NJC

RSC Publishing

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c3nj00656e

Selective activation of secondary C–H bonds by an iron catalyst: insights into possibilities created by the use of a carboxyl-containing bipyridine ligand†

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Received (in Porto Alegre, Brazil) 18th June 2013,
Accepted 2nd August 2013

DOI: 10.1039/c3nj00656e

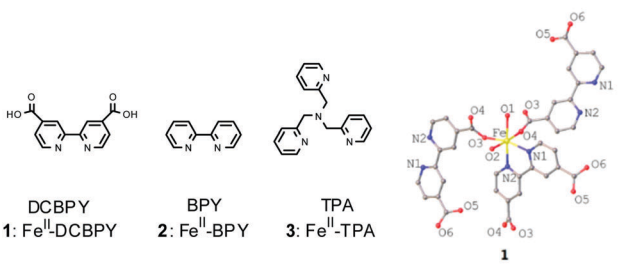
www.rsc.org/njc

In this work, we report the discovery of a carboxyl-containing iron catalyst **1** (Fe^{II}-DCBPY, DCBPY = 2,2′-bipyridine-4,4′-dicarboxylic acid), which could activate the C–H bonds of cycloalkanes with high secondary (2°) C–H bond selectivity. A turnover number (TN) of 11.8 and a 30% yield (based on the H_2O_2 oxidant) were achieved during the catalytic oxidation of cyclohexane by **1** under irradiation with visible light. For the transformation of cycloalkanes and bicyclic decalins with both 2° and tertiary (3°) C–H bonds, **1** always preferred to oxidise the 2° C–H bonds to the corresponding ketone and alcohol products; the 2°/3° ratio ranged between 78/22 and >99/1 across 7 examples. ^{18}O isotope labelling experiments, ESR experiments, a PPh_3 method and the catalase method were used to characterize the reaction process during the oxidation. The success of **1** showed that, in addition to using a bulky catalyst, high 2° C–H bond selectivity could also be achieved using a less bulky molecular iron complex as the catalyst.

Introduction

The functional oxidation of inert paraffin carbon–hydrogen (C–H) bonds has recently received increasing attention because the process can generate complex molecules from simpler ones.[1] However, the selectivity of the C–H bond activation is very difficult to control when multiple non-equivalent C–H bonds are present in the substrate molecule. In particular, the remaining challenge is the selective cleavage of 2° C–H bonds before 3° C–H bonds with smaller bond dissociation energies (BDE).[2] Despite the wide application of catalytically regiospecific oxidations of inactive C–H bonds, the majority of transition metal catalysts preferentially activate 3° C–H bonds.[1–5] This preference facilitates the abstraction of the hydrogen atom on the 3° C–H site with active oxidants, such as iron–oxo species, followed by the rebounding of an alkyl radical to form alcohols as products. However, nature has evolved many iron-containing enzymes, such as the soluble methane monooxygenases (s-MMO), which achieve the required 2° C–H bond oxidation, even in the presence of weaker 3° C–H bonds.[6] This selectivity could be attributed to the non-covalent or charged lock-and-key interactions between the substrates and the intricate binding pockets of the enzymes.[7] Very recently, a synthetic bulky polyoxometalate catalyst $[\gamma\text{-}HPV_2W_{10}O_{40}]^{4-}$ was reported to perform highly regioselective oxidations on the 2° C–H bonds of cycloalkanes with H_2O_2.[8] Inspired by this, we attempted to develop a less bulky molecular iron catalyst using carboxyl-containing ligands (see Scheme 1) and we expected **1** to realise the selective activation of 2° C–H bonds.

In previous disclosures, some iron complexes were used to accelerate the catalytic oxidation of organic compounds through irradiation with light.[9,10] We therefore found that using a ligand that was modified to include carboxylic groups on the 4,4′-positions of 2,2′-bipyridine significantly improved the reactivity of iron-complex. For example, in addition to higher photocatalytic activity, **1** could facilitate the use of more dioxygen in the oxidation with H_2O_2 than its parent complex **2**



Scheme 1 Three catalysts and their corresponding ligands.

