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2,2,2-Trifluoroacetophenone: An Organocatalyst for an Environmentally Friendly Epoxidation of Alkenes

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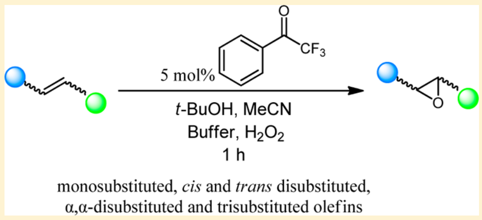
Supporting Information

ABSTRACT: A cheap, mild, fast, and environmentally friendly oxidation of olefins to the corresponding epoxides is reported using polyfluoroalkyl ketones as efficient organocatalysts. Namely, 2,2,2-trifluoroacetophenone was identified as an improved organocatalyst for the epoxidation of alkenes. Various olefins, mono-, di-, and trisubstituted, are epoxidized chemoselectively in high to quantitative yields utilizing 2−5 mol % catalyst loading and H_2O_2 as the green oxidant.



INTRODUCTION

Alkene epoxidation has always been a dominant reaction in organic synthesis both in industry and academia, since epoxides are versatile intermediates for the synthesis of a plethora of valuable compounds.[1] The initial spark for the exploration of olefin epoxidation was given by Katsuki and Sharpless when they reported the asymmetric epoxidation of allylic alcohols utilizing a titanium complex.[2] Following the inspiring contributions by Jacobsen[3] and Katsuki,[4] a variety of metal complexes appeared in the literature for the racemic and the enantioselective epoxidation of olefins.[5] With the advent of organocatalysis,[6] much effort has been devoted to the development of metal-free molecules for the epoxidation of alkenes. The first attempt to use pure organic compounds as a stoichiometric oxidant for the epoxidation of alkenes goes back to 1909 when Prileschajew uses the well-known *m*-CBPA.[7] However, the lion's share in the epoxidation of olefins can be attributed to dioxiranes rather than peracids. Among the pioneers in the dioxirane field were Adam, Mello, and Curci.[8] Furthermore, real advances in the field were made by the groups of Yang,[9] Denmark,[10] and Shi,[11] who demonstrated that dioxirane derivatives from chiral ketones could be employed in substoichiometric quantities (10−100%) to afford epoxides from medium to high enantioselectivities. Moreover, efficient epoxidation protocols have been introduced using peracids[12] and sulfur ylides.[13] Efficient epoxidation of alkenes with environmentally benign H_2O_2 as an oxidant has drawn much attention because it is cheap, clean, safe, and gives water as the only byproduct.[14] Toward this direction, Shi and co-workers have employed trifluoroacetone as the dioxirane precursor in conjunction with H_2O_2 instead of Oxone.[15] However, an increased amount of H_2O_2 (4 equiv) was required, as well as maintaining a low reaction temperature (0 °C), while catalyst loading and reaction time varied from 10 to 30 mol % and from 4 to 10 h, respectively. Thus, the development of efficient and inexpensive catalysts for the epoxidation of alkenes is still a challenge in green chemistry. Recent advances on the use of organocatalysts for epoxidation reactions have been disclosed.[16]

We have recently diverted our attention on the development of a strategy that enables the use of commercially available activated ketones as a synthetically versatile and operationally trivial mode of activation of a green oxidant like H_2O_2. Hydrogen peroxide by itself is a poor oxidant for organic oxidations. Thus, it has to be coupled with a catalyst in order to form a reactive intermediate that will efficiently execute the oxidation. Nitriles have been employed in the past for such activation.[17] Perfluoroalkyl ketones, especially hexafluoroacetone and 1,1,1-trifluoroacetone, have been employed in the past for oxidation reactions, but usually in stoichiometric amounts.[18−20] Only limited examples exist in the literature, where substoichiometric amounts of perfluoroalkylketone are employed.[15,19c,d] However, in these cases, large amounts of MeCN or H_2O_2 have to be employed and long reaction times are required. It is known that perfluoroalkyl ketones in aqueous environment exist mainly in their hydrate form (Figure 1). This hydrate in conjunction with hydrogen peroxide could lead to either a perhydrate or a dihydroperoxide. This perhydrate, upon reaction with MeCN and H_2O_2, could create a more

