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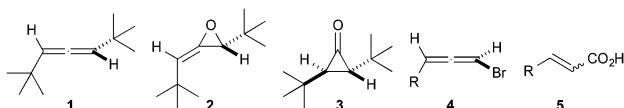
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The first stable bromoallene oxides were obtained by the DMDO epoxidation of 1-bromo-1,3-di-*tert*-alkylallenes, producing the first crystalline allene oxide of any kind. The epoxidations are regioselective for the bromine-bearing $\Delta^{1,2}$ alkene, and also face selective producing single diastereomer *E*-olefin products.

The allene oxide functional group and its valence tautomeric cyclopropanone and oxyallyl cation forms are of significant interest.^{1,2} The first room-temperature stable allene oxide was reported in 1968 by peracid epoxidation of 1,3-di-*tert*-butylallene **1** to give epoxide **2**.^{‡,3} It was subsequently converted into its corresponding isomeric cyclopropanone **3** on heating thereby establishing their relative thermodynamic stabilities. However, despite this early success, only a handful of further allene oxides have been successfully characterised.^{4–10} Nevertheless, these studies have helped to establish that stable allene oxides can be obtained when (i) the epoxide is kinetically stabilised by steric protection against S_N2 attack, and (ii) when cyclopropanone formation *via* the presumed intermediacy of an oxyallyl cation is non-favoured.^{1c}



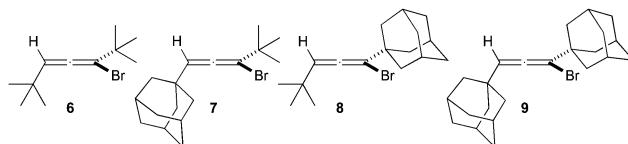
We have recently reported¹¹ that DMDO epoxidation of 3-*n*-alkyl-1-bromo-allenes **4** give rise directly to α,β -unsaturated carboxylic acids **5** by presumed spontaneous rearrangement of bromo-allene oxides – an unprecedented functional group in the literature¹² – to bromocyclopropanones and subsequent Favorskii rearrangement.

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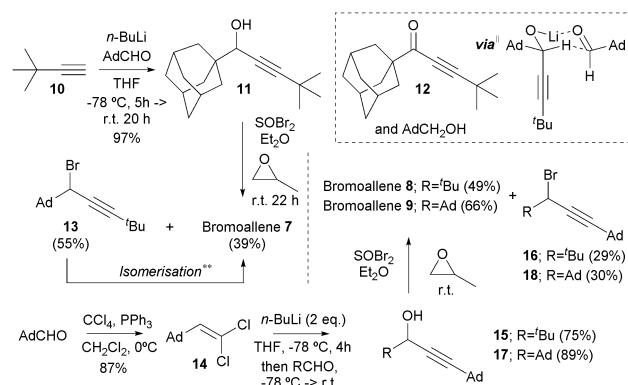
† Electronic supplementary information (ESI) available: Experimental procedures and characterising data for **7–9**, **11–24**; copies of ^1H and ^{13}C NMR spectra for all compounds including NOE, DEPT-135, correlation spectroscopy and bromide induced isotopic shifts where appropriate. CCDC 1485934 (**9**) and 1485935 (**19**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c6cc06395k

In that work, an analysis of the mechanism revealed that epoxidation of either olefin of the bromoallene would lead to the same product and so the site of initial epoxidation could not be identified. With the intention of identifying the preferred position of epoxidation in bromoallenes, we now report the first stable bromoallene oxides.



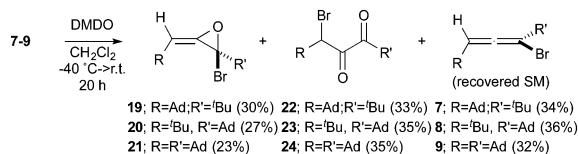
With the above literature precedents in mind, we selected known 1-bromo-1,3-di-*tert*-butylallene **6** – reported as a colourless liquid – as a suitable substrate for epoxidation.¹³ However, in our hands it proved to be inseparable from its propargylic bromide isomer, was found to be somewhat volatile, and consequently epoxidation experiments proved inconclusive. Instead, we targeted novel adamantyl-containing bromoallenes **7–9**, which proved to overcome these difficulties (*vide infra*).

