomplished using the Omnic ESP software. Measurements were performed at 2 cm^{-1} resolution (256 scans). W. R. Fawcett, G. Liu and A. A. Kloss, *J. Chem. Soc., Faraday Trans.*, 1994, 2697.

20 ADF 2.3.0, Theoretical Chemistry, Vrije Universiteit, Amsterdam; (*a*) E. J. Baerends, D. E. Ellis and P. Ros, *Chem. Phys.*, 1973, **2**, 41; (*b*) G. te Velde and E. J. Baerends, *J. Comput. Phys.*, 1992, **99**, 84; (*c*) C. Fonseca Guerra, J. G. Snijders, G. te Velde and E. J. Baerends, *Theor. Chem. Acc.*, 1998, **99**, 391.

21 S. H. Vosko, L. Wilk and M. Nusair, *Can. J. Phys.*, 1980, **58**, 1200.

22 A. D. Becke, *Phys. Rev. A*, 1988, **38**, 3098.

23 J. P. Perdew, *Phys. Rev. B*, 1986, **33**, 8822.

24 L. Versluis and T. Ziegler, *J. Chem. Phys.*, 1988, **322**, 88.