

Mechanistic study on benzylic oxidations catalyzed by bismuth(III) salts: X-ray structures of two bismuth–picolinate complexes

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Abstract

We report studies that are consistent with benzylic oxidation reactions catalyzed using bismuth(III) salts proceeding via a radical mechanism. Additionally, X-ray structures of two potential bismuth–picolinate complex intermediates are reported.
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The oxidation of benzylic C–H bonds is of fundamental importance in the scale-up synthesis of arene carboxylic acids, aryl ketones and other compounds.¹ Traditionally, these reactions involve the use of stoichiometric quantities of potent oxidants such as potassium permanganate or potassium dichromate.² In the last decade, chemists have been developing alternative processes using Co,³ Cr,⁴ Mn,⁵ Rh,⁶ Ru,⁷ Zn⁸ and Fe⁹ species among others.¹⁰ With increasing environmental concerns, focus on non-toxic, benign catalysts has assumed greater importance. Since, bismuth(III) salts are of low toxicity and often Lewis acidic, numerous synthetic procedures have been reported using such salts.¹¹ Recently, we have developed a bismuth-catalyzed oxidation of alkylarenes to the corresponding ketones or carboxylic acids using *t*-butyl hydroperoxide as the stoichiometric oxidant.¹² In this Letter, we describe some mechanistic studies of this reaction.

Previously, we reported that experiments on bismuth-catalyzed benzylic oxidation reactions in the presence of 2,6-di-*t*-butyl-4-methylphenol (**1**) and 2-methyl-1-phenyl-

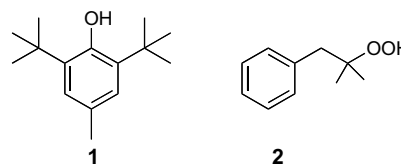


Fig. 1.

prop-2-yl hydroperoxide (**2**) were consistent with a free radical mechanism operating during the reaction (Fig. 1).¹²

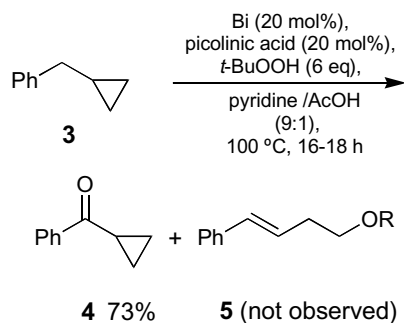
Nevertheless, when benzylcyclopropane (**3**) was used as a substrate, no rearranged product **5** (R=H, *Or*-Bu) was detected and only the corresponding ketone **4** was isolated in 73% yield (Scheme 1).

Consequently, we decided to further investigate this apparent mechanistic inconsistency. It has been well documented that ring-opening reactions of cyclopropylalkyl radicals are generally dependent on enthalpic, polar and steric effects.¹³ Indeed, the predominant reaction pathway is strongly dependent on the substituents present on the cyclopropane (Scheme 2).

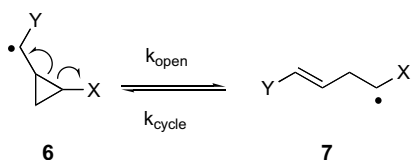
In the case of cyclopropane **3**, Ingold and co-workers^{13a} demonstrated that the ring opening of this radical is a reversible process with the cyclized form predominant at 22 °C. Based on these results, it is reasonable to suggest

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Scheme 1.

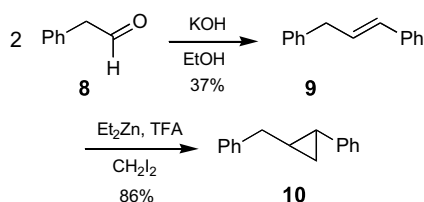


Scheme 2.