Bromoallene **7** was prepared by the initial lithiation of terminal alkyne **10** and addition to adamantanecarboxaldehyde[§] to give propargylic alcohol **11** (Scheme 1). Temperature control in this



Scheme 1 Synthesis of bromoallenes **7–9** (Ad = 1-adamantyl).





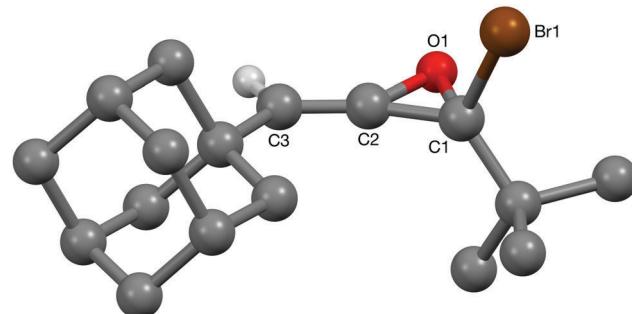
Scheme 2 Epoxidation of bromoallenes 7–9.

transformation proved critical, otherwise significant quantities of ketone **12** and 1-adamantanemethanol were formed.[¶] Using the conditions of Corey,¹³ alcohol **11** was transformed into bromoallene **7** along with the expected, but now separable, propargylic bromide **13**.^{**} Next, the action of the carbon tetrachloride–triphenylphosphine reagent combination¹⁴ on adamantanecarboxaldehyde as a α,α,α -trisubstituted aldehyde provided ready access to vinylidichloride **14**¹⁵ free from any complicating dichloroalkane formation.¹⁶ Corey–Fuchs type acetylidy anion formation,¹⁷ and *in situ* trapping¹⁸ with pivaldehyde and adamantanecarboxaldehyde gave propargylic alcohols **15** and **17** respectively in good yields.^{††} Bromoallenes **8** and **9** were subsequently obtained by subsequent reaction with thionyl bromide along with the corresponding expected, and again separable, propargylic bromides **16** and **18**.^{‡‡}

The incorporation of adamantyl groupings rendered the three bromoallenes **7–9** to be solid, bromoallene **9** proved to be crystalline, and its structure was solved by X-ray crystallography.^{‡§§} With these compounds in hand, attention turned to epoxidation.^{¶¶}

In the event, epoxidation of each of bromoallenes **7–9** with DMDO¹⁹ provided monoepoxidation products as *E*-1-bromoallene oxides **19–21**^{||} as single diastereoisomers respectively, along with bromodiketones **22–24**,^{***} and recovered bromoallene starting materials after column chromatography (Scheme 2).^{†††} Importantly, under the conditions of the experiment and the isolation and purification regime, there was no evidence for the formation of any corresponding α,β -unsaturated carboxylic acids *via* intersecting bromoallene oxide–bromocyclopropanone–Favorskii rearrangement.¹¹ These experiments therefore establish that (i) bromoallene oxides of this type are kinetically stabilised with respect to rearrangement by the bulky alkyl substituents; (ii) for these bromoallenes, epoxidation occurs preferentially at the bromine-bearing $\Delta^{1,2}$ alkene and (iii) epoxidation occurs with complete face selectivity away from the alkyl grouping at C-3 of the allene.^{‡‡‡} Moreover, the uniformity of the product distributions obtained with the different bromoallenes **7–9** show that the *tert*-butyl and adamantyl groups behave as effectively identical and interchangeable substituents in this situation, but with the advantage that the incorporation of an adamantyl group increases the prospect of crystallinity. Indeed, bromoallene oxide **19** proved to be crystalline and its structure was determined by X-ray crystallography (Fig. 1). To the best of our knowledge this is the first X-ray crystallographic structural elucidation of any allene oxide.^{§§§}²⁰

We probed the origins of the observed regioselectivity and diastereoselectivity using DFT theory (ω B97XD/TZVP, QZVP/PCM = acetone as continuum solvent).²¹ An NBO analysis on

Fig. 1 X-ray crystal structure of bromoallene oxide **19**.

