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Graphical Abstract

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Biphasic copper-catalyzed C–H bond activation of arylalkanes to ketones with *tert*-butyl hydroperoxide in water at room temperature

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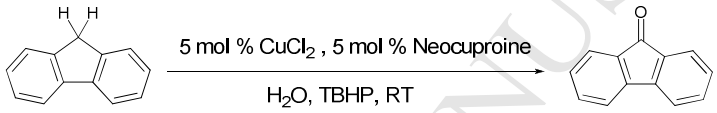

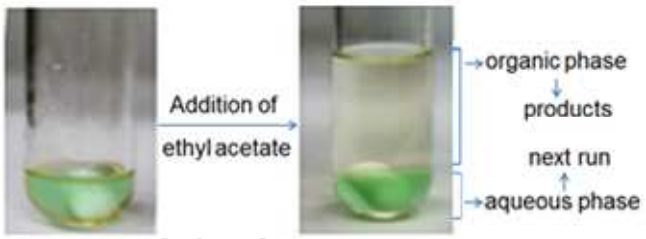

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ABSTRACT

A facile C–H bond activation of arylalkanes to their corresponding ketones catalyzed by copper salts using *tert*-butyl hydroperoxide as an oxidant in water at room temperature is described. Easy product separation, simple reaction procedures (without using base or phase transfer catalysis), and catalyst recycling make the catalytic system attractive. It is also active beyond activated benzylic methylene positions and could tolerate factionalized arylalkanes with diverse groups.

1. Introduction

Aromatic compounds are integral parts of various natural products and key intermediates for the synthesis of drugs, perfumes, insecticides, and photo initiators.[1] Traditionally, their synthesis through acylation of aromatic compounds catalyzed by acids requires harsh reaction conditions, and stoichiometric amounts of oxidants, resulting in the formation of toxic and corrosive wastes.[2] Oxidation of methylene groups of alkylaromatics to benzylic ketones using stoichiometric quantities of $KMnO_4$ as an oxidant produces a large volume of wastes, and product separation is also difficult.[3] The Industrial production of benzylic ketones using oxygen and a cobalt catalyst in acetic acid is often limited due to the corrosive nature of the solvent and the homogeneous feature of the catalyst.[4] Several methods using homogeneous,[5] heterogeneous,[6] and metal-free[7] catalysts are reported for the synthesis of ketones by benzylic C–H bond activation of alkylaromatics. Despite the importance of such a process, green as well as economic protocols are still scarce.

In this context, a process with inexpensive catalyst and benign oxidant are considered to be environmentally friendly. However, a process with a reasonable catalyst/oxidant combination can be overshadowed by a single parameter, i.e., solvent, as it is the main contributor to the organic wastes. Thus, instead of a catalyst/oxidant combination, solvent is also an important factor from the environmental perspective of such a process.[8] Among the solvents, water, a green solvent, is not only non-toxic, non-flammable, and abundantly available, but also exhibits different reactivity in comparison to organic solvents.[9] Reactions in water can enhance the reaction rate and the selectivity owing to its hydrophobic effect.[9c] In addition, aqueous biphasic systems offer easy separation of the product (dissolved in the organic phase) and the catalyst (resides in the water phase).[9a] Thus, the development of a catalytic system operating in water is highly desirable.

Regarding the catalyst, the use of copper salts or complexes as the catalyst has gained much prominence recently because of their viability, reduced handling hazard, good functional group tolerance, and scalability in synthetic procedures.[5a,e,f] On the other hand, in consideration of the oxidant, cheap and readily available 70% aqueous *tert*-butyl hydroperoxide (TBHP) is used frequently as a promising alternate to H_2O_2 in combination with various metal catalysts.[10] Moreover, TBHP has fewer handling risks than does H_2O_2 in water,[10g,h] and its reduction to a volatile and non-toxic[10d,g,11] alcohol by-product simplifies purification. Thus, the catalytic combination of Cu/TBHP/H_2O can provide economic, environmental, and separation benefits.

