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FULL PAPER

Palladium-Catalyzed Direct Oxidative Coupling of Iodoarenes with Primary Alcohols Leading to Ketones: Application to the Synthesis of Benzofuranones and Indenones

Basuli Suchand, Chinnabattigalla Sreenivasulu and Gedu Satyanarayana*

Abstract: In the present study, a palladium-catalyzed direct oxidative acylation through cross-dehydrogenative coupling has been investigated, utilizing readily available primary alcohols as acylating sources. Overall, this oxidative coupling proceeds *via* three distinct transformations such as oxidation, radical formation and cross-coupling in one catalytic process. This protocol does not involve the assistance of a directing group or activation of the carbonyl group by any other means. Further, this reaction made use of no toxic CO gas as carbonylating agent; instead, feedstock primary alcohols have been utilized as acylation source. Notably, enabled the synthesis of benzofuranones and indenones. Significantly, this strategy was also applied to the synthesis of *n*-butylphthalide, fenofibrate, pitofenone and neo-lignan.

Introduction:

In the recent times, functionalization of chemical compounds by virtue of transition metal-catalysis[1] has stood forefront in the field of synthetic organic chemistry. This has brought a vast advance in the areas of catalysis as well. For instance, acylation is an important C–C bond forming transformation, which has broad application in organic synthesis.[2] One of its major uses is the preparation of aryl ketones, which are of chemical feedstock.[3] Also, ketone constitute the structural framework of various natural and pharmaceutical products.[4] In this context, recently, transition-metal catalyzed direct acylation has turned out to be as an alternative viable strategy[5] when compared with the traditional methods for C–C bond forming reactions, such as, Friedel-Crafts acylation,[6] Grignard/Barbier reaction with aldehydes and followed by oxidation[7] (Scheme-1a), or Grignard reaction with nitriles[8] and organometallic 1,2-additions to Weinreb amides.[9] In addition, transition-metal catalyzed acylation utilizes a number of readily available chemical precursors, namely aldehydes,[10a] α-diketones,[10b] α-oxocarboxylic acids,[10c] benzylic ethers,[10d] methyl arenes,[10e] styrenes[10f] and benzyl bromides.[10g] Despite being functional, utilizing aldehydes bear some sort of drawbacks. Apart from being comparatively pricy and highly reactive, aldehydes

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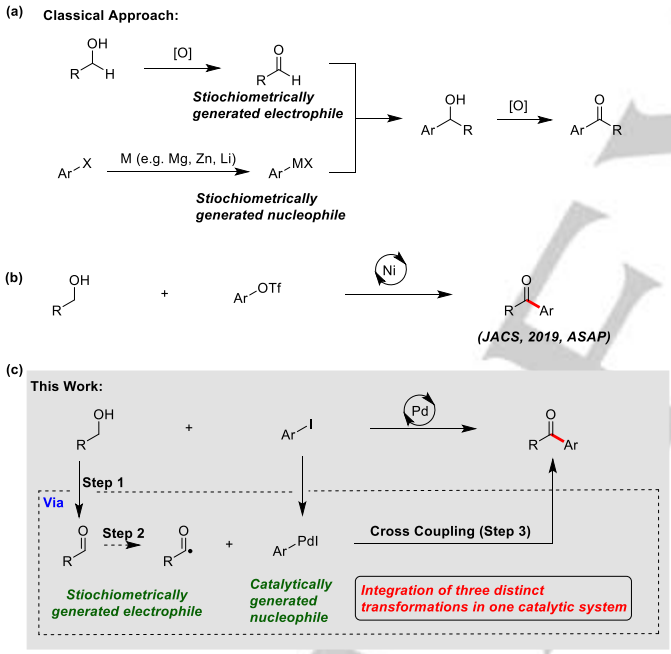
are prone to undergo aldol and Tishchenko-type side reactions.[11] Moreover, by virtue, alcohols have also been identified as good acyl sources,[12] due to their low toxicity, economic, stable and commercially available. However, they are seldom directly employed in the C–C bond forming cross-coupling reactions. Thus, this kind of reaction can be proceeded through multiple oxidation state-manipulating steps, in single catalytic process through oxidation and acyl or benzoyl radical formation and cross-coupling reactions (Scheme-1c).



Scheme 1: Classical approach and our strategy.

Thus, investigative studies to develop such strategies could aid various chemical transformations and form multiple bonds in one-pot operation. To the best of our knowledge, primary alcohols are being more abundant acyl surrogates that have been scarcely explored for the formation of ketones. This prompted us to check the feasibility by using primary alcohols as acylating agents, for the direct cross-coupling (acylation) without the assistance of any directing group. During the manuscript preparation a seminal report has been published by Stephen G. Newman group (Scheme 1b), wherein organotriflates and primary alcohols have been employed for the cross dehydrogenative coupling to synthesize ketones, in the presence of a nickel catalyst.[13]

Aside from the direct acylation, the strategic approach for the one-pot synthesis of bioactive molecule displays good economy concerning step count when compared to well-established classical method(s). For instance, indenone cores are omnipresent bicyclic motifs, with proficient biological properties and can be served as synthons as well,[14] in the synthesis of natural products. Till now, numerous synthetic routes have been described for their synthesis. For example, transition-metal catalyzed annulations of alkynes were accomplished using carbon monoxide (CO) as carbonylating agent.[15] Also, annulations of internal alkynes with 2-halobenzaldehydes or 2-(methoxycarbonyl)phenylboronic acids or 2-bromophenylboronic acids or 2-iodobenzonitriles have been developed,[16] under transition-metal

catalysis. Furthermore, radical mediated cyclizations have also been utilized for the preparation of indenones.[17] Despite good number of attempts, some of the methods holds few drawbacks. Particularly, regioselectivity is a major issue under transition-metal mediated cyclizations, especially, when unsymmetrical alkynes were employed as annulation partners.[18] Hence, it is highly desirable to establish the synthesis of indenones with high regioselectivity.

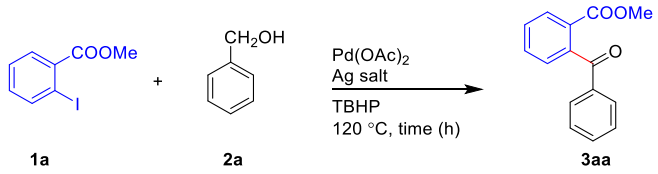
Extending our investigations in transition-metal catalysis,[19] recently, a [Pd]-catalyzed environmentally benign acylations was reported, for the synthesis of various ketones.[20a] Subsequently, its precision was seen in the one-pot synthesis of indenones,[20b] 4-aryl-2-quinolinone,[20c] phthalazine and phthalazinones.[23d] Herein, we describe an oxidative strategy, in which alcohols have been employed as acylating agents, under palladium-catalyzed direct acylations. Alcohols are less toxic, stable, and widely available and are inexpensive compared to α-oxocarboxylic acid and aldehydes. Also, we applied this approach to the one-pot synthesis of indenones by employing intramolecular aldol condensation reaction on in-situ generated di-ketones. In addition, the strategy was applied to the synthesis of natural as well as pharmaceutical products.

