Solvent-free Hydroxylation of C-H bonds by Fe-complex: A Green Approach for Activation of Small Molecules and Macromolecules

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ABSTRACT: One approach to mitigate the crisis of plastic waste is “chemical upcycling”, in which waste plastic is converted into products with higher economic value. Towards this goal, several metal-catalyzed post-functionalization of polymers have been reported, with variable success, mostly on account of lack of selectivity, use of harsh reaction conditions, and use of environmentally unfriendly solvents. In this work, we demonstrate selective hydroxylation of the backbone 3° C-H bonds in polyolefin macromolecules using in-house developed $(Et_4N)_2[Fe^{III}$-(Ph,Me-bTAML)] (**3**) complex and solid $Na_2CO_3.1.5\ H_2O_2$ (SPC; Sodium percarbonate) under solvent-free mechanochemical conditions. The reaction condition only employs simple mechanochemical grinding at room temperature. The polar functional group -OH was successfully incorporated into the polymer backbone without any chain degradation and crosslinking. The same reaction conditions were also employed to selectively hydroxylate small organic molecules including complex natural products. The rate and selectivity of the reaction towards 3° C-H bonds far exceed that performed under homogeneous conditions. Mechanistic investigation indicates the formation of the well-characterized oxoiron(V) intermediate upon mechanical grinding of **3** and SPC. The high selectivity observed under solvent-free conditions is due to the elimination of solvent-induced side-reaction of this intermediate. This represents a very sustainable process since it uses environmentally benign reagents (iron complex, “oxygen bleach”), thus eliminating the use of hazardous solvents. The workup protocol involves simple washing with water where both the spent catalyst and the oxidant are soluble.

INTRODUCTION

Selective oxidation of alkane C-H bonds to obtain value-added oxidized congeners has far-reaching implications as they open up new possibilities for chemical synthesis. Several Fe and Mn complexes have been developed to activate H_2O_2 and catalyze predictive, selective, and scalable hydroxylation of 3° and 2° C-H bonds.[1, 2, 3] This includes Fe-bTAML complexes, belonging to an extended family of TAML activators, that activate *m*CPBA and NaOCl to catalyze the 3° C-H bond oxidation of a wide range of organic substrates including complex natural products.[4, 5] In addition to challenges in catalyst design, the choice of the reaction medium and the solvent in particular, is critical. The main challenges lie in the choice of a solvent that is oxidatively robust and solubilizes the catalyst and the oxidant. This limits the choice of solvents rendering CH_3CN as the most preferred solvent in most of the protocols. Moreover, solvents constitute ~90% of the total system by mass,[6] and since the recovery of solvents is extremely challenging, it raises serious concerns about environmental safety. Additionally, the use of polar solvents like acetonitrile limits the substrate scope when non-polar hydrocarbons are used as substrates.

Another interesting extension of such selective bioinspired oxidations is modifying or enhancing the properties of synthetic macromolecules through simple C-H functionalization methods. This is an emerging area of interest in the field of polymer science with potential applications in improving the functional properties of non-polar polymers or in sustainably upcycling end-of-life plastics and generating new, functional materials with properties that are difficult to access through traditional synthetic routes.[7, 8, 9] The need to use large quantities of solvent to solubilize polymers has limited the traditional application of such methods. Such upcycling reactions can be made practical if these reactions can be performed under solvent-free conditions.

In the past few decades, there have been significant advances made in “solvent-free” solid-solid reactions.[10, 11] Among various methodologies, mechanochemical grinding or ball-milling has been established as a useful tool as it often provides advantages over standard solvent-based methods. However, examples of oxidation reactions under solvent-free conditions are rare; the IBX-mediated oxidation of alcohols being one of them.[12] Solvent-free mechanochemical hydroxylation of unactivated C-H bonds using transition metal catalysts and terminal oxidants has not yet been reported in the literature. This is extremely challenging since the reactive high-valent oxometal intermediates formed under such conditions would be extremely reactive and lead to very fast decomposition (*via* ligand oxidation) due to the increased local concentration.

Fe-bTAML complexes, on the contrary, are extremely robust towards oxidative degradation.[4] We report the first-ever catalytic C-H bond hydroxylation under mechanochemical conditions using an environmentally friendly iron complex and oxidant. In this report, we employ a Ph-modified Fe-bTAML, which catalyzes C-H oxidation using $Na_2CO_3.1.5\ H_2O_2$ (“oxygen bleach”) as the oxidant under solvent-free

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conditions using mechanochemical grinding (Figure 1). The reaction scope includes macromolecules like polystyrene and poly(hexene-1), which are selectively hydroxylated under these conditions. This represents a truly "green" process since both the Fe-bTAML catalyst and oxidant are known to be non-toxic and the only purification required involves washing the excess oxidant and inactivated catalyst in water, thus eliminating the use of hazardous organic solvents during the entire course of the reaction and work-up.

RESULTS AND DISCUSSION

Previous reports from our laboratory have demonstrated the utility of Fe-bTAML catalyst (**1, 2**) towards the oxidation of C-H bonds selectively with *m*CPBA/NaOCl as a terminal oxidant in acetonitrile/buffer under homogeneous conditions.[4, 5] The reaction involves the in-situ generation of an oxoiron(V) species followed by H-atom abstraction and, the subsequent 'rebound step' to hydroxylate unactivated C-H bonds.[4]

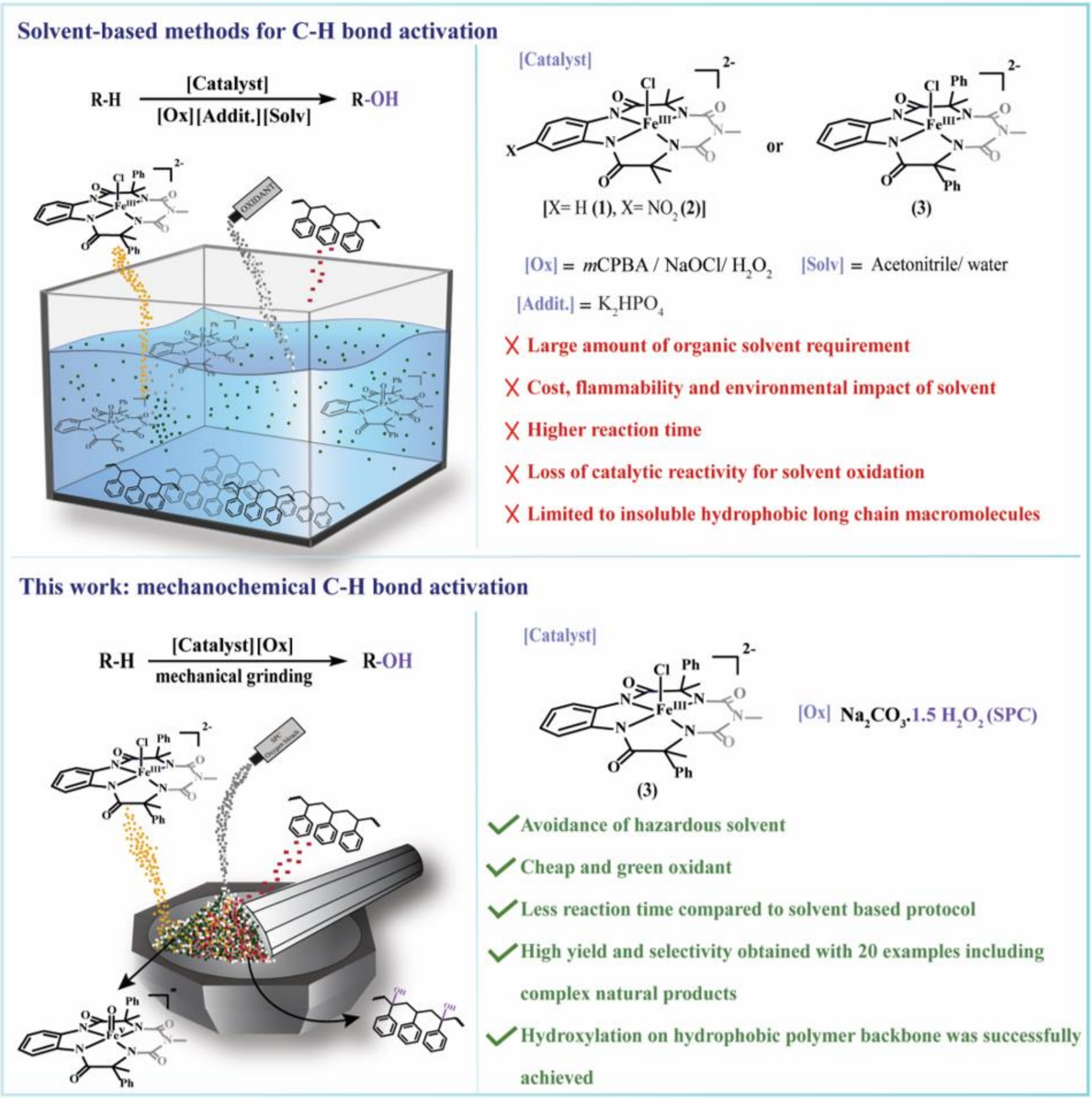


Figure 1. C-H activation by Fe-bTAML in acetonitrile-water medium and Mechanochemical C-H bond activation by Fe-bTAML under solvent-free condition

The role of solvents in these reactions is solely for solubilizing the reactants, thus, enabling the proximity between them. However, acetonitrile is incapable of solubilizing large and non-polar hydrophobic molecules like synthetic macromolecules. Additionally, the huge amount of organic solvent present, which has a plethora of C-H bonds, can also get oxidized resulting in unwanted byproducts, lower yields, high catalyst loading, and longer reaction time. Another major drawback of this catalytic system lies in the use of *m*CPBA as an oxidant to afford selective oxidation. Since pure *m*CPBA is explosive when used in large amounts, the scale-up of this reaction may prove limiting.[13] Moreover, *m*CPBA generates an organic acid as a byproduct that degrades the catalyst. Additionally, neutralizing and discarding the acid residue results in undesired waste. On the other hand, sodium percarbonate (SPC) ($Na_2CO_3.1.5H_2O_2$), which is used as a bleach in everyday life, is a versatile and cheap oxidant that under mechanochemical activation liberates H_2O_2.[14] However the Fe-bTAML framework remained reluctant to activate sodium percarbonate and we speculated that the inactiveness of sodium percarbonate with the regular Fe-bTAML is because of the dimer formation in mechanochemical conditions, as has been observed in the solution. Recently, a "picket-fence" derivation of bTAML with phenyl groups attached to the ligand framework, ($(Et_4N)_2[Fe^{III}$-(Ph,Me-bTAML)] (**3**), has been developed (Figure 1).[15] **3** has been found to activate H_2O_2 in solution for the selective oxidation of unactivated C-H bonds. Therefore, the urge to develop a sustainable catalytic system involving green oxidants under solvent-free conditions prompted us to explore the hydroxylation of C-H bonds ranging from small molecules to commodity polymers by employing **3** as the catalyst and $Na_2CO_3.1.5$ H_2O_2 (SPC) as an oxidant. Addition of $Na_2CO_3.1.5$ H_2O_2 (SPC) to **3** led to an intense color change from orange to green (Figure 2A). The UV-Vis spectra of this green-colored species indicated the absence of spectral features at 370 nm (characteristic of the starting Fe^{III} complex) and the concomitant appearance of new spectral features at 447 nm and 637 nm (Figure 2B. b). EPR analysis of this green species showed spectral features characteristic of S=1/2 with g values of 2.13, 2.03, and 1.99 at 85 K (Figure 2B. a). HRMS examination of this green species revealed one prominent ion at a mass-to-charge ratio of 553.1054 (calculated m/z (M-) 553.1049 (100%)); the isotopic distribution pattern corresponds to **3'** (Figure S1). It should be noted that similar UV-Vis spectral characteristics and EPR spectra were observed when either *m*CPBA or H_2O_2 was added to **3** in CH_3CN: H_2O solution. In this case, the peak shift was observed from 380 nm to 442 nm and 625 nm and the EPR displayed rhombic S=1/2 species with g = 1.985, 1.950, 1.755.[15] This intermediate has been conclusively identified by us earlier as the oxoiron(V) intermediate based on mass spectroscopy, EPR, and Mössbauer spectroscopy.[15] Furthermore, the mixing of *m*CPBA to **3** under solvent-free mechanical grinding conditions also led to the same green-colored intermediate and showed identical spectral features in both UV-Vis and EPR spectroscopy to that obtained with $Na_2CO_3.1.5$ H_2O_2 (SPC). All these pieces of evidence point out that in all likelihood addition of SPC to **3** under mechanical grinding led to the formation of the oxoiron(V) intermediate (**3'**) in the solid-state.

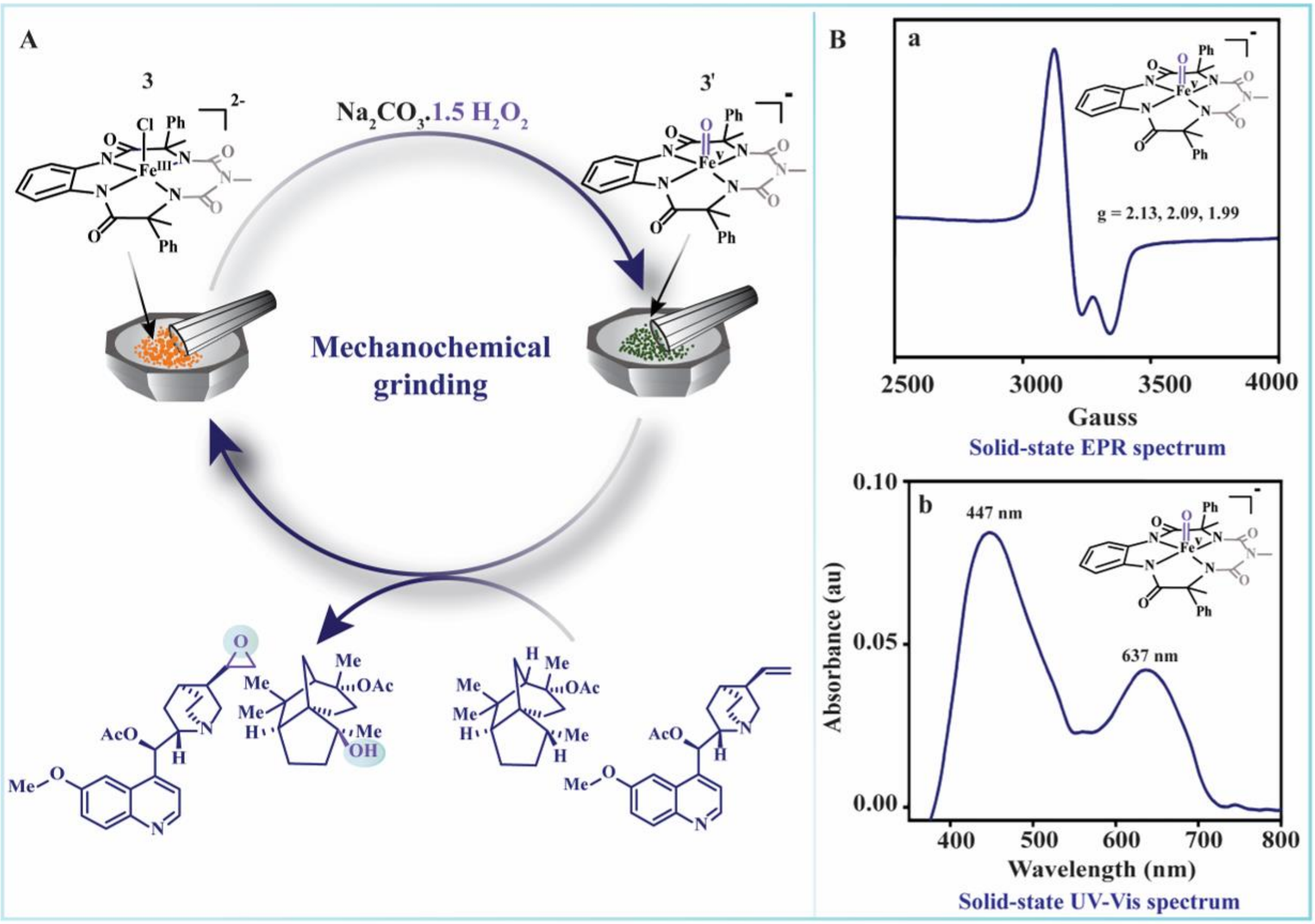
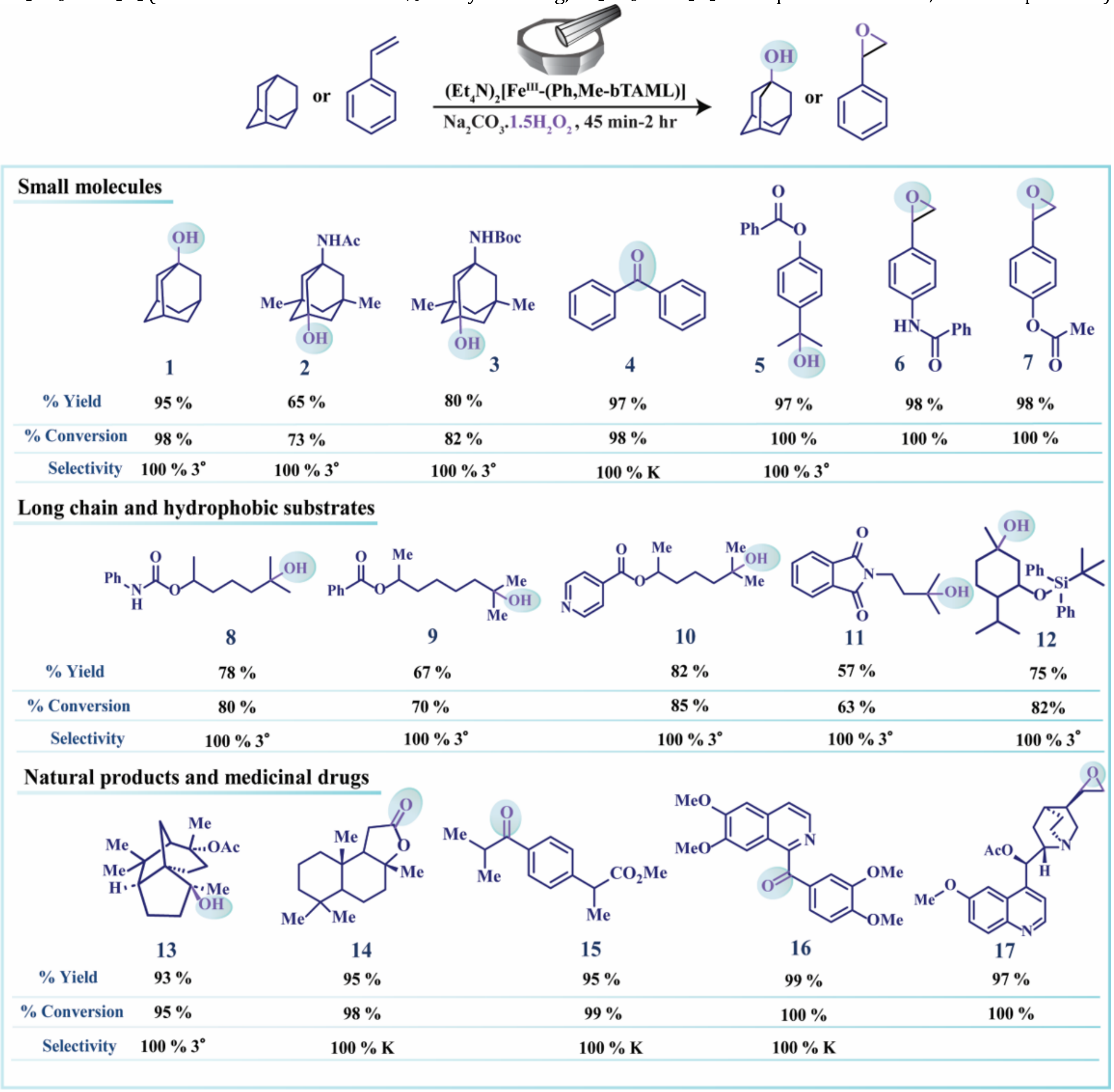


Figure 2. A. Solvent-free formation of oxoiron(V) reactive intermediate upon addition of $Na_2CO_3.1.5$ H_2O_2 (SPC; (Oxygen Bleach) to **3**; **B.** Characterization of oxoiron(V) (**3′**) reactive intermediate by solid-state spectroscopic techniques (a. EPR spectrum, b. UV-Vis spectrum)

Catalytic oxidation of ambroxide was attempted with **3** as the catalyst (5 mol% of substrate) and $Na_2CO_3.1.5\ H_2O_2$ (SPC) as the oxidant (1.1 eqv. of substrate; added in equal ten portions over a period of 45 min with continuous grinding). Analysis of the solid mixture after 45 min showed the exclusive formation of the product sclareolide in >95% yield. Control experiments performed without the presence of **3** or by addition of $FeCl_3$ as the catalyst showed no product formation. The high valent oxoiron(V) (**3'**) species formed upon mechanical grinding of **3** and SPC, under solvent-free conditions, is capable of oxidizing a series of substrates having moderate to high BDE within a time span of 45 min to 2 h (Table 1).