Recently, we reported the oxidative cleavage of alkene double bonds to their corresponding carbonyl compounds with oxygen catalyzed by a water soluble copper complex [Cu(μ-Cl)Cl(phen)]$_2$[12] (which was synthesized in high yield using a

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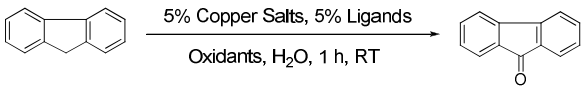
simple method)[13] and copper salts with neocuproine (2,9-dimethyl-1, 10-phenanthroline) with TBHP in water (denoted as catalytic system **A**).[14] In continuation of our explorations in developing a simple and sustainable catalytic process for the oxidation of organic substrates, herein we report a facile and selective C–H bond activation of arylalkanes to their corresponding carbonyl compounds catalyzed by Cu(II)/Cu(I) salts using TBHP as an oxidant in water at room temperature without using any phase transfer catalyst or base. The catalyst is recyclable and retains its high activity up to several cycles.

2. Results and discussion

To optimize the reaction conditions, the reactions of fluorene with different ligands, copper salts, and oxidants were carried out under identical conditions. The results are summarized in Table 1.

Among different bidentate bipyridine ligands (Table 1, entries 1-4), neocuproine completes the oxidation reaction in an hour in the presence of $CuCl_2 \cdot 2H_2O$ and water with high yield (Table 1, entry 1). Reactions in the absence of $CuCl_2$ (entry 5) and/or ligand (entry 6) affording comparable product yields with that of only TBHP (entry 7) suggest that TBHP is responsible for the conversion. In addition, no reaction was observed when TBHP was removed from the $CuCl_2$/neocuproine/TBHP catalytic system (entry 8) or when $CuCl_2$ was used in the absence of neocuproine and TBHP (entry 9).

Table 1 Optimization of the reaction conditions for the oxidation of fluorene in different copper salts, oxidants, and ligands.[a]



Entry	Ligands	Oxidants	Copper Salts	Conv./GC Yield (%)	Select. (%)
1	neo[b]	TBHP	$CuCl_2$	100/98	98
2	phen	TBHP	$CuCl_2$	12/3	25
3	bipy[c]	TBHP	$CuCl_2$	13/4	31
4	DMP[d]	TBHP	$CuCl_2$	14/4	29
5	neo	TBHP	no	14/6	43
6	no	TBHP	$CuCl_2$	15/5	33
7	no	TBHP	no	18/7	39
8	nuo	no	$CuCl_2$	–	–
9	no	no	$CuCl_2$	–	–
10	neo[e]	TBHP[e]	$CuCl_2$	100/89	89
11[f]	neo	TBHP	CuCl	100/99	99
12	neo	TBHP	$CuBr_2$	100/98	98
13	neo	TBHP	CuBr	100/99	99
14	neo	TBHP	CuI	100/98	98
15	neo	TBHP	$Cu(NO_3)_2$	66/54	82
16	neo	TBHP	$CuSO_4$	18/13	72
17	neo	TBHP	$Cu(OAc)_2$	97/95	98
18	neo	H_2O_2	$CuCl_2$	–	–
19	neo	THFH[g]	$CuCl_2$	7/2	29
20	neo	CHP[h]	$CuCl_2$	91/85	94

[a]Reaction conditions: fluorene (0.2 mmol), copper salts (0.01 mmol), ligands (0.01 mmol), oxidants (1.4 mmol) 70% aq. TBHP, H_2O (0.7 mL).
[b]neocuproine.
[c]bipyridine.
[d]4,7-dimethyl-1,10-phenanthroline.
[e]5M-6M decane solution, solid $CuCl_2 \cdot 2H_2O$.
[f]fluorene (0.4 mmol), neocuproine (0.02 mmol), TBHP (2.8 mmol), CuCl (0.02 mmol).
[g]THF-hydroperoxide.
[h]cumene hydroperoxide.

These observations support the individual inertness of $CuCl_2$ and neocuproine toward the reaction. In the presence of other bidentate ligands (entries 2-4), the yields are comparable to that of only TBHP (entry 7) suggesting that these ligands are inert toward the reaction. Thus, both copper and neocuproine are needed for the catalytic reactions (entry 1). The cause behind reactivity and product selectivity enhancements by neocuproine as compared to other ligands (entries 2-4) is not clear. Reactivity enhancement due to the inductive effect of a methyl substituent should be minor as the ligand 4,7-dimethyl-1,10-phenanthroline (DMP) with a similar methyl substituent shows a lower reactivity (entry 4). The structures of the ligands are shown in Chart 1.