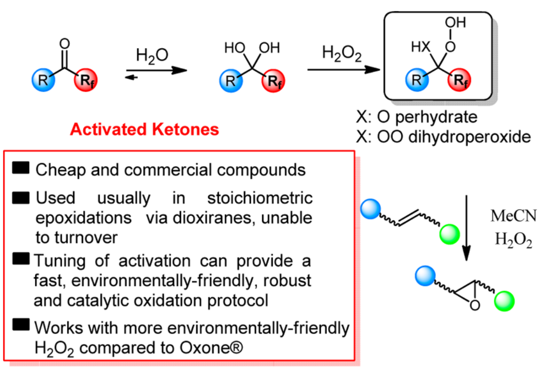


Figure 1. Proposed mode of activation.

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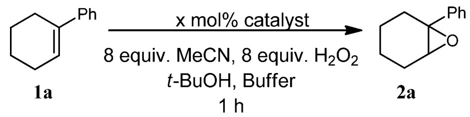
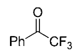
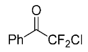
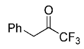
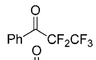
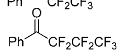
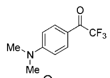
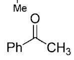
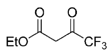
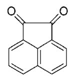
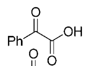
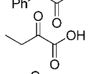
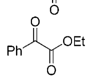
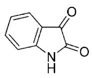
Table 1. Catalyst Optimization for the Epoxidation of 1-Phenylcyclohexene



Entry	Catalyst	Catalyst loading (mol %)	Yield (%)[a]
1	No catalyst	-	11
2		5	>99
3[b]		5	>99 (99)
4		2	>99 (99)
5[c]		1	58
6		5	92
7		5	59
8		5	98
9		5	98
10		5	27
11		5	12
12		5	43
13		5	21
14		5	11
15		5	12
16		5	9
17		5	14

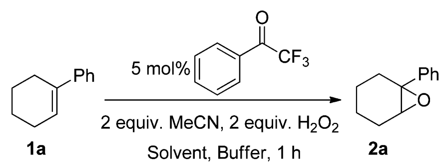
[a]Yield determined by GC−MS analysis, isolated yield in parentheses. [b]2 equiv of MeCN and H_2O_2 were utilized. [c]Reaction time 24 h.

reactive intermediate that could perform the oxidation of the substrate and would regenerate the catalyst to be employed in another catalytic cycle. We have been previously engaged in the synthesis of activated ketones as potent and selective enzyme inhibitors.[21,22] Coupled with our own previous experience in organocatalysis[23] and oxidations,[24] we considered the application of activated ketones as catalysts for the epoxidation of olefins in an effort to provide an improved oxidation protocol to the existing literature knowledge.

■ RESULTS AND DISCUSSION

A variety of activated ketones, namely ketoacids, ketoesters, ketoamides, perfluoroalkyl ketones, and 1,2-diketones were tested as catalysts for the oxidation of 1-phenylcyclohexene to the corresponding epoxide using H_2O_2 as the oxidant (Table 1). Initially, the reaction was performed in the absence of catalyst and the product was formed in just 11% yield (entry 1, Table 1). Activated ketones were then employed, utilizing 8 equiv of H_2O_2 and MeCN in a mixed solvent system, which contained *tert*-butyl alcohol and an aqueous buffer solution (0.6 M K_2CO_3; 4×10^{-5} M EDTA tetrasodium salt, pH 11). When 2,2,2-trifluoroacetophenone was employed, the product was formed in quantitative yield (entry 2, Table 2). In the literature, large excess or stoichiometric quantities are required in order for oxidations to reach completion. However, the reaction

Table 2. Solvent Optimization for the Epoxidation of 1-Phenylcyclohexene

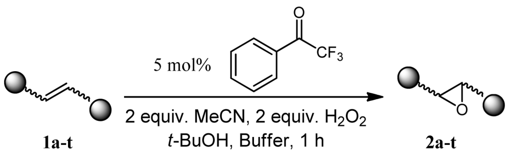


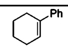
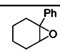
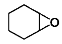
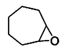
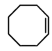
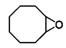
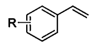
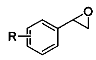
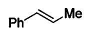
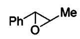
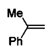
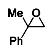
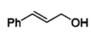
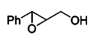
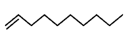
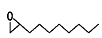
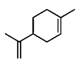
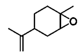
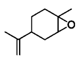
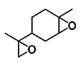
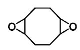
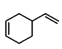
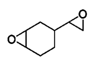
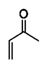
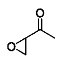
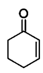
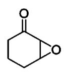
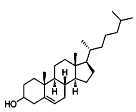
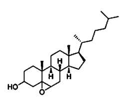
entry	solvent	yield[a] (%)
1	*t*-BuOH	>99
2	*i*-PrOH	82
3	MeOH	trace
4	Et_2O	60
5	EtOAc	95
6	CH_2Cl_2	33
7	$CHCl_3$	40
8	DMSO	35
9	DMF	49