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† Electronic supplementary information (ESI) available. See DOI: 10.1039/c3nj00656e

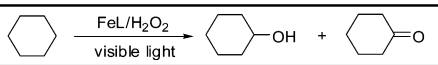
(Fe^{II}–BPY, BPY = 2,2′-bipyridine). Recently, a single crystal structure of **1** was successfully determined by Li *et al.* (right side of Scheme 1, H atoms have been omitted for clarity);[11] **1** resembles the typical N,N,O-coordinated structures of many non-heme mononuclear iron enzymes.[12] Its Fe–$O_{carboxylate}$ bond lengths, which are 2.111(2) Å and 2.148(1) Å, are longer than the previously reported bond lengths between a carbonyl and iron (2.00–2.08 Å), as well as an amide carbonyl and iron (2.043–2.047 Å).[13] The Fe–$N_{bipyridine}$ lengths (2.186(3) Å and 2.178(2) Å) are also longer than those found in **2**, which has Fe–$N_{aromatic}$ ≈ 1.98 Å,[14] and tetradentate tripodal coordinated Fe^{II}–TPA (**3**, TPA = tris-(2-pyridylmethyl)amine) with Fe–$N_{pyridine}$ lengths of 1.92–1.99 Å.[15] The coordination of **1** is loose and is therefore envisioned to cover more space with its stereo-electronic effects for selective C–H cleavage.

Results and discussion

Catalytic and photocatalytic activity in the oxidative transformation of cyclohexane

A typical oxidation of cyclohexane by H_2O_2 was first performed in an aqueous CH_3CN solution at room temperature (Table 1), in which we evaluated the activity of the three iron catalysts (Scheme 1) mainly by their turnover numbers (TN) (represented by the products, including both cyclohexanol (A) and cyclohexanone (K), per catalyst). As determined by GC, no products were formed without H_2O_2 in either the absence or presence of visible light irradiation for all the iron catalysts tested. To obtain the best TN, both the reactant and mixed solvent ratios needed to be optimised. With the optimal reactive conditions, **1** exhibited superior reaction properties and provided a TN of 11.8 after 20 hours (Table 1, entry 8), which was 1–2 orders of magnitude greater than Fe^{II} (Table 1, entry 1), **2** (Table 1, entry 3) and **3** (Table 1, entry 5). Similar to the results previously reported for the degradation of organic pollutants in water,[9,17] visible light irradiation significantly enhanced the TN observed for the cyclohexane transformation (Table 1, entries 8 and 9). Unfortunately, the A/K ratio generated by **1** was quite low and this catalytic oxidation did not remain in the alcohol stage. However, the cyclohexanone formation was not caused by cyclohexanol over-oxidation or autoxidation in this case, which was indicated by our control experiments; cyclohexanol, when used as the initial reactant, could not transform into the ketone over an identical reaction time. Therefore, cyclohexanone formation should be attributed to the involvement of a long-lived alkyl radical $R^{\bullet}$. This species would subsequently capture dioxygen to form ROOH, which is commonly decomposed into equal parts of alcohol and ketone. To confirm this pathway, two independent experiments were carried out with $^{18}O_2$ and $H_2{}^{18}O$ to detect the origin of the O atom in the formed cyclohexanol. Incorporation of the O-atom from H_2O_2 was calculated based on two other values from H_2O and O_2. During the ^{18}O labelling experiments, the oxygen atom in the product alcohol was primarily from O_2 (≈67% for entry 8, Table 1), while H_2O_2 contributed ≈32%. In addition, Ar purge experiments were conducted to remove O_2 from the system and subsequently the product yield decreased precipitously; therefore, O_2 is a participant in the transformation of alkanes by **1**.