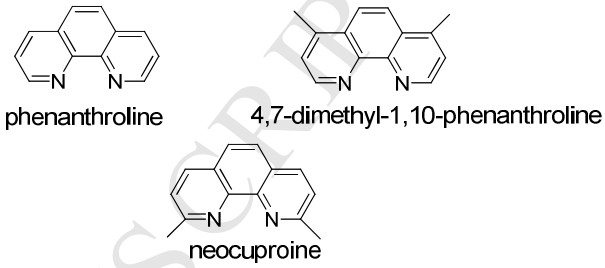


Chart 1

Both Cu(I) and Cu(II) salts (entries 1 and 11-17) are effective in catalyzing the reaction. However, the counterions have significant impact on the reactivity toward activation.[5a] Thus, $Cu(NO_3)_2$ (entry 15) and $CuSO_4$ (entry 16) are less reactive than other copper salts (entries 1, 11-14, 17). Reactions with Cu halides afforded similar product yields irrespective of their oxidation states and counterions (entries 1 and 11-14), indicating that they may have similar active species and follow a similar reaction path in the reactions. The active species should be Cu(II) and Cu(I) moieties formed *in situ* in the redox reaction in the catalytic cycle. The typical green color of Cu(II) observed in the reaction mixture further supports the above hypothesis (Fig. 1).

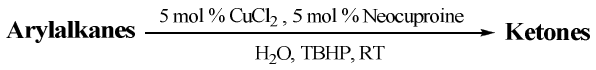
Among different oxidants, H_2O_2 is not active (entry 18), whereas organic peroxides, 2-hydroperoxy-tetrahydrofuran (THFHP) is less active as compared to *tert*-butyl hydroperoxide (TBHP) and cumene hydroperoxide (CHP) (entries 1, 19 and 20). Hence, the order of reactivity is TBHP ~ CHP > THFHP > H_2O_2. Formation and stabilisation of the usual free radical intermediates (generated during oxidation) may be facilitated according to the positive inductive effect of alkyl substituent of organic peroxides, and accordingly they then interact with the substrates for their conversion.[14] TBHP is miscible in both water and organic phase in the reaction mixture and thus favors close interaction with the organic reagent and results in smooth oxidation. Water soluble H_2O_2 cannot provide such miscibility and interaction toward hydrophobic arylalkanes, and therefore oxidation reaction is limited.

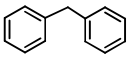
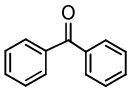
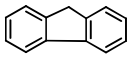
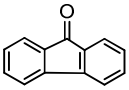
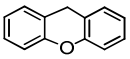
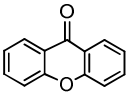
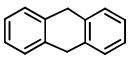
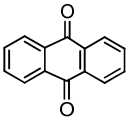
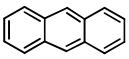
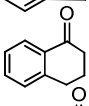
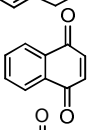
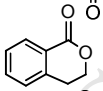
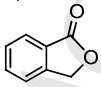
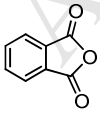
To evaluate the role of water as a solvent, we used TBHP in decane and solid $CuCl_2 \cdot 2H_2O$ without adding water (entry 10). The reactions are smooth both in aqueous TBHP (organic solvent free) and TBHP in decane. Yields and selectivity in the former case is better than those in the latter case (entries 1 and 10). This indicates that reactions in water may proceed in the organic phase, and water not only forms a biphasic system but also influences the product selectivity of the reaction to some extent.[9c] It is also advantageous to use the biphasic system because water is unavoidable in product separation and reused of the aqueous

phase, containing the catalyst (Fig. 1). The catalytic system was then applied to various arylalkanes in water. The results are summarized in Table 2.

It is noted that monoarylalkane (Table 2, entry 1) is less reactive than diarylalkane (entry 2). When aryl substituents are part of a tricyclic substrate, oxidation is even faster (entries 3-5). Bicyclic arylalkanes (entries 6 and 7) are more reactive than acyclic arylalkanes (entries 1 and 2) indicating that the aromatic substituent plays a pivotal role in affecting the reactivity.

Table 2 Oxidation of arylalkanes into ketones[a]



Entry	Arylalkanes	Products	Time (h)	Conv. (%)	GC Yields[b] /Select. (%)
1			17	98	97 (91)/99
2			7	>99	93 (89)/94
3			1	100	99 (95)/99
4			1	100	99 (95)/99
5		 	1	100	81 (76)/81 10 (–) /10
6			1	100	56 (51)/56
7		 	1	100	29 (25)/29 33 (29)/33
8			1	100	78 (72)/78
9		 	1	100	24 (21)/24 41 (37)/41

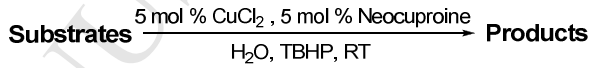
[a]Reaction conditions: arylalkanes (0.2 mmol), $CuCl_2{\cdot}2H_2O$ (0.01 mmol), neocuproine (0.01 mmol), H_2O (0.7 mL), *tert*-butyl hydroperoxide (1.4 mmol).