[a]Yield determined by GC−MS analysis.

conditions are quite crucial for decreasing the amount of the reaction promoter.[25] Decreasing the amount of MeCN and H_2O_2, both to 2 equiv, had no impact on the yield (entry 3, Table 1). When the catalyst loading was decreased to 2 mol %,

Table 3. Substrate Scope of the Epoxidation Utilizing 2,2,2-Trifluoroacetophenone as the Catalyst



Entry	Susbstrate	Product	Yield (%)[a]
1			99
2			98[b]
3			98
4			98
			
5	R: H		98
6	R: 4-Cl		94
7	R: 3-Br		91
8	R: 4-*t*-Bu		97
9	R: 4-Me		99
10			98
11			97
12[c]			81
13[d]			97
14[e]			81
15			98
16[f]			98
17[f]			88
18			98[b]
19			99[b]
20[g]			98

[a]Yield of isolated product. [b]Yield determined by GC−MS analysis. [c]Reaction time 2 h. [d]5 equiv of H_2O_2 and MeCN, reaction time 24 h. [e]*Cis*:*trans* 60:40. [f]4 equiv of H_2O_2 and MeCN. [g]dr 60:40.

a quantintative yield was obtained (entry 4, Table 1). A further decrease to 1 mol % catalyst loading led to a noticeable decrease of reaction efficiency (entry 5, Table 1). Perfluoroalkyl ketones are known to be highly activated carbonyl compounds; that is why they have been employed as inhibitors for the serine hydrolase enzymes.[22] The decrease of the carbonyl activation had a strong effect in the reaction outcome, since the substitution of one fluorine atom by a chlorine led to a decreased yield (entry 6, Table 1). Further decrease on the activation of the carbonyl compound by replacing the phenyl

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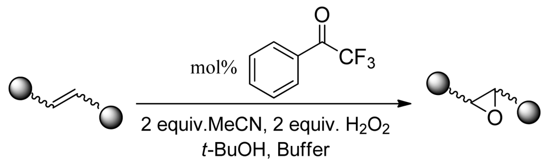
moiety by benzyl led to mediocre yield (entry 7, Table 1). Polyfluoroalkyl ketones led to similar high yields (entries 8 and 9, Table 1), while electron-rich aromatic moieties led to decreased yields (entry 10, Table 1). When acetophenone was employed as the catalyst, an extremely low yield was observed highlighting the need of the perfluoroalkyl moiety to activate the carbonyl compound in order to act as the oxidation catalyst (entry 11, Table 1). Ethyl 4,4,4-trifluoro-3-oxobutanoate as well as other activated compounds as diketones, ketoacids, ketoesters, and ketoamides were also tested, but in all cases, low to moderate yields were obtained (entries 12−17, Table 1).

Identifying 2,2,2-trifluoroacetophenone as the best catalyst, a solvent screening was carried out in order to evaluate the best reaction conditions (Table 2). *tert*-Butyl alcohol proved the best solvent (entry 1, Table 2). Other solvents led to lower reactivities (entries 2−9, Table 2). A number of other parameters were also investigated in order to find the optimum reaction conditions.[25] In comparison with literature, this protocol leads to reduction in catalyst loading, reaction time, and the amount of H_2O_2 while maintaining excellent yields.

