A bridgehead adamantyl peroxyl radical has been prepared and isolated in the gas phase by the reaction of a distonic radical anion with dioxygen in a quadrupole ion-trap mass spectrometer.

The 1-adamantyl radical has been identified as a reactive intermediate in organic synthesis and has also been implicated in the metal-catalysed oxidation of adamantane. Bridgehead radicals of this type are unusual due to the enforced pyramidal distortion about the radical centre, which is in contrast to the near planarity of conventional alkyl radicals. This geometric distortion of bridgehead radicals results in an enhanced reactivity compared with analogous unrestricted radicals. As such, the unusual structure and reactivity of bridgehead radicals presents an extremely attractive target for investigation in the isolation if the gas phase.

While the gas phase thermochemistry and spectroscopy of the 1-adamantyl radical has been probed by indirect methods and its structure has been predicted by calculation, no reliable procedure for the preparation, isolation and reaction of this intermediate has previously been described. In the present study we have prepared a gas phase radical anion which includes a bridgehead adamantyl radical and a carboxylate anion moiety isolated from each other by the rigid adamantane cage. Kenttamaa has shown that distonic radical ions can provide useful models for free radical reactivity and indeed we observe a facile gas phase reaction of this tert-adamantyl radical with adventitious dioxygen in an ion-trap mass spectrometer. These data provide the first direct observation of a tert-adamantyl peroxyl radical.

Negative ion electrospray ionization (ESI) of a 10 μM aqueous acetonitrile solution of 1,3-adamantane dicarboxylic acid on an LTQ ion-trap mass spectrometer (ThermoFinnigan, Waltham, MA) yields both [M-H]- and [M-2H]2- parent ions at m/z 223 and 111, respectively. Collision induced dissociation (CID) of the dianion yields an [M-2H-CO2]- radical anion at m/z 178 via decarboxylation and concomitant loss of an electron (Scheme 1).

The decarboxylation of dicarboxylic dianions has been described as a gentle and regiospecific method for the synthesis of radical anions in the gas phase, although it has not previously been applied to saturated systems. The activation energy required for this process can be estimated at ΔEa ~ 100 kJ mol-1 for carboxylate anions separated by less than 5 Å from a like charge. An ion of m/z 178 has been reported as a fragment in CID spectra of various 3-substituted adamantane carboxylates and as such an alternative preparation of this ion from the deprotonated Barton ester, 3-(N-oxy carbonyl-2(1H)-pyridinethione)-adamantane-1-carboxylic acid (D), was devised. This compound was synthesized from 1,3-adamantane dicarboxylic acid by established methods and the gas phase [M-H] anion, E, was prepared by ESI of a 10 μM methanolic solution. CID of E produced abundant m/z 178 ions, via homolytic dissociation of the labile O-N bond and subsequent decarboxylation of the nascent oxycarbonyl radical. Both gas phase syntheses of the m/z 178 radical anion (Scheme 1) are consistent with the formation of the adamantyl radical, C. The molecular structure and energy of C was calculated at the B3LYP/6-31+G(d)/HF/6-31+G(d) level of theory using the Gaussian03 suite of programs and the structure is presented in Fig. 1.
Figure 1(b). The geometry about the radical centre is closely related to the unsubstituted 1-adamantyl radical calculated at the same level of theory (Figure 1a), with analogous bond lengths and angles differing by less than 0.01 Å or 1°. This structural congruence suggests that the charge-tagged adamantyl radical, C, is a good model for its neutral homologue.

Rearrangement of 1-adamantyl radicals via β-scission is not normally observed in solution, indeed the reverse, ring closing reaction occurs with surprising efficiency. Ring opening of 1-adamantyl radicals via β-scission has, however, been reported during gas phase pyrolysis of radical precursors. In order to assess the likelihood of a such a reaction occurring in this system we computed the activation barrier for this process. The activation barrier to β-scission in the parent 1-adamantyl radical was calculated to be $E_a = 103$ kJ mol$^{-1}$, while a barrier of $E_a = 81$ kJ mol$^{-1}$ was computed for the charge-tagged homologue C. A barrier of this magnitude is sufficient to prevent rearrangement of the tert-adamantyl radical in this experiment given: (i) the gentle methods of radical formation, (ii) CID in an ion-trap instrument does not produce energetic secondary collisions, and (iii) the rapid thermalization of ions by the helium buffer gas.