Table 1. Mechanochemical solvent-free oxidation of alkanes and alkenes including complex natural products using **3** and $Na_2CO_3.1.5\ H_2O_2$ (reaction condition= 1-5 mol% catalyst loading, $Na_2CO_3.1.5\ H_2O_2$: 1-2 eqv. w.r.t substrate, room temperature)



Small molecules

	1	2	3	4	5	6	7
% Yield	95 %	65 %	80 %	97 %	97 %	98 %	98 %
% Conversion	98 %	73 %	82 %	98 %	100 %	100 %	100 %
Selectivity	100 % 3°	100 % 3°	100 % 3°	100 % K	100 % 3°		

Long chain and hydrophobic substrates

	8	9	10	11	12
% Yield	78 %	67 %	82 %	57 %	75 %
% Conversion	80 %	70 %	85 %	63 %	82%
Selectivity	100 % 3°	100 % 3°	100 % 3°	100 % 3°	100 % 3°

Natural products and medicinal drugs

	13	14	15	16	17
% Yield	93 %	95 %	95 %	99 %	97 %
% Conversion	95 %	98 %	99 %	100 %	100 %
Selectivity	100 % 3°	100 % K	100 % K	100 % K	

Small molecules (1, 2, 3, 4, 5: Table 1) were hydroxylated using **3** (1-5 mol% of substrate) and $Na_2CO_3.1.5\ H_2O_2$ (SPC) as the oxidant (1.1-1.5 eqv. of substrate; added in equal portions over a period of 45 min (1,4,5: Table 1)-1.30 hours (2,3: Table 1) with continuous grinding). The GC-MS analysis of the reaction mixtures led to a very high yield (ranging from >70% to 100%) and selectivity was predominant at 3° position over 2° for derivatives of adamantane (1,2,3: Table 1). Substrates containing a C4 to C6 chain on substituted phthalimide (11: Table 1), isonicotinate groups (10: Table 1), and phenyl rings (8, 9: Table 1) were oxidized by **3** (5 mol%) selectively at the distant

3° C-H centers to yield their corresponding alcohols with high yield (60%-80%) showing great tolerance for arene and heteroatoms in hydroxylation reactions catalyzed by **3**. The bulky TBDPS group-protected menthol (12: Table 1) was hydroxylated at the least sterically hindered 3° C-H bond selectively with a 75 % yield within 1 hour reaction time while the time taken in solvent-based methods is 5 times more, which can be attributed to the side reactions including solvent oxidation. Several complex natural products and medicinal drugs were converted to highly value-added oxidized congeners (13, 14, 15, 16: Table 1) with a yield >95% (**3** loading: 2-5 mol%) within a very short reaction time. (+)-Cedryl acetate, a cedrol derivative was converted to its strain-released hydroxylated product (13: Table 1) at least sterically hindered 3° C-H bond with > 95% yield within 1 hour. Papaverine, belonging to a group of medicine called vasodilators, was oxidized to yield ketone (16: Table 1) at the benzylic position in >95% yield within 45 min of grinding. Epoxides are an important class of compounds in organic synthesis. We could successfully extend the mechanochemical solvent-free reaction protocol to synthesize epoxides with 100 % yield within 30 min from derivatives of styrene (6,7: Table 1) with 1 mol% loading of **3** and $Na_2CO_3.1.5\ H_2O_2$ (SPC) as the oxidant (1.1 eqv. of substrate). Acetate-protected Quinine, being a compound of interest in treating malaria, was completely converted to its corresponding epoxide within 45 min of mechanochemical grinding (17: Table 1) (100% product yield).

The solid-state hydroxylation reaction using **3** and SPC not only eliminated the need for solvents but also led to improved yields, reaction rates, and selectivity (Table S1). For example, (+)-cedryl acetate was converted to its oxidized product with 95% yield within 1 hour while ~60 % product was obtained in the solution phase (acetonitrile-water) after 7 hours. The improved selectivity of 3° C-H bonds over 2° C-H bonds was observed in the oxidation of adamantane, where almost no trace of 2-adamantanone was observed in the GC-MS. These high reaction rates and improved regioselectivity are unprecedented when compared to hydroxylation reactions carried out in solutions using bioinspired catalytic systems such as Fe-PDP, Fe-MCPP, etc.[1,2]

The efficient catalytic C-H oxidation reactions with small molecules encouraged us to extend the methodology for the oxidation of hydrocarbon-based synthetic macromolecule, namely, polystyrene (PS). Being a major contributor to landfill,[16] the vinyl backbone of polystyrene seemed attractive to us since hydroxylating the backbone could lead to upcycling this material into a value-added product. We employed a PS sample, with a nominal molecular weight M_w 2,200 (PSLW; Đ = 1.06). Hydroxylation reaction was performed on the PS sample under solvent-free conditions using **3**. Room temperature activation of **3** (0.0024 mmol, 2 mol% of monomer) using green oxidant $Na_2CO_3.1.5\ H_2O_2$ (2-3 eqv. of monomer; added in equal portions over a period of 4-5 h with continuous grinding) under mild mechanical force by a pestle kickstarted the hydroxylation reaction of polystyrene (PSLW: 0.12 mmol) to afford hydroxylated polystyrene. FTIR analysis of the hydroxylated polystyrene (PSLWOH) displayed a new peak at 3485 cm^{-1} that is consistent with the hydroxyl group stretch (Figure 3C). The absence of any FTIR stretch around 1700 cm^{-1} ruled out the possibility of carbonyl group incorporation that could have occurred *via* oxidation at the secondary C-H bond. The incorporation of hydroxyl groups was further evaluated by ^{1}H NMR spectroscopy. ^{1}H NMR spectra of oxidized polystyrene samples in $CDCl_3$ contained a new broad signal around 3 ppm corresponding to the hydroxyl groups (Figure S3). Although IR and ^{1}H NMR spectroscopic analyses indicated the presence of hydroxyl functional groups on the polystyrene, no characteristic resonances were observed in the ^{13}C NMR spectrum, presumably due to the poor sensitivity of these quaternary carbons. However, β carbon atoms of the hydroxyl group were unambiguously identified by ^{1}H–^{13}C HMBC NMR spectroscopy (Figure S4) thus indicating that hydroxylation occurred at the tertiary position selectively. Integrating the peak at 3 ppm of PSLWOH unveils the presence of 2 to 3 hydroxyl groups per 21 monomer unit or 4 to 6 hydroxyl groups per 100 monomer unit. The molecular weight of the hydroxylated polystyrene (PSLWOH, M_n = 2800 Da, M_w = 3100 Da, Đ = 1.09) was found to be similar to that of the virgin polystyrene (PSLW, M_n = 2700 Da, M_w = 3100 Da, Đ = 1.15) (Figure 3B). This similarity in molecular weights provides evidence that the polymer does not undergo chain fragmentation or crosslinking process during the oxidation reaction. The surface chemical composition of oxidized polystyrene was analyzed using an X-ray photoelectron spectrometer (XPS) to confirm the oxygen incorporation in the polymer backbone. [17] For untreated polystyrene, the XPS spectrum consists of a peak at 283.6 eV which corresponds to the C-C/C-H bonds in polystyrene backbone (Figure S5). A new peak at 285.03 eV obtained in XPS analysis of the hydroxylated polystyrene corresponds to the C-OH bonds (Figure S6), thereby confirming the hydroxyl group incorporation upon mechanochemical treatment of polystyrene with **3** and SPC. Thus, mechanochemical activation of H_2O_2 in the solid-state by bioinspired bTAML framework led to successful hydroxylation on a styrenic polymer backbone with 10 mol% hydroxyl functional group incorporation per chain.

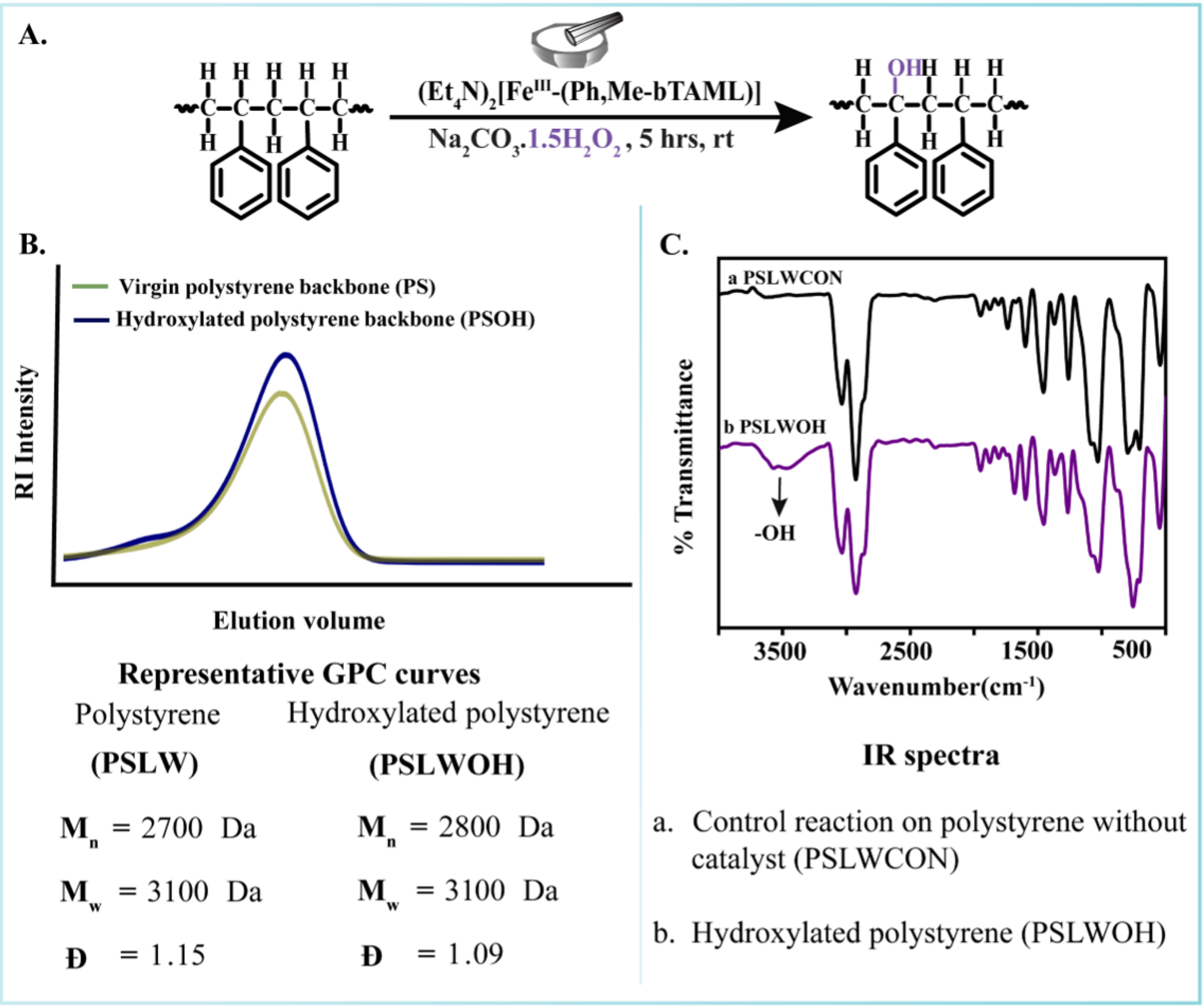


Figure 3. A. Schematic diagram of polystyrene hydroxylation employing **3** and SPC **B**. Representative GPC curves of virgin polystyrene (PSLW) and polystyrene after hydroxylation (PSLWOH) **C.** IR spectrum of **a.** Control reaction on polystyrene without catalyst (PSLWCON) **b.** Hydroxylated polystyrene (PSLWOH)

Catalyst **3** in the presence of a green oxidant SPC ($Na_2CO_3.1.5\ H_2O_2$) under mechanochemical conditions, oxidized the benzylic C-H (Ar-C-H) bond selectively to a benzhydrol group (Ar-C-OH). The presence of active benzylic C-H bonds made it feasible for polystyrene to be catalytically post-functionalized under ambient conditions. On the other hand, upcycling of polypropylene, another major commodity plastic, remains a challenge. Polypropylene is constituted of a long hydrophobic carbon chain making it difficult to solubilize in conventional solvents thereby restricting the catalytic reactivity for performing post-functionalization modifications. Poly(hexene-1) (PH), structurally related to polypropylene, was chosen therefore to explore the catalytic efficacy of **3** under the mechanochemical solvent-free conditions.

Post-functionalization reaction on PH was performed under solvent-free conditions using **3**. Room temperature activation of **3** (0.0024 mmol, 2 mol% of monomer) using green oxidant SPC (2-3 eqv. of monomer; added in equal portions over a period of 5-6 h with continuous grinding) under mild mechanical force afforded hydroxylated poly(hexene-1) (Figure 4A). IR stretch at 3360 cm^{-1} confirms the incorporation of -OH group in the backbone whereas the absence of any carbonyl stretches at 1700 cm^{-1} indicated the absence of carbonyl group in the backbone (Figure 4B). ^{13}C NMR analysis of the reaction mixture gave rise to a new peak at 45 ppm (Figure 4C). This peak did not show up in DEPT pointing out it to be a tertiary center (Figure 4D). This led us to conclude that the hydroxy functionalization is occurring at the tertiary position. Further ^{1}H-^{13}C correlation between α-carbon attached to the -OH group and protons at the β-position of the branched chain was established from the HMBC NMR spectra (Figure 4E).

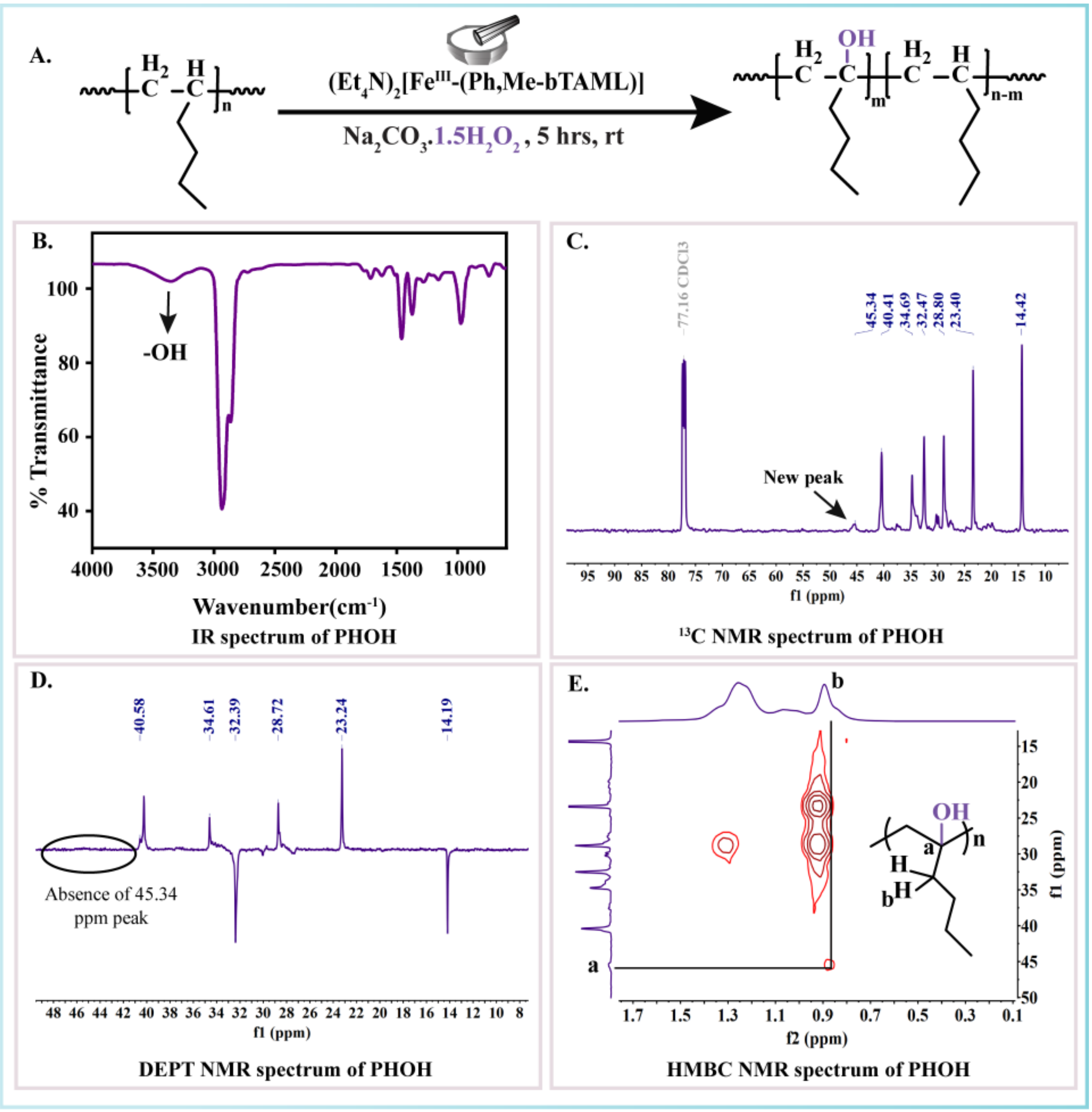


Figure 4. **A**. Schematic diagram of poly(hexene-1) hydroxylation employing **3** and SPC **B.** IR spectrum of hydroxylated poly(hexene-1) (PHOH) **C.** ^{13}C NMR spectrum of poly(hexene-1) after functionalization; new peak at 45.34 ppm **D.** DEPT NMR spectrum; absence of peak at 45.34 ppm points out functionalization at tertiary center **E.** ^{1}H-^{13}C HMBC NMR correlates α carbon (45.34 ppm) attached to -OH group with protons at β position of the branched chain

Metal-catalyzed oxidation of hydrocarbon polymer backbone has been reported earlier. Polymer oxyfunctionalization was reported by Hillmyer and his co-workers where they employed a manganese porphyrin complex, imidazole, a phase transfer agent, and oxone to oxyfunctionalize polyolefin backbone in dichloromethane solution.[18] This method led to the insertion of 0.4- 1.1 hydroxyl groups per 100 backbone carbons after 5 days of reaction time. A biomimetic ruthenium porphyrin system for the oxidation of polyisobutene, was reported by Hartwig and group.[19] This procedure yielded oxidized polyisobutene with 0.6% to 2.3% ketone group incorporation. It involved the use of organic solvents, environmentally non-benign oxidants, and ruthenium as a metal center. It is worth noting that all the reported methodologies on metal-catalyzed oxyfunctionalization of hydrocarbon polymers involve the use of undesirable chlorinated organic solvents like dichloromethane, dichloroethane, and trichlorobenzene due to the limited solubility of polymers. Further, the by-products of the oxidants used (oxone, *m*CPBA, 2,6-dichloropyridine-N-oxide) in these methodologies possess a serious environmental threat (such as *m*-chlorobenzoic acid) and would be unsuitable for large-scale applications. In contrast, the present protocol accomplishes chemical functionalization of a vinyl or olefin polymer in a "solvent-free" condition using a robust non-toxic iron complex **3** and widely-used non-toxic, inexpensive and green oxidant SPC opens up possibilities of modifying commercial polymers under conditions that can be industrially practised. The only work-up required after the reaction is a water wash, where both the catalyst and the oxidant by-products are soluble. We believe that similar to Fe-TAMLs, complex **3** does not have any long-term toxic effects on the environment. The aqueous wash after the completion of the reaction can be released into the wastewater without any additional treatment.