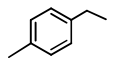
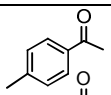
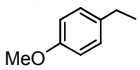
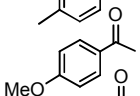
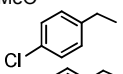
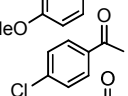
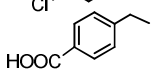
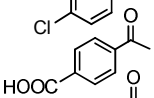
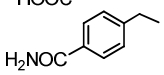
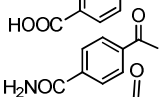
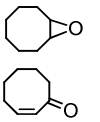
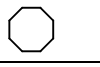
[b]GC yield using internal standard 1,4-di-*tert*-butylbezene and isolated yields in parenthesis.

Furthermore, substrates with a single methylene group were converted selectively to their corresponding carbonyl compounds without any side products (entries 1-4). Hence, in these cases (entries 2-4), we obtained pure product (avoiding the cumbersome task of separation) by drying the ethyl acetate extract or filtering the solid without chromatographic workup (entry 4). Thus, the yields are also better or comparable to the literature values.[5e] On the other hand, substrates with more than one methylene group are involved in over-oxidation (entries 5-9), and in a few cases afforded more than one product (entries 5, 7, and 9). However, as a whole, the products are obtained in good to moderate in yields and more or less comparable to the literature values.[5e]

To evaluate the tolerance of this catalytic system toward the functionalized arylalkanes with diverse groups and to elaborate activity of this process toward methylene groups beyond the activated benzylic position were also carried out. The results are summarized in the Table 3. Arylalkanes bearing a methyl, methoxy, and chloride, carboxylic acid and amide groups are tolerated and yielded methylene oxidative product ketones with high to moderate yields (Table 3, entries 1-5). Moreover, substrates with electron withdrawing groups (entries 3-5) are less reactive than those with electron donating group (entries 1 and 2).

Table 3. Oxidation of functionalized arylalkanes and substrates containing different type of methylene groups.[a]



Entry	Substrates	Products	Time (h)	Conv. (%)	GC Yield[b] Select. (%)
1			15	99	51 (46)/52
2			7	100	96 (92)/96
3			19	95	89 (85)/94
4			30	95	– (81)/85
5			40	87	54 (49)/62
6			40	33	31 (25)/94
7			15	100	65 (58)/65
8			30	100	21 (15) /21 trace
9			20	86	37(31)/43

[a]Reaction conditions: as it is like Table 1 for arylalkanes.

[b]GC yield using internal standard 1,4-di-*tert*-butylbezene and isolated yields in parenthesis.

On the other hand, methylene group adjacent to a heterocyclic ring in 2-ethylpyridine and 2-ethylthiophene, which are usually regarded as difficult substrates in oxidation involving transition metals due to their strong coordinating ability, were also converted into the corresponding carbonyl compounds with moderate yields (entries 6 and 7).[5f] Oxidation of cyclooctene afforded cyclooctene oxide instead of methylene oxidative product (entry 8). This indicates the allylic methylene group is

less active than the allylic double bond. Oxidation of cyclooctane gave cyclooctanone, indicating that the aliphatic methylene group is also active toward this catalytic system.

To check the sustainability of the catalyst, we observed that the Cu(II) catalyst retained its activity through the end of the reaction because further conversion of arylalkanes to the corresponding ketone occurred when additional arylalkanes (e.g., fluorene) and TBHP were added to the aqueous layer containing the dissolved catalyst after the product separation. The product 9-fluorenone was transferred to the organic layer, leaving soluble copper catalyst in water when ethyl acetate was added into the reaction mixture under stirring (Fig. 1). Leaching of the ligand neocuproine into organic phase during product separation was not observed based on the NMR spectra (see the supporting information Fig S10-11) of the isolated product (through drying the ethyl extract without chromatographic workup). It is mostly coordinated to the dissolved copper complex in the aqueous phase.