Table 1 Cyclohexane oxidation by various iron catalysts[a]



Entry	Catalyst	I[b]	TN	A/K[c]	O-atom of alcohol from H_2O_2/H_2O/O_2[d] (%)
1[e]	Fe^{II}	+	0.5	0.31	57/0/43
2[e]	Fe^{II}	−	0.5	0.31	57/0/43
3	**2**	+	0.7	0.56	49/0/51
4	**2**	−	0.4	0.32	70/0/30
5	**3**	+	0.1	0.52	—
6	**3**	−	0.1	0.36	—
7[f]	**3**	−	3.2	5.0	70/27/3
8[g]	**1**	+	11.8	0.71	32/1/67
9	**1**	−	1.4	0.54	55/1/44

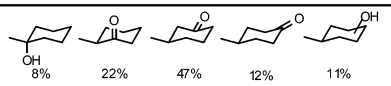
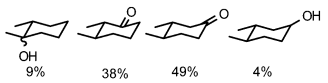
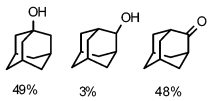
[a] Reaction conditions: 1.5 mM iron catalyst, 1.5 M alkane substrate and 60 mM H_2O_2 in 2.5 mL CH_3CN–H_2O solution (CH_3CN–H_2O (v/v) = 60/40), 20 h reaction time. [b] I = irradiation. + = visible irradiation (λ > 420 nm), − = without visible irradiation. [c] A = cyclohexanol, K = cyclohexanone. [d] Incorporation of the O-atom from H_2O_2 was calculated based on the two other values from H_2O and O_2, which were detected through experiments with $H_2{}^{16}O_2$/$H_2{}^{18}O$/$^{16}O_2$ and $H_2{}^{16}O_2$/$H_2{}^{16}O$/$^{18}O_2$, respectively. [e] Fe^{II} = $Fe^{II}(ClO_4)_2{\cdot}6H_2O$. [f] 1.5 mM iron catalyst, 1.5 M alkane substrate and 15 mM H_2O_2 in 2.5 mL CH_3CN with 1000 equiv. H_2O relative to **3**. [g] The quantum yield ($\varnothing$) based on the irradiation at wavelength λ = 520 nm was about $\varnothing$ = 0.23%, which was obtained by the previously described method.[16] For the detailed method, see the Experimental section.

Generally, alkyl peroxides (ROOH) readily decompose in catalytic systems,[18] but occasionally these molecules do not decompose over time and subsequently accumulate at high concentrations. In the injector of the G, the peroxides decomposed to form mixtures of products and led to incorrect results. According to well-known methods[18] we used Ph_3P to treat the reaction samples, as a test to reveal whether ROOH had accumulated. Our results showed that the product distribution was unchanged after treatment with Ph_3P, which illustrated that ROOH (if formed) had already decomposed before GC analysis. In addition, the catalase method[19] was utilised to detect ROOH accumulation in the reaction that was catalysed by **1**. As expected, ROOH had not accumulated during the transformation of the substrate (Fig. S4, ESI†). As an excellent non-heme iron catalyst,[15] **3** had a TN of 3.2 and a high A/K ratio of 5 in CH_3CN (Table 1, entry 7), whereas its catalytic activity was quite low in aqueous CH_3CN solutions (Table 1, entries 5 and 6). In CH_3CN, the oxygen atom of the product alcohol was only ≈3% from O_2 and ≈70% from H_2O_2 during the catalytic process with **3**; this value was consistent with that reported by Que and Chen.[15] These preliminary results implied that **1** differed from **3** in both the process of the substrate activation and the active oxidant species.

Anomalous 2°/3° selectivity for transformations of cycloalkane

When mono- and di-substituted methylcyclohexanes were employed as substrates (see Table 2), **1** exhibited surprisingly high 2°/3° selectivity (78/22–92/8) for all of the oxidative products (A + K). **1** exhibits a high selectivity for secondary products with

Table 2 Selective oxidation of cycloalkanes by **1** under visible irradiation[a]

Entry	Substrate	Products (selectivity)	TN	2°/3°[b]
1		 OH 8% 22% 47% 12% 11%	6.3	92/8
2		 HO 22% (*cis*/*trans*=55/45) 4% 29% 7% 38%	7.2	78/22
3		 OH 9% 38% 49% 4% (*cis*/*trans*=56/44)	6.5	91/9
4		 OH OH 49% 3% 48%	4.8	51/49

[a] Reaction conditions: 1.5 mM iron catalyst, 1.5 M alkane substrate and 60 mM H_2O_2 in 2.5 mL CH_3CN–H_2O solution (CH_3CN–H_2O (v/v) = 60/40), 20 h reaction time. [b] 2°/3° = (all 2° alcohol + ketone)/all 3° alcohols.