CONCLUSION

In summary, we report a solvent-free approach for the oxidation of 3° C-H bonds using a Fe-bTAML complex, which is known to be environmentally benign, and SPC, an oxygen bleach", that is used in regular household applications. To date, C-H hydroxylation reactions have been performed under homogeneous conditions with the use of organic solvents such as CH_3CN. These reactions are performed under relatively dilute conditions to minimize intermolecular catalyst degradations. We show for the first time that these reactions can be carried out under solvent-free conditions by mechanical grinding. In addition to a series of organic substrates including natural products, we have extended the reaction to vinyl and olefin polymers, which are model substrates for commodity polymers, such as polystyrene and polyolefins. This is particularly interesting since the reduced solubility of polyolefins in organic solvents poses a huge challenge in performing such functionalization reactions. The solid-state reaction described herein outperforms the same reaction performed under homogeneous conditions in terms of both selectivity (3° *vs* 2°) and reactivity. Such exclusive hydroxylation of 3° C-H bonds in the presence of 2° C-H bonds is unprecedented. The only work-up required, especially when macromolecules are used, is a water wash which dissolves both the spent catalyst and the oxidant. In theory, this spent liquid could be easily discharged into wastewater without any additional treatment, as has been shown earlier. The reaction mechanism shows the formation of the well-characterized oxoiron(V) in the solid-state.

ASSOCIATED CONTENT

Supporting Information: Synthesis, and characterization details are provided in the Supporting Information file. 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 interests.

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Supporting Information

Solvent-free Hydroxylation of C-H bonds by Fe-complex: A Green Approach for Activation of Small Molecules and Macromolecules

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1. Materials

$(Et_4N)_2Fe^{III}$-(Ph,Me-bTAML) **(3)** was synthesized by standard reported protocol.[1] meta-chloroperbenzoic acid (*m*CPBA) was purchased from Sigma-Aldrich with 77% purity and was further purified by standard protocol.[2] $Na_2CO_3.1.5\ H_2O_2$ was purchased from Alfa-aesar. All the substrates were either bought from TCI, Sigma-Aldrich, and Alfa-aesar or made by standard synthetic procedures.[3] All the solvents used were previously purified and dried by standard methods.[2] Polystyrene was purchased from Thermo Fischer Scientific. Poly(hexene-1) was prepared in the laboratory by a standard method described below. Polystyrene samples were dissolved in dichloromethane and reprecipitated in MeOH thrice for purification.

2. Methods and instrumentation

2.1 Ultraviolet-Visible Spectroscopy (UV-Vis)

Solid-state UV-visible absorption spectra were measured using a Jasco V-670 spectrophotometer at room temperature.

2.2 Electron Paramagnetic Resonance Spectroscopy (EPR)

Electron Paramagnetic Resonance (EPR) spectroscopy measurements were carried out on a uniform mixture of catalyst embedded in silica followed by the addition of the corresponding oxidant. EPR spectroscopic data was obtained by a Bruker spectrometer (Bruker, EMXmicro) operating at X-band frequency and magnetic field modulation of 100 kHz. All the experiments were conducted at 9.31 GHz microwave frequency and 10 G modulation amplitude at 85 K.

2.3 Gas Chromatography-Mass Spectrometry (GC-MS)

Gas Chromatography-Mass Spectrometry (GC-MS) was conducted on a Thermo Scientific ISQ QD Mass Spectrometer attached with Thermo Scientific TRACE 1300 gas chromatograph using an HP-5 ms capillary column (30 m × 0.25 mm × 0.25 µm, J&W Scientific) with helium as the carrier gas. The method was set as: oven temperature program, 18 min; initial temperature, 60°C, hold for 2.00 min; ramp-1, 15 °C min^{-1} to 180°C, hold for 1 min; ramp-2, 20 °C to 280°C, hold for 1 min; injector temperature, 230 °C; detector temperature, 280 °C.

2.4 Nuclear Magnetic Resonance Spectroscopy (NMR)

^1H NMR, ^{13}C NMR, DEPT, and HMBC spectroscopic data were obtained from both 400 MHz and 500 MHz Bruker spectrophotometers. Tetramethysilane was used as an internal standard (δH 0.00). $CDCl_3$ and DMSO-d_6 were used as NMR solvents.

2.5 Infrared spectroscopy (IR)

FTIR Perkin-Elmer spectrophotometer was used to obtain FT-IR spectra. Polymer samples were dissolved in dry and degassed DCM and drop cast on a NaCl plate. Before collecting the data complete drying of the sample on the plate was done.

2.6 Mass spectrometry

HRMS was performed in a Bruker mass spectrophotometer using an electrospray ionization source using acetonitrile as an eluent.

2.7 Gel permeation chromatography (GPC)

Gel permeation chromatography (GPC) was performed to record the molecular weights and dispersity (Đ) of polymers in DMF solvent at 40 °C at 0.8 mL/min flow rate. The GPC instrument contained a Waters 2414 refractive index (RI) detector, a Waters 1515 HPLC pump, one PolarGel-M guard column (50 × 7.5 mm), and two PolarGel-M analytical columns (300 × 7.5 mm). The instrument was calibrated against polystyrene (PS) standards and molecular weights and Đ values were calculated from the calibration graph. Before performing SEC, polymer solutions were filtered through a 0.45 μm syringe filter.

2.8 X-ray photoelectron spectroscopy (XPS)

X-ray photoelectron spectroscopy (XPS) was performed in a PHI VersaProbe 4 spectrometer equipped with an Al K_α X-ray source with 225 eV pass energy used. Survey scan was recorded with 55 eV pass energy.

3. Experimental section

3.1 UV-Vis spectroscopic studies of oxoiron(V) in solid state

(1 mg, 0.001 mmol) of **3** was embedded in a small amount of silica in a mortar. To this well-grounded mixture, 10 eqv. (0.01 mmol) of $Na_2CO_3.1.5H_2O_2$ was added at room temperature. The color of the reaction mixture was changed from yellow to green. The green species obtained was characterized as oxoiron(V) (**3'**) intermediate by UV-Vis spectroscopy. Characteristic peaks at 447 nm and 637 nm were obtained for **3'** (Figure 2).

3.2. HRMS analysis

HRMS data was obtained after the formation of **3'** in the solid state by adding $Na_2CO_3.1.5H_2O_2$ (10 eqv., 0.005 mmol) to **3** (0.42 mg, 0.0005 mmol) followed by rapid addition of dry acetonitrile and direct injection in the detector (Figure S1).

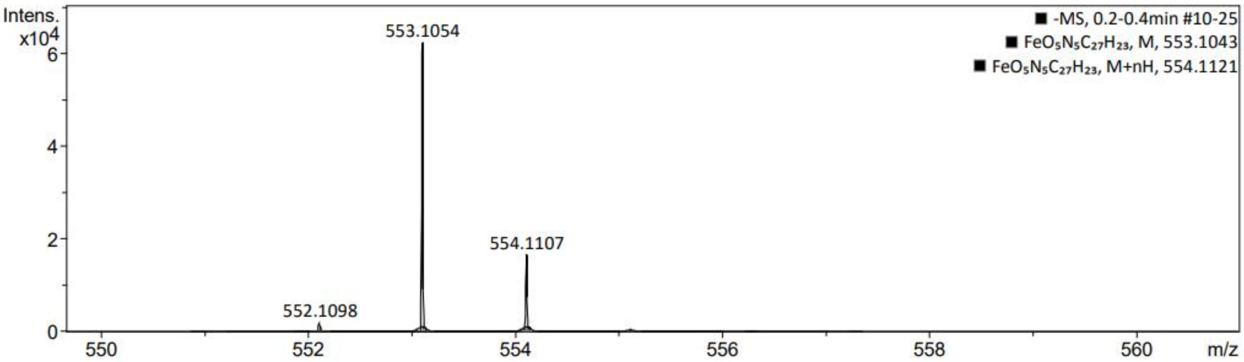


Figure S1. HRMS of **3'** Experimental m/z (M-) 553.1043 (100%); calculated m/z (M-) 553.1049 (100%)

3.3 EPR spectroscopic studies of 3' in solid state

(1 mg, 0.001 mmol) of **3** was embedded in a small amount of silica in a mortar. To this well-grounded mixture, (10 eqv., 0.01 mmol) of $Na_2CO_3.1.5H_2O_2$ was added at room temperature. The color of the reaction mixture was changed from yellow to green upon grinding by pestle. The green species obtained was characterized as oxoiron(V) (**3'**) intermediate by EPR spectroscopy. EPR spectroscopy was done at 85K in an EPR tube loaded with green color species followed by freezing in liquid nitrogen. The spectrum obtained shows an orthorhombic species with S=1/2 and g values of 2.13, 2.03, and 1.99 (Figure 2).

3.4 Reaction conditions and product quantification for small molecules

All the hydroxylation and epoxidation reactions were carried out at room temperature under solvent-less conditions. To a mortar, **3** (0.0005 mmol, 1-5 mol %) and substrate (0.01 mmol - 0.050 mmol) were added. To this well-grounded mixture oxidant ($Na_2CO_3.1.5H_2O_2$) was added iteratively (2 eqv. each time w.r.t. catalyst) until the catalyst color bleaches out. For the complete reaction total of 1-2 eqv. oxidant was added with respect to the substrate. Most of the reactions were completed within 45 min - 2 h unless specifically mentioned. After completion of the reaction, the reaction mixture was extracted in ethyl acetate and washed twice with water for the complete removal of excess catalyst and oxidant. The organic layer was filtered through a plug of basic alumina and was subjected to GC-MS for product identification and quantification. Bromobenzene was used as an internal standard. The yield and conversion were estimated using the response factor of authentic substrates and products.

3.5 Polymerization of 1-hexene

The Mg-Ti Ziegler type catalyst was synthesized according to previously published literature.[4] 1-hexene polymerization was performed in a specially designed and developed deep freezer roller. 0.250 g (0.156 mmol) of the catalyst was weighed in a specially designed schlenk in a glove box. In a separate schlenk flask, 30 mL of dry 1-hexene was taken and cooled down to 0 °C. To this schlenk flask, 1.35 mL (3.132 mmol) of MMAO-12 was added and the reaction mixture was stirred for 10 minutes. Then this reaction content was added to the precooled schlenk ampule in which the catalyst was taken. The ampule was closed immediately with an airtight teflon stop cock and transferred to the deep freezer roller which was already set at 0° C with the desired rolling speed (50 RPM). The ampule was then rolled for 24 hours. After that polymerization was quenched by pouring the reaction mixture into the acidified methanol. The precipitated polymer was separated, washed with methanol, and dried under vacuum for 12 hours (~11 g). The resultant polymer was characterized by ^{1}H, ^{13}C NMR spectroscopy and GPC.

3.6 Hydroxylation reaction on macromolecules

3.6.1 Polystyrene (PSLW)

(2 mg, 0.0024 mmol) of **3** was taken in a mortar. To the catalyst **3**, 50 eqv. (12.48 mg, 0.12 mmol) of polystyrene (M_w = 3100 Da, Đ = 1.15) was added. Stoichiometry was calculated with styrene monomer unit. Catalyst and polystyrene were mixed thoroughly with a pestle followed by iterative addition of $Na_2CO_3.1.5H_2O_2$ in 5 eqv. with respect to the catalyst. The reaction took place under solvent-less conditions in a mortar under mechanical grinding by a pestle. The reaction was continued for almost 5 h until the complete color of the catalyst was gone. After completion of the reaction, the reaction mixture was washed with water to ensure complete removal of excess catalyst and oxidant. The reaction mixture was then extracted in ethyl acetate and was run through a small plug of basic alumina. Drying of the reaction mixture was done very carefully under reduced pressure at 50°C for 5 h.

Control experiment: A similar reaction was performed excluding the catalyst to confirm the role of **3** in polystyrene hydroxylation reaction. The reaction mixture was extracted similarly and dried well under reduced pressure at 50°C for 5 h.

3.6.2 Poly(hexene-1) (PH)

(2 mg, 0.0024 mmol) of **3** was taken in a mortar. To the catalyst **3**, 50 eqv. (10.08 mg, 0.12 mmol) of poly(hexene-1) was added. Stoichiometry was calculated with 1-hexene monomer unit. Catalyst and poly(hexene-1) were mixed thoroughly with a pestle followed by iterative addition of $Na_2CO_3.1.5H_2O_2$ in 5 eqv. with respect to the catalyst. The reaction took place under solvent-less conditions in a mortar under mechanical grinding by a pestle. The reaction was continued for almost 5 h until the complete color of the catalyst was gone. After completion of the reaction, the reaction mixture was washed with water to ensure complete removal of excess catalyst and oxidant. The reaction mixture was then extracted in dichloromethane and was run through a small plug of basic alumina. Drying of the reaction mixture was done very carefully under reduced pressure at 50°C for 5 h.

Control experiment: A similar reaction was performed excluding the catalyst to confirm the role of **3** in poly(hexene-1) hydroxylation reaction. The reaction mixture was extracted similarly and dried well under reduced pressure at 50°C for 5 h.

3.7 Characterization of hydroxylated polystyrene and poly(hexene-1) backbone

3.7.1 IR measurements

After successful drying of the samples obtained both from **3** catalyzed hydroxylation of polystyrene and control experiment, they were solubilized in purified dry and degassed dichloromethane. Thin films were made by drop-casting a minimum amount of the solution on NaCl plates. The plate was dried under reduced pressure very well before data collection. Complete drying is necessary to rule out any chances of moisture absorption.

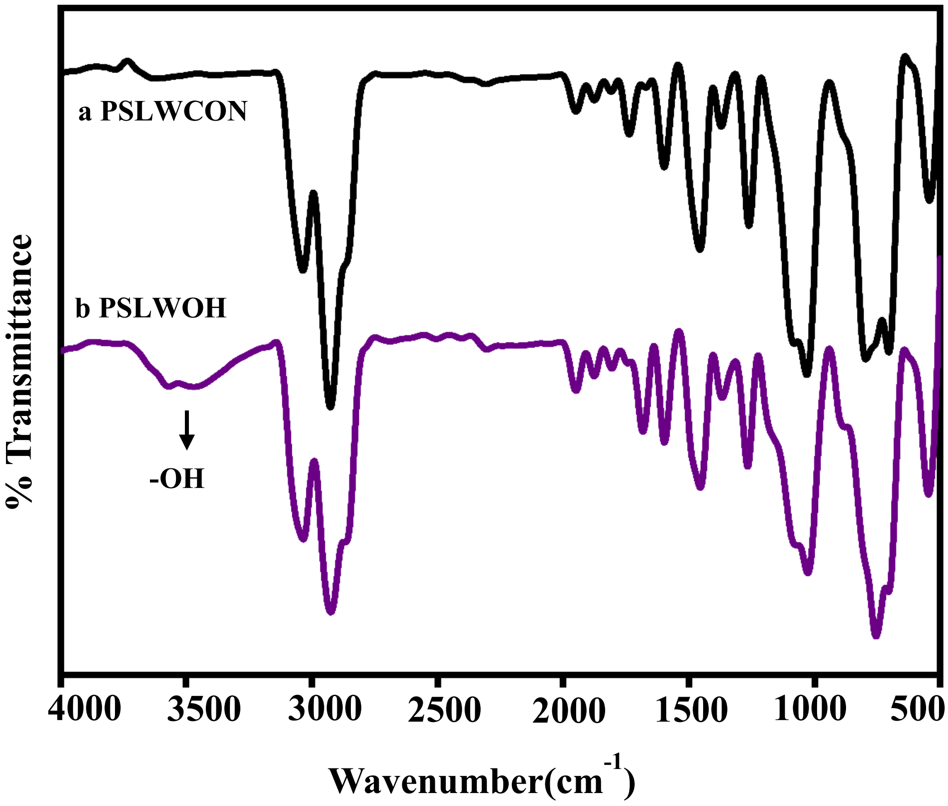


Figure S2. Infra-red spectrum of a. Control reaction on polystyrene (PSLW) without catalyst (PSLWCON) b. Hydroxylated polystyrene (PSLWOH)