Results and discussion:

To initiate our investigations to identify the optimal conditions, initially, we examined the reaction of *ortho*-iodomethylbenzoate **1a** with benzyl alcohol **2a**, under our established conditions (i.e. reported conditions for acylations of iodoarenes with benzaldehydes[20a]). Notably, the desired ketone **3aa** was formed in 47% yield (Table 1, entry 1). From our earlier observations, it was clear that *t*-butyl hydroperoxide (TBHP) was the best oxidant and silver oxide (Ag_2O) was the optimum additive. Hence, it was thought to explore the reaction with regards to the quantity of alcohol (acylating source) and also it was expected that the alcohols would be converted into the corresponding aldehydes in-situ by oxidizing agent TBHP that in turn could acylate the iodoarene. As expected, by increasing amount of benzyl alcohol **2a** to 5.0 equiv, the yield of the ketone **3aa** was slightly improved (Table 1, entry 2). Fair amount of **3aa** was obtained with 6.0 equiv of benzyl alcohol **2a** (Table 1, entry 3). However, further increase of **2a** could not show notable improvement in the yield (Table 1, entry 4). Thus, it was concluded that 6.0 equiv of **2a** be the optimal amount of alcohol **2a**. From our previous reports, it was also noted that sufficient amount of TBHP was necessary to facilitate the acylation and to furnish the products in good yields. Since the present case deals with alcohols, utilized 6.0 equiv of TBHP/H_2O (Table 1, entry 5). To our delight, ketone **3aa** was isolated in 64% yield. However,

further increase of TBHP did not improve in the product **3aa** yield (Table 1, entry 6).

Table 1. Optimization studies for the acylation product **3aa**.[a]



1a 2a 3aa

Entry	Alcohol (equiv)	Additive (equiv)	Oxidant (equiv)	Time (h)	Yield (%)[b]
1	4.0	Ag_2O (1.2)	4.0	22	47
2	5.0	Ag_2O (1.2)	4.0	21	55
3	6.0	Ag_2O (1.2)	4.0	22	60
4	7.0	Ag_2O (1.2)	4.0	22	60
5	**6.0**	**Ag_2O (1.2)**	**6.0**	**20**	**64**
6	6.0	Ag_2O (1.2)	7.0	20	63
7	7.0	Ag_2O (1.2)	7.0	20	64
8	6.0	Ag_2O (1.5)	6.0	20	64
9	6.0	Ag_2CO_3 (1.2)	6.0	23	59
10	6.0	AgOAc (1.2)	6.0	22	58

[a]Unless otherwise mentioned, all the reactions were carried out by using 105.0 mg (0.40 mmol) of aryl iodide **1a**, 5 mol% of $Pd(OAc)_2$, at 120 °C temperature. [b]Isolated yields of chromatographically pure products.

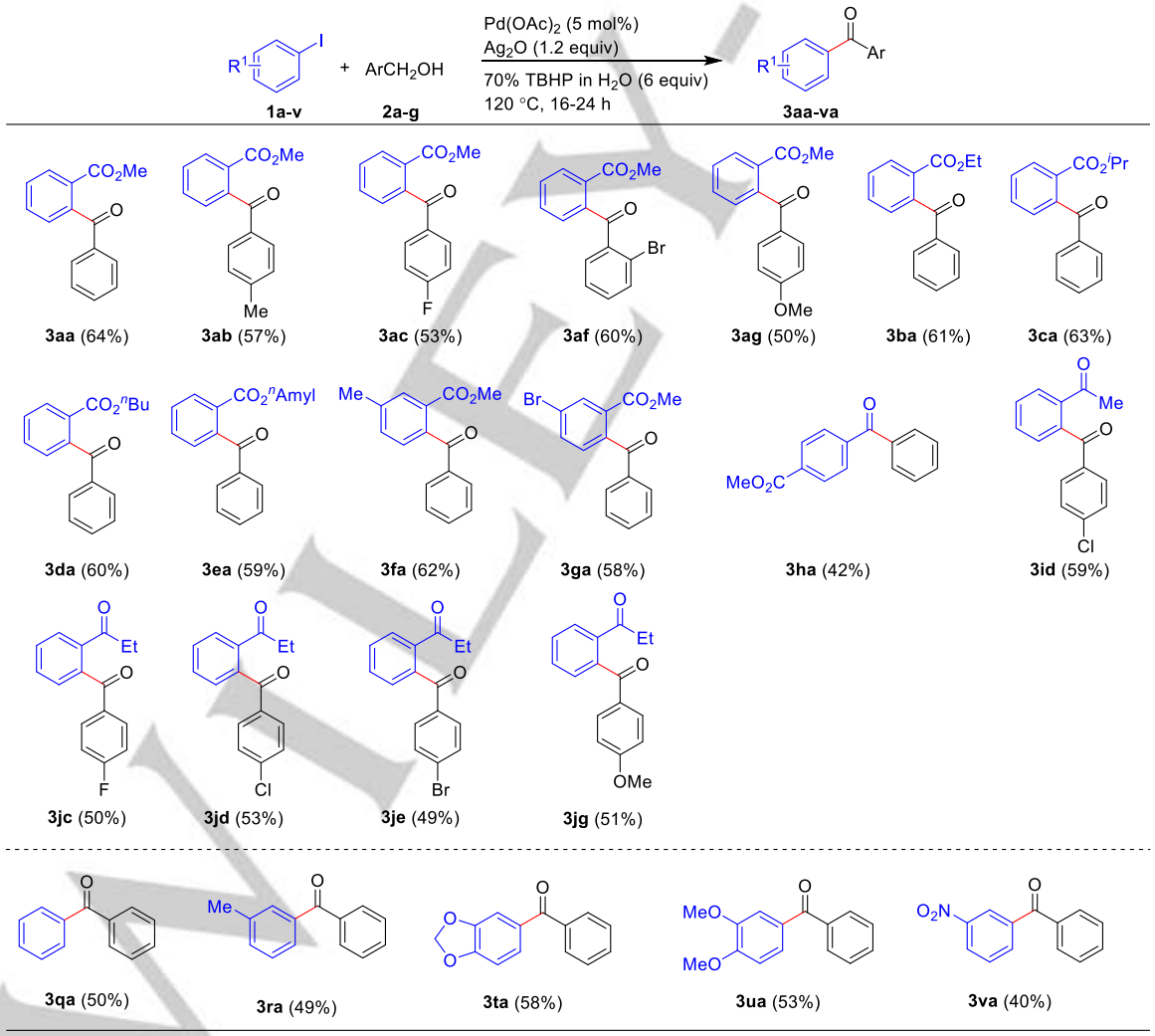
No further improvement was found upon increasing the amount of both alcohol **2a** and TBHP/H_2O (Table 1, entry 7). As identified by the previous reports, silver salt (Ag_2O) was an effective additive for [Pd]-catalyzed direct acylation reactions. Thus, the reaction with slightly increased amount of Ag_2O (1.5 equiv), could not raise the yield (Table 1, entry 8). On the other hand, the reaction in the presence of Ag_2CO_3 and AgOAc were not much effective (Table 1, entries 9 & 10).

With the above conditions (Table 1, entry 5), next, we evaluated the scope and generality of this acylation between various iodoarenes **1a-v** and benzyl alcohols **2a-g**. Gratifyingly, the process was viable and delivered the corresponding diaryl ketones **3aa-va**, in moderate to fair yields (Table 2). The method was successful with electron withdrawing ester and ketone moieties connected to iodoarenes. The acylation reaction was feasible to a variety of benzyl alcohols bearing a wide range of functional groups. For example, in addition to the simple benzyl alcohol **2a**, the reaction was smooth with electron activating Me (**2b**) and OMe (**2g**) groups on the aromatic ring of benzyl alcohols.

Significantly, amenable to the electron deactivating substituents [e.g. F (**2c**), Cl (**2d**), Br (**2e** & **2f**)]. Further, the reaction was also feasible with iodoarenes bearing Me, OMe and methylenedioxy groups including simple iodobenzene (**1q-u**) and afforded the ketones **3qa-ua** (Table 2). Remarkably, acylation was successful with iodoarene **1v** having strong electron withdrawing nitro functionality and gave the product **3va**, albeit in moderate yields (Table 2).

