A simple procedure for C–C bond cleavage of aromatic and aliphatic epoxides with aqueous sodium periodate under ambient conditions

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Abstract

The sodium periodate mediated oxidative cleavage of the C–C bond of 12 epoxides is reported with yields of the corresponding carbonyl compounds in up to 91%. This is a two-step reaction that proceeds through a rate-limiting epoxide opening to a vicinal diol that is cleaved in situ to the corresponding carbonyl compound. This method serves as a chemoselective alternative to ozonolysis.

The oxidative cleavage of olefins has been extensively studied in organic synthesis. 1 However, the cleavage of C–C bonds via epoxides is a less explored route. A major advantage of accessing carbonyl compounds through epoxides rather than olefins is that selective epoxidation can be performed on compounds with multiple double bonds. 2 This creates another possibility for site-specific oxidative cleavage of olefins (Scheme 1). A similar strategy was utilized in the synthesis of the multi-functionalized molecule (−)-terpestacin. 3

The most common method for oxidative cleavage is ozonolysis, a process that can be dangerous on larger scales. 4 Alternative one-pot processes include the use of RuCl₃·H₂O 5 or OsO₄ 6 for vicinal dihydroxylation in combination with oxidants such as NaIO₄, oxone, and NaOCl to facilitate the conversion of the glycol to the carbonyl compound. The ability of periodate to cleave vicinal diols led us to study the cleavage of the C–C bond of epoxides, which we assumed would proceed through a diol intermediate. 7 It has been reported that the treatment of the vicinal diol derived from limonene with sodium periodate does facilitate C–C bond cleavage, resulting in the ketoaldehyde. 8 The two-step process involving isolation of the diol was low yielding but the one-pot treatment of the epoxide with periodate at elevated temperature does afford the oxidative cleavage product in higher yield. 8a However, the generality of this method was not tested with other terpene epoxides. A few cases in the literature have reported the reaction of periodic acid (HIO₄) or metaperiodic acid (H₅IO₆) with epoxides, resulting in the corresponding carbonyl compound. 9 These reactions were only demonstrated on a small number of epoxides and employed harsh reaction conditions, often with elevated temperatures. To the best of our knowledge, a systematic study of the reaction of epoxides, both aliphatic and aromatic, with aqueous sodium periodate has not been performed. In this Letter,
the one-pot cleavage of the C–C bonds of several epoxides in the absence of catalyst is explored (Scheme 2).

During the course of our work, Ochiai demonstrated the novel use of iodosylbenzene for the one-pot oxidative cleavage of olefins. In some cases, a considerable amount of epoxide was detected and implicated as a reaction intermediate. A few aromatic epoxides were then tested in the reaction with iodosylbenzene to yield substituted benzaldehydes. Similar findings were reported in a recent paper by Liu, in which a Mn-porphyrin catalyst was used in combination with NaIO₄ to facilitate the oxidative cleavage of olefins. Although no epoxide was detected, the reaction was thought to proceed through an epoxide intermediate, with the epoxidation being the rate-limiting step. The authors were able to cleave the C–C bond of cyclohexene oxide and styrene oxide using their method; however, authors were able to cleave the C–C bond of cyclohexene with the epoxidation being the rate limiting step. The was thought to proceed through an epoxide intermediate, in the absence of catalyst is explored (Scheme 2).

The one-pot cleavage of the C–C bonds of several epoxides with sodium periodate and to provide a slightly acidic environment to dissolve the reaction. In some cases, a considerable amount of rearrangement product was observed and nopinone was observed using a variety of solvents and solvent mixtures including water, methanol, and THF. A similar ring rearrangement occurred in the reaction with α-pinene oxide as well. We then turned our interest toward simpler aliphatic and aromatic epoxides. Water was chosen as one of the co-solvents in order to partially dissolve the periodate and to provide a slightly acidic environment to promote epoxide opening. We also found that both THF and CH₃CN solvents worked well for this reaction and all subsequent reactions were performed using either THF/H₂O or CH₃CN/H₂O.