3.7.2 NMR measurements

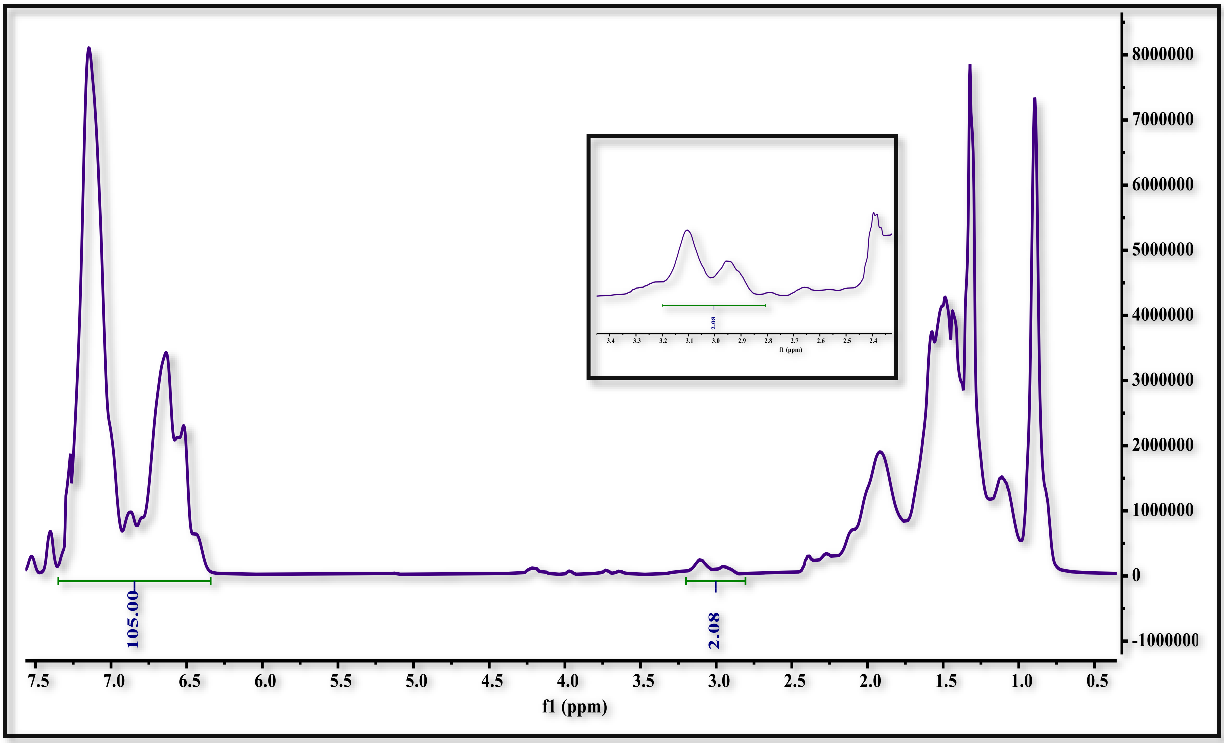


Figure S3. ^{1}H NMR spectrum of **PSLWOH** in $CDCl_3$, obtained from **3'** catalyzed C–H bond hydroxylation of **PSLW** (M_n = 2700 Da, M_w = 3100 Da, Đ = 1.15)

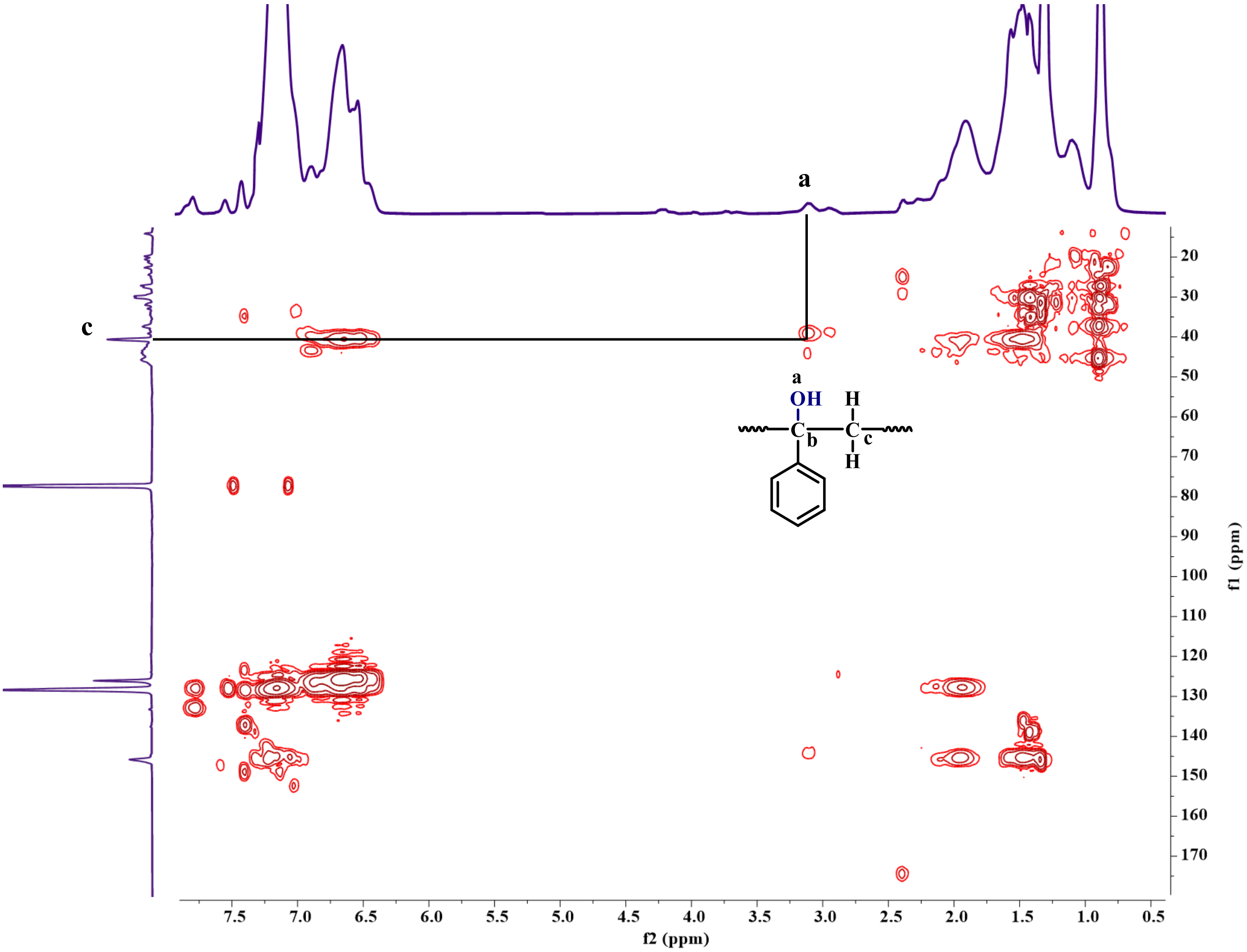


Figure S4. ^{1}H-^{13}C HMBC NMR spectrum of **PSLWOH**, obtained from **3'** catalyzed C–H bond hydroxylation of **PSLW** (M_n = 2700 Da, M_w = 3100 Da, Đ = 1.15), measured in $CDCl_3$ at room temperature

3.7.3 X-ray photoelectron spectroscopy (XPS) data

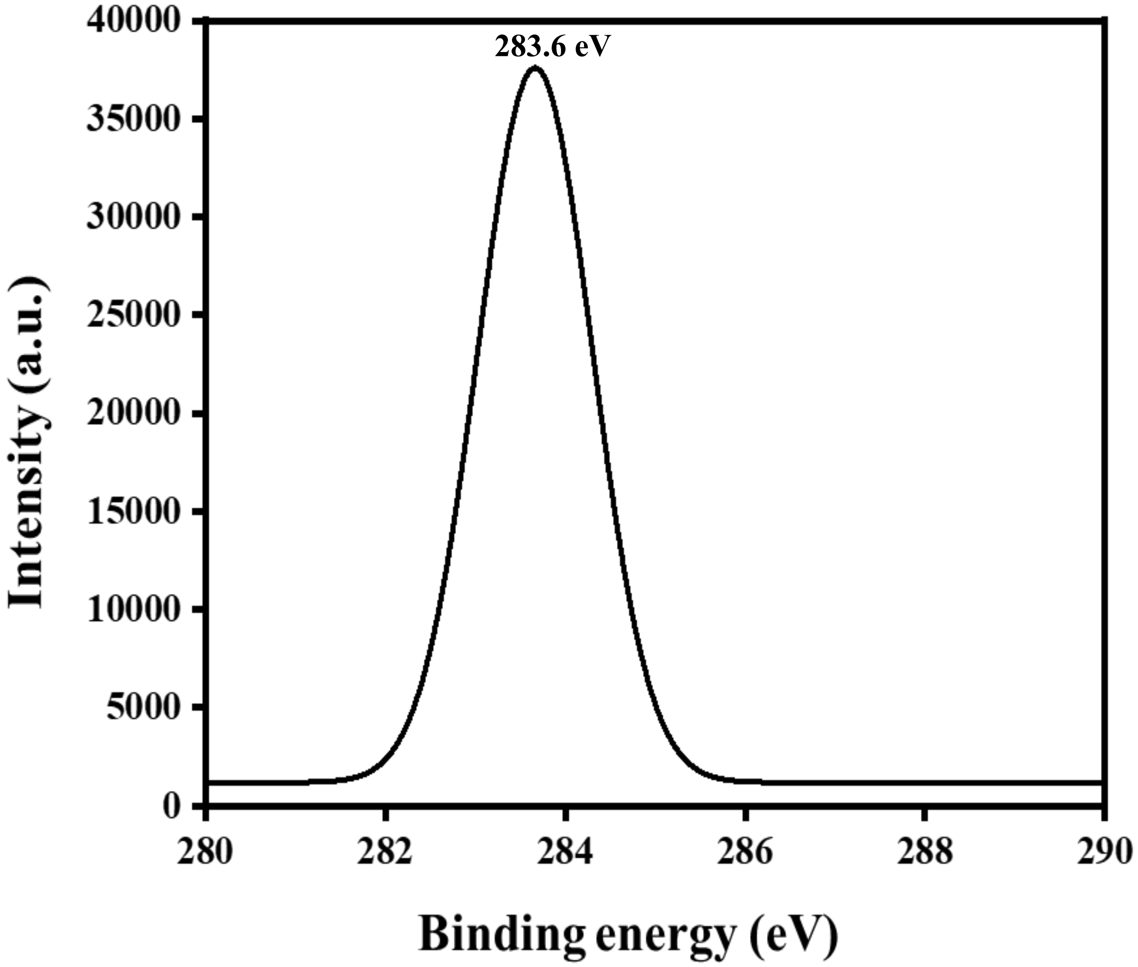


Figure S5. XPS spectrum of **PSLW** (M_n = 2700 Da, M_w = 3100 Da, Đ = 1.15)

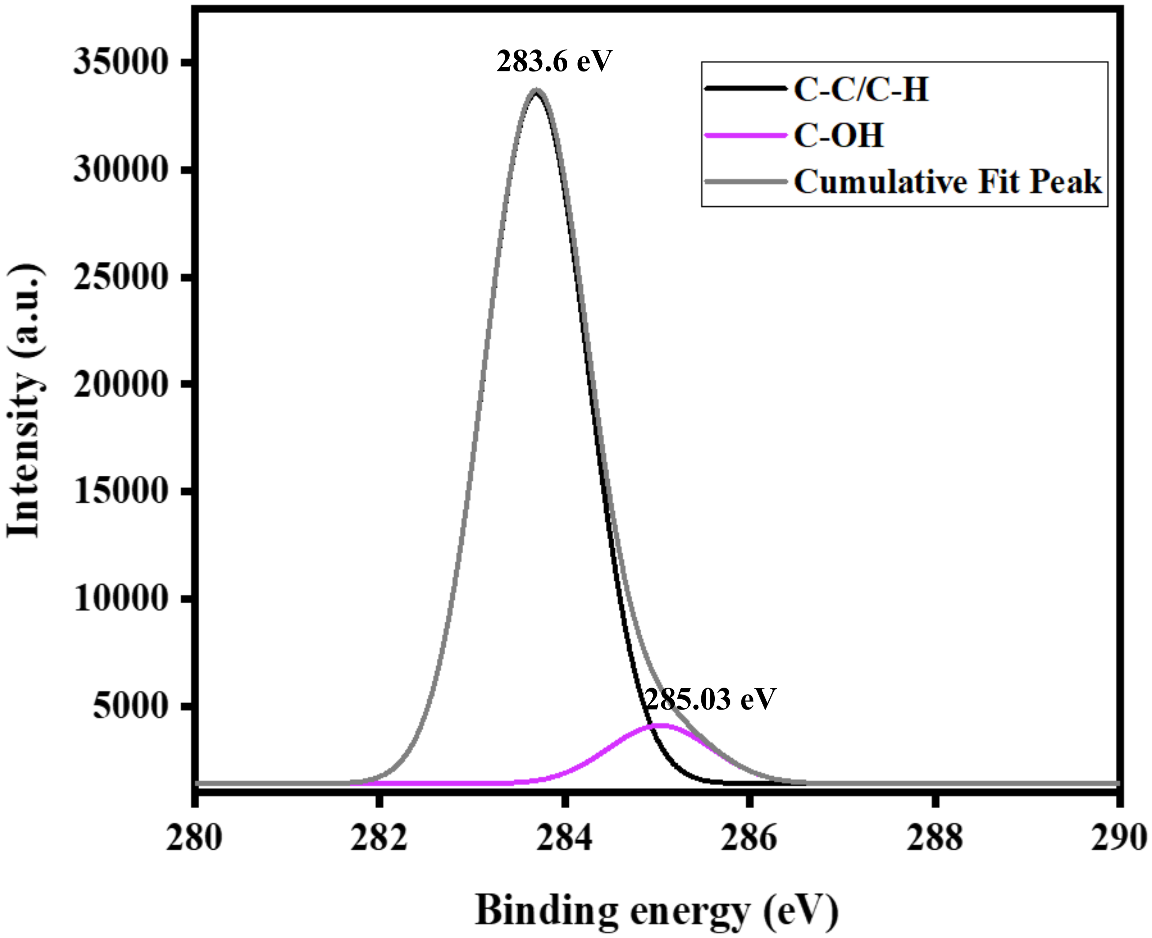
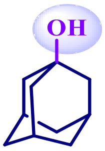


Figure S6. XPS spectrum of **PSLWOH**, obtained from **3'** catalyzed C–H bond hydroxylation of **PSLW** (M_n = 2700 Da, M_w = 3100 Da, Đ = 1.15)

3.8 GC-MS traces for product quantification; reactions catalyzed by **3** and $Na_2CO_3.1.5H_2O_2$

Figure S7. GC-MS of 1-Adamantanol



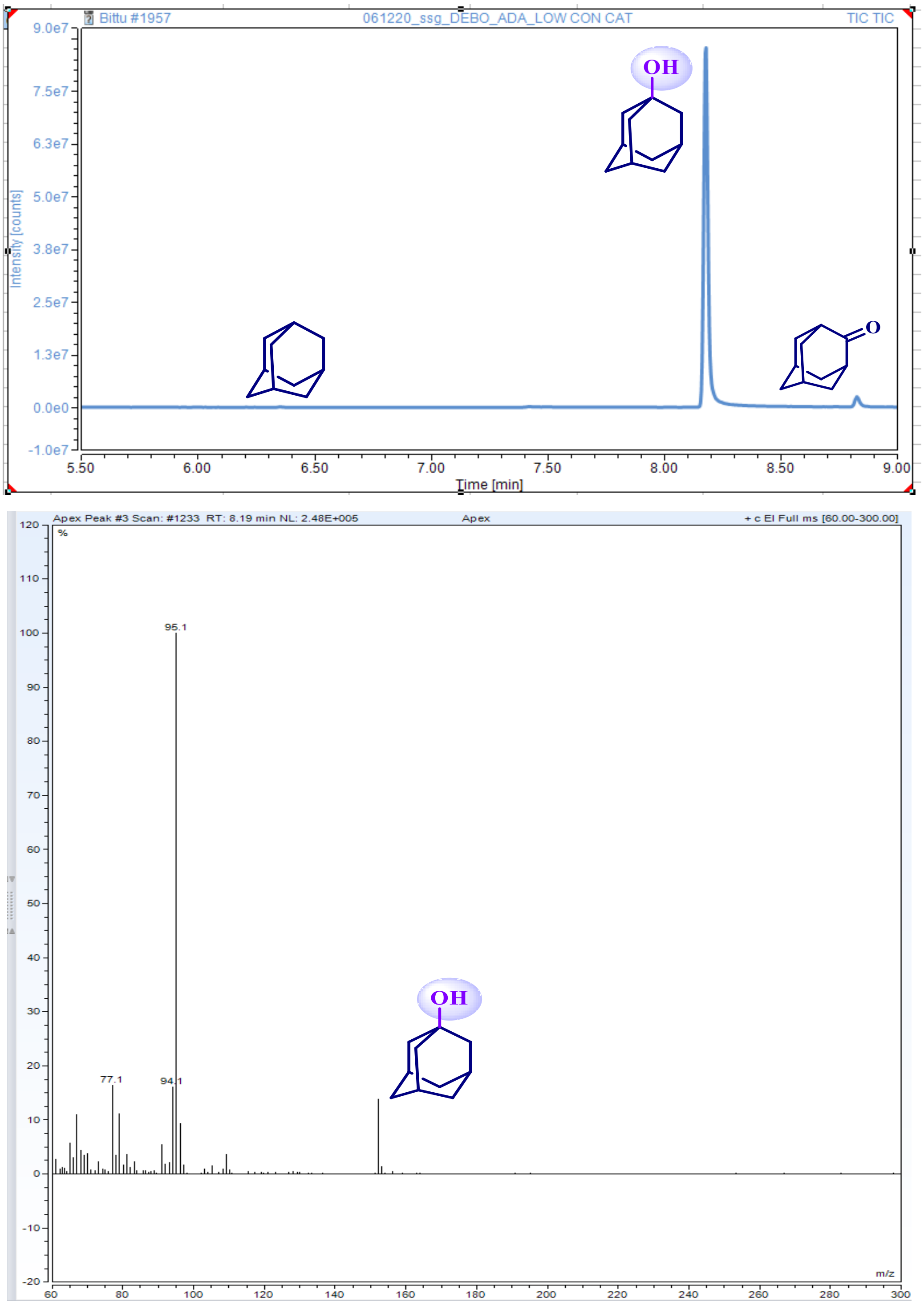
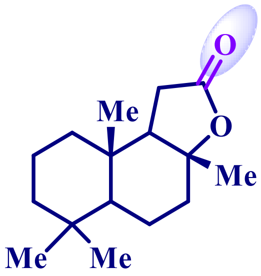
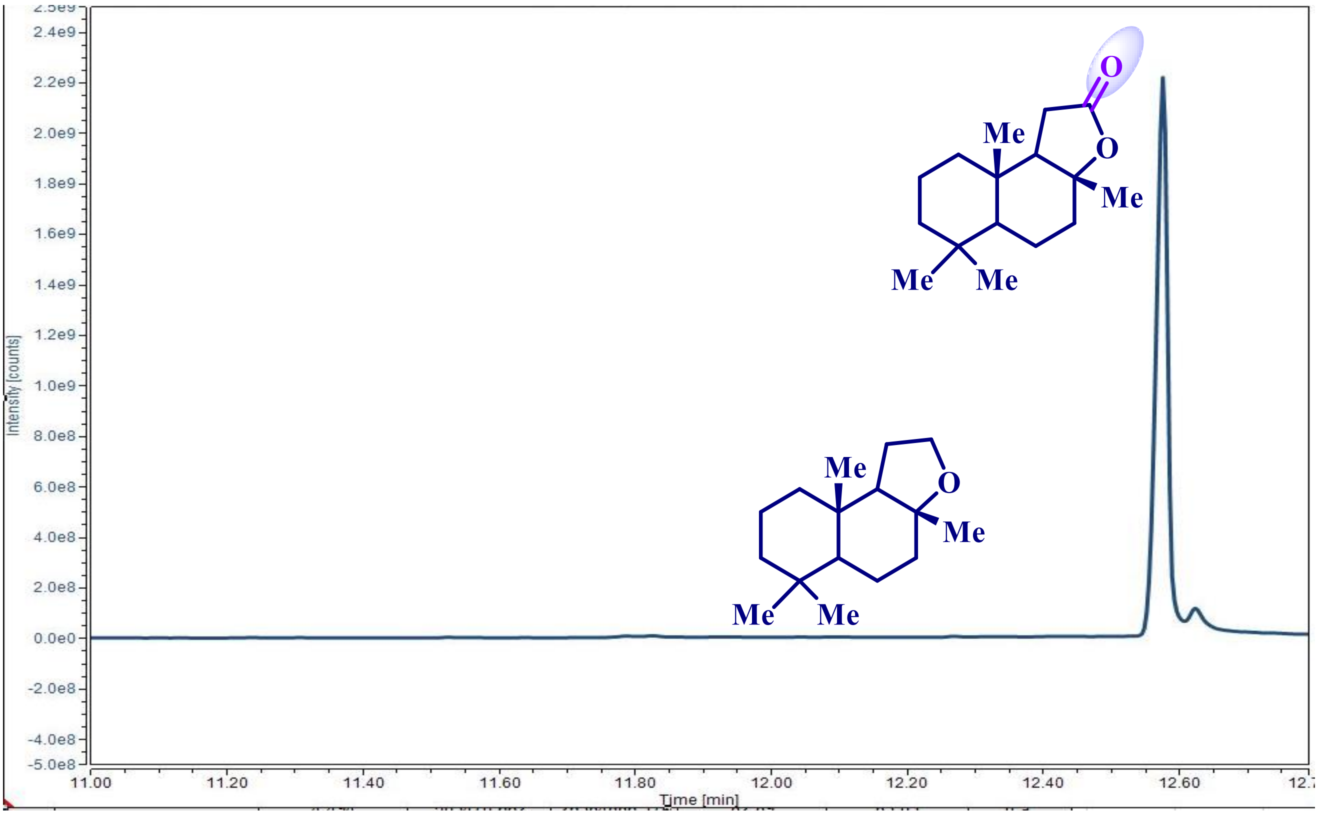