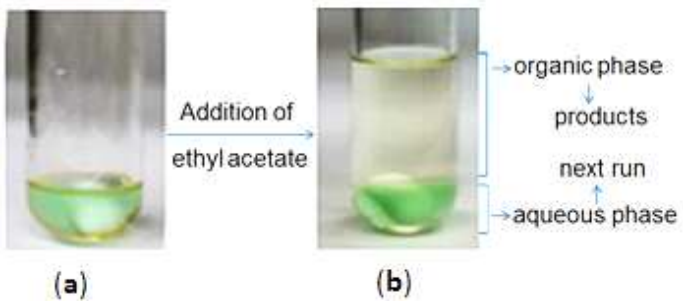


Fig. 1. (a) Reaction mixture in water, **(b)** organic phase containing products and the aqueous phase including copper catalyst after addition ethyl acetate.

The ethyl acetate layer was decanted for the product and the aqueous layer containing the catalyst is used for further oxidation. The reaction was repeated 7 times similarly with similar activity using the same catalyst dissolved in the aqueous layer each time (Fig. S1). The aqueous phase containing the catalyst was charged only with fresh substrate and TBHP each time with continued stirring as usual for the oxidation. It is also noted that the utility of TBHP is smooth for a gram scale conversion when water is a reaction medium.[10g, h]

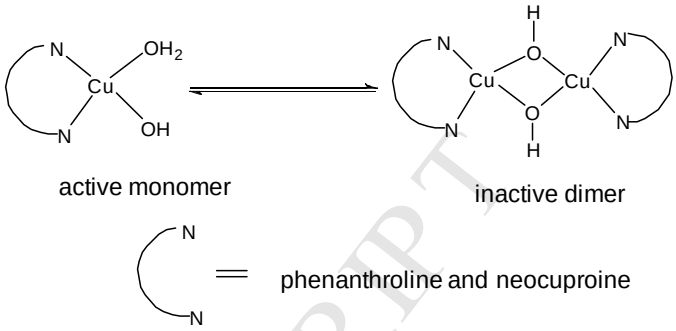
In general, in peroxide activation reactions, several reactive oxidizing species (i.e., oxygen-centered radicals) are generated.[15] For the case of metal ion catalyzed hydroperoxy reactions; the most important function of the catalyst is the decomposition of the relatively stable hydroperoxides into radicals.[16] Addition of the radical scavenger 2,6-di-*tert*-butyl-4-methylphenol in our system inhibited the cleavage reaction, indicating the presence of a free radical pathway.[16] According to the literature, copper ions can react with TBHP and generate alkoxyl ($RO^{\bullet}$) and peroxyl ($ROO^{\bullet}$) radicals from overall conversion of two molecules TBHP (Scheme 1)[5a,17].

$$CuCl_2 + TBHP \longrightarrow CuCl + tBuOO^{\bullet} + HCl$$

$$CuCl + TBHP \longrightarrow Cu(OH)Cl + tBuO^{\bullet}$$

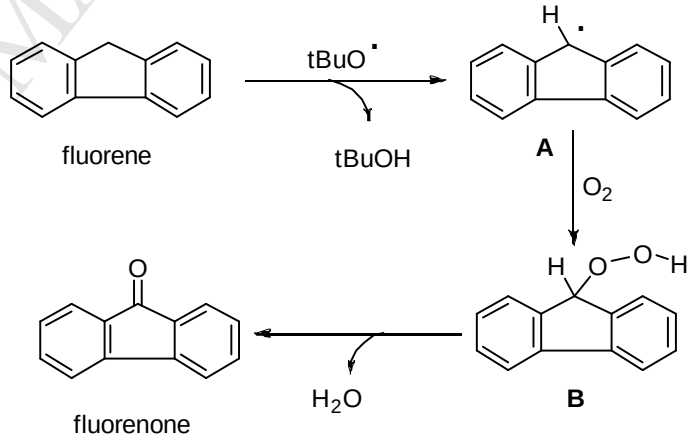
Scheme 1. Proposed decomposition path of TBHP by copper salt

Equilibrium between catalytically active monomer and inactive dimer of copper complexes with bidentate bipyridyl ligands in neutral solution is reported (Scheme 2).[18] At room temperature, the equilibrium favors the active monomeric form in the case of neocuproine due to its steric effect of methyl substituent.[18a,b] Thus, efficient oxidation for using neocuproine is observed.



Scheme 2. Monomeric and dimeric forms of copper complexes with bidentate bipyridyl ligands.