The substrate scope of the oxidation was then explored (Table 3). Initially, cyclic olefins were utilized providing the products in high to quantitative yields (entry 1−4, Table 3). A series of monosubstituted styrenes were then tested (entry 5−9, Table 3). Substitution at either the *meta-* or *para*-position had a minor effect on the reaction outcome, and the products were obtained in almost quantitative yield. Except from disubstituted *cis* olefins (entries 1−4, Table 3), disubstituted *trans* olefins are well tolerated, since *trans-β*-methylstyrene led to high yield (entry 10, Table 3). Furthermore, *α,α*-disubstituted styrenes can be employed in this protocol, leading to high yields (entry 11, Table 3). Allylic alcohols can be also employed successfully as demonstrated by the use of cinnamyl alcohol (entry 12, Table 3). Terminal olefins, like 1-decene, proved to be difficult substrates, and an increase of the amount of H_2O_2 and MeCN, as well as longer reaction time, were required to lead to high yields (entry 13, Table 3). Trisubstituted olefins are well tolerated since the natural product limonene provided limonene oxide in high yield proving regioselectivity in favor of the cyclic olefin (entry 14, Table 3), whereas limonene oxide provided the coresponding diepoxide quantitatively (entry 15, Table 3). When 1,4-cyclooctadiene was utilized, the corresponding diepoxide was isolated in very high yield (entry 16, Table 3), while 4-vinylcyclohex-1-ene provided four diastereomers of the product in slightly lower yield (entry 17, Table 3). In addition, electron-deficient alkenes, which in some cases are problematic, were utilized successfully providing the corresponding products in high yield (entries 18 and 19, Table 3), proving the efficiency and broad application of this oxidation protocol. Finally, the epoxidation of the natural steroid cholesterol can be successfully carried out (entry 20, Table 3), and the epoxide product is of wide interest for further steroid synthesis.[26]

In order to clarify the reaction mechanism, control experiments were carried out (Scheme 1).[25] In the absence of H_2O_2, no reaction took place, confirming that H_2O_2 is the oxidant of the reaction. However, H_2O_2 by itself or in the combination with the catalyst was not capable of performing the oxidation because in the absence of MeCN, oxidation is negligible. Furthermore, when only 0.5 equiv of MeCN was employed, 48% of the oxidation occurred. The amount of the acetonitrile is of critical importance because at least 1 equiv of acetonitrile is required to obtain full oxidation of the starting

Scheme 1. Mechanistic Investigations of the Reaction

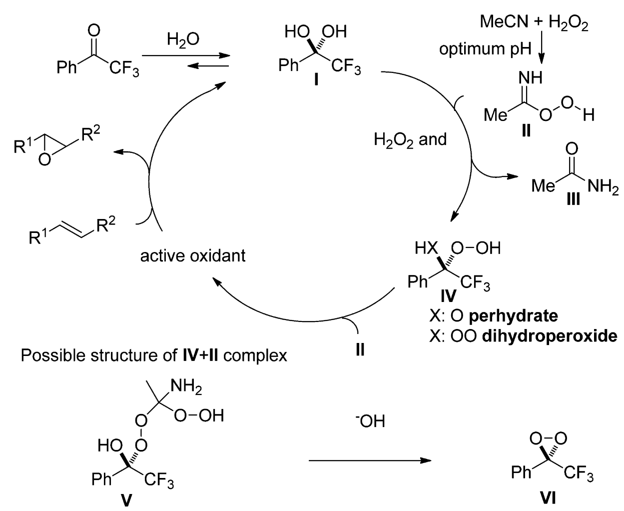


10% mol catalyst, MeCN, H_2O_2, t-BuOH, Buffer	>99% yield (18 h)
10% mol catalyst, MeCN, **No H_2O_2**, t-BuOH, Buffer	0% yield (18 h)
10% mol catalyst, **No MeCN**, H_2O_2, t-BuOH, Buffer	6% yield (18 h)
No catalyst, MeCN, H_2O_2, t-BuOH, Buffer	traces (18 h)
10% mol catalyst, 50 mol% MeCN, H_2O_2, t-BuOH, Buffer	48% yield (18 h)
Reaction Conditions and **Tempo**	>99% yield (18 h)
Reaction Conditions and **BHT**	>99% yield (18 h)

material. It is safe to presume that an intermediate is formed, which is a peroxycarboximidic acid, similar to the intermediate that Payne and co-workers have proposed in their epoxidation reaction.[17a] Furthermore, this intermediate oxidant is sluggish in promoting the reaction by itself, since in the absence of the catalyst only traces of the product were observed. Evidence that supports the peroxycarboximidic acid intermediate is the observation of the formation of acetamide at the end of the reaction both by GC−MS analysis and ^{1}H NMR. At this stage, the crucial role of the pH of the solution has to be highlighted in order for the peroxycarboximidic acid intermediate to be generated (see the Supporting Information for the role of pH in the reaction outcome). To eliminate the possibility of radical intermediates in this protocol, the following control experiments were performed (Scheme 1). The reaction was performed in the presence of known radical traps, like Tempo and BHT. The reaction outcome was independent to the addition of the radical traps, proving that this protocol does not contain any radical intermediates.