Figure S8. GC-MS of Sclareolide





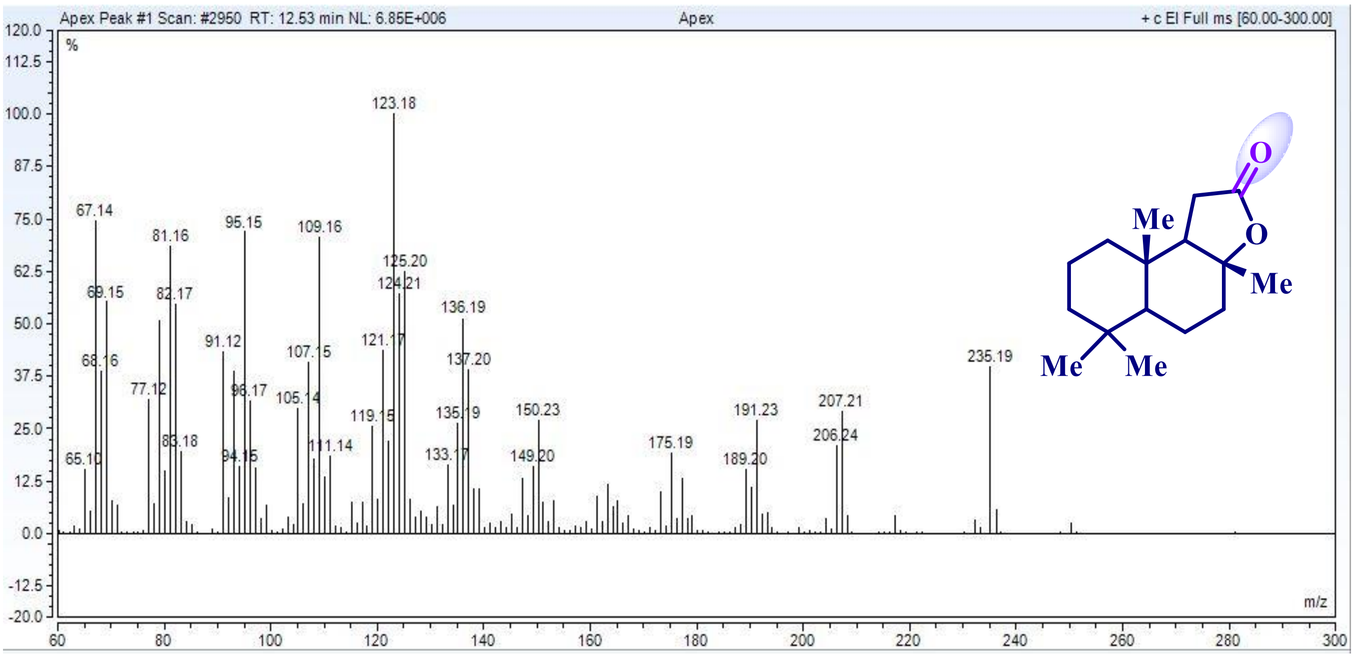
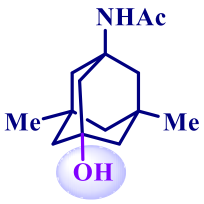
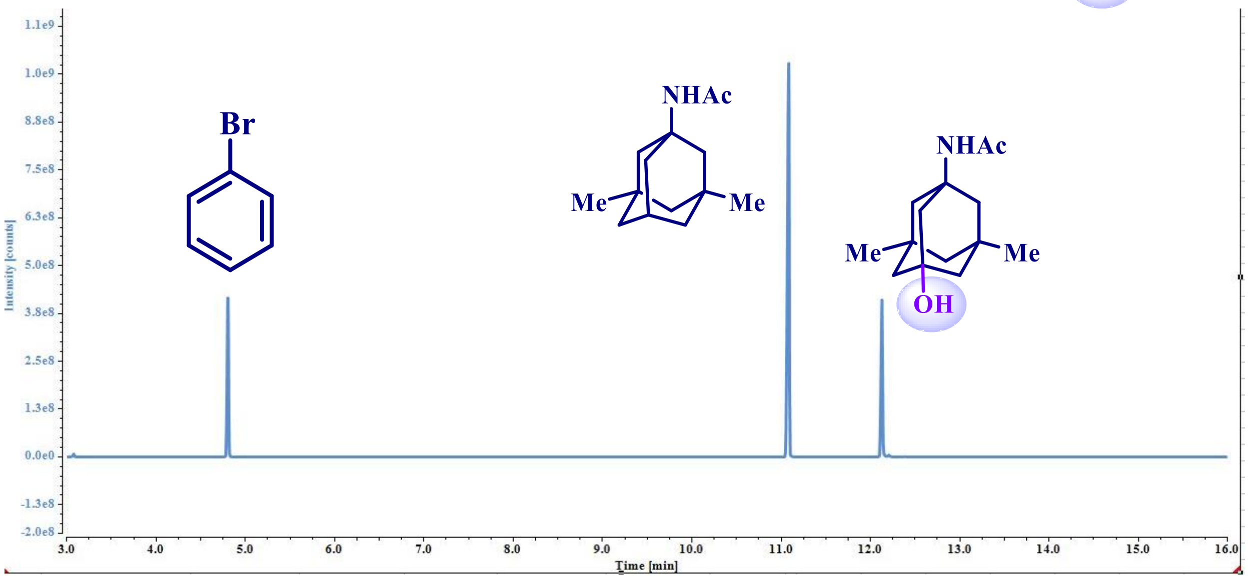


Figure S9. GC-MS of 3-hydroxy-5,7-dimethyladamantan-1-yl)acetamide





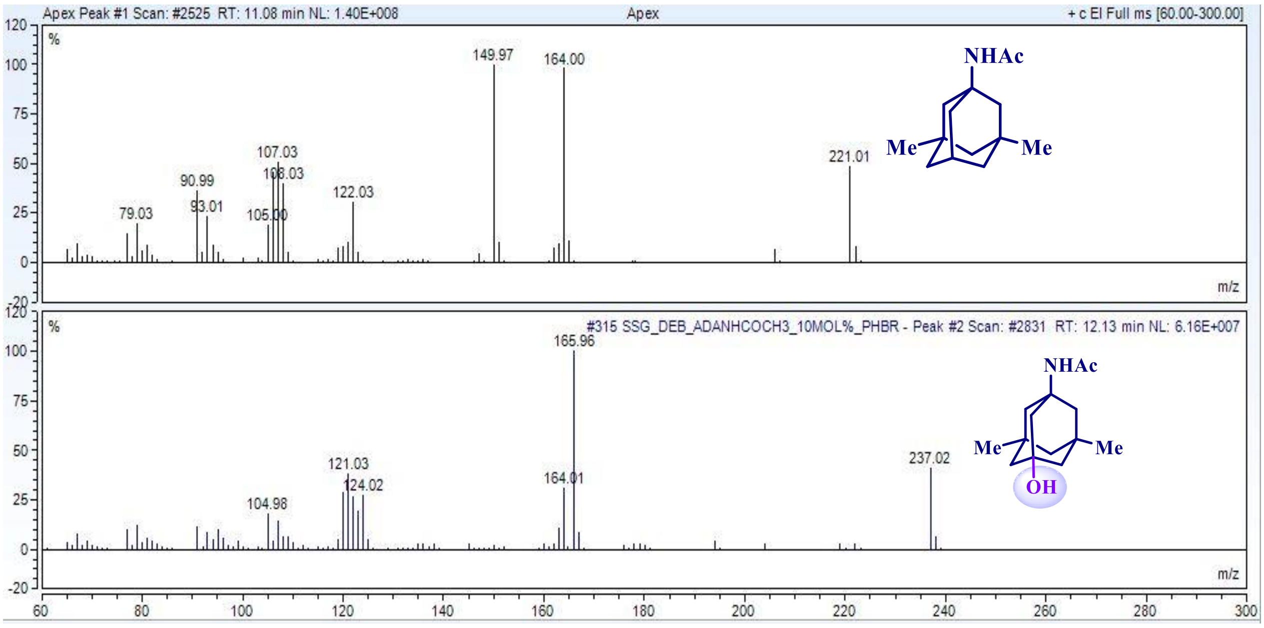
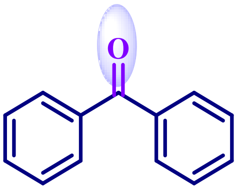
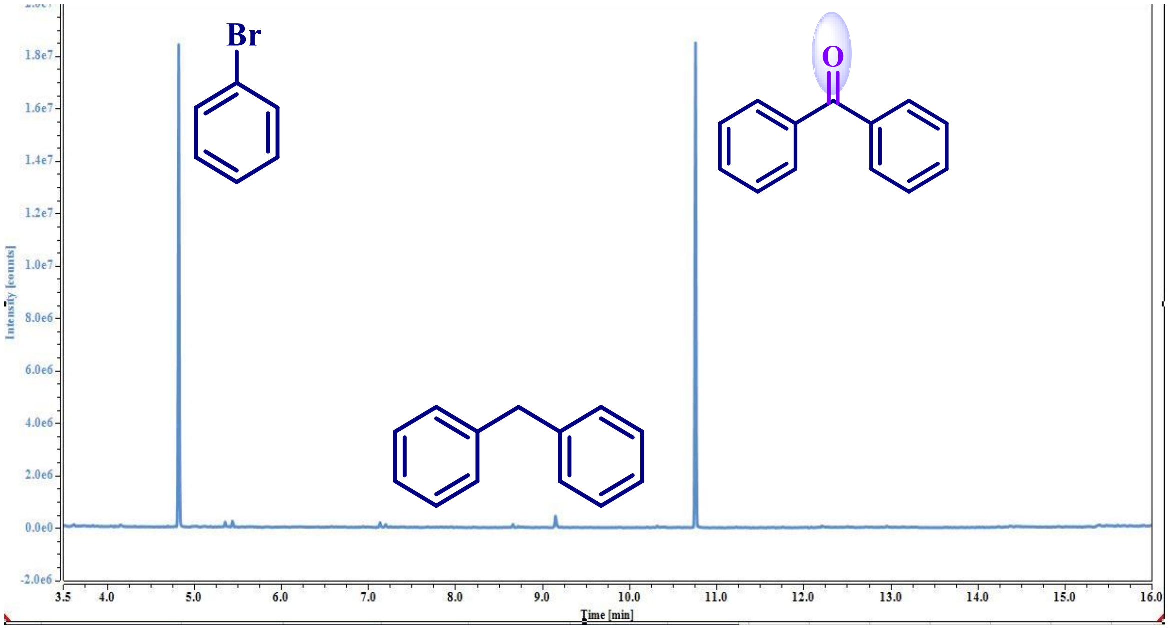


Figure S10. GC-MS of Benzophenone





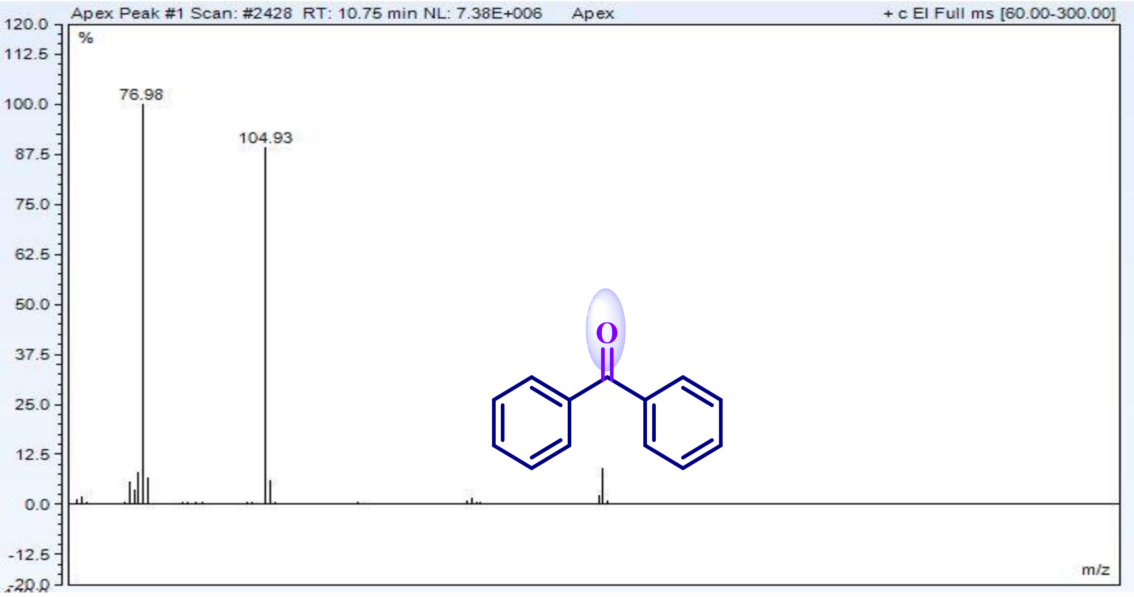
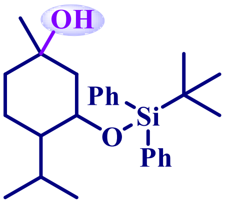
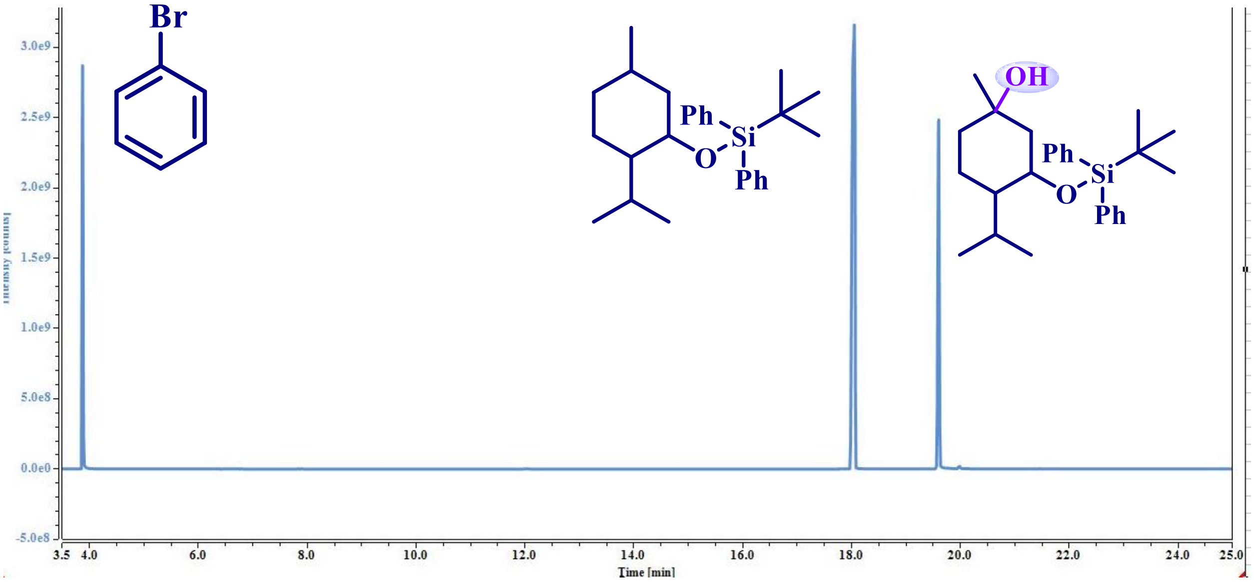
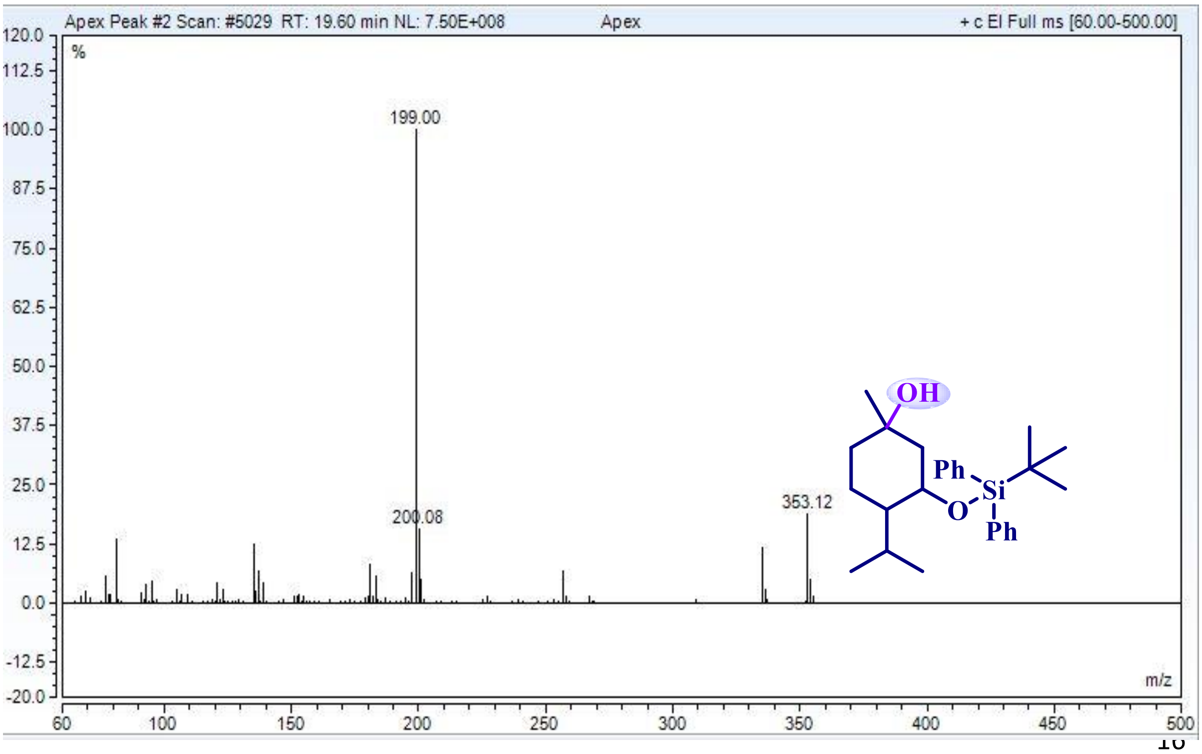