Based on the literature[19] and the above results, a plausible reaction pathway is proposed in Scheme 3. The *in situ* generated alkoxyl radical $tBuO^{\bullet}$ abstracts one of the hydrogen atoms from fluorene to produce fluorene radical **A** which is then reacted with oxygen (atmospheric or generated by decomposition of peroxyl $ROO^{\bullet}$ radical) to form fluorene peroxide derivative **B**.[19c,d] Finally, oxidative decomposition of **B** afforded the desired product fluorenone.



Scheme 3. Proposed pathways for oxidation of arylalkanes to ketones by TBHP.

3. Conclusions

We report a catalytic system which operates in water featuring sustainability criteria such as stability, activity, easy product separation (drying the ethyl extract or filtration of the solid product in few cases without chromatographic workup), simple operation, and recycling of the catalyst (the catalyst can be recycled up to seven times without any loss of activity). Moreover, diversity in group tolerance toward functionalized arylalkanes and in activation of C–H bonds beyond activated benzylic methylene positions are noteworthy. In addition, a smooth gram scale preparation indicates the capability of the catalytic system toward large scale preparation in the future.

Further use of the system to other oxidative reactions is under exploration.

4. Experimental section

4.1. General

All chemicals were obtained from commercial sources and used without further purification. 2-hydroperoxytetrahydrofuran was synthesized according to literature.[20] Gas chromatographic analyses were performed on an Agilent 6890 instrument with a FID detector and an Aglient 30 m x 0.53 mm x 3.0 μm HP-1 capillary column. Product isolation was carried out by TLC (Merck, TLC silica gel 60 F_{254} 25 Aluminum sheets 20x20 cm). NMR spectra were recorded in $CDCl_3$ on a Bruker AV 300 MHz, at room temperature.

4.2. Typical procedure for arylalkanes oxidation

A stock solution of $CuCl_2 \cdot 2H_2O$ in water (0.0171 g/mL) was prepared (by dissolving 0.171 g in 10 mL H_2O). To a Teflon screw cap glass tube, catalyst **A** (100 μL of a stock solution, 0.01 mmol of $CuCl_2$, 2.1 mg, 0.01 mmol of neocuproine) was added. Then 0.7 mL of H_2O, 0.2 mmol of arylalkanes, and 70% aq. *tert*-butyl hydroperoxide (200 μL, 1.4 mmol) were added in each case. The mixture was stirred vigorously at room temperature till to its reaction time specified in the Table 2 and Table 3. The reaction mixture was then diluted with ethyl acetate and the products dissolved in ethyl acetate layer were analyzed by GC using internal standard 1,4-di-*tert*-butylbenzene (19.4 mg, 0.1 mol). For product separation, the aqueous phase was extracted with ethyl acetate (3x10 mL). The combined extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated and product isolation was carried out by TLC. The pure products of benzophenone, 9-fluorenone (Table 2, entries 2 and 3) and 4-methoxyacetophenone (Table 3 entry 2) were obtained from drying their ethyl acetate extract without chromatographic workup. Filtration of the reaction mixture afforded pure 9-xanthenone (Table 2, entry 4).

4.2.1. Acetophenone:[5q,r,7b] TLC (hexane/ethyl acetate = 95:5) gave acetophenone as a colorless liquid; yield: 22.0 mg (91%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.69 (d, *J* = 7.5, 2H), 7.28 (t, *J* = 7.2, 1H), 7.17 (t, *J* = 7.8, 2H), 2.29 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 197.5, 136.7, 132.6, 128.1, 127.8, 26.0.

4.2.2. 4-Methoxyacetophenone:[5h,q,r] Drying of ethyl acetate extract under vacuum gave pure 4-metoxyacetophenone as a colorless solid; yield: 27.1 mg (92%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.90 (d, *J* = 8.7, 2H), 6.89 (d, *J* = 9.0, 2H), 3.83 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 196.7, 163.4, 130.5, 113.6, 55.4, 26.3.

4.2.3. 4-Chloroacetophenone:[5r] TLC (hexane/ethyl acetate = 95:5) gave 4-chloroacetophenone as a colorless liquid; yield: 26.3 mg (85%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.79 (d, *J* = 8.7, 2H), 7.32 (d, *J* = 9.9, 2H), 2.50 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 196.3, 139.1, 135.2, 129.4, 128.5, 26.1.

4.2.4. Benzophenone:[5h,q,7b,d] Drying of ethyl acetate extract under vacuum gave pure benzophenone as a colorless solid; yield: 31.5 mg (89%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.79 (d, *J* = 7.8, 4H), 7.59-7.54 (m, 2H), 7.48-7.43 (m, 4H), ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 196.6, 137.5, 132.3, 130.0, 128.2.