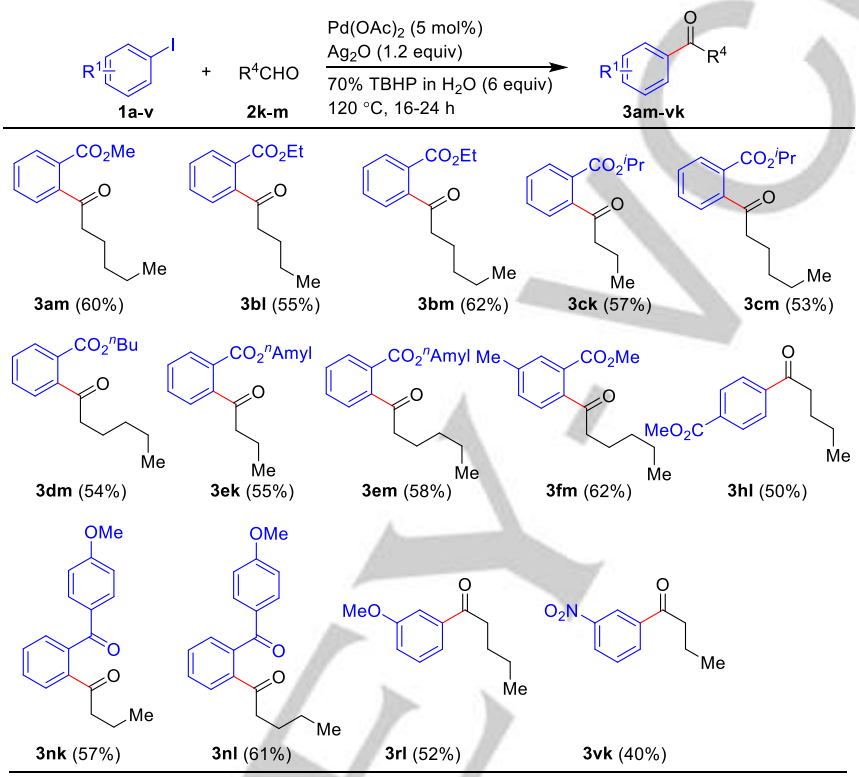
Besides this study, to describe the permissibility of the process, we investigated the reaction with aliphatic alcohols **2k-m**. As anticipated, the protocol was quite successful and afforded variety of ketones **3am-vk** possessing different functionalities on their aromatic rings (Table 3).

Table 2: Scope and generality of formation of ketones **3aa-va**.[a,b]



Reaction conditions: [a]all the reactions were carried out by using aryl iodide **1** (0.40 mmol), alcohol **2** (2.4 mmol), $Pd(OAc)_2$ (5 mol%), Ag_2O (0.48 mmol) and TBHP (2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 16-24 h. [b]Isolated yields of chromatographically pure products.

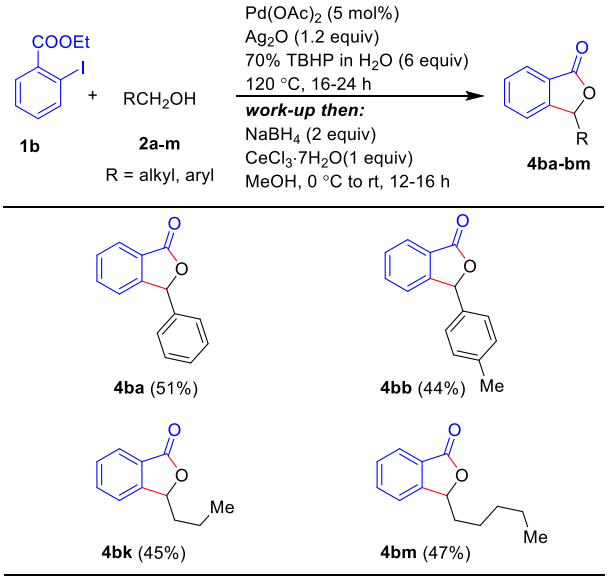
Table 3: Scope and generality of formation of ketones **3am-vk**.[a,b]



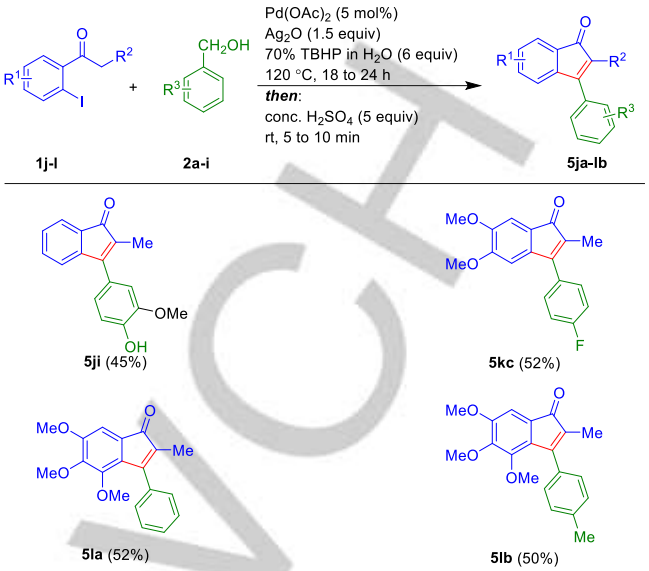
Reaction conditions: [a]all reactions were carried out by using aryl iodide **1** (0.40 mmol), alcohol **2** (2.4 mmol), $Pd(OAc)_2$ (5 mol%), Ag_2O (0.48 mmol) and TBHP (2.4 mmol), the resulting reaction mixture was stirred at 120 °C for 16-24 h. [b]Isolated yields of chromatographically pure products.

Furthermore, to illustrate the scope of the present strategy, it was executed for the synthesis of biologically significant scaffolds, benzofuranones (Table 4). Unlike our earlier report, the desired lactones were obtained by reducing the concentrated crude reaction mixture of *ortho*-ketoesters (i.e. after work-up) with $NaBH_4$. Thus, benzofuranones **4ba-bm** were isolated in moderate overall yields (Table 4).

Table 4: Scope and generality of formation of benzofuranones **4ba-bm**.[a,b]



Reaction conditions: [a]i) all reactions were carried out by using aryl iodide **1** (0.40 mmol), alcohol **2** (2.4 mmol), $Pd(OAc)_2$ (5 mol%), Ag_2O (0.48 mmol) and TBHP (2.4 mmol), the resulting reaction mixture was stirred at 120 °C for 16-24 h; ii) then to the concentrated crude reaction mixture of keto-ester, were added $NaBH_4$ (0.80 mmol), $CeCl_3·7H_2O$ (0.40 mmol), and MeOH (1 mL) and stirred at 0 °C to rt for 12-16 h. [b]Isolated yields of chromatographically pure products.



Reaction conditions: [a]i) all reactions were carried out by using aryl iodide **1** (0.40 mmol), alcohol **2** (2.4 mmol), $Pd(OAc)_2$ (5 mol%), Ag_2O (0.48 mmol) and TBHP (2.4 mmol), the resulting reaction mixture was stirred at 120 °C for 16-24 h; ii) then to the cooled reaction mixture to rt, was added conc. H_2SO_4 (2.0 mmol) and stirred at rt for 5-10 min. [b]Isolated yields of chromatographically pure products.