representative reactant bromoallene **6** reveals the $\Delta^{2,3}$ localized occupied π -orbital is higher in energy (by 0.014 Hartree) than the $\Delta^{1,2}$ orbital, suggesting that the intrinsic electronic nucleophilic reactivity of the allene is at the 2,3 position. However, transition state models of the reaction with DMDO as electrophile reveals the 1,2 isomers are 1.2 (QZVP) or 1.4 (TZVP) kcal mol⁻¹ lower in ΔG_{298}^\ddagger for bromoallene **6** and 1.2 (TZVP) for bromoallene **9**. For the simplest possible bromoallene ($\text{H}_2\text{C}=\text{C}=\text{CHBr}$, not shown) the 2,3 transition state at the π -face *anti*-periplanar to the Br is favoured by 0.4 kcal mol⁻¹ over the 1,2 isomer and by 1.3 kcal mol⁻¹ over 2,3-*syn*-periplanar attack (TZVP). Taken together, these calculations reveal that although the bromine atom is inherently deactivating for the $\Delta^{1,2}$ olefin, it also acts to sterically protect the *syn*-periplanar face of the $\Delta^{2,3}$ olefin. For bromoallenes **7–9**, since the bulky alkyl group on C-1 protects the other face of $\Delta^{2,3}$ olefin and the C-3 alkyl group inhibits Z-1-bromoallene oxide formation, $\Delta^{1,2}$ attack leading to the *E*-1-bromoallene oxides **19–21** emerges as the most facile.

In conclusion, we have demonstrated that stable bromoallene oxides can be obtained by DMDO epoxidation of 1-bromo-1,3-di-*tert*-alkylallenes, and the first X-ray crystal structural elucidation of any allene oxide has thereby been accomplished. The epoxidation for these bromoallenes is selective for the bromine-bearing $\Delta^{1,2}$ alkene, and with exclusive face selectivity to produce *E*-1-bromoallene oxides.^{¶¶¶} The thermal stability of these bromoallene oxides is the subject of current investigations and will be reported in due course.

We thank Mr Jaren Soo for preliminary investigations with compound **6**.

Notes and references

[‡] Interestingly, a definitive structure for allene oxide **2** was not given in the original report and two geometrical isomeric structures were proffered. Our results (*vide infra*) support this to be the *E*-allene oxide as drawn.

[§] Readily prepared from 1-adamantanemethanol by PCC oxidation.[‡]

[¶] See ESI[†] for experimental details. See also ref. 21.

^{||} We invoke an unprecedented irreversible hydride transfer from the initially formed secondary lithium alkoxide $\text{AdCH}(\text{C}\equiv\text{C}^*\text{Bu})\text{OLi}$ to still unreacted AdCHO in a concerted six-membered TS to explain this observation. In this process steric compression of the adamantyl- sp^3 centre is relieved, and the formation of conjugated ynone **12** acts as a thermodynamic driving force. Formation of the lithium alkoxide from alcohol **11** by the action of *n*-BuLi, and subsequent addition of AdCHO gave also ynone **12**.

** Unwanted bromide **13** was found to slowly isomerise to bromoallene **7** on standing as a neat liquid, or this could be induced by the action of LiCuBr_2 in refluxing THF. As a representative experiment, after 20 h at reflux, allene **7** and bromide **13** were obtained as a 1.35:1 mixture respectively.

†† Temperature control was found to be essential to prevent hydride transfer to give products of the type $\text{RCOC}\equiv\text{CAd}$ and RCH_2OH .

‡‡ Bromides **16** and **18** also isomerised on standing (tlc analysis) into their respective bromoallenes.