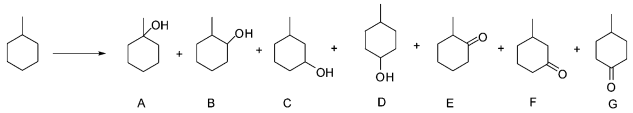
both *cis*- and *trans*-DMC (DMC = 1,2-dimethylcyclohexane); however, its 3° alcohol products could not maintain stereospecificity, which was most likely due to the epimerisation of a long-lived radical R• or carbonium intermediate (*cis*/*trans* = 55/45 for *cis*- and 56/44 for *trans*-) (entries 2 and 3 of Table 2). Interestingly, some iron systems with enhanced 2° C–H selectivity demonstrated selectivity for only *cis*-DMC or *trans*-DMC.[20] For example, the H_2O_2 based system using non-heme iron catalyst Fe(*S*,*S*-PDP),[20a] that was recently reported, gave a normal selectivity of 2°/3° = 20/80 for *cis*-DMC but a reverse 2°/3° ratio of 67/33 for *trans*-DMC. Several iron systems exhibited a normal 2°/3° selectivity such as **3** (25/75) and $[Fe^{II}(N_4Py)]^{2+}$ (<1/99) during the oxidation of DMC (Table S2, ESI†).[3,5] During the oxidation of adamantane, which had a special steric effect that led to the oxidation of the 3° C–H bond (entry 4 of Table 2). **1** afforded a higher 2°/3° value of 51/49 than the bulky polyoxometalate (2°/3° = 15/85),[8] which indicated that the steric effect of adamantane was not the parameter that controlled the regiospecific oxidation; instead, the selectivity of **1** for 2° C–H bonds might be determined by the catalyst structure.

Some classic examples have demonstrated that, in addition to chemically stoichiometric oxidations with peracid and dioxirane, transition-metal-catalysed systems without bulky ligands nearly always exclusively favour the formation of 3° alcohols (see entries 4–11 of Table 3 and Table S2, ESI†).[21] Iron systems with no ligands (a Fenton system, entry 6 of Table 3), which generate •OH radicals as the main oxidant, display enhanced selectivity toward tertiary sites, which indicates that the •OH radicals did not afford such specific 2° selectivity. Visible light irradiation had no effect on the 2°/3° selectivity for alkanes; therefore, the selectivity was not induced by visible light irradiation. Except for the use of the bulky polyoxometalate catalyst $[\gamma\text{-}HPV_2W_{10}O_{40}]^{4-}$,[8] such clear selectivity for the 2° C–H bond in the presence of weaker and more electron-rich 3° C–H bonds could not be obtained with transition metal catalysts until now. Catalyst **1** demonstrated high selectivity, which could only be obtained using carboxyl-based oxidants, such as peracetic acid or *m*-CPBA.[22]

The effect of substrates with different C–H bonds on the 2°/3° selectivity

We investigated the photocatalytic oxidation of other cycloalkanes with different 2° and 3° C–H bonds (Table 4). The electron-donating, alkyl-substituted cycloalkanes (Table 4, entries 1 and 2) and the bicyclic decalins (Table 4, entries 3 and 4), which had significantly different steric and stereoelectronic effects, afforded, without exception, 3° alcohols and 2° ketones as the minor and major products, respectively; the remarkably high 2°/3° ratios of the products ranged from 87/13 to >99/1. This specific selectivity for 2° C–H bonds in a wide range of substrates is very similar to that of the polyoxometalate catalyst.[8] Although these C–H bonds were non-equivalent towards