Figure S11. GC-MS of (3-((tert-butyldiphenylsilyl)oxy)-4-isopropyl-1-methylcyclohexan-1-ol)

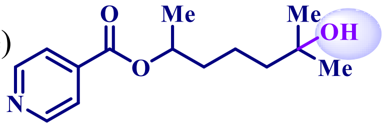






https://doi.org/10.26434/chemrxiv-2024-7f3dr **ORCID:** https://orcid.org/0000-0002-3729-1820

Figure S12. GC-MS of (6-hydroxy-6-methylheptan-2-yl isonicotinate)



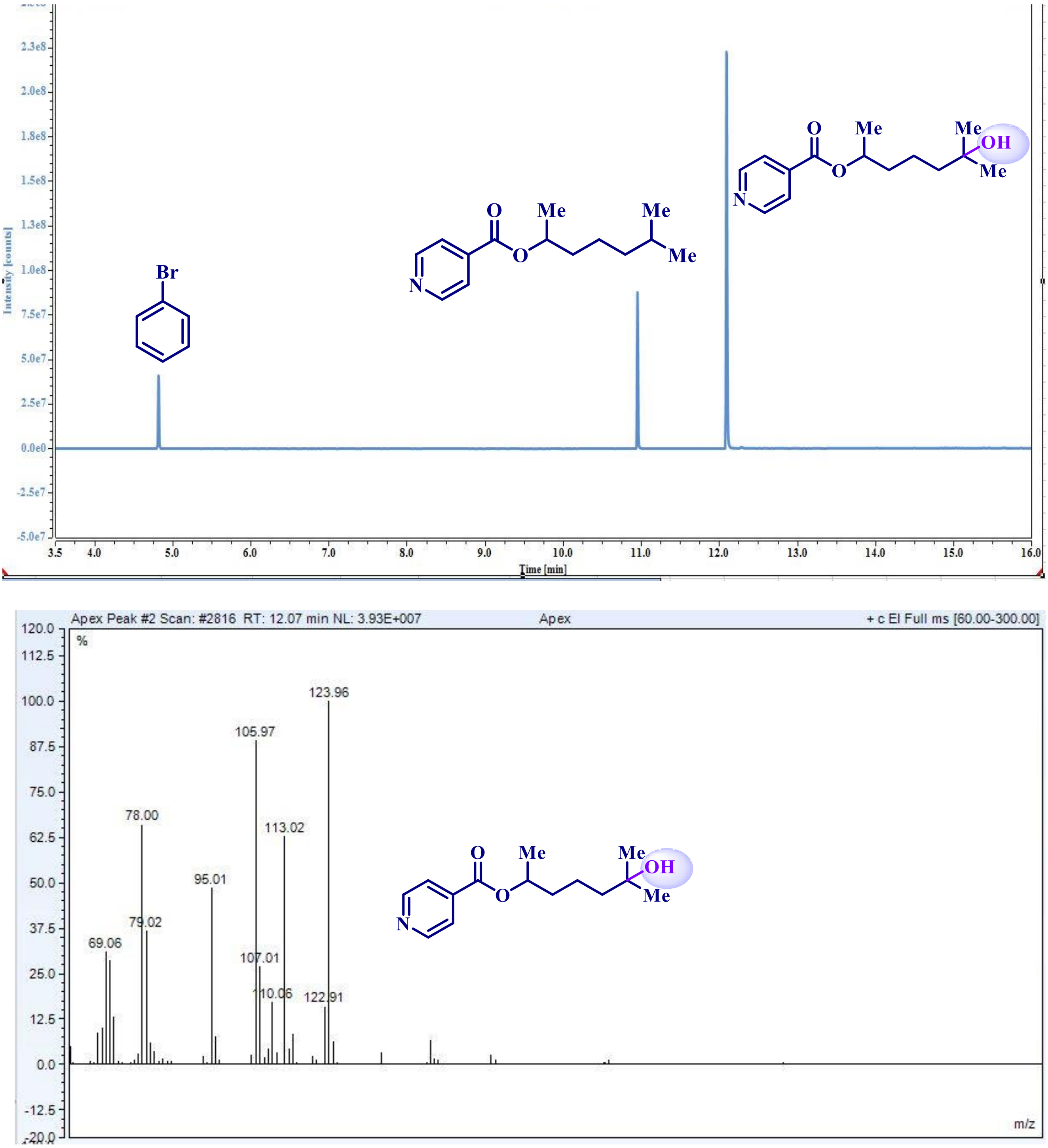
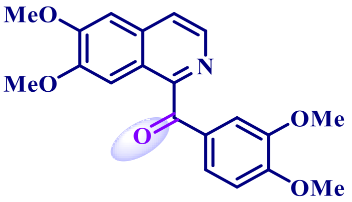
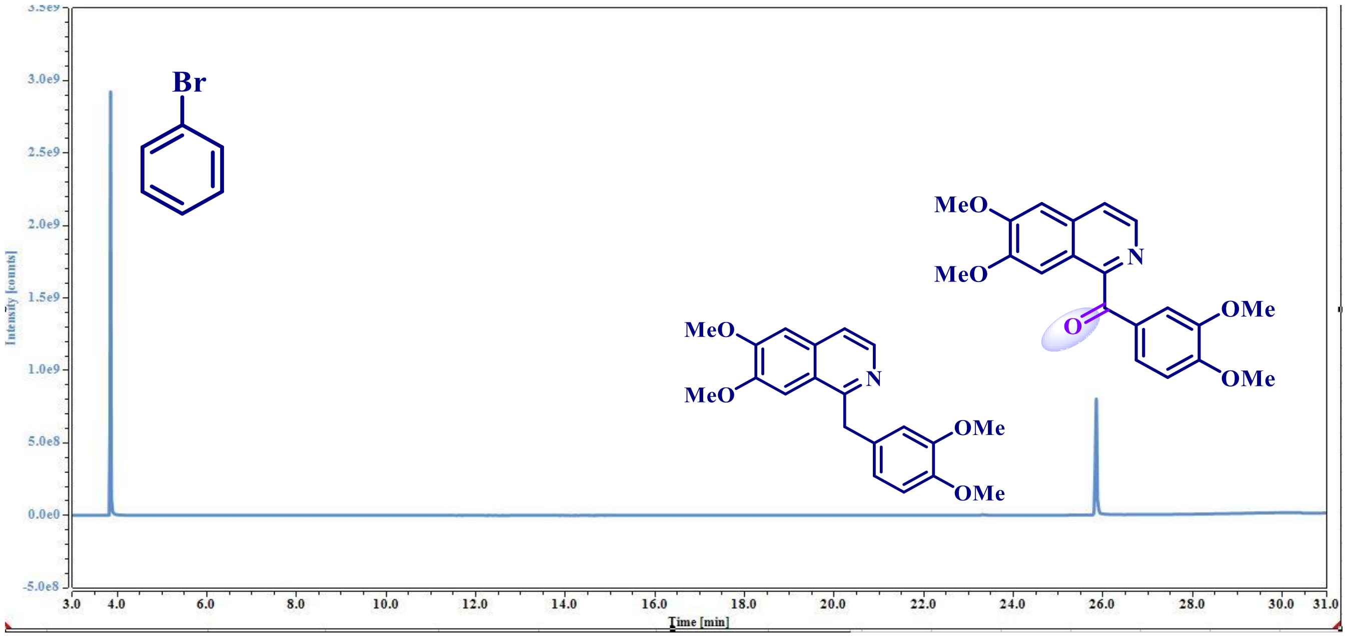


Figure S13. GC-MS of ((6,7-dimethoxyisoquinolin-1-yl) (3,4 dimethoxyphenyl)methanone)





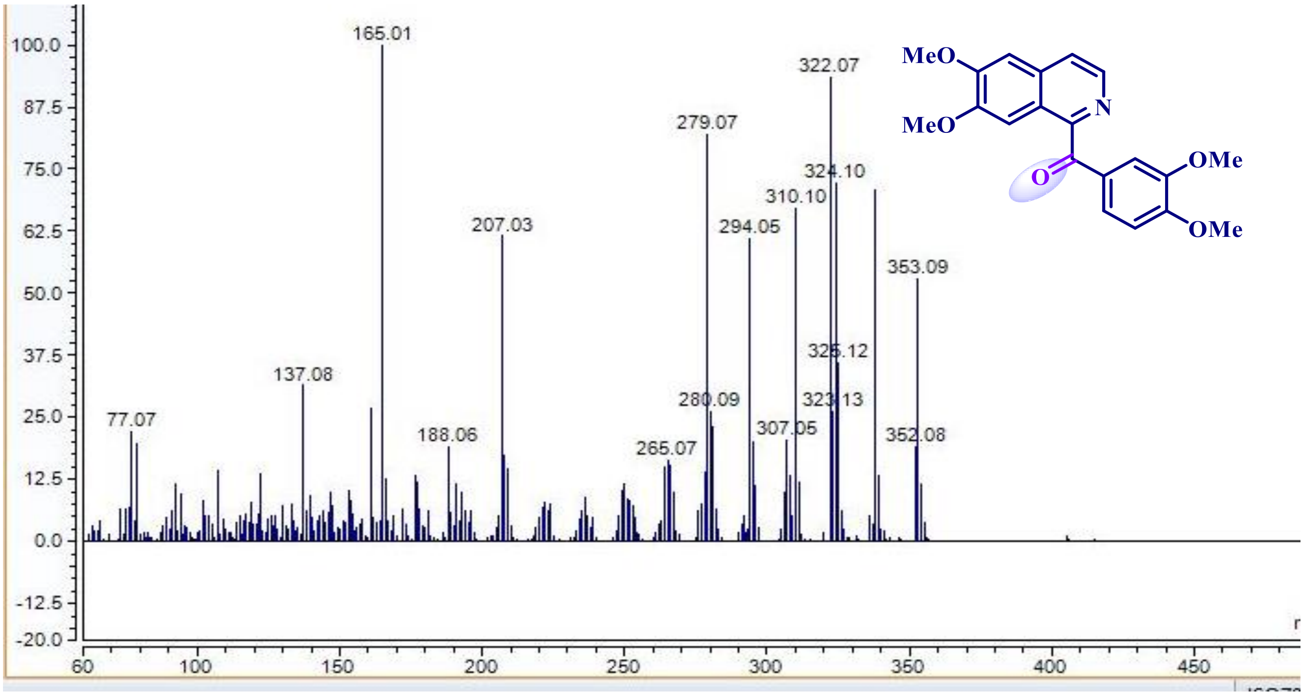
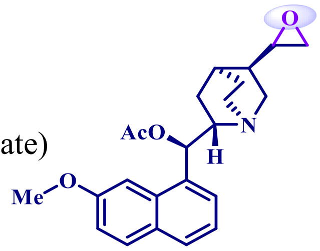


Figure S14. GC-MS of ((R)-(7-methoxynaphthalen-1-yl)((1S,2S,4S,5R)-5-((S)-oxiran-2-yl)quinuclidin-2-yl)methyl acetate)



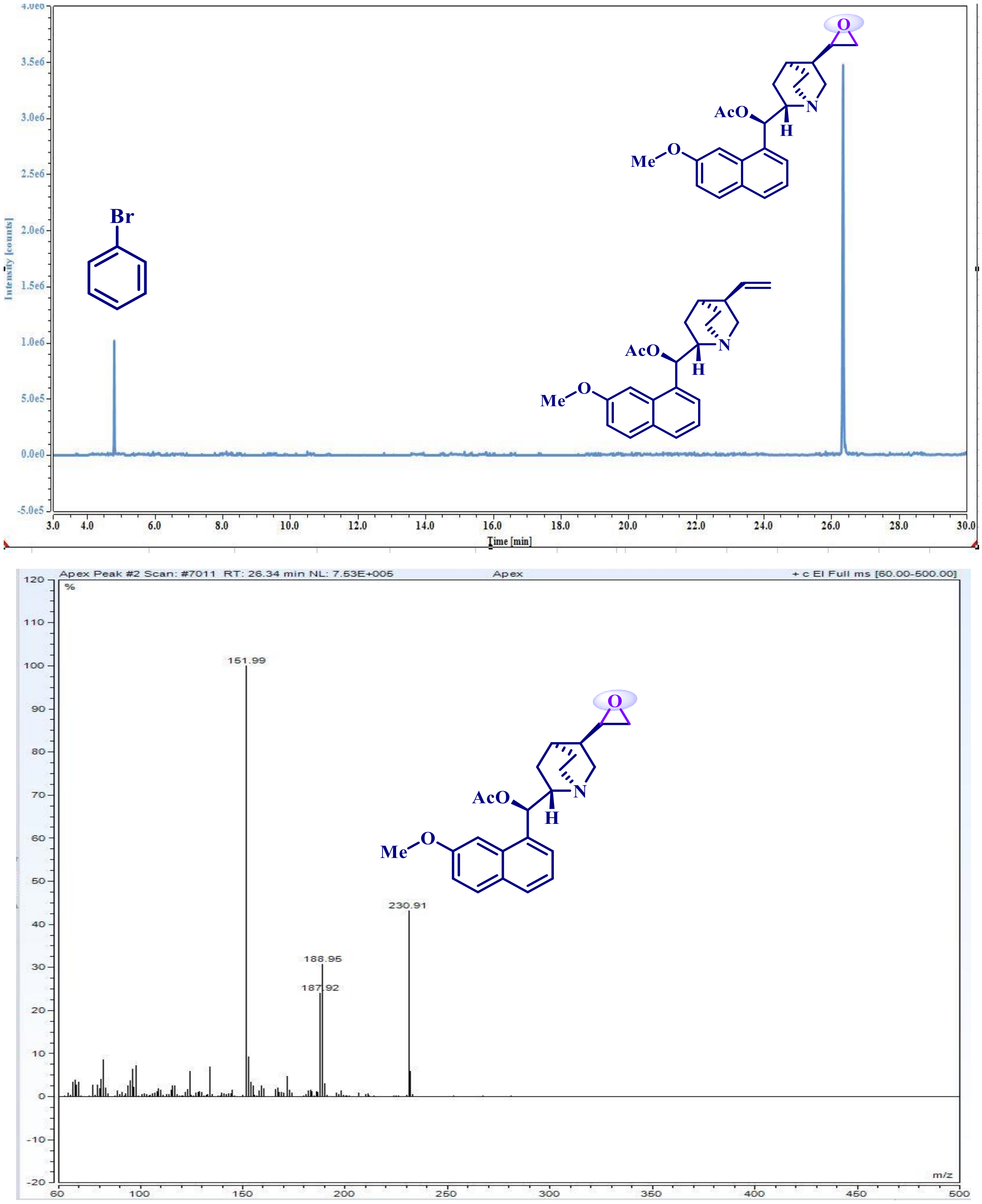
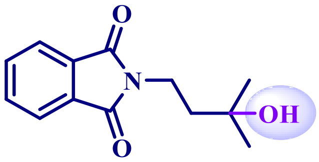
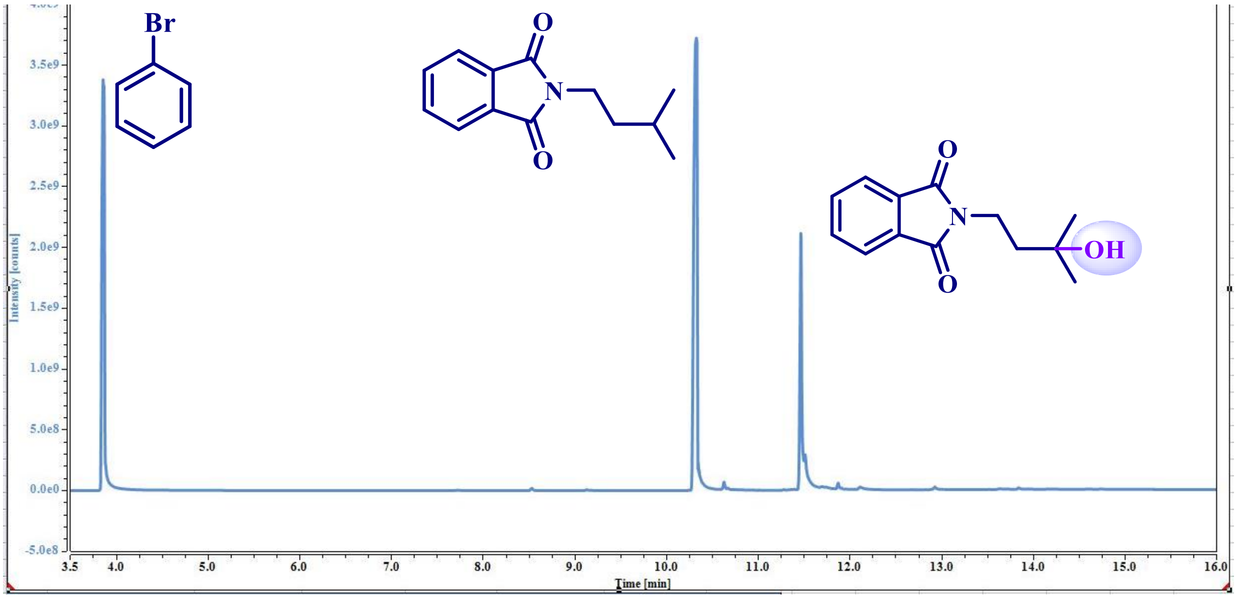


Figure S15. GC-MS of (2-(3-hydroxy-3-methylbutyl)isoindoline-1,3-dione)