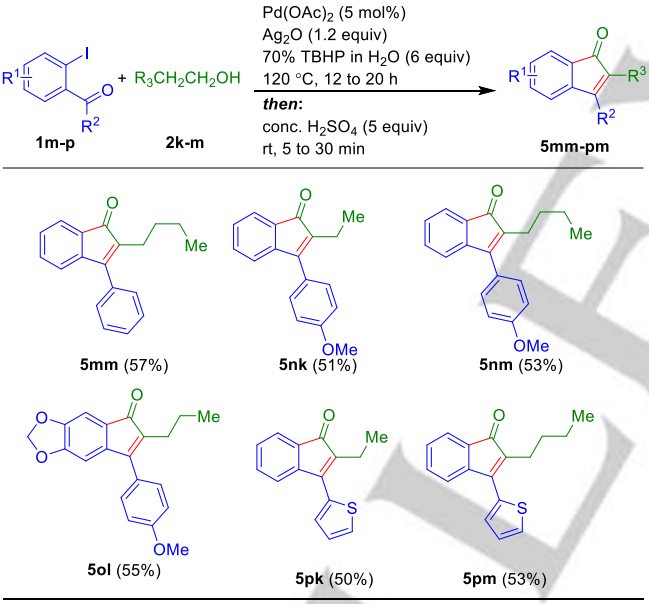
To exemplify the synthetic significance of this protocol, next, it was aimed for one-pot synthesis of indenones. As established by our previous report, this could be feasible *via* acid mediated intramolecular aldol condensation of in-situ generated diketone derivatives. Thus, after confirming the formation of 1,2-diketobenzene, using thin-layer-chromatography (TLC), to the reaction mixture, was added to conc. H_2SO_4, at room temperature. As predicted, the acylation reaction and subsequent intramolecular aldol condensation in one-pot was successful and gave the desired indenones **5ja-lb** (Table 5).

Table 5: Scope and generality of one-pot synthesis of indenones **5ja-lb**.[a,b]

Furthermore, particularly, to demonstrate the utility of the one-pot protocol, for the synthesis of indenones, the reaction was carried out between *ortho*-iodobenzophenones **1m-p** with various aliphatic alcohols **2k-m**. Pleasingly, the strategy exhibited good adaptability and delivered the expected indenones **5mm-pm** (Table 6). Remarkably, the reaction was consistent with heteroaromatic *ortho*-iodobenzophenone **1p**. As a matter of fact, in the involvement of electron-rich aromatic systems (iodoarenes and benzyl alcohol) the direct formation of indenones was seen in minor quantities, before subjecting the aldol condensation reaction of in-situ formed 1,2-diketone intermediate with conc. H_2SO_4 (Table 6, **5ol**). Presumably, the aldol condensation of 1,2-

diketone bearing both electron rich aromatic rings, would have been triggered either by the silver ions (Ag^+) of Ag_2O or the carboxylic acid that might be produced from the corresponding benzyl alcohol in the presence of oxidizing agent TBHP.

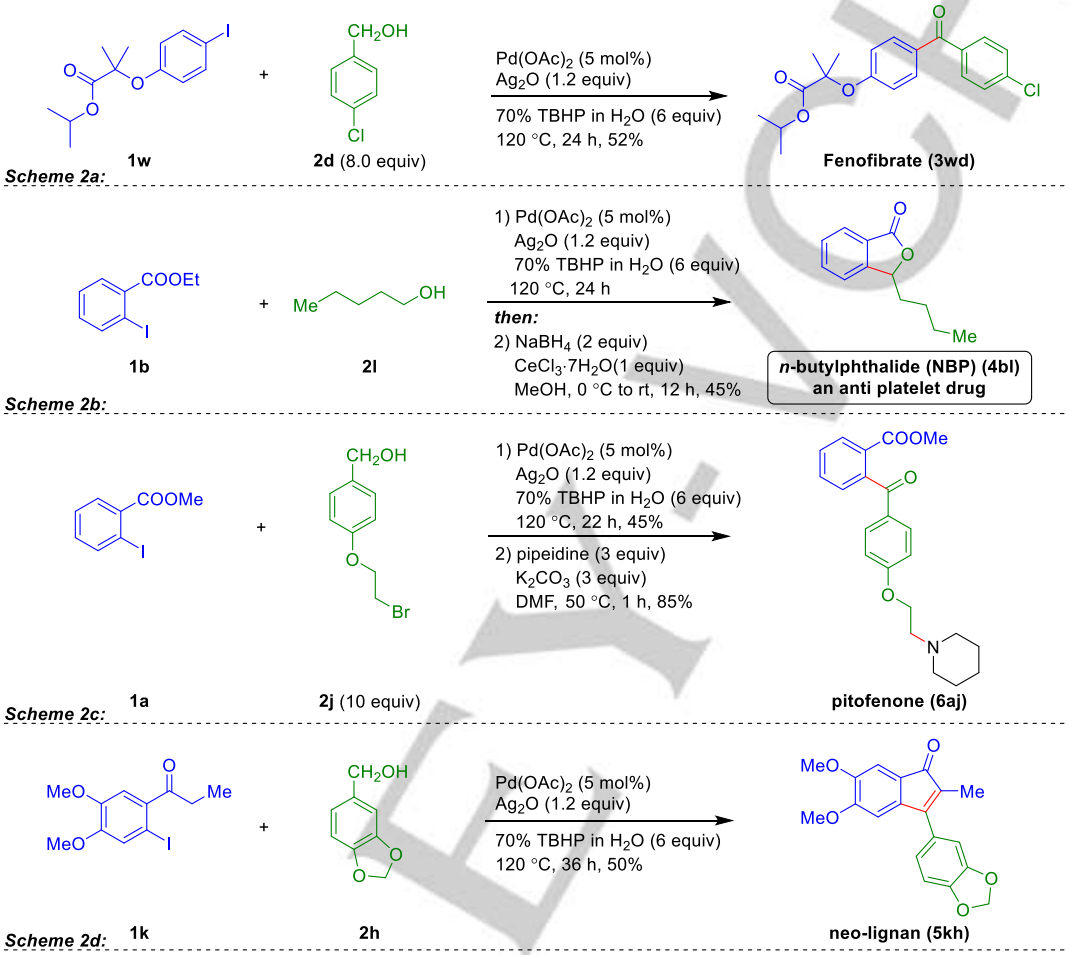
Table 6: Scope and generality for the synthesis of indenones **5mm-pm**.[a,b]



Reaction conditions: [a]i) all reactions were carried out by using aryl iodide **1** (0.40 mmol), alcohol **2** (2.4 mmol), $Pd(OAc)_2$ (5 mol%), Ag_2O (0.48 mmol) and TBHP (2.4 mmol). The reaction mixture was stirred at 120 °C for 16-24 h; ii) then to the cooled reaction mixture to rt, was added conc. H_2SO_4 (2.0 mmol) and the resulting reaction mixture was stirred at rt for 5-30 min. [b]Isolated yields of chromatographically pure products.