4.2.5. 9-Fluorenone:[5h,q,r,7b,d] Drying of ethyl acetate extract under vacuum gave pure 9-fluorenone as a yellow solid; yield: 34.2 mg (95%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.60 (d, *J* = 7.8, 2H), 7.46-7.40 (m, 4H), 7.26-7.21 (m, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 193.8, 144.4, 134.1, 129.0, 124.2, 120.2.

4.2.6. Anthracene-9,10-dione:[5q,r,7d] TLC (hexane/ethyl acetate = 95:5) gave anthracene-9,10-dione as a light brown solid; yield: 31.6 mg (76%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 8.31–8.28 (dd, *J* = 5.5, 3.1, 4H), 7.80-7.77 (dd, *J* = 5.4, 3.3, 4H), ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 183.1, 134.1, 133.6, 127.2.

4.2.7. 9-Xanthenone:[5h,q,r,7d] Filtration gave pure 9-xanthenone as a colorless solid; yield: 37.1 mg (95%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 8.29 (d, *J* = 7.8, 2H), 7.66 (t, *J* = 7.8, 2H), 7.42 (d, *J* = 8.4, 2H) 7.32 (t, *J* = 7.5, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 177.1, 156.1, 134.7, 126.6, 123.8, 121.8, 117.9.

4.2.8. Indan-1-one:[5h,q,r,7d] TLC (hexane/ethyl acetate = 95:5) gave indan-1-one as a colorless solid; yield: 13.5 mg (51%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.71 (d, *J* = 7.8, 1H), 7.59-7.51 (m, 1H), 7.43 (d, *J* = 7.8, 1H), 7.34-7.28 (m, 1H) 3.09 (t, *J* = 5.8, 2H), 2.66-2.62 (m, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 206.9, 155.1, 137.0, 134.5, 127.2, 126.6, 123.6, 36.1, 25.7.

4.2.9. 1-Tetralone:[5h,q,7d] TLC (hexane/ethyl acetate = 95:5)) gave 1-tetralone as a colorless liquid; yield: 14.6 mg (25%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.99 (d, *J* = 7.8, 1H), 7.45-7.40 (m, 1H), 7.32-7.20 (m, 2H), 2.92 (t, *J* = 6.0, 2H), 2.61 (t, *J* = 6.6, 2H), 2.14-2.05 (m, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 198.2, 144.4, 133.3, 132.6, 128.7, 127.1, 126.5, 39.1, 29.6, 23.2.

4.2.10. Naphthalene-1,4-dione:[5h] TLC (hexane/ethyl acetate = 95:5) gave naphthalene-1,4-dione as a light yellow solid; yield: 19.4 mg (29%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 8.07-8.04 (dd, *J* = 5.7, 3.3, 2H), 7.73 (dd, *J* = 5.7, 3.6, 2H), 6.95 (s, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 185.0, 138.7, 133.9 131.9, 126.4.

4.2.11. Isochroman-1-one:[7d] TLC (hexane/ethyl acetate = 95:5) gave isochroman-1-one as a colorless solid; yield: 21.4 mg (72%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.92 (d, *J* = 7.8, 1H), 7.43-7.38 (m, 1H), 7.24 (t, *J* = 7.5, 1H), 7.14 (d, *J* = 7.5, 1H), 4.38 (t, *J* = 6.0, 2H), 2.92 (t, *J* = 6.0, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 164.7, 139.2, 133.3, 129.8, 127.2, 127.0, 124.9, 67.0, 27.4.

4.2.12. Phthalide:[7d] TLC (hexane/ethyl acetate = 95:5) gave phthalide as a colorless solid; yield: 11.2 mg (21%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.85 (d, *J* = 0.9, 1H), 7.66-7.61 (m, 1H), 7.47 (t, *J* = 7.5, 2H), 5.27 (s, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 171.0, 146,5, 133.9, 128.9, 125.5, 122.1, 69.6.

4.2.13. Phthalic anhydride:[5v] TLC (hexane/ethyl acetate = 95:5) gave phthalic anhydride as a colorless solid; yield: 21.8 mg

(37%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 8.02-7.99 (dd, *J* = 5.4, 3.3, 2H), 7.92-7.89 (dd, *J* = 5.5, 3.0, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 162.7, 136.1, 131.3, 125.7.