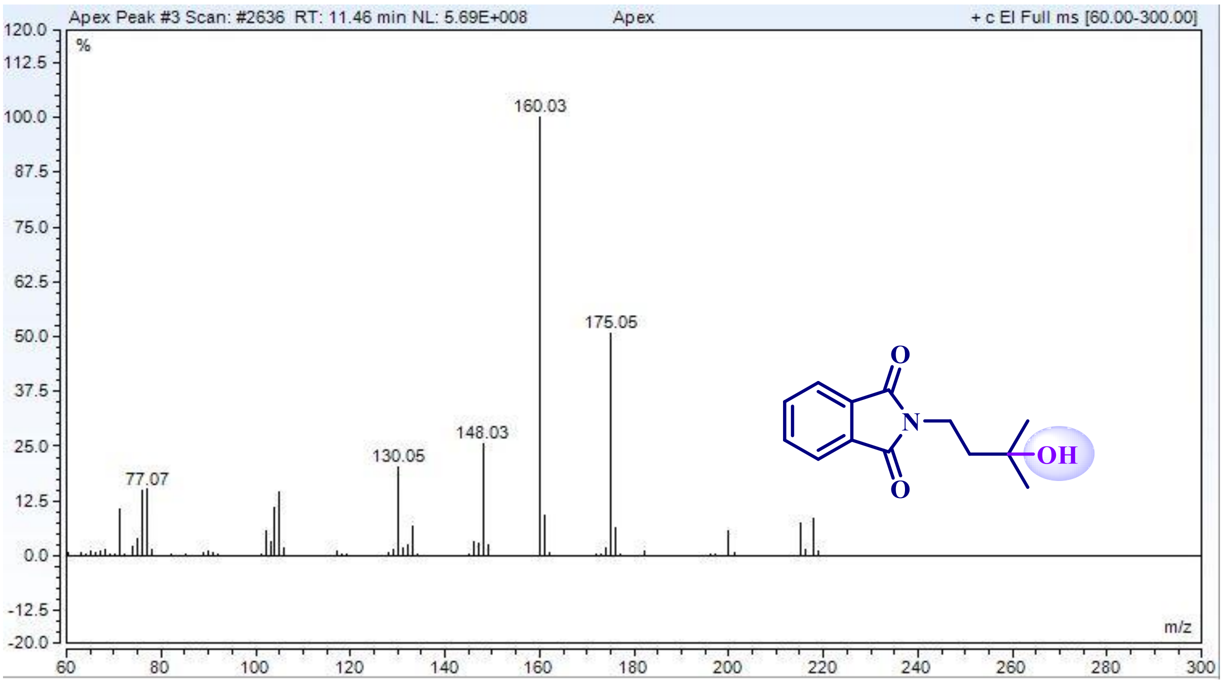
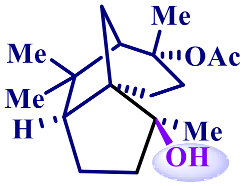
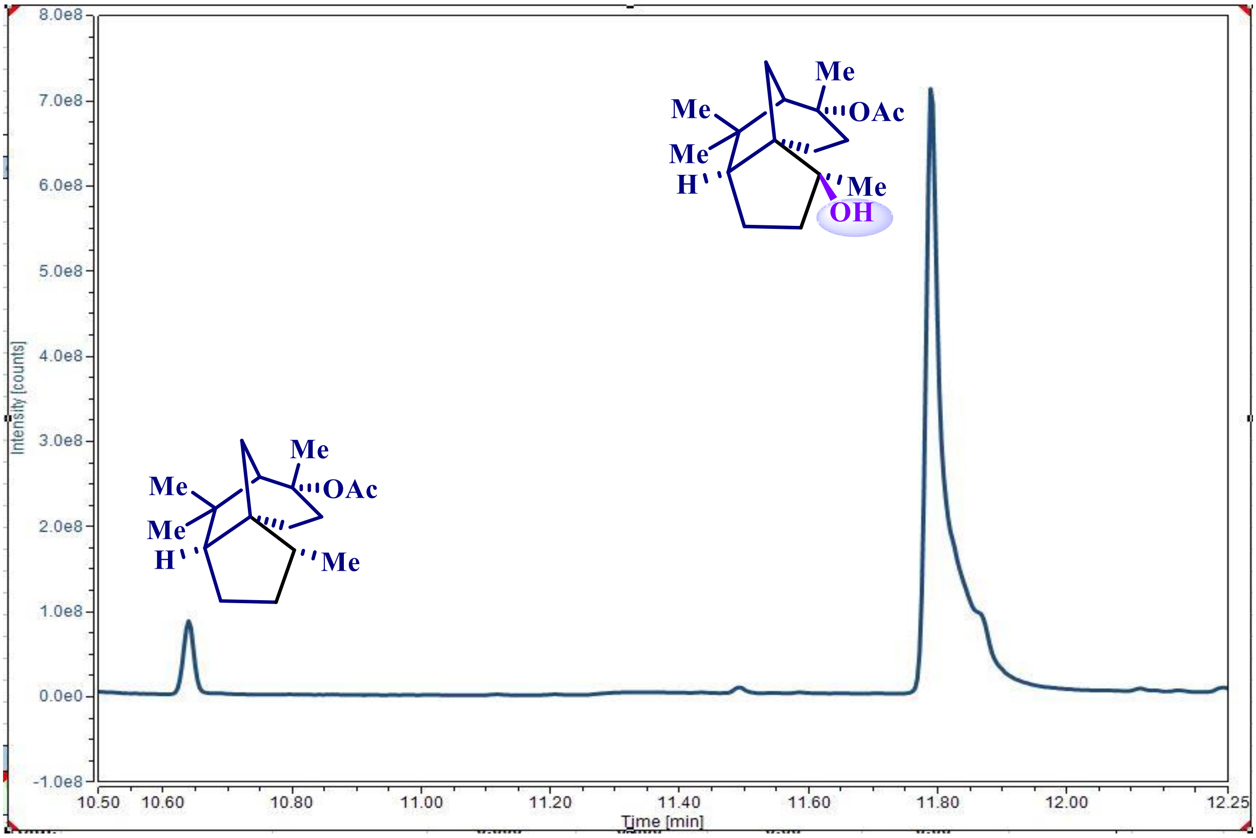


Figure S16. GC-MS of (2,6,6,8-tetramethyl-8-tricyclo[5.3.1.0^{1,5}]undecanyl) acetate





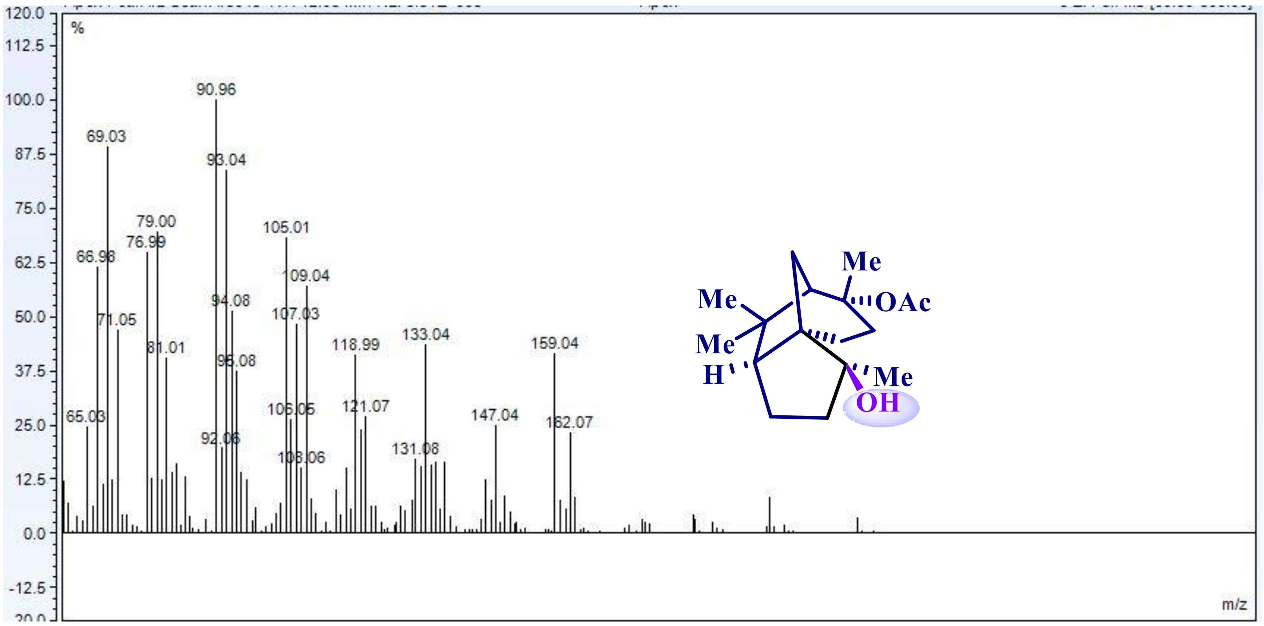
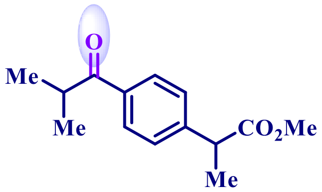
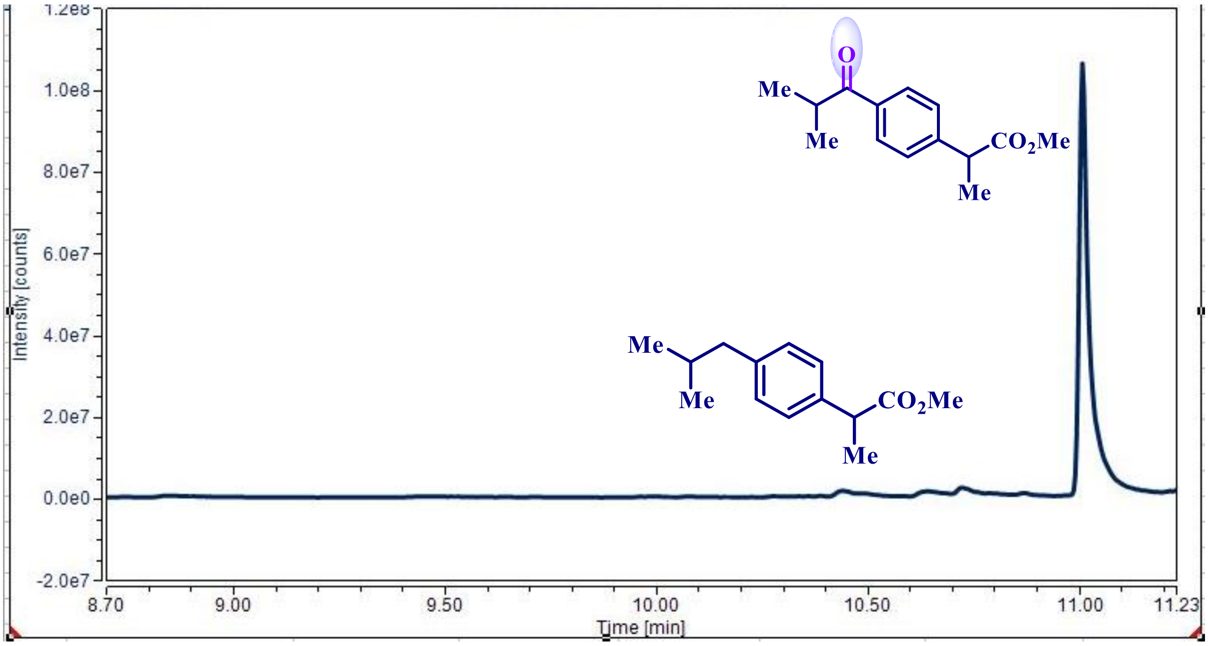


Figure S17. GC-MS of (methyl 2-(4-isobutylphenyl)propanoate)





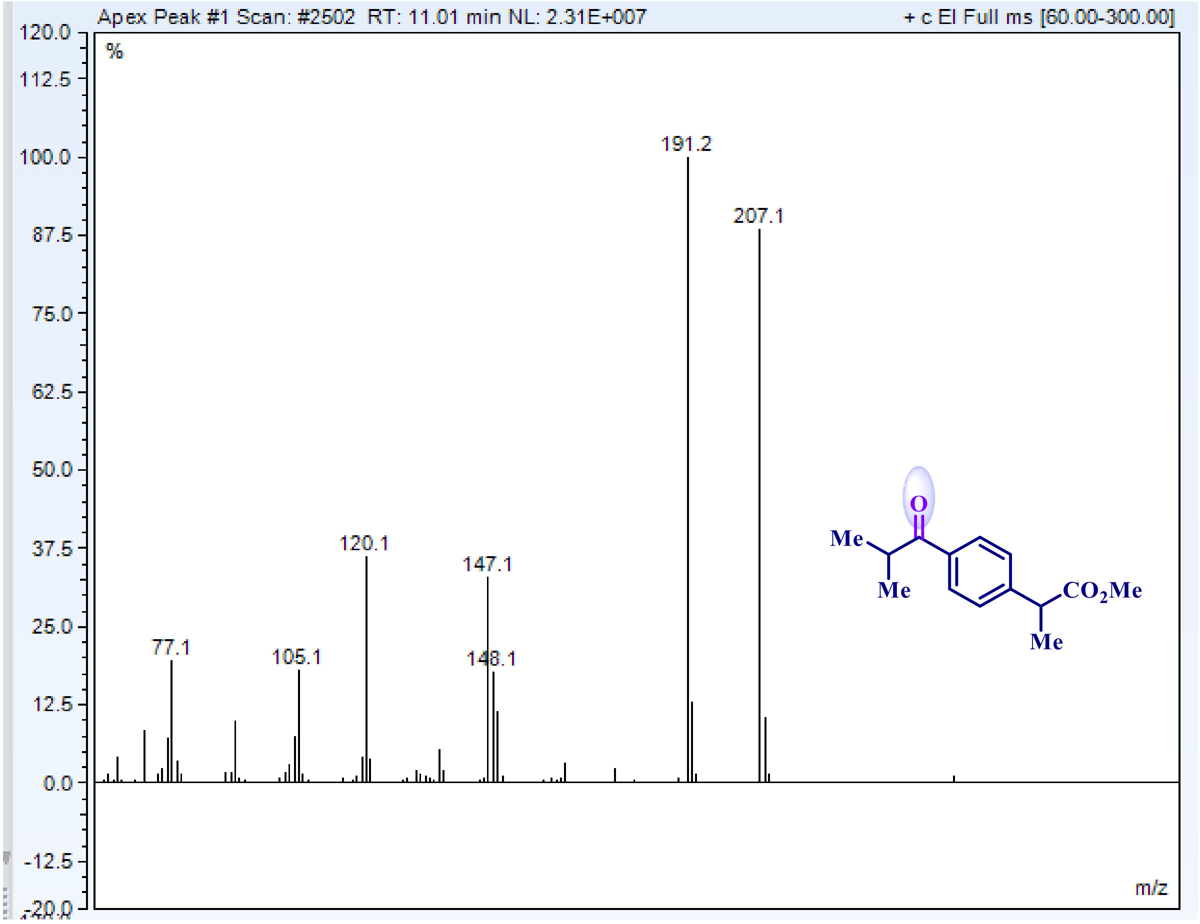
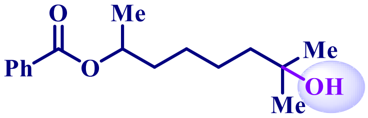
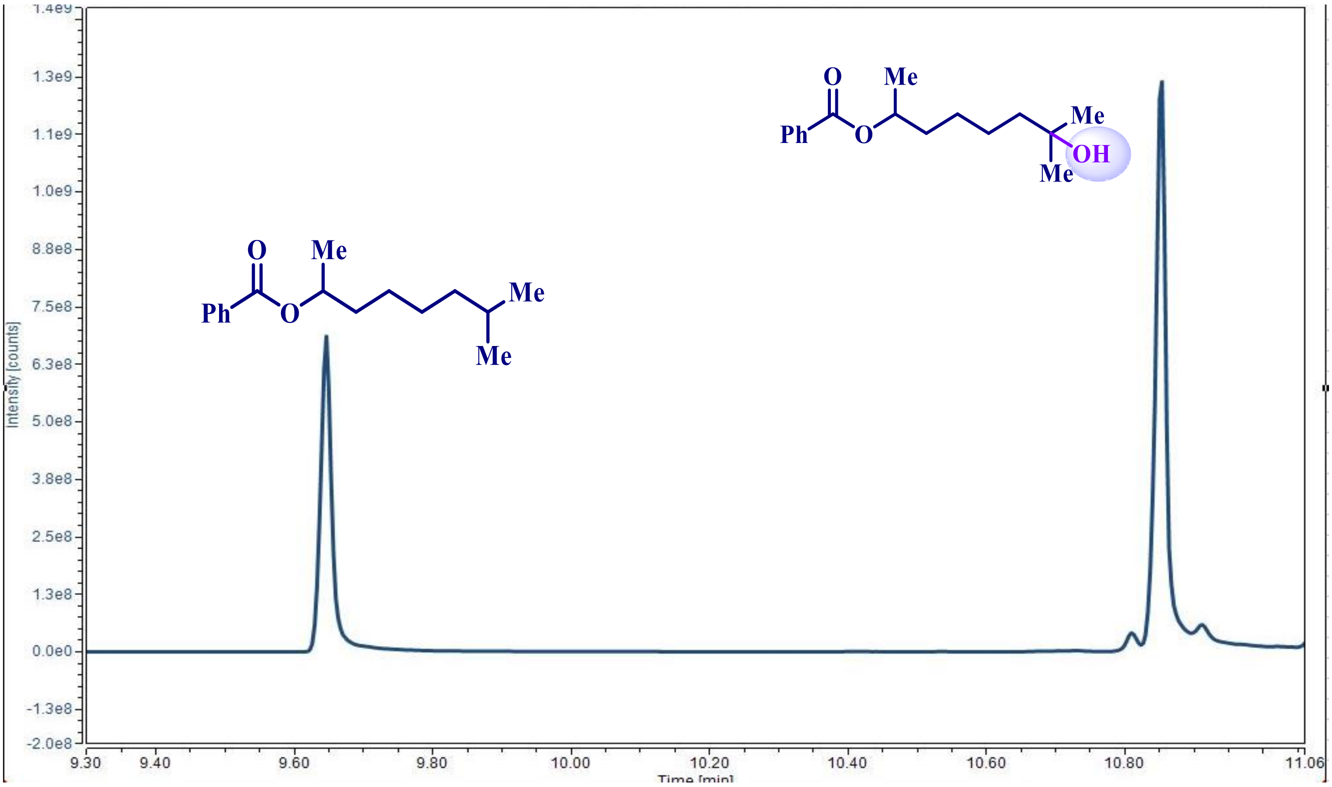


Figure S18. GC-MS of (6-hydroxy-6-methylheptan-2-yl)