Stemming from previous knowledge acquired in our laboratory,[21,24] perfluoroalkyl aryl ketones exist mainly in their hydrate form in the aqueous environment of the reaction. Indeed, ^{19}F NMR experiments showed that although in organic solvents, 2,2,2-trifluoroacetophenone exists in the keto form, in a D_2O-buffer solution, the hydrate form (compound I, Scheme 2) is the predominant species (see the Supporting Information). Upon addition of *t*-BuOH and MeCN, no change was observed. Once H_2O_2 was added, immediately a new peak was

Scheme 2. Proposed Reaction Mechanism



observed in the ^{19}F NMR spectrum. This presumably corresponds to compound **IV** (a perhydrate in Scheme 2), since the same peak is observed in the ^{19}F NMR when no MeCN is used (see the Supporting Information).[24,25] If no olefin is added, perhydrate **IV** was slowly transformed to a new compound, which is assumed to be the corresponding dihydroperoxide. This compound was sluggish in catalyzing the epoxidation. Taking into consideration these data, the following catalytic cycle is proposed (Scheme 2). Initially, the perfluoroalkyl ketone is hydrated in the presence of water leading to its hydrate form **I** (Scheme 2). Once the optimum pH is employed (aqueous buffer K_2CO_3 0.6M, 4 × 10^{-5} M EDTA tetrasodium salt, measured pH 11), acetonitrile and H_2O_2 react to form peroxycarboximidic acid **II**. The hydrate form of the perfluoroalkyl ketone is oxidized by H_2O_2 and **II** forming perhydrate **IV** and leaving as byproduct acetamide **III**. Perhydrate **IV** then reacts with **II** forming the active oxidant species of the reaction.[24] An intermediate, **V**, that corresponds to the addition of perhydrate **IV** to **II** has been detected by MS. This intermediate under the basic conditions of the reaction could collapse and form dioxirane **VI**. According to the work of Yang, Denmark, and Shi, dioxirane is asssumed to be the active oxidant of this protocol. Since our catalytic system does not behave like a typical dioxirane,[27] we cannot rule out the possibility of **V** or other intermediates to be the active oxidant species. Finally, upon addition of the alkene, the epoxide is obtained, and at the same time recycling of the catalyst occurs through generation of the hydrate **I**.

■ CONCLUSIONS

In summary, we have managed to establish an improved, green, efficient, inexpensive, and fast oxidative protocol for the epoxidation of alkenes utilizing 2,2,2-trifluoroacetophenone as the catalyst in combination with the green oxidant H_2O_2. This constitutes an overall improvement in the existing knowledge in the literature, since for the first time, low catalyst loadings (2−5 mol %) are employed to provide the epoxidation product in just 1 h in excellent yields. The fine-tuning of the activation of the ketone employed as the catalyst in combination with the appropriate reaction conditions were the key factors for this improvement. A broad variety of olefins, mono-, di-, and trisubstituted were well tolerated. The mechanism of the reaction was studied and active intermediates are proposed.

■ EXPERIMENTAL SECTION

General Procedure for the Epoxidation of Alkenes. Alkene (1.00 mmol) was placed in a round-bottom flask followed by 2,2,2-trifluoro-1-phenylethanone (9.0 mg, 0.05 mmol). *tert*-Butyl alcohol (1.5 mL), aqueous buffer solution (1.5 mL, 0.6 M K_2CO_3, 4 × 10^{-5} M EDTA tetrasodium salt), acetonitrile (0.11 mL, 2.00 mmol), and 30% aqueous H_2O_2 (0.23 mL, 2.00 mmol) were added consecutively. The reaction mixture was allowed to stir for 1 h at room temperature. The crude product was purified using flash column chromatography (various mixtures of petroleum ether/Et_2O or petroleum ether/EtOAc) to afford the desired product.