4.2.14. 4-Methylaectophenone:[7d] TLC (hexane/ethyl acetate = (95:5) gave acetophenone as a colorless liquid; yield: 12.0 mg (46%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.76 (d, *J* = 8.4, 2H), 7.15 (d, *J* = 8.1, 2H), 2.47 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 197.6, 143.7, 134.6, 129.1, 128.3, 26.4, 21.5.

4.2.15. 2-Acetylthiophenee:[5u] TLC (hexane/ethyl acetate = 95:5) gave acetophenone as a colorless liquid; yield: 14.7 mg (58%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.51–7.49 (m, 1H), 7.45-743 (m, 1H), 6.93-6.9 (m, 1H), 2.34 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 190.3, 144.2, 133.5, 132.4, 127.9, 26.5.

4.2.16. 2-Acetylpyridine:[5t] TCL (hexane/ethyl acetate/ dichloromethane = 55:5:40) gave acetophenone as a colorless liquid; yield: 12.0 mg (25%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 8.46 (d, *J* = 4.5, 1H), 7.82-790 (m, 1H), 7.65-7.59 (m, 1H), 7.29-725 (m, 1H), 2.50 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 199.6, 153.3, 148.8, 136.6, 126.9, 121.3, 25.5.

4.2.17. 4-Acetylbenzamide:[5s] TLC (hexane/ethyl acetate = 30:70) gave 4-acetylbenzamide as a colorless solid; yield: 16.0 mg (49%). ^{1}H NMR (300 MHz, DMSO-d6) δ ppm 8.15 (s, 1H), 8.00 (s, 4H), 7.58 (s, 1H), 2.61 (s, 3H); ^{13}C NMR (300 MHz, DMSO-d6) δ ppm 197.7, 167.2, 138.7, 138.1, 128.1,127.8, 26.9.

4.2.18. 4-Acetylbenzoic acid:[5h,7d] TLC (hexane/ethyl acetate = 50:50) gave 4-acetylbenzoic acid as a colorless solid; yield: 27.0 mg (81%). ^{1}H NMR (300 MHz, DMSO-d6) δ ppm 13.30 (s, 1H), 8.04 (s, 4H), 2.62 (s, 3H); ^{13}C NMR (300 MHz, DMSO-d6) δ ppm 197.7, 166.6, 139.8, 134.5, 129.5, 128.3, 26.9.

4.2.19. Cyclooctene oxide:[5s] TLC (hexane/ethyl acetate = 95:5) gave cyclooctene oxide as a colorless liquid; yield: 8.0 mg (15%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 2.71–2.68 (m, 2H), 1.97-1.91 (m, 2H), 1.44-1.03 (m, 10H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 55.3, 26.4, 26.1, 25.4.

4.2.20. Cyclooctannone:[5r] TLC (hexane/dichloromethane = 50:50) gave cyclooctanone as a colorless liquid; yield: 15.0 mg (31%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 2.37–2.32 (m, 4H), 1.85-1.77 (m, 4H), 1.52-1.44 (m, 4H), 1.34-1.32 (m, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ ppm 218.4, 42.1, 27.3, 25.8, 24.8.

4.3. The control reactions with fluorene and 2,6-di-*tert*-butyl-4-methylphenol (radical scavenger) and TBHP in decane solution

A stock solution of $CuCl_2{\cdot}2H_2O$ in water (0.0171g/mL) was prepared (by dissolving 0.171 g in 10 mL H_2O). To a Teflon screw cap glass tube, catalyst **A** (100 μL of a stock solution; 0.01 mmol of $CuCl_2$, 2.1 mg, 0.01 mmol of neocuproine), 2,6-di-*tert*-butyl-4-methylphenol (308.0 mg, 1.4 mmol), fluorene (33.9 mg, 0.2 mmol) were added. Then 0.7 mL of H_2O and 70% aq. *tert*-butyl hydroperoxide, (200 μL, 1.4 mmol) was added in the above reaction tube. The mixture was stirred vigorously at room temperature for 1h. It was then diluted with ethyl acetate and the products dissolved in ethyl acetate layer were analyzed by GC using internal standard 1,4-di-tert- butylbezene (19.4 mg, 0.1 mol). For a control reaction without water, a solution of 70% aq. TBHP (240 uL, 1.4 mmol) in decane solution and fluorene (33.9 mg, 0.2 mmol) were added to a solid mixture of $CuCl_2{\cdot}2H_2O$ (1.7 mg, 0.01 mmol) and neocuproine (2.1 mg, 0.01 mmol). Then the reaction was continued as above for 1h and the products identified by GC diluting with ethyl acetate.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/.....

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