Isolation of $m/z$ 178 (formed by either pathway in Scheme 1) in the ion-trap in an MS$^3$ experiment results in the formation of an ion of $m/z$ 210 after trapping times of 30 ms or more. Figure 2 shows that increasing the trapping time for the $m/z$ 178 anion results in a significant increase in the abundance of $m/z$ 210 with the latter ion accounting for more than 50% of the ion current after trapping for 5 s (Figure 2). These data suggest that the $m/z$ 178 ions are adding 32 Da by ion-molecule reaction with background gas in the ion-trap mass spectrometer. The possibility of formation of non-specific methanol adducts was excluded by repeating the experiments using both aqueous acetonitrile and D$_2$-methanol as electrospray solvents. In each case the data obtained were identical to that shown in Figure 2. Furthermore, trapping of the non-bridgehead 3-carboxylate-1-cyano-1-methyl-propyl radical anion also resulted in the addition of 32 Da while the even-electron [M-H$^-$] anion of 1,3-adamantane dicarboxylic acid showed no such reaction (see Supplementary Information). These data indicate that the observed ion-molecule reaction is a specific free radical process and points to a radical-radical reaction of C with adventitious oxygen.

The addition of dioxygen was further supported by the observation of an isotope peak at $m/z$ 212 with a relative abundance 0.4% that of $m/z$ 210 and consistent with formation of the adamantyl peroxy radical F.

The reaction of alkyl radicals with dioxygen to form alkyl peroxy radicals in the gas phase are well described. These reactions are exothermic (e.g., $\Delta_{\text{298}}^{\text{mol}} [\text{CH}_3\text{CH}_2 + \text{O}_2 \rightarrow \text{CH}_3\text{CH}_2\text{O}_2] = -149 \pm 11$ kJ mol$^{-1}$) and thus excess energy must be removed by a third stabilizing collision. In this instance, the addition of dioxygen to the adamantyl radical C yielding the tert-adamantyl peroxy radical, F (Figure 1c) is calculated to be exothermic by -169 kJ mol$^{-1}$ with excess energy presumably dissipated by collisions with helium buffer gas. The influence of the charge on the reaction is likely to be small given that (i) the charge and radical centre are rigidly separated by more than 4 Å and (ii) the neutral reaction partner is non-polar. The structural assignment of $m/z$ 210 to the tert-adamantyl peroxy radical, F, is strongly supported by its CID spectrum (Figure 3). The fragment ion at $m/z$ 178 corresponds to direct dissociation of the C-O bond and loss of O$_2$ (-32 Da), while the $m/z$ 193 ion corresponds to loss of a hydroxyl radical (-17 Da).

Schaefer and co-workers have computed activation energies for dissociation of ethyl peroxy radical and found that $E_a[\text{CH}_3\text{CH}_2\text{O} \rightarrow \text{C}_2\text{H}_4 + \text{OH}]$ is greater than $E_a[\text{CH}_3\text{CH}_2\text{O} \rightarrow \text{CH}_3\text{CH} + \text{O}_2\text{H}]$ by just 25 kJ mol$^{-1}$. In the tert-adamantyl peroxy system, this trend should be reversed, with the epoxide channel favoured over the alkene forming reaction due to the high degree of strain involved in formation of an adamantane. This mechanism, shown in Scheme 2, is therefore consistent with the observed neutral loss of hydroxyl radical from a tert-adamantyl peroxy radical.

In this study we have prepared a distonic radical anion with charge and radical centres both sterically and electronically isolated from each other by the rigid adamantane cage. This is in contrast to previous studies of distonic radical ions which have utilized rigid...
but polarizable aromatic templates.\textsuperscript{9,10} The adamantyl radical centre was found to react rapidly with dioxygen, independent of the charged moiety, to form a hitherto uncharacterized \textit{tert}-adamantyl peroxyl radical. Distonic radical anions of this type show great potential for elucidation of bridgehead radical and peroxyl radical reactivity.

S.J.B. and D.G.H. acknowledge the financial support of the Australian Research Council (DP0452849) and the generous allocation of supercomputing resources from the Australian Partnership for Advanced Computing (ANU, Canberra). We acknowledge the technical support and advice of Mr Larry Hick.

Notes and references

\textsuperscript{†} Density of oxygen in the ion-trap manifold could be as high as $10^{10}$ molecules cm\textsuperscript{-3}.

\textsuperscript{‡} The process of adding O\textsubscript{2} to C and removing it by CID of the peroxyl adduct, F, can be repeated three times for the same ion population.