1-Phenyl-7-oxabicyclo[4.1.0]heptane (2a):[28] colorless oil; 173 mg, 99% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 7.44−7.24 (5H, m), 3.10−3.06 (1H, m), 2.40−1.98 (4H, m), 1.72−1.23 (4H, m); ^{13}C (50 MHz, $CDCl_3$) δ 142.5, 128.2, 127.1, 125.3, 61.8, 60.1, 28.8, 24.7, 20.1, 19.7; MS 175 (M + H$^+$, 52).

7-Oxabicyclo[4.1.0]heptane (2b):[29] colorless oil; 97 mg, 98% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 3.16−3.10 (2H, m), 1.97−1.77 (4H, m), 1.48−1.35 (2H, m), 1.28−1.07 (2H, m); ^{13}C (50 MHz, $CDCl_3$) δ 52.6, 24.9, 19.8; MS 99 (M + H$^+$, 23).

8-Oxabicyclo[5.1.0]octane (2c):[30] colorless oil; 110 mg, 98% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 3.10−3.01 (2H, m), 1.97−1.84 (4H, m), 1.62−1.35 (6H, m); ^{13}C (50 MHz, $CDCl_3$) δ 55.9, 30.8, 28.6, 24.4; MS 113 (M + H$^+$, 36).

9-Oxabicyclo[6.1.0]nonane (2d):[30] colorless oil; 124 mg, 98% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 2.94−2.81 (2H, m), 2.18−2.04 (2H, m), 1.60−1.17 (10H, m); ^{13}C (50 MHz, $CDCl_3$) δ 55.6, 26.4, 26.2, 25.5; MS 127 (M + H$^+$, 32).

2-Phenyloxirane (2e):[31] colorless oil; 118 mg, 98% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 7.42−7.23 (5H, m), 3.88 (1H, dd, *J* = 3.8 and 2.6 Hz), 3.17 (1H, dd, *J* = 5.5 and 3.8 Hz), 2.82 (1H, dd, *J* = 5.5 and 2.6 Hz); ^{13}C (50 MHz, $CDCl_3$) δ 137.5, 128.3, 128.0, 125.3, 52.1, 51.0; MS 121 (M + H$^+$, 41).

2-(4-Chlorophenyl)oxirane (2f):[31] colorless oil; 145 mg, 94% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 7.28 (2H, d, *J* = 8.6 Hz), 7.17 (2H, d, *J* = 8.6 Hz), 3.80 (1H, dd, *J* = 3.9 and 2.6 Hz), 3.11 (1H, dd, *J* = 5.4 and 3.9 Hz), 2.72 (1H, dd, *J* = 5.4 and 2.6 Hz); ^{13}C (50 MHz, $CDCl_3$) δ 136.0, 133.7, 128.5, 126.7, 51.6, 51.1; MS 155 (M + H$^+$, 45).

2-(3-Bromophenyl)oxirane (2g):[32] colorless oil; 181 mg, 91% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 7.40−7.32 (2H, m), 7.20−7.12 (2H, m), 3.75 (1H, dd, *J* = 4.1 and 2.5 Hz), 3.07 (1H, dd, *J* = 5.5 and 4.1 Hz), 2.68 (1H, dd, *J* = 5.5 and 2.5 Hz); ^{13}C (50 MHz, $CDCl_3$) δ 139.8, 131.0, 129.8, 128.1, 124.6, 124.0, 51.4, 51.1; MS 199 (M + H$^+$, 21).

2-(4-(*tert*-Butyl)phenyl)oxirane (2h):[33] colorless oil; 171 mg, 97% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 7.41 (2H, d, *J* = 8.5 Hz), 7.25 (2H, d, *J* = 8.5 Hz), 3.87 (1H, dd, *J* = 3.9 and 2.7 Hz), 3.16 (1H, dd, *J* = 5.5 and 3.9 Hz), 2.84 (1H, dd, *J* = 5.5 and 2.7 Hz), 1.35 (9H, s); ^{13}C (50 MHz, $CDCl_3$) δ 151.6, 134.8, 125.3, 125.2, 52.2, 51.0, 34.5, 31.2; MS 177 (M + H$^+$, 25).