Next, we turned our attention to highlight the applications of this acylation protocol. The strategy was successfully applied to the synthesis of fenofibrate, pitofenone, *n*-butylpthalide and one-pot synthesis of natural product neo-lignan (Scheme 2). Thus, the reaction between iododerivative **1w** with *p*-chlorobenzyl alcohol **2d**, under the standard acylation conditions, furnished fenofibrate **3wd** with 52% yield (Scheme 2a). Notably, the synthesis of *n*-butylphthalide **4bl** was accomplished starting from *ortho*-iodoethylbenzoate **1b** with amyl alcohol **2l**. It is worth noting that **4bl** was obtained by using a single column chromatography technique upon reducing the concentrated crude reaction mixture of keto-ester with $NaBH_4$ and subsequent intramolecular nucleophilic attack/condensation step of alkoxide intermediate onto the ester functionality (Scheme 2b). Delightfully, the antispasmodic drug, pitofenone **6aj**, was achieved in just two steps (Scheme 2c). This certainly illustrate the efficacy of the present strategy. Most significant utility of the present protocol is its application in the one-pot synthesis of the natural product, neo-lignan **5kh**. The compound was afforded by subjecting *ortho*-iodoketone **1k** with benzyl alcohol **2h**, under standard acylation conditions and without the need of using conc. H_2SO_4. This is because of the fact that either of these aromatic rings are electron rich enough and hence, a mild acidity present in the reaction either in the form of silver ions or in the form of carboxylic acid, would be good enough to drive the

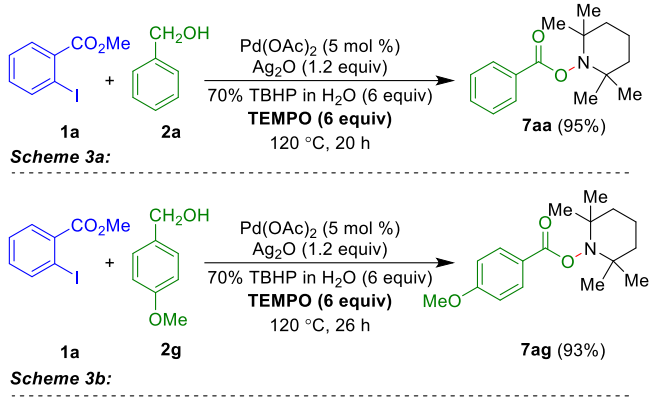
subsequent intramolecular aldol condensation step. The natural product neo-lignan **5kh** was obtained in 50% yield in one-pot (Scheme 2d). These above applications, certifies the synthetic utility of the present methodology.



Scheme 2: Synthesis of fenofibrate, pitofenone, *n*-butylphthalide and neo-lignan.

Next, we sought to explore the mechanism of the reaction. In our previous work,[20a] it was proved that the reaction proceeds *via* radical path from aldehydes. Thus, it is predicted that the present case would follow a radical mechanism. Hence, to further prove it, the reaction was performed between *ortho*-iodoester **1a** and benzyl alcohol **2a** in the presence of 2,2,6,6-tetramethylpiperidinyloxy (TEMPO), a free radical scavenger, under standard conditions. Gratifyingly, as predicted, the aldehyde radical trapped 2,2,6,6-tetramethylpiperidinyl ester **7aa** was formed in 95% yield (Scheme 3a). The chemical structure of **7aa** was also established by single crystal X-ray diffraction analysis (Figure 1). Even, *para*-methoxybenzyl alcohol **2g** was also underwent same reaction with **1a** and furnished **7ag** in excellent yield (Scheme 3b). Based on the above trapping experiments, it can be confirmed that initially aldehyde is generated from the corresponding alcohol *via* oxidation reaction facilitated by TBHP. This aldehyde in turn will undergo further oxidation and gets converted into aldehyde-radical by the same TBHP oxidant. The insitu generated aldehyde radical can undergo cross-coupling with aryl-palladium species which

is formed from an independent pathway thruogh the oxidative insertion of palldium catalyst across the C–I bond. Finally, reductive elimination leads to the formation of target product ketone.



Scheme 3: Trapping of reactions with TEMPO.

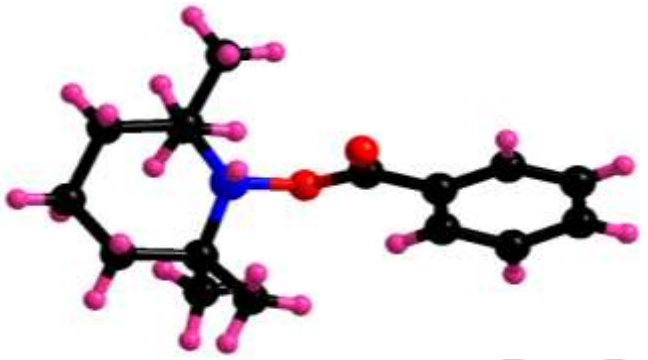


Figure 1: Single crystal structure of **7aa** (CCDC: 1935118).

Conclusion:

In conclusion, we have described a [Pd]-catalyzed direct coupling reaction of iodiarenes with alcohols, for the synthesis of a wide range of ketones. This protocol involves the use of simple and readily available benchtop alcohols and in-situ served as acyl radicals by the oxidizing agent TBHP. This methodology has been utilized to afford the variety of benzofuranones using a single column chromatography technique and one-pot synthesis of indenones. Moreover, enabled the synthesis of drug molecules such as fenofibrate, petofenone, *n*-butylphthalide and naturally occurring neo-lignan.

Experimental:

IR spectra were recorded on a FTIR spectrophotometer. ^{1}H NMR spectra were recorded on 400 MHz spectrometer at 295 K in $CDCl_3$; chemical shifts (δ ppm) and coupling constants (Hz) are reported in standard fashion with reference to either internal standard tetramethylsilane (TMS) (δ_H =0.00 ppm) or $CHCl_3$ (δ_H = 7.25 ppm). ^{13}C NMR spectra were recorded on 100 MHz spectrometer at RT in $CDCl_3$; chemical shifts (δ ppm) are reported relative to $CHCl_3$ [δ_C = 77.00 ppm (central line of triplet)]. In the ^{13}C NMR, the nature of carbons (C, CH, CH_2 and CH_3) was determined by recording the DEPT-135 spectra. In the ^{1}H-NMR, the following abbreviations were used throughout: s = singlet, d = doublet, t = triplet, q = quartet, qui =quintet, sept = septet, dd = doublet of doublet, m = multiplet and br. s = broad singlet. High-resolution mass spectra (HR-MS) were recorded on Q-TOF electron spray ionization (ESI) mode and atmospheric pressure chemical ionization (APCI) modes. Melting points were determined on an electrothermal melting point apparatus and are uncorrected. All small scale reactions were carried out using Schlenk tube. Reactions were monitored by TLC on silica gel

using a combination of hexane and ethyl acetate as eluents. Reactions were generally run under nitrogen atmosphere. Acme's silica-gel (60–120 mesh) was used for column chromatography (approximately 20 g per one gram of crude material). All catalysts, reagents and reactants were procured from commercial suppliers (Sigma Aldrich, Merck, Hychem and Avra) and used as received. Solvents, used for work up and chromatographic procedures were purchased from commercial suppliers (Madin Lifesciences, Standard Reagents Spectrochem) and distilled prior to use.

GP-1 [**General Procedure for Preparation of ketones 3**]**:**

To an oven dried Schlenk tube, were added aryl iodide **1** (81.0-127.0 mg, 0.40 mmol), alcohol **2** (259.0-448.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 16-24 h. TLC monitored the progress of the reaction, for the formation **3** until the reaction was completed. The reaction mixture was cooled to room temperature, diluted with aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate) furnished the products **3aa-va** (36.0-76.0 mg, 40-64%).

GP-2 [**General Procedure for Preparation of Benzofuranones 4**]**:**

To an oven dried Schlenk tube, were added *ortho*-iodo ester **1b** (110.0 mg, 0.40 mmol), alcohol **2** (177.0-293.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 16-24 h. The progress of the product **3** formation was monitored by TLC till the reaction was completed. The reaction mixture was allowed to cool to room temperature, diluted with aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure then kept in high vacuum for 10 minutes. Then, to this magnetically stirred reaction mixture solution of keto ester in MeOH (1 mL), were added sequentially $CeCl_3.7H_2O$ (149.0 mg, 0.40 mmol) and $NaBH_4$ (30.0 mg, 0.80 mmol). The reaction mixture was stirred at 0 °C to room temperature for 12 to 24 h. The progress of the product **4ba-bm** formation was monitored by TLC. The reaction mixture was quenched with H_2O and then extracted with ethyl acetate (3 × 10 mL). Purification of the crude material by silica-gel column

chromatography (petroleum ether/ethyl acetate) furnished the product **4ba-bm** (32.0-43.0 mg, 44-51%).