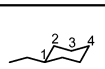
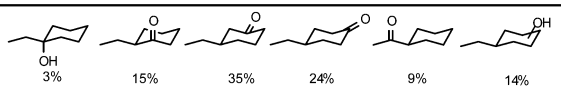
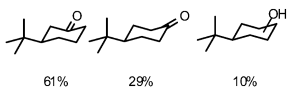
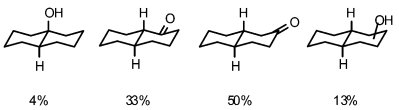
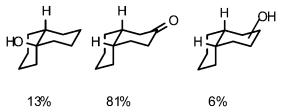
Table 3 Comparison of regioselectivity and product distribution in the different oxidations of ethylcyclohexane



Entry	System	Selectivity[a] (%) A	B	C	D	E	F	G	Others	[2°]/[3°]	TN	Ref.
1	**1**–H_2O_2 (this work)	8	11			22	47	12	—	92/8	6.3	
2	$[(n\text{-}C_4H_9)_4N]_4[\gamma\text{-}HPV_2W_{10}O_{40}]$–$H_2O_2$	19	6	44	24	1	4	2	—	81/19	28.8	8
3	Cytochrome P450[b]	25	8	43	23				1[f]	75/25	—	23
4	Mn(TPP)–PhIO[c]	36	29	5	26	2	2		—	64/36	3.4	24
5	Mn(TPP)–PhIO[d]	37	3	8	15	17	20		—	63/37	3.0	24
6	$Fe(ClO_4)_3$–H_2O_2	41	55						4[f]	56/44	—	21*e*
7	$Cu(H_3L)(NCS)$–TBHP[e]	53	46						2[f]	47/53	—	25
8	$RuCl_3$–IO_4^-	67	—	—	—	20	7	6	—	33/67	523	26
9	CF_3COOH	88	4	4	4	—	—	—	—	12/88	—	23
10	Methyl(trifluoromethyl)dioxirane	92	—	—	—	—	8	—	—	8/92	1.0	27
11	$CrO_2(OAc)_2$–H_5IO_6	>99	—	—	—	—	—	—	—	<1/99	13	28

[a] Selectivity (%) = product (mol)/total products (mol) × 100. [b] Obtained from rat-liver microsomes. [c] Performed under anaerobic conditions. [d] Performed under aerobic conditions. [e] L = *N*,*N*,*N*′,*N*′-tetrakis(2-hydroxyethyl)ethylenediamine. [f] Hexahydrobenzylalcohol.

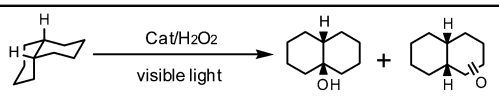
Table 4 Selective oxidation of cycloalkanes by **1** under visible light irradiation[a]

Entry	Substrate	Products (selectivity)	TN	2°/3°[b]	[Ketones]/[2° alcohols]
1		 3% 15% 35% 24% 9% 14%	4.7	97/3 (86/14)	86/14
2		 61% 29% 10%	5.2	>99/1 (83/17)	90/10
3		 4% 33% 50% 13%	6.8	96/4[c] (80/20)	87/13
4		 13% 81% 6%	7.6	87/13[d] (80/20)	93/7

[a] Reaction conditions: 1.5 mM iron catalyst, 1.5 M alkane substrate and 60 mM H_2O_2 in 2.5 mL CH_3CN–H_2O solution (CH_3CN–H_2O (v/v) = 60/40), 20 h reaction time. [b] 2°/3° = (all 2° alcohol + ketone)/all 3° alcohols. Number in parentheses were theoretically calculated 2°/3° value as statistic average for all 2° and 3° C–H bonds. [c] *cis*-9-Decalol/*trans*-9-decalol = 20/80. [d] *cis*-9-Decalol/*trans*-9-decalol = 28/72.