2-(*p*-Tolyl)oxirane (2i):[34] colorless oil; 133 mg, 99% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 7.19−7.15 (4H, m), 3.83 (1H, dd, *J* = 4.1 and 2.5 Hz), 3.12 (1H, dd, *J* = 5.5 and 4.1 Hz), 2.79 (1H, dd, *J* = 5.5 and 2.5 Hz), 2.35 (3H, s); ^{13}C (50 MHz, $CDCl_3$) δ 138.1, 134.9, 129.0, 125.5, 52.2, 50.9, 20.8; MS 135 (M + H$^+$, 32).

2-Methyl-3-phenyloxirane (2j):[34] colorless oil; 132 mg, 98% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 7.38−7.22 (5H, m), 3.55 (1H, d, *J* = 2.0 Hz), 3.07 (1H, qd, *J* = 5.2 and 2.0 Hz), 1.45 (3H, d, *J* = 5.2 Hz); ^{13}C (50 MHz, $CDCl_3$) δ 137.7, 128.4, 127.9, 125.5, 59.5, 59.0, 17.9; MS 135 (M + H$^+$, 47).

2-Methyl-2-phenyloxirane (2k):[34] colorless oil; 130 mg, 97% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 7.41−7.26 (5H, m), 2.95 (1H, d, *J* = 5.4 Hz), 2.79 (1H, d, *J* = 5.4 Hz), 1.74 (3H, s); ^{13}C (50 MHz, $CDCl_3$) δ 141.0, 128.2, 127.4, 125.2, 57.0, 56.7, 21.7; MS 135 (M + H$^+$, 28).

(3-Phenyloxiran-2-yl)methanol (2l):[34] reaction time 2 h; colorless oil; 122 mg, 81% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 7.40−7.22 (5H, m), 3.99 (1H, dd, *J* = 12.7 and 2.2 Hz), 3.90 (1H, d, *J* = 2.2 Hz), 3.72 (1H, dd, *J* = 12.7 and 4.2 Hz), 3.23 (1H, dt, *J* = 4.2 and 2.2 Hz), 2.41 (1H, br s); ^{13}C (50 MHz, $CDCl_3$) δ 136.6, 128.3, 128.1, 125.6, 62.3, 61.1, 55.4; MS 151 (M + H$^+$, 33).

2-Octyloxirane (2m):[35] reaction time 24 h; colorless oil; 152 mg, 97% yield; ^1H NMR (200 MHz, $CDCl_3$) δ 2.95−2.86 (1H, m), 2.74 (1H, t, *J* = 5.1 Hz), 2.45 (1H, dd, *J* = 5.1 and 2.7 Hz), 1.64−1.18 (14H, m), 0.91−0.86 (3H, m); ^{13}C (50 MHz, $CDCl_3$) δ 52.3, 47.1, 32.5, 31.8, 29.7, 29.6, 29.4, 25.8, 22.7, 14.1; MS 157 (M + H$^+$, 29).

(4*R*)-1-Methyl-4-(prop-1-en-2-yl)-7-oxabicyclo[4.1.0]heptane (2n):[36] colorless oil; 123 mg, 81% yield; mixture of *cis*:*trans* diastereomers (60:40); ^1H NMR (200 MHz, $CDCl_3$) δ 4.73−4.66 (0.8H, m), 4.64 (1.2H, m), 3.04 (0.6H, t, *J* = 5.5 Hz), 2.98 (0.4H, d, *J* = 5.1 Hz), 2.40−1.10 (7H, m), 1.67 (1.8H, s), 1.65 (1.2H, s), 1.30 (1.2H, s), 1.29 (1.8H, s); ^{13}C (50 MHz, $CDCl_3$) δ 149.2, 149.0, 109.2, 109.0, 60.5, 59.2, 57.6, 57.4, 40.7, 36.3, 30.9, 30.8, 30.0, 28.7, 26.1, 24.5, 24.3, 23.2, 21.2, 20.3; MS 153 (M + H$^+$, 35).

(4*S*)-1-Methyl-4-(2-methyloxiran-2-yl)-7-oxabicyclo[4.1.0]heptane (2o):[37] colorless oil; 165 mg, 98% yield; mixture of four diastereomers; ^1H NMR (200 MHz, $CDCl_3$) δ 3.05−2.93 (1H, m), 2.64−2.45 (2H, m), 2.14−1.39 (7H, m), 1.27 (3H, s), 1.19−1.14 (3H, m); ^{13}C (50 MHz, $CDCl_3$) δ 60.3, 59.9, 59.0, 58.7, 58.6, 58.5, 57.7, 57.6, 57.3, 57.2, 53.3, 53.1, 52.8, 52.6, 39.8, 39.2, 36.2, 35.3, 34.7, 30.1,

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30.0, 28.6, 28.5, 28.3, 27.6, 26.5, 26.3, 24.3, 24.2, 23.5, 23.2, 22.9, 22.8, 21.2, 21.1, 18.6, 18.1, 18.0, 17.3; MS 169 (M + H^+, 18).