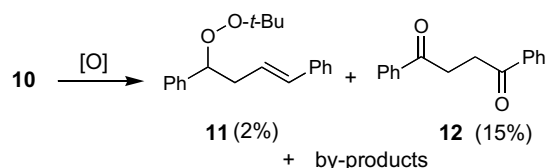
that in the oxidation of cyclopropane **3**, the formation of ketone **4** is preferred and this substrate is not an optimum probe of radical intermediates. Thus, we examined *trans*-1-benzyl-2-phenylcyclopropane (**10**) since the derived radical **6** (X=Y=Ph) is predominantly ring opened as **7** (Scheme 3).¹⁴

Following literature precedent,¹⁵ phenylacetaldehyde (**8**) was condensed under alkaline conditions to give *trans*-1,3-diphenylpropene (**9**) in 37% yield. Subsequently, Simmons–Smith cyclopropanation¹⁶ gave the desired substrate **10**. Cyclopropane **10** was subjected to a benzylic oxidation catalyzed by bismuth(0) and picolinic acid with excess of *t*-butyl hydroperoxide. Based on the recovery of starting material **10**, conversion in this reaction was less than 70%. Interestingly, the corresponding ketone was not observed (by NMR and MS of the reaction mixture) but two other products, peroxide **11** and dione **12**, were isolated in poor yields (Scheme 4).

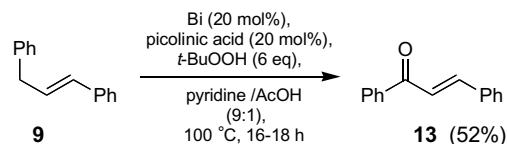
The formation of products **11** and **12** was consistent with the operation of a radical rearrangement reaction during oxidation. Of particular note, the isolation of peroxide **11** was consistent with the presence of *t*-butyl peroxy radicals (*t*-BuOO \cdot). Secondly, these results underlined the importance of the nature of the substrate as a mechanistic probe.



Scheme 3.



Scheme 4.



Scheme 5.

Encouraged by these results, we explored the scope of our bismuth-catalyzed oxidation to determine whether the addition of oxygen to an alkene could occur to form the corresponding oxirane (Scheme 5).

Bismuth-catalyzed oxidation of *trans*-1,3-diphenylpropene (**9**) gave only isolated chalcone (**13**) in 52% yield along with the recovered starting material (42%). The NMR spectrum of the reaction mixture did not show the presence of an epoxide derivative. This result showed that the oxidation procedure is selective towards the benzylic position over the alkene.

The synthesis and characterization of bismuth(III) picolinates was examined to gain a better understanding of the inner sphere ligands during the catalysis. Several pyridine and pyrazinecarboxylates of bismuth(III) have been reported in the literature, including bismuth picolinate.¹⁷ All these insoluble, polymeric complexes were characterized mainly by IR spectroscopy. However, Postel et al.^{17a} have reported the crystal structure of the mononuclear bismuth 2,6-pyridinedicarboxylate complex.

The common procedure^{17b} to prepare these complexes is by heating the ligand with bismuth oxide in water under reflux for 1–2 days. Unfortunately, the resulting products from this procedure are highly insoluble in most solvents. Thus, we prepared the bismuth–picolinate complex via bismuth(III) ethoxide,¹⁸ which was allowed to react with excess picolinic acid. This gave a white powder that was partially soluble in hot DMSO and to our delight gave white crystals, from DMSO and acetic acid, suitable for an X-ray crystallographic study (Fig. 2).¹⁹

The X-ray structure of **14** revealed an eight-coordinate bismuth center with four chelating picolinate ligands (Fig. 2); the coordination at the metal is bi-capped trigonal prismatic (see Fig. S2 in the Supplementary data). Adjacent anionic units are linked by the sodium cation (not drawn in the picture) to form a chain polymer along the crystallographic *b* axis direction (see Fig. S3).

To gain further insight on the bismuth species involved in the benzylic oxidation reaction, we sought to characterize the powder resulting from the reaction of bismuth(0) with picolinic acid in the presence of the oxidant but with-

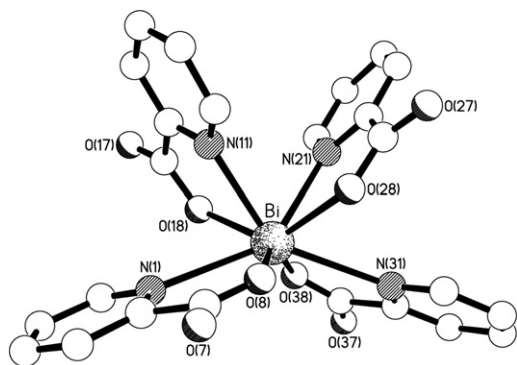


Fig. 2. The molecular structure of the complex anion present in the crystals of **14**.

out the substrate present.¹⁹ After considerable efforts, we isolated a novel polymeric complex, the structure of which was determined by X-ray crystallography (Fig. 3).