GP-4 [**General procedure for preparation of indenones 5**]**:**

To an oven dried Schlenk tube, were added *ortho*-iodoketone **1j-p** (104.0-153.0 mg, 0.40 mmol) and alcohols **2a-m** (177.0-370.0 mg, 2.4 mmol) in the presence of $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol) and allowed the reaction mixture to stir at 120 °C for 18-28 h. Progress of the reaction was monitored by TLC till the *ortho*-iodoketone **1i-p** was completed. Then the reaction mixture was removed from oil bath and allow to reach room temperature and then added conc. H_2SO_4 (0.1 mL, 2.0 mmol) and allowed the reaction mixture stirred at room temperature. Progress of the products **5** formation was monitored by TLC till the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the products **5ja-pm** (48.0-71.0 mg, 45-57%) as viscous liquid/solid.

Methyl-2-benzoyl-5-methylbenzoate (**3fa**)**:** GP-1 was carried out with aryl iodide **1f** (110.0 mg, 0.40 mmol), aromatic alcohol **2a** (259.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 20 h. The progress of the product **3fa** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 98:02 to 97:03) furnished the product **3fa** (63.0 mg, 62%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.80, R_f(**3fa**)=0.40, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2934, 2853, 1728, 1673, 1444, 1273, 1091, 929, 836, 714 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.82 (s, 1H Ar-H), 7.73 (dd, 2H, *J*=8.3 and *J*=1.4 Hz, Ar-H), 7.54-7.50 (m, 1H Ar-H), 7.43-7.38 (m, 3H Ar-H), 7.31 (d, 1H, *J*=7.8 Hz, Ar-H), 3.55 (s, 3H, OCH_3), 2.45 (s, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=197.1 (s, C=O), 166.7 (s, O–C=O), 140.0 (s, Ar-C), 138.6 (s, Ar-C), 137.4 (s, Ar-C), 132.9 (d, Ar-CH), 132.8 (d, Ar-CH), 130.4 (d, Ar-CH), 129.4 (s, Ar-C), 129.1 (d, 2C, Ar-CH), 128.4 (d, 2C, Ar-CH), 128.0 (d, Ar-CH), 52.0 (q, O*C*H_3), 21.1 (q, *C*H_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{16}H_{15}O_3]^+$=$[M+H]^+$: 255.1016; found 255.1006.

Methyl 2-benzoyl-5-bromobenzoate (**3ga**)**:** GP-1

was carried out with aryl iodide **1g** (136.0 mg, 0.40 mmol), aromatic alcohol **2a** (259.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 22 h. The progress of the product **3ga** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 98:02 to 97:03) furnished the product **3ga** (74.0 mg, 58%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1g**)=0.70, R_f(**3ga**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2927, 2855, 1722, 1674, 1596, 1501, 1435, 1278, 1142, 1086, 935, 848, 762 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=8.17 (d, 1H, *J*=1.9 Hz, Ar-H), 7.76 (dd, 1H, *J* = 8.1, 2.0 Hz, Ar-H), 7.74-7.70 (m, 2H, Ar-H), 7.58-7.53 (m, 1H Ar-H), 7.45-7.41 (m, 2H Ar-H), 7.28 (d, 1H, *J*=8.3 Hz, Ar-H), 3.61 (s, 3H, OCH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=195.9 (s, C=O), 165.1 (s, O–C=O), 140.3 (s, Ar-C), 136.8 (s, Ar-C), 135.3 (d, Ar-CH), 133.3 (d, Ar-CH), 133.0 (d, Ar-CH), 131.0 (s, Ar-C), 129.4 (d, Ar-CH), 129.2 (d, 2C, Ar-CH), 128.6 (d, 2C, Ar-CH), 123.8 (s, Ar-C), 52.5 (q, O*C*H_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{15}H_{12}Br^{79}O_3]^+$=$[M+H]^+$: 318.9964; found 318.9949; $[C_{15}H_{12}Br^{81}O_3]^+$=$[M+H]^+$: 320.9944; found 320.9928.

1-[2-(4-Fluorobenzoyl)phenyl]propan-1-one (3jc): GP-1 was carried out with aryl iodide **1j** (104.0 mg, 0.40 mmol), aromatic alcohol **2c** (302.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 23 h. The progress of the product **3jc** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 85:15) furnished the product **3jc** (51.2 mg, 50%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10), R_f(**1j**)=0.90, R_f(**3jc**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3059, 2927, 2857, 1675, 1583, 1479, 1362, 1263, 1163, 1089, 1020, 930, 732 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.87 (dd, 1H, *J*=6.8 and 1.9 Hz, Ar-H), 7.78–7.73 (m, 2H, Ar-H), 7.64–7.53 (m, 2H, Ar-H), 7.38–7.35 (m, 1H, Ar-H), 7.10–7.04 (m, 2H, Ar-H), 2.92 (q, 2H, *J*=7.3 Hz, CH_2), 1.09 (t, 3H, *J*=7.3 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=201.4 (s, C=O), 196.3 (s, C=O), 165.5 (d, ^1J=254 Hz, Ar-CF), 140.6 (s, Ar-C), 137.4 (s, Ar-C), 133.6 (d, ^4J=2.9 Hz, Ar-C-CF), 131.9 (d, 2C, CH), 131.8 (d, Ar-CH), 129.7 (d, CH), 128.6 (d, Ar-CH), 128.1 (d, Ar-CH), 115.6 (d, Ar-CH), 115.4 (d, Ar-CH), 32.8 (t, CH_2), 7.9 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{16}H_{14}FO_2]^+$=$[M+H]^+$: 257.0972; found 257.0968.

1-[2-(4-Chlorobenzoyl)phenyl]propan-1-one (3jd): GP-1 was carried out with aryl iodide **1j** (104.0 mg, 0.40 mmol), aromatic alcohol **2d** (342.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 23 h. The progress of the product **3jd** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 85:15) furnished the product **3jd** (57.8 mg, 53%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10), R_f(**1j**)=0.80, R_f(**3jd**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3060, 2927, 2857, 1675, 1583, 1263, 1089, 929, 730 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.88 (dd, 1H, *J*=6.8 and 1.9 Hz, Ar-H), 7.68–7.65 (m, 2H, Ar-H), 7.63–7.55 (m, 2H, Ar-H), 7.39–7.35 (m, 3H, Ar-H), 2.92 (q, 2H, *J*=7.3 Hz, CH_2), 1.08 (t, 3H, *J*=7.3 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=201.3 (s, C=O), 196.6 (s, C=O), 140.4 (s, Ar-C), 139.3 (s, Ar-C), 137.4 (s, Ar-C), 135.6 (s, Ar-C), 132.0 (d, Ar-CH), 130.6 (d, 2C, CH), 129.8 (d, Ar-CH), 128.7 (d, 2C, CH), 128.7 (d, Ar-CH), 128.1 (d, Ar-CH), 32.7 (t, CH_2), 7.9 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{16}H_{14}ClO_2]^+$=$[M+H]^+$: 273.0677; found 273.0665.