oxidation,[2,8,20] a simple statistical hypothesis was proposed: if 3° and 2° C–H bonds have equal and random reactivity (see the statistic average values in parentheses in Table 4), then a preference for the 2° C–H bond was displayed by **1** and the 3° selectivity was below its average value. Similar to the polyoxometalate catalyst,[8] which resulted in at least six 2° products (see entry 2 of Table 3), **1** generated multiple products for all of the substituted cyclohexanes. This result illustrated that these catalysts were predisposed towards the cleavage of 2° C–H bonds, but they could not distinguish between 2° C–H sites with different chemo-environments. In addition, a higher chemoselectivity toward ketones was observed for the four substituted substrates (A/K = 14/86–7/93) than the unsubstituted cyclohexanes (A/K = 42/58–35/65, see Table 1), which clearly implies that the **1**-mediated ketone formation is not a simple over-oxidation or autoxidation.

Table 5 Oxidation of *cis*-decalin by **1**, **2** and **3** as well as Fe^{II}[a]



Catalyst	Substrate	[2°]/[3°]
1	*cis*-Decalin	87/13
2	*cis*-Decalin	40/60
2[b]	*cis*-Decalin	42/58
3	*cis*-Decalin	45/55
Fe^{II}	*cis*-Decalin	21/79
Fe^{II}	Ethyl cyclohexane	58/42
Fe^{II}	*tert*-Butyl cyclohexane	55/45

[a] Reaction conditions: 1.5 mM iron catalyst, 1.5 M alkane substrate and 60 mM H_2O_2 in 2.5 mL CH_3CN–H_2O solution. [b] Solutions contains excess acetic acid (2000 equiv. relative to the iron catalyst).

Possible mechanisms for the creation of 2°/3° selectivity

White and Chen proposed that an *in situ*-formed bulky oxidant could cause a reversal of the 2°/3° selectivity during the oxidation of *trans*-DMC.[20a] However, the substrate-independent selectivity of **1** should be attributed to the carboxyl groups that are located on the BPY ligand. To elucidate the role of the carboxyl groups on **1**, we compared **1** with **2** and **3** (both without carboxyl groups in the skeleton of the ligand) during the oxidation of *cis*-decalin (Table 5) under identical reaction conditions. As expected, **2** and **3** did not demonstrate an obviously high selectivity towards 2°/3° C–H bonds. Excess acetic acid, which was added to a reaction with **2**, did not strongly affect the selectivity of **2**, which excluded the possibility that the selectivity of **1** was simply induced by the carboxylic acid. For **3**, it is well known that a high-valent iron–oxo species was generated to induce the homolytic cleavage of the weaker 3° C–H bond *via* H atom abstraction and the subsequent rebounding of the short-lived alkyl radical to give the alcohol products. Simultaneously, the iron-catalysed oxidation without the ligand (conventional Fenton reaction) *via* the •OH radical pathway furnished a lower 2°/3° selectivity (21/79); this selectivity was close to the previously reported value,[29] as well as being lower than both **2** and **3**. To confirm this result, two other substrates (ethyl cyclohexane and *tert*-butyl cyclohexane) were used to extend this comparison using the iron catalyst without any ligand (Fenton system). The oxidation occurred preferentially at the tertiary sites; the 2°/3° selectivity was 58/42 and 55/45 for ethyl cyclohexane and *tert*-butyl cyclohexane, respectively. Furthermore, ESR experiments were conducted to detect the presence of any •OH radicals in both the **1**-catalysed oxidation and the Fenton system under identical conditions. In agreement with the previous catalytic results,[30] the trapped DMPO–•OH radical adduct easily formed under the Fenton system and the signal exhibited was strong at room temperature. However, no obvious DMPO–•OH adduct was observed during the **1**-catalysed oxidation (Fig. S5, ESI†), which further indicated that **1**, at least, did not generate a long-lived free radical derivative of the substrate *via* an •OH radical. The origin of the special selectivity remained speculative and there are two

possible explanations for the origin of the selectivity. One possibility was that a carbonium intermediate of the substrates might form over the course of the reaction; therefore, the carboxyl groups, which have with a negative charge on the ligand, might interact with the carbonium intermediate and provide the stereo-electronic effects to make the 2° C–H cleavage favourable. Another possibility was that peracid was formed *in situ* by the reaction of the carboxyl groups on the ligand of **1** and H_2O_2; the oxygen atom could subsequently be reacted with the 2° C–H site through a non-covalent interaction, which has also observed during non-catalytic oxidations with peracetic acid or *m*-CPBA.[21a] The pendent carboxyl groups of **1** play important roles in the selective oxidation. However, both explanations need more evidence and further studies.