Six aliphatic epoxides, including terminal epoxides, were screened in the cleavage reaction (Table 1). Facile conversion of cyclohexene oxide, limonene oxide, and 3-carene oxide was achieved in moderate to high yields with just 2 equiv of sodium periodate (entries 4–6). The lower yield of adipaldehyde is likely due to the high volatility of the product. Less reactive substrates, such as epoxycyclooctane and 1,2-epoxy-9-decene (entries 1 and 3), required at least 4 equiv of periodate to facilitate the full consumption of starting material. The reaction carried out in the THF/H₂O solvent system gave impure aldehyde, contaminated with a significant amount of unidentified by-products. However, aqueous acetonitrile eliminated this by-product and gave essentially analytically pure aldehyde product (entry 1). It is possible that the lipophilic tails of these epoxides are forming micelles, preventing the polar epoxide heads from reacting with aqueous periodate. The reactions of 1,2-epoxy-9-decene and limonene oxide (entries 3 and 5) demonstrate the chemoselectivity of this reaction, which is complementary to conventional ozonolysis.

Periodate cleavage is known to prefer cis-diols as substrates, whereas acid-induced epoxide opening is known to create a trans-diol intermediate. While this may not be of consequence to linear epoxides, it is somewhat unexpected to observe such facile conversion of the cyclic examples. This leads us to believe that isomerization of the diol may be occurring under the acidic reaction conditions. It is also worth noting that in the case of epoxydodecane, a significant amount of unreacted starting material was recovered (Table 1, entry 2). This implies that epoxide opening is the rate-limiting step of the reaction. The trisubstituted epoxides generally gave products in higher yield compared to monosubstituted epoxides, reflecting the ease of epoxide hydrolysis in the former.

Initial attempts to perform this reaction on styrene oxide in THF/H₂O resulted in a mixture of benzaldehyde and phenacetalddehyde. The production of the latter is due to a rearrangement that occurs before ring opening. Carrying out the reaction in CH₃CN/H₂O exclusively provided benzaldehyde in 84% isolated yield (entry 7). It should be pointed out that the reaction of styrene with iodosylbenzene gave phenacetalddehyde in 85% yield along with 5% benzaldehyde, whereas styrene oxide gave only benzaldehyde in 89% yield, which is comparable to the results realized in our reaction.

Extension to halogenated aromatic epoxides gave fair to moderate yields for p-fluoro, p-chloro, and o-bromo-styrene oxide (Table 1, entries 8–10). We believe these lower yields may be due to the incomplete hydrolysis of the epoxide. The recovery of starting material in the o-bromo derivative leads us to believe that the epoxide-opening is the rate-limiting step. Disubstituted aromatic epoxides such as the TBS-protected cinnamyl epoxide and trans-stilbene oxide (entries 11 and 12) gave comparable results.
The oxidative cleavage of the C–C bond of 12 different epoxides has been demonstrated in yields up to 91%. We believe this is a two-step reaction that proceeds through a rate-limiting epoxide ring-opening, leading to a vicinal diol intermediate that is highly reactive toward periodate oxidation. Apparently, the trans-diols formed from cyclic epoxides isomerize under the acidic reaction conditions before undergoing C–C bond cleavage. More highly substituted epoxides appear to be more reactive, which may be due to the ease of initial epoxide opening. This aqueous one-pot procedure provides access to a variety of different carbonyl compounds, which are important intermediates in organic synthesis. This method, in combination with known selective epoxidation methods, should provide an appealing alternative to ozonolysis.

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References and notes

Representative procedure for the C–C cleavage of epoxides. To a round-bottom flask equipped with a magnetic stir-bar, finely powdered sodium periodate (20–50 mmol, 99% pure) was stirred with the appropriate solvent mixture (40 mL) for five minutes. The epoxide (10 mmol) was then added and the reaction mixture was stirred at room temperature. Upon reaction completion, as monitored by TLC, the white precipitate that had formed was filtered away and washed with 30 mL Et₂O, creating two distinct layers. The aqueous layer was extracted with two 30 mL portions of Et₂O, washed with water and brine, dried (MgSO₄), filtered, and concentrated in vacuo. Although most examples provided pure carbonyl compounds the crude reaction mixtures could be purified via column chromatography on silica gel eluting with EtOAc/hexanes.