The X-ray analysis of crystals **15** showed only three picolinate ligands per bismuth (cf. four in **14**), and so there is no need for any additional cation; the coordination at the metal is again bi-capped trigonal prismatic (see Fig. S7). The structure is an extended coordination polymer (Fig. 3) with ligand bridges between the adjacent bismuth centers (cf. the sodium bridges in **14**). The bismuth has an oxidation state of three and each metal is coordinated by three picolinate ligands.

Interestingly, when the benzylic oxidation reaction was carried out using complex **15** in the presence of tetrahydronaphthalene, pyridine/acetic acid and *t*-BuOOH, α -tetralone was obtained in 76% yield, which is similar to the yield from the usual oxidation reaction. This result is consistent with picolinic acid acting as an inner sphere ligand for bismuth in our benzylic oxidation reactions.

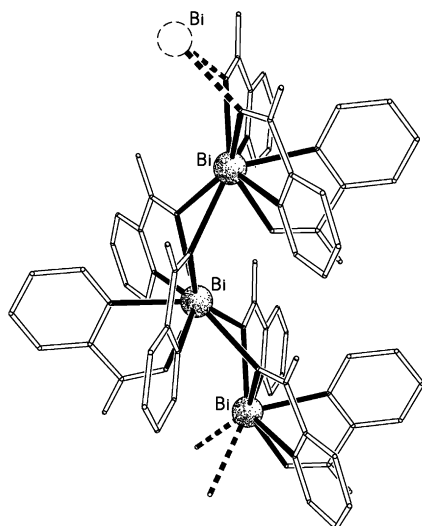


Fig. 3. Part of one of the extended polymer chains present in the crystals of **15**.

In conclusion, we have shown that bismuth-catalyzed benzylic oxidation most reasonably proceeds via the formation of the radical of the stoichiometric oxidant, *t*-butyl hydroperoxide and benzylic radicals. In addition, we also report the first examples of two modestly soluble bismuth picolinate complexes, which may be involved in the catalytic cycle.

Acknowledgements

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Supplementary data

Supplementary data (full details of the X-ray crystal structures for **14** and **15**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.04.044.

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19. *Procedures for the syntheses of bismuth picolinate complexes:*
*Preparation of Bi(OEt)₃.*¹⁸ Na (1.67 g, 72.6 mmol) was added to EtOH (50 mL) at 0 °C and the suspension was stirred until gas evolution had ceased. BiCl₃ (7.67 g, 24.3 mmol) in distilled THF (60 mL) was added resulting in the formation of a white precipitate. This was heated to reflux for 16 h and concentrated to approximately 50% of its original volume (by distillation) under reduced pressure. The residue was centrifuged and the supernatant liquid transferred via a syringe to a dry, pre-weighed Schlenk tube. Evaporation of the solvent at room temperature, under reduced pressure, gave bismuth ethoxide (3.48 g, 41%) as a white solid.
Preparation of Na[Bi(picolinate)₄] **14**. Picolinic acid (3.48 g, 31 mmol) in pyridine and AcOH (8:1 ratio; 45 mL) was added to bismuth ethoxide (3.48 g, 9.9 mmol) in a Schlenk tube via a syringe under Ar. The mixture was stirred overnight at room temperature, the resulting precipitate was filtered off and washed with pyridine leaving a white powder (550 mg). This powder was partially dissolved in hot DMSO and filtered. The resulting filtrate was diluted with a mixture of PhMe and DMSO (9:1) and allowed to stand affording white crystals. In the X-ray structure (CCDC 675457) shown in Fig. 2, the sodium cation and the 2.5 water molecules per metal have been omitted for clarity.
Preparation of bismuth–picolinate complex 15. Picolinic acid (0.49 g, 4 mmol) and *t*-BuOOH in H₂O (70%; 16 mL, 120 mmol) were added to a suspension of Bi(0) (0.83 g, 4 mmol) in distilled pyridine (10 mL) and AcOH (1.25 mL). The mixture was heated at 100 °C for 16 h in a sealed vessel. The precipitate was washed with distilled H₂O (3 × 10 mL) and dried leaving a white powder (650 mg), which was partially dissolved in hot DMSO and filtered. The resulting filtrate was diluted with a mixture of PhMe and DMSO (9:1) and allowed to stand affording white crystals (CCDC 675458).