Conclusions

In summary, the iron catalyst **1**, which utilised BPY ligands that were modified with carboxyl groups, was found to not only exhibit better catalytic activity during the oxidation of alkanes, but also achieved a reverse oxidative selectivity for 2° over 3° C–H bonds. Although **1** currently affords only intractable mixtures of ketones and the TN for **1** is not comparable to the most active catalyst,[8] our results provide an alternative approach, which is to mimic iron enzymes that contain a 2-His-1-carboxylate coordination environment, and realise the favourable activation of 2° C–H bonds.

Experimental

The iron catalysts were all prepared as described previously.[9,15] Catalyst **1** was prepared by mixing $Fe^{II}(ClO_4)_2{\cdot}6H_2O$ with 3 equiv. of DCBPY ligand in H_2O. Catalyst **2** was prepared by mixing $Fe^{II}(ClO_4)_2{\cdot}6H_2O$ with 3 equiv. of BPY ligand in CH_3CN. Catalyst **3** was prepared by mixing equimolar amounts of $Fe^{II}(ClO_4)_2{\cdot}6H_2O$ and TPA ligand in CH_3CN.

The reaction conditions were as follows: photocatalytic experiments were conducted under visible light irradiation through a cut-off filter (λ > 420 nm), with a 500 W halogen lamp (Philip) as the visible light source. The light source was positioned inside a cylindrical Pyrex vessel that was surrounded by a Pyrex jacket that contained circulating water to cool the lamp. The reaction mixture comprised the iron catalyst (1.5 mM), alkane substrate (1.5 M) and H_2O_2 (60 mM) in a solution of CH_3CN–H_2O (2.5 mL, CH_3CN–H_2O (v/v) = 60/40). H_2O_2 was added to a vigorously stirred CH_3CN solution over *ca.* 45–75 s. The reaction time was 20 h. In all cases, bromobenzene was added as an internal standard. The products were extracted with ether and dried over $MgSO_4$ before GC analysis. The samples were analysed twice, once before and once after the treatment of PPh_3. Because the TN for **2**, **3** and $Fe^{II}(ClO_4)_2{\cdot}6H_2O$ were too small in solutions that contained too much H_2O and the ratio for CH_3CN–H_2O had no effect on the selectivity, the reaction with **2** and **3** was conducted in the pure CH_3CN solution rather than an aqueous CH_3CN–H_2O (60/40) solution to improve the accuracy of the experiments exhibited in Table 5.

The quantum yield ($\varnothing$) was detected using a monochromatic light filter (λ = 520 nm). $\varnothing$ is defined as the number of product molecules N_{mol} (5.7×10^{14} molecules per s, calculated based on the enhancement of product yields brought by the photo irradiation) relative to the number of photons $N_{photons}$ absorbed by the photocatalyst:

$$\varnothing = \frac{N_{mol(molecules\ per\ s)}}{N_{photons(photons\ per\ s)}}$$

$N_{photons}$, the amount of photons absorbed or scattered by the photocatalyst, was calculated following the equation:

$$N_{photons} = E_{abs} \times 10^{-3}\ C_f S$$

where E_{abs} is the light energy scattered by the lamp (62 mW cm^{-2}), C_f is the reciprocal of the average light energy of each photon (2.6×10^{18} W^{-1} s^{-1}) emitted by the lamp at 520 nm and S is the entrance area of the light reactor (1.5 cm^2).