1-[2-(4-Bromobenzoyl)phenyl]propan-1-one (3je): GP-1 was carried out with aryl iodide **1j** (104.0 mg, 0.40 mmol), aromatic alcohol **2e** (449.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 24 h. The progress of the product **3je** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 85:15) furnished the product **3je** (62.0 mg, 49%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10), R_f(**1j**)=0.80, R_f(**3je**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3059, 2926, 2856, 1676, 1584, 1480, 1409, 1263, 1090, 929, 730 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.88 (dd, 1H, *J*=6.8 and 1.9 Hz, Ar-H), 7.63–7.52 (m, 6H, Ar-H), 7.37–7.34 (m, 1H, Ar-H), 2.92 (q, 2H, *J*=7.3 Hz, CH_2), 1.08 (t, 3H, *J*=7.3 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=201.2 (s, C=O), 196.8 (s, C=O), 140.3 (s, Ar-C), 137.3 (s, Ar-C), 135.9 (s, Ar-C), 132.0 (d, Ar-CH), 131.7 (d, 2C, CH), 130.7 (d, 2C, CH), 129.8 (d, Ar-CH), 128.7 (d, Ar-CH), 128.0 (d, Ar-CH), 128.0 (s, Ar-C), 32.7 (t, CH_2), 7.9 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{16}H_{14}Br^{79}O_2]^+$=$[M+H]^+$: 317.0172; found 317.0158; $[C_{16}H_{14}Br^{81}O_2]^+$=$[M+H]^+$: 319.0151; found 319.0138.

1-[2-(4-Methoxybenzoyl)phenyl]propan-1-one (3jg): GP-1 was carried out with aryl iodide **1j** (104.0 mg, 0.40 mmol), aromatic alcohol **2g** (331.0

mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 23 h. The progress of the product **3jg** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 85:15) furnished the product **3jg** (54.7 mg, 51%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10), R_f(**1j**)=0.80, R_f(**3jg**)=0.20, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2924, 2855, 1667, 1581, 1351, 1271, 1195, 1014, 873, 716 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.82 (dd, 1H, *J*=7.3 and 1.9 Hz, Ar-H), 7.74–7.70 (m, 2H, Ar-H), 7.59–7.52 (m, 2H, Ar-H), 7.38–7.36 (m, 1H, Ar-H), 6.90–6.87 (m, 2H, Ar-H), 3.83 (s, 3H, O*CH*$_3$), 2.89 (q, 2H, *J*=7.3 Hz, *CH*$_2$), 1.08 (t, 3H, *J*=7.3 Hz, *CH*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=201.8 (s, C=O), 196.5 (s, C=O), 163.4 (s, Ar-C), 140.8 (s, Ar-C), 137.8 (s, Ar-C), 131.8 (d, 2C, Ar-CH), 131.5 (d, Ar-CH), 130.1 (s, Ar-C), 129.5 (d, Ar-CH), 128.4 (d, Ar-CH), 128.2 (d, Ar-CH), 113.6 (d, Ar-CH), 55.4 (q, CH_3), 33.2 (t, CH_2), 8.0 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{17}H_{17}O_3]^+$=$[M+H]^+$: 269.1172; found 269.1165.

Methyl 2-hexanoylbenzoate (**3am**)**:** GP-1 was carried out with aryl iodide **1a** (105.0 mg, 0.40 mmol), aromatic alcohol **2m** (245.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 24 h. The progress of the product **3am** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 98:02 to 97:03) furnished the product **3am** (56.2 mg, 60%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1a**)=0.90, R_f(**3am**)=0.40, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2916, 1723, 1662, 1491, 1440, 1271, 1038, 942, 751 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.85 (dd, 1H, *J*=7.3 and 1.4 Hz, Ar-H), 7.53 (td, 1H, *J*=7.3 and 1.4 Hz, Ar-H), 7.45 (td, 1H, *J*=7.3 and 1.4 Hz, Ar-H), 7.32 (dd, 1H, *J*=7.3 and 1.4 Hz, Ar-H), 3.85 (s, 3H, OCH_3), 2.76 (t, 2H, *J*=7.8 Hz, CH_2), 1.74–1.67 (m, 2H, CH_2), 1.37–1.30 (m, 4H, CH_2), 0.89–0.86 (m, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=205.8 (s, C=O), 167.2 (s, O–C=O), 143.2 (s, Ar-C), 132.0 (d, Ar-CH), 129.8 (d, Ar-CH), 129.6 (d, Ar-CH), 128.4 (s, Ar-C), 126.2 (d, Ar-CH), 52.4 (q, CH_3), 42.7 (t, CH_2), 31.3 (t, CH_2), 23.7 (t, CH_2), 22.4 (t, CH_2), 13.9 (q, *C*H_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{14}H_{19}O_3]^+$=$[M+H]^+$: 235.1329; found 235.1332.

Ethyl-2-hexanoylbenzoate (**3bm**)**:** GP-1 was carried out with aryl iodide **1b** (110.0 mg, 0.40 mmol), aromatic alcohol **2m** (245.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48

mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for xx h. The progress of the product **3bm** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 98:02 to 97:03) furnished the product **3bm** (61.5 mg, 62%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1b**)=0.90, R_f(**3bm**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2927, 1663, 1593, 1456, 1252, 1180, 1025, 929, 755, 604 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.86 (dd, 1H, *J*=7.5 and 1.2 Hz, Ar-H), 7.52 (td, 1H, *J* = 7.5 and 1.4 Hz, Ar-H), 7.45 (td, *J* = 7.6 and 1.4 Hz, Ar-H), 7.32 (dd, *J* = 7.5 and 1.0 Hz, Ar-H), 4.33 (q, 2H, *J*=7.0 Hz, OC*H*$_2$CH$_3$), 2.77 (t, 2H, *J*=7.0 Hz, CH_2), 1.77–1.65 (m, 2H, CH_2), 1.35–1.30 (m, 7H, CH_2), 0.87 (t, 3H, *J*=7.0 Hz, OCH$_2$C*H*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=205.8 (s, C=O), 166.7 (s, O–C=O), 143.2 (s, Ar-C), 131.9 (d, Ar-CH), 129.8 (d, Ar-CH), 129.5 (d, Ar-CH), 128.8 (s, Ar-C), 126.2 (d, Ar-CH), 61.5 (t, *C*H$_2$), 42.8 (t, CH_2), 31.3 (t, CH_2), 22.7 (t, CH_2), 22.4 (t, CH_2), 14.0 (q, *C*H$_3$), 13.8 (q, *C*H$_3$) ppm. HR-MS (ESI$^+$) m/z calculated for $[C_{15}H_{21}O_3]^+$=$[M+H]^+$: 249.1485; found 249.1487.

Isopropyl 2-butyrylbenzoate (**3ck**)**:** GP-1 was carried out with aryl iodide **1c** (116.0 mg, 0.40 mmol), aromatic alcohol **2k** (177.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 24 h. The progress of the product **3ck** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 98:02 to 97:03) furnished the product **3ck** (53.4 mg, 57%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1c**)=0.90, R_f(**3ck**)=0.40, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3064, 2982, 1712, 1676, 1585, 1472, 1388, 1272, 1089, 926, 843,737 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.86 (dd, 1H, *J*=7.8 and 0.9 Hz, Ar-H), 7.52 (td, *J* = 7.5 and 1.4 Hz, 1H), 7.45 (td, *J* = 7.6 and 1.4 Hz, 1H), 7.31 (m, 1H, Ar-H), 5.20 (sep, 1H, *J*=6.3 C*H*$(CH_3)_2$), 2.78 (m, 2H), 1.78–1.69 (m, 2H, CH_2), 1.32 (d, 6H, *J*=6.3 C*H*$(CH_3)_2$), 0.98 (t, 3H, *J*=7.3 Hz, C*H*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=205.7 (s, C=O), 166.2 (s, O–C=O), 143.1 (s, Ar-C), 131.7 (d, Ar-CH), 129.8 (d, Ar-CH), 129.5 (d, Ar-CH), 129.3 (s, Ar-C), 126.2 (d, Ar-CH), 69.2 (d, *C*H$(CH_3)_2$), 44.8 (t, CH_2), 21.6 (q, 2C, CH(*C*H$_3$)$_2$), 17.4 (t, CH_2), 13.7 (q, *C*H$_3$) ppm. HR-MS (ESI$^+$) m/z calculated for $[C_{14}H_{19}O_3]^+$=$[M+H]^+$: 235.1329; found 235.1330.