§§ The regioisomeric structures of bromoallenes **7** and **8** follow by the nature of the $\text{S}_{\text{N}}2'$ reaction in which they are formed (ref. 13). These structures are further supported by characteristic NOE enhancements and HMBC correlations.‡

¶¶ At the outset, in a simplistic model, we predicted that epoxidation of a bromoallene would be electronically disfavoured at the $\Delta^{2,3}$ alkene position due to the deactivating donation of its π -cloud into the periplanar C-Br σ^* orbital. However, it was unclear whether the mesomeric activating release of a bromine lone pair into the $\Delta^{1,2}$ alkene would overcome its inductive deactivating effect.

||| The bromoallene oxides **19–21** showed characteristic allene oxide vinyl resonances in their ^1H NMR spectra (CDCl_3) at 4.84, 4.97 and 4.83 ppm respectively allowing immediate identification of regiochemistry of epoxidation. Their respective ^{13}C NMR resonances (CDCl_3) at C-3 (100.2, 100.3, 100.4 ppm) match perfectly with an allene oxide of the type $^1\text{BuCH}=\text{C}-(\text{O}-)\text{CHR}$ (100.3 ppm, ref. 6). Characteristic IR stretches for all bromides **19–21** at 1806 cm^{-1} show them to be allene oxides (see ref. 1c).

*** We invoke the formation of bromodiketones **22–24** via further epoxidation of bromoallene oxides **19–21** to give their respective bromospirodiepoxides, followed by ring-opening rearrangement to the diketones with bromide anion loss from C-1 and gain at C-3 (for the ring-opening rearrangement of spirodiepoxides of trisubstituted allenes with halide anions see ref. 10b). They were assigned these structures on the basis of their characteristic diketone stretches in their IR spectra (**22**: 1713, 1694 cm^{-1} ; **23**: 1719, 1690 cm^{-1} ; **24**: 1717, 1692 cm^{-1}), the presence of two carbonyl resonances in their ^{13}C NMR spectra (**22**: 206.3, 190.9 ppm; **23**: 206.3, 191.0 ppm; **24**: 205.9, 191.2 ppm), and a ^{13}C NMR resonance at *ca.* 59 ppm (**22**: 58.8 ppm; **23**: 58.2 ppm; **24**: 59.1 ppm) that displays a bromine induced isotopic shift (for **22**, $\Delta\delta = 1.6$ ppm).‡ NOEs from $\text{H} \rightarrow \text{R}$ (**22**, NOESY; **23**, 4.58%) confirm the bromide has shifted rather than a possible hydride shift (interchanging R and R'). However, their expected molecular ions with the characteristic bromine isotope pattern could not be observed by mass spectrometry, and only m/z 135 (Ad^+) was observed by EI^+ or Cl^+ methods (for **23**, **24**).

††† The yields represent the optimized yields for the bromoallene oxides using 3.0 equivalents of DMDO where the total mass recoveries from these experiments are >90%. The use of 1.5 equivalents gave the bromoallene oxides **19–21** in 21%, 19% and 21% isolated yield respectively, with (for **7** and **8**) 8% and 6% of **22** and **23**, and recovered starting materials **7** (68%) and **8** (74%) for >95% total mass recovery. The use of 5.0 equivalents (for **7** and **8**) led instead to the predominant formation of the corresponding bromodiketones **22** and **23** where no bromoallene oxides were observed.

‡‡‡ These results are also congruent with the reported epoxidations of tri(alkyl)substituted allenes (ref. 4 and 10b) where (i) the most substituted alkene is epoxidised, and (ii) the epoxidation occurs with face selectivity for the resulting *E*-olefin.

§§§ A search of the Cambridge Structural Database (version 5.37, Feb-2016 update) for an allene oxide moiety returned only 3 hits, all of which are epoxyC60fullerenes. The O-C bond lengths in the epoxide moiety of bromoallene oxide **19** show a marked asymmetry. Whilst that to the sp^3 carbon [O1–C1 1.453(6) \AA] is close to the average C–O bond length in epoxides with two sp^3 carbon centres [1.446 \AA], that to the sp^2 carbon of the adjacent C=C double bond is significantly shorter [O1–C2 1.388(7) \AA]. The C–C bond of the epoxide moiety [C1–C2 1.435(8) \AA] is also shorter than the average for epoxides with two sp^3 carbon centres [1.467 \AA]. The C2–C3 double bond [1.304(8) \AA] is unchanged from the average seen in allene systems [1.317 \AA] (data for average bond lengths of C=C double bonds in allene units, and in epoxides with two sp^3 carbon centres came from statistical analyses of searches of the Cambridge Structural Database).

¶¶¶ The question of the preferred site of epoxidation in 1-bromo-3-alkyl allenes (ref. 11) remains experimentally unresolved however.

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