The isotope-labelling experiments were carried out as follows: in experiments with $H_2{}^{18}O$, $H_2{}^{18}O$ (97% ^{18}O-enriched) was used as a solvent rather than H_2O (entries 1–6 and 8 and 9 of Table 1), whereas 1000 equiv. $H_2{}^{18}O$, which was relative to the catalyst, was added to the solution before the addition of H_2O_2 (entry 7 of Table 1). In the experiments with $^{18}O_2$ (96% ^{18}O-enriched), the reaction mixtures were degassed with five freeze–vacuum–thaw cycles before the reaction; the reaction was performed under an atmosphere of $^{18}O_2$. The ^{16}O and ^{18}O isotope distribution was determined *via* the relative abundances of the products. The substrates were purified according to the reported procedure.[31] The cycloalkanols (3-ethylcyclohexanol, 3-*tert*-butylcyclohexanol, and 1-decalinol) were synthesised by the Ru/Al_2O_3-catalysed hydrogenation of the corresponding phenols or naphthol (3-ethylphenol, 3-*tert*-butylphenol, and 1-naphthol) with H_2 (20–50 atm).[32] The cycloalkanones (3-ethylcyclohexanone, 3-*tert*-butylcyclohexanone, and 2-decalinone) were synthesised *via* the oxidation of the corresponding alcohols (3-ethylcyclohexanol, 3-*tert*-butylcyclohexanol, and 2-decalinol) with $K_2Cr_2O_7$. *cis*-9-Decalinol and *trans*-9-decalinol were synthesised by the stereospecific hydroxylation of *cis*-decalin and *trans*-decalin with *m*-CPBA/I_2, respectively.[33] 1-Ethylcyclohexanol was synthesised *via* the $LiAlH_4$-catalysed reduction of 1-ethynyl-1-cyclohexanol with H_2.[34] *cis*-DMC and *trans*-DMC were synthesised through the oxidation of DMC, which was catalysed by **3**/H_2O_2, respectively.[15] The diastereomeric mixtures of the synthesised or commercially available reagents were separated by GC (Agilent).

The DPD (*N*,*N*′-dialkyl-*p*-phenylenediamine) method that was employed for the peroxide measurements was used for the detection of both H_2O_2, as well as any ROOH intermediate that was formed during the oxidation of the alkanes.[19a] The catalase enzyme, which was used for detecting the presence of a ROOH intermediate,[19b] was added before the DPD and POD (horseradish peroxidase). The concentration of the total peroxides (which included organoperoxides and H_2O_2) that formed during the irradiation was determined after a reaction time of 5 h. A spectrophotometric DPD method was employed

(λ = 551 nm, ε = 21 000 M^{-1} cm^{-1}); the DPD reagent was oxidised by either H_2O_2 and/or the organoperoxides and was based on the peroxidase-catalysed reaction. It is known that the catalase enzyme can eliminate H_2O_2 from a mixture of H_2O_2 and organoperoxides. If the catalase is added to a solution that contains H_2O_2 and organoperoxides before the DPD method is used, then this DPD method assays only the organoperoxides. We can therefore discriminate between H_2O_2 and the organoperoxides to determine if the alkyl peroxides ROOH were decomposed over the course of the reaction or accumulated at a high concentration.

The electron spin resonance (ESR) signals of the radicals that were trapped by DMPO were detected at ambient temperature with a Bruker ESR 500 E spectrometer under the same reaction conditions that were used for the other reactions. A 30 μL sample of the solution was collected at a specified time and transferred to a quartz capillary for ESR measurement. The settings for the ESR spectrometer were as follows: centre field, 3443 G; sweep width, 100 G; microwave frequency, 9.64 GHz; modulation frequency, 100 kHz; power, 10.05 mW. To minimise experimental errors, the same quartz capillary tube was used for all EPR measurements. The temperature was controlled with a standard temperature accessory and was monitored before and after each measurement.

Acknowledgements

Financial support from 973 projects (No. 2010CB933503 and 2013CB632405), the NSFC (No. 21137004, 21077110 and 21273445), and CAS is greatly appreciated.

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