5,10-Dioxatricyclo[7.1.0.04,6]decane (2p):[38] colorless oil; 137 mg, 98% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.05−2.95 (4H, m), 2.04−1.82 (8H, m); ^{13}C (50 MHz, $CDCl_3$) δ 56.1, 21.9; MS 141 (M + H^+, 52).

3-(Oxiran-2-yl)-7-oxabicyclo[4.1.0]heptane (2q):[39] colorless oil; 123 mg, 88% yield; mixture of four diastereomers; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.24−3.14 (2H, m), 2.80−2.66 (2H, m), 2.55−2.46 (1H, m), 2.28−1.08 (7H, m); ^{13}C (50 MHz, $CDCl_3$) δ 56.0, 55.7, 55.6, 55.5, 52.5, 52.4, 52.3, 52.2, 51.7, 51.6, 50.9, 50.8, 46.3, 46.2, 45.7, 45.4, 35.7, 35.2, 32.7, 31.9, 27.4, 27.2, 27.0, 25.8, 24.3, 24.1, 23.6, 23.2, 22.9, 22.7, 21.4, 20.2; MS 141 (M + H^+, 37).

1-(Oxiran-2-yl)ethanone (2r):[40] colorless oil; 84 mg, 98% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.38 (1H, dd, J = 4.6 and 2.5 Hz), 3.01 (1H, dd, J = 5.7 and 4.6 Hz), 2.88 (1H, dd, J = 5.7 and 2.5 Hz), 2.02 (3H, s); ^{13}C (50 MHz, $CDCl_3$) δ 205.8, 53.8, 45.8, 23.7; MS 86 (M^+, 21).

7-Oxabicyclo[4.1.0]heptan-2-one (2s):[5h] colorless oil; 111 mg, 99% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.66−3.54 (1H, m), 3.26 (1H, d, J = 4.0 Hz), 2.63−2.48 (1H, m), 2.33−2.19 (1H, m), 2.12−1.88 (3H, m), 1.71−1.66 (1H, m); ^{13}C (50 MHz, $CDCl_3$) δ 205.7, 55.8, 55.0, 36.1, 22.7, 16.9; MS 112 (M^+, 11).

(6aS,6bS,9R,9aR,11aS,11bR)-9a,11b-Dimethyl-9-((R)-6-methylheptan-2-yl)hexadecahydrocyclopenta[1,2]phenanthro-[8a,9-b]oxiren-3-ol (2t):[41] white solid; mp 132−134 °C; 395 mg, 98% yield; mixture of diastereomers (60:40); ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.01−3.81 (0.4H, m), 3.79−3.61 (0.6H, m), 3.07 (0.6H, d, J = 2.1 Hz), 2.92 (0.4H, d, J = 4.4 Hz), 2.42 (1H, br s), 2.22−1.70 (6H, m), 1.70−0.78 (22H, m), 1.03 (1.2H, s), 0.96 (1.8H, s), 0.89 (1.2H, s), 0.87 (1.2H, s), 0.85 (3.6H, s), 0.82 (3H, s), 0.61 (1.8H, s), 0.58 (1.2H, s); ^{13}C (50 MHz, $CDCl_3$) δ 69.4, 68.7, 66.5, 64.2, 63.6, 59.8, 57.0, 56.4, 56.3, 56.0, 51.5, 42.7, 42.5, 42.4, 42.1, 39.9, 39.6, 39.5, 39.4, 37.4, 36.3, 35.9, 34.9, 34.8, 32.7, 32.6, 30.9, 29.9, 29.8, 28.9, 28.4, 28.3, 28.2, 28.0, 24.4, 24.2, 24.0, 23.6, 23.0, 22.8, 22.2, 20.8, 18.8, 17.1, 16.1, 12.1, 12.0; MS 403 (M + H^+, 19).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General remarks, catalyst and conditions optimization including NMR data, as well as mechanistic investigations. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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