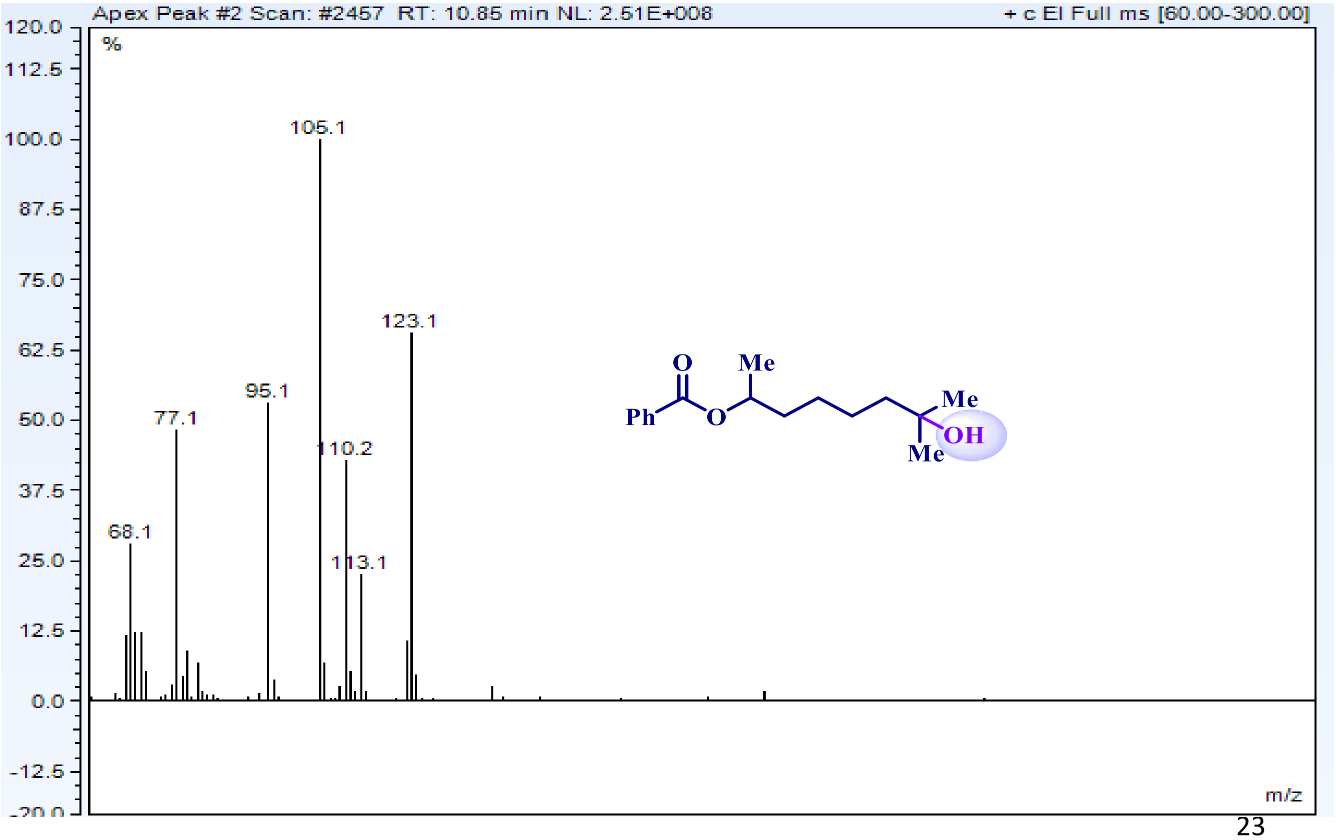
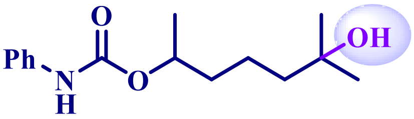


Figure S19. GC-MS of (6-hydroxy-6-methylheptan-2-yl phenylcarbamate)



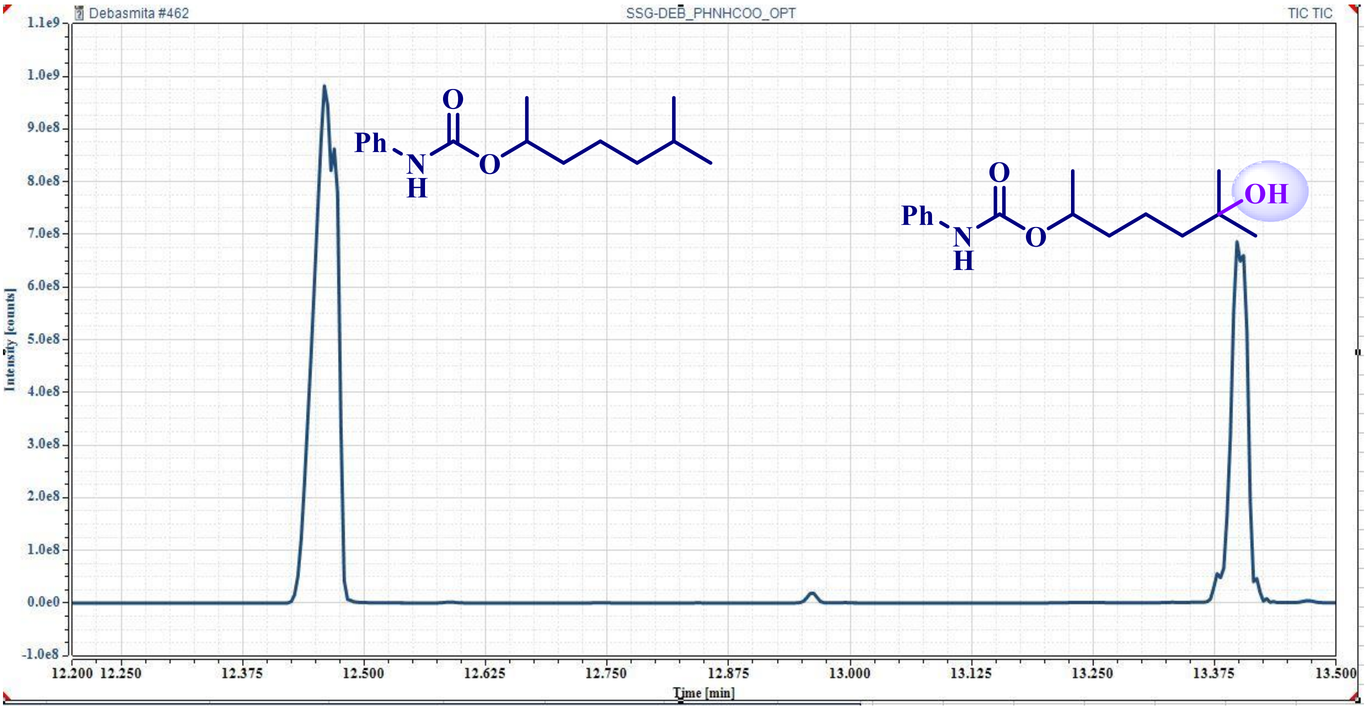
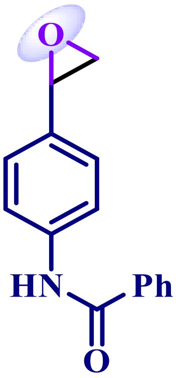


Figure S20. GC-MS of (N-(4-(oxiran-2-yl)phenyl)benzamide)



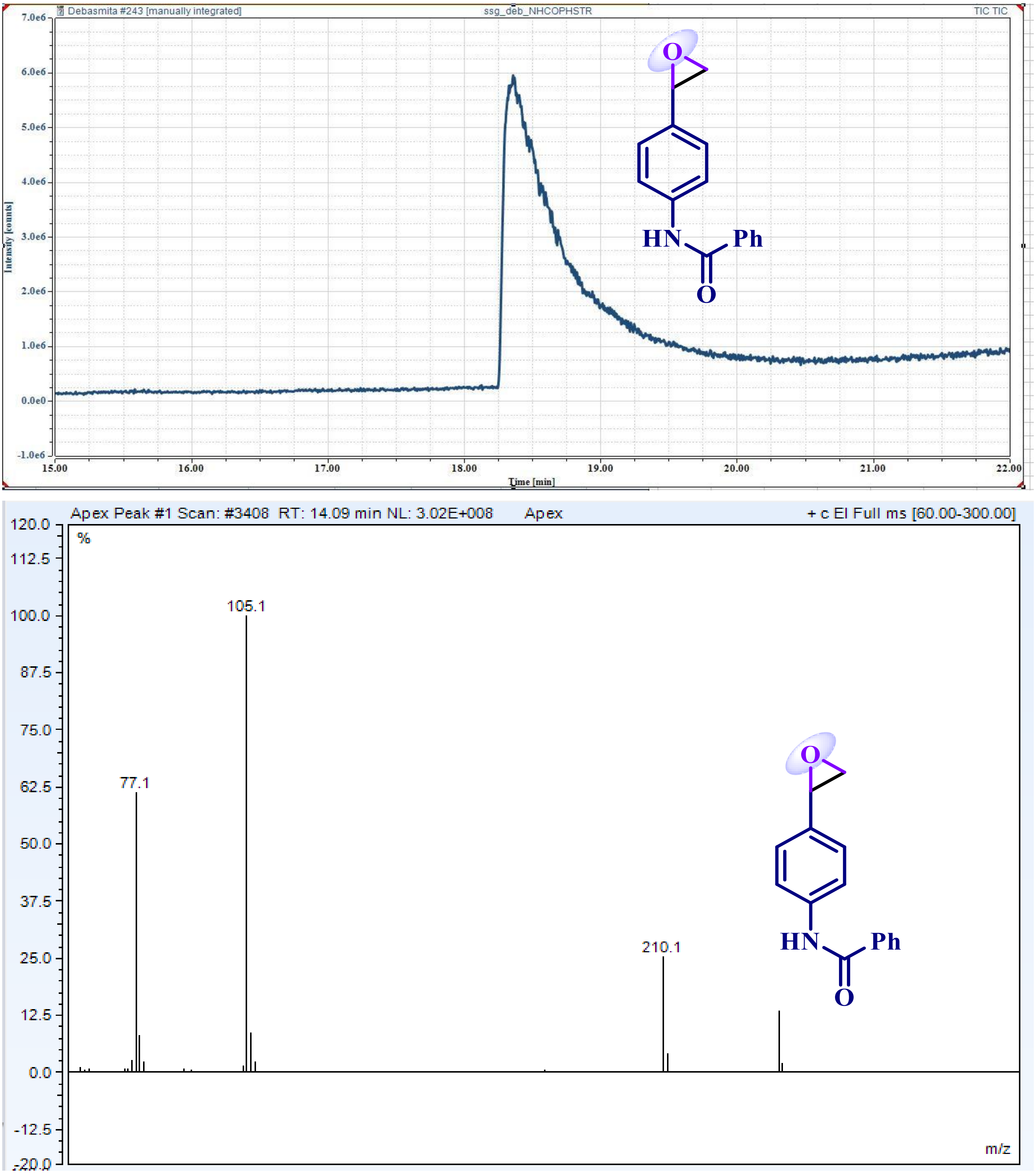
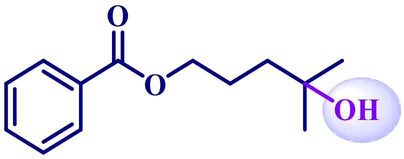
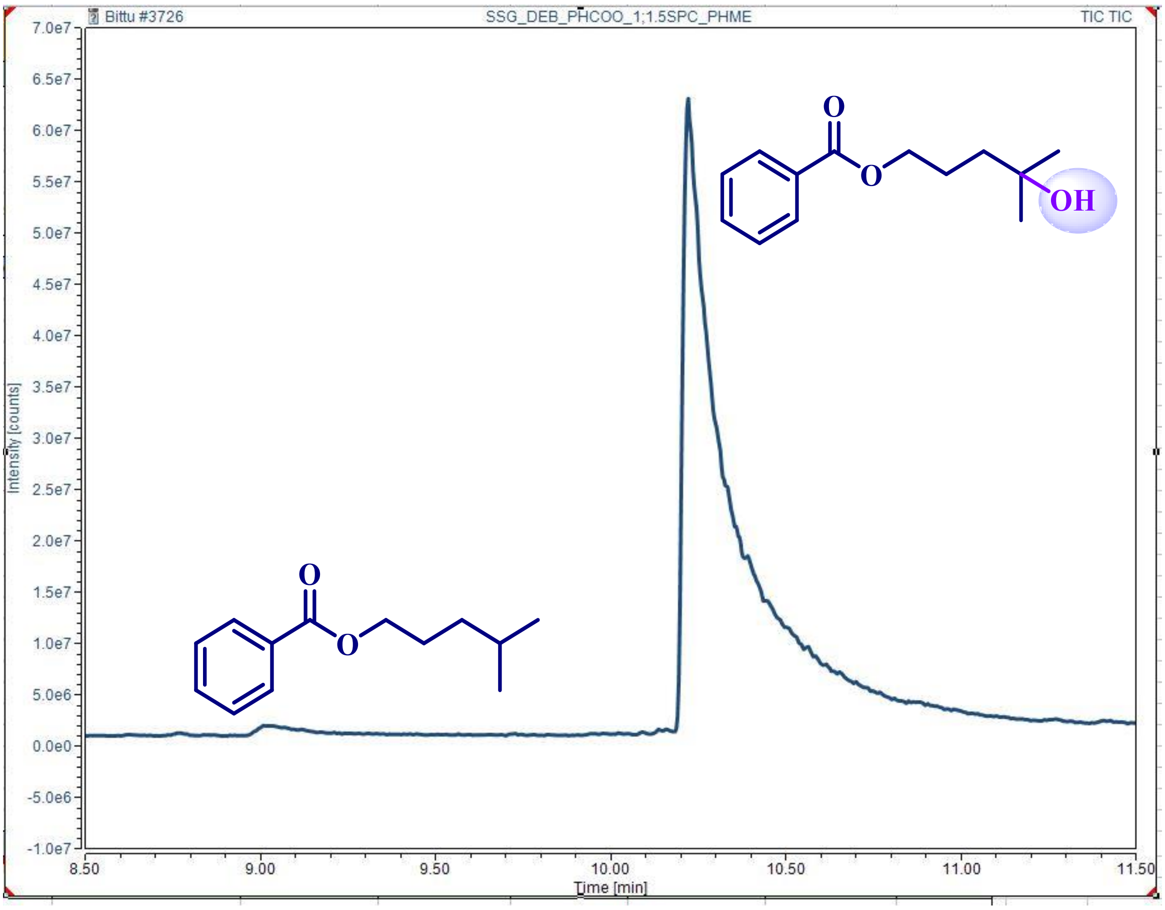


Figure S21. GC-MS of (4-hydroxy-4-methylpentyl benzoate)





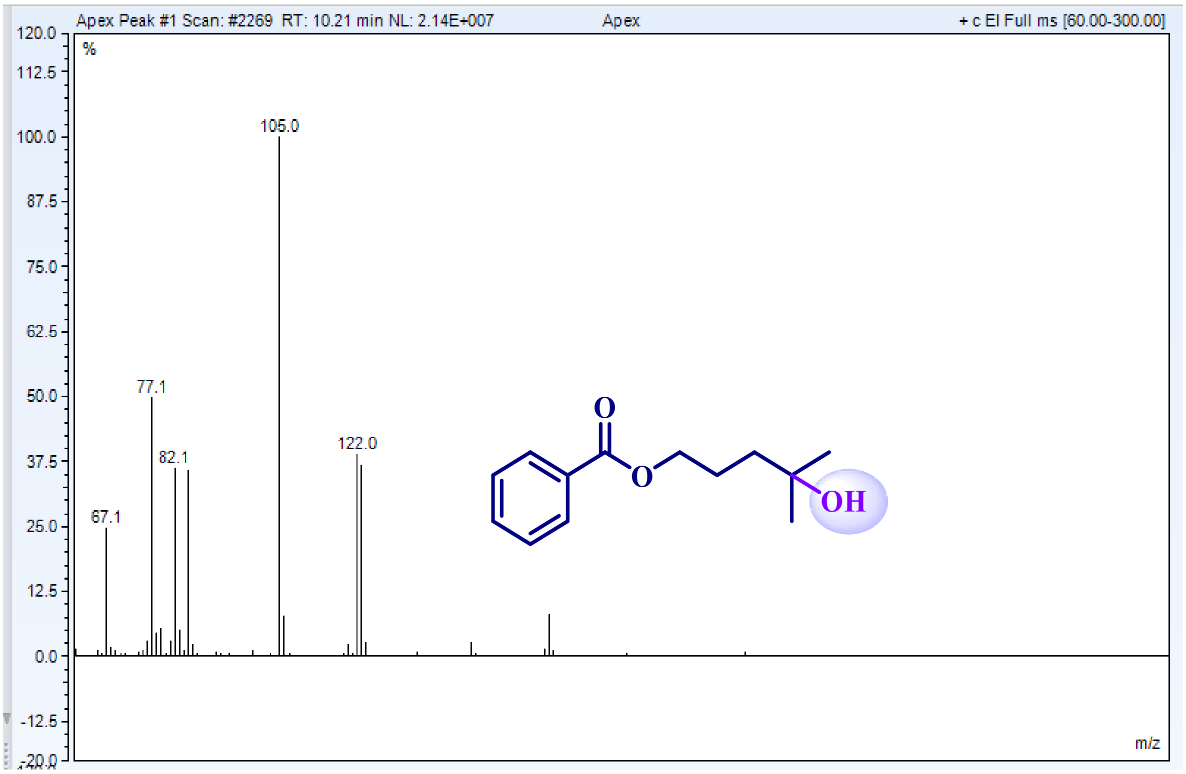
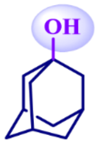
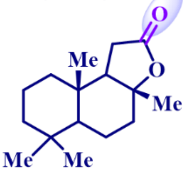
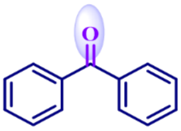
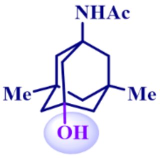
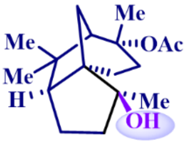
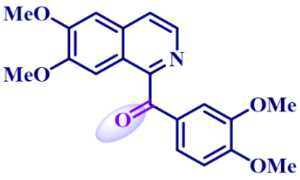
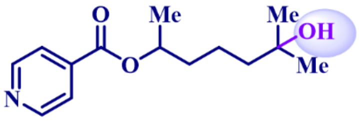
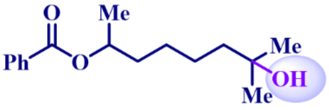


Table S1. Comparison table of product yield and time for solvent-based homogeneous method[1,3] vs Mechanochemical solvent free C-H bond oxidation loading using Fe-bTAML as catalyst

Substrates	**% Yield (selectivity;3°:2°), time** **Solvent-based method**	**% Yield (selectivity;3°:2°), time** **Solvent-free mechanochemical method**
	**53% (98:2), 6 h**	**95%(>100:1), 45 min**
	**90%, 5 h**	**96%, 45 min**
	**99%, 2 h**	**99%, 30 min**
	**52%, 7 h**	**65%, 1 h**
	**80%, 6 h**	**93 %, 1 h**
	**68%, 3 h**	**98 %, 1 h**
	**66%, 3 h**	**82%, 1.5 h**
	**33% , 3 h**	**67% , 1 h**

References

1) Jana, S.; De, P.; Dey, C.; Dey, S. G.; Dey, A.; Gupta, S. S. Highly Regioselective Oxidation of C–H Bonds in Water using Hydrogen Peroxide by a Cytochrome P450 mimicking Iron Complex. *Chemical Science* **2023**, DOI: 10.1039/D3SC03495J
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3) Jana, S.; Ghosh, M.; Ambule, M.; Sen Gupta, S. Iron Complex Catalyzed Selective C–H Bond Oxidation with Broad Substrate Scope. *Org. Lett.* **2017**, *19* (4), 746–749.
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