Isopropyl 2-hexanoylbenzoate (**3cm**)**:** GP-1 was carried out with aryl iodide **1c** (116.0 mg, 0.40 mmol), aromatic alcohol **2m** (245.0 mg, 2.4 mmol),

$Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 23 h. The progress of the product **3cm** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 98:02 to 97:03) furnished the product **3cm** (55.6 mg, 53%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1c**)=0.90, R_f(**3cm**)=0.40, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2982, 1674, 1585, 1472, 1392, 1273, 1089, 1014, 927, 844, 736 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.85 (d, 1H, J=7.8 Hz, Ar-H), 7.51 (td, 1H, J = 7.5 and 1.2 Hz, Ar-H), 7.44 (td, 1H, J = 7.6 and 1.3 Hz, Ar-H), 7.31 (dd, 1H, J = 7.5, 0.9 Hz, Ar-H), 5.20 (sep, 1H, J=6.3 C*H*$(CH_3)_2$), 2.78 (m, 2H), 1.74–1.67 (m, 2H, CH_2), 1.34–1.31 (m, 10H), 0.90–0.86 (m, 3H, C*H*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=205.8 (s, C=O), 166.2 (s, O–C=O), 143.2 (s, Ar-C), 131.7 (d, Ar-CH), 129.8 (d, Ar-CH), 129.5 (d, Ar-CH), 129.2 (s, Ar-C), 126.1 (d, Ar-CH), 69.2 (d, CH), 42.9 (t, CH_2), 31.3 (t, CH_2), 23.7 (t, CH_2), 22.4 (t, CH_2), 21.6 (q, 2C, CH_3), 13.9 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{16}H_{23}O_3]^+$=$[M+H]^+$: 263.1642; found 263.1647.

Butyl 2-hexanoylbenzoate (**3dm**)**:** GP-1 was carried out with aryl iodide **1d** (121.0 mg, 0.40 mmol), aromatic alcohol **2m** (245.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 24 h. The progress of the product **3dm** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 98:02 to 97:03) furnished the product **3dm** (59.6 mg, 54%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1d**)=0.90, R_f(**3dm**)=0.40, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2979, 2929, 1712, 1672, 1587, 1465, 1392, 1269, 1089, 927, 843, 744 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.88 (dd, 1H, J=7.8 and 0.9 Hz, Ar-H), 7.54 (td, 1H, J = 7.5 and 1.3 Hz, Ar-H), 7.47 (td, 1H, J = 7.6 and 1.4 Hz, Ar-H), 7.33 (dd, 1H, J=7.5 and 1.2 Hz, Ar-H), 4.28 (t, 2H, J=6.6 Hz, O*C*$H_2$$CH_2CH_2CH_3$), 2.88–2.73 (m, 2H), 1.73–1.66 (m, 4H, CH_2), 1.47–1.38 (m, 2H), 1.36–1.31 (m, 4H), 0.95 (t, 3H, J=7.3 Hz, C*H*$_3$), 0.90–0.87 (m, 3H, C*H*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=206.0 (s, C=O), 166.8 (s, O–C=O), 143.4 (s, Ar-C), 131.9 (d, Ar-CH), 129.9 (d, Ar-CH), 129.6 (d, Ar-CH), 128.8 (s, Ar-C), 126.2 (d, Ar-CH), 65.5 (t, CH_2), 42.9 (t, CH_2), 31.4 (t, CH_2), 30.5 (t, CH_2), 23.7 (t, CH_2), 22.5 (t, CH_2), 19.2 (t, CH_2), 13.9 (q, CH_3), 13.7 (q, *C*H_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{17}H_{25}O_3]^+$=$[M+H]^+$: 277.1798; found 277.1800.

Pentyl 2-butyrylbenzoate (**3ek**)**:** GP-1 was carried out with aryl iodide **1e** (127.0 mg, 0.40 mmol), aromatic alcohol **2k** (177.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 23 h. The progress of the product **3ek** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 98:02 to 97:03) furnished the product **3ek** (57.7 mg, 55%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1e**)=0.90, R_f(**3ek**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2949, 2866, 1718, 1669, 1584, 1457, 1265, 1128, 1080, 929, 726 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.87 (dd, 1H, *J*=7.3 and 0.9 Hz, Ar-H), 7.53 (td, 1H, *J* = 7.5 and 1.4 Hz, Ar-H), 7.46 (td, 1H, *J* = 7.6 and 1.4 Hz, Ar-H), 7.33 (dd, 1H, *J*=7.8 and 0.9 Hz, Ar-H), 4.26 (t, 2H, *J*=6.8 Hz, OCH_2), 2.79–2.75 (m, 2H), 1.76–1.67 (m, 4H, CH_2), 1.38–1.32 (m, 4H), 0.98 (t, 3H, *J*=7.3 Hz, CH_3), 0.92–0.88 (m, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=205.8 (s, C=O), 166.8 (s, O–C=O), 143.3 (s, Ar-C), 131.9 (d, Ar-CH), 129.8 (d, Ar-CH), 129.5 (d, Ar-CH), 128.8 (s, Ar-C), 126.2 (d, Ar-CH), 65.8 (t, CH_2), 44.8 (t, CH_2), 28.2 (t, CH_2), 28.0 (t, CH_2), 22.3 (t, CH_2), 17.5 (t, CH_2), 13.9 (q, CH_3), 13.7 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{16}H_{23}O_3]^+$=$[M+H]^+$: 263.1642; found 263.1643.

Pentyl 2-hexanoylbenzoate (**3em**)**:** GP-1 was carried out with aryl iodide **1e** (127.0 mg, 0.40 mmol), aromatic alcohol **2m** (211 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 23 h. The progress of the product **3em** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 98:02 to 97:03) furnished the product **3em** (67.3 mg, 58%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1e**)=0.90, R_f(**3em**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2953, 1718, 1670, 1584, 1458, 1267, 1132, 1082, 929, 726 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.87 (dd, 1H, *J*=7.8 and 0.9 Hz, Ar-H), 7.53 (td, 1H, *J* = 7.5 and 1.4 Hz, Ar-H), 7.46 (td, 1H, *J* = 7.6 and 1.4 Hz, Ar-H), 7.32 (dd, 1H, *J*=7.5 and 1.2 Hz, Ar-H), 4.26 (t, 2H, *J*=6.8 Hz, OCH_2), 2.84–2.73 (m, 2H), 1.75–1.68 (m, 4H, CH_2), 1.37–1.31 (m, 8H), 0.92–0.87 (m, 6H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=205.9 (s, C=O), 166.8 (s, O–C=O), 143.3 (s, Ar-C), 131.9 (d, Ar-CH), 129.8 (d, Ar-CH), 129.5 (d, Ar-CH), 128.8 (s, Ar-C), 126.2 (d, Ar-CH), 65.8 (t, CH_2), 42.9 (t, CH_2), 31.4 (t, CH_2), 28.2 (t, CH_2), 28.0 (t, CH_2), 23.7 (t, CH_2), 22.5 (t, CH_2), 22.3 (t, CH_2), 13.9 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for

$[C_{18}H_{27}O_3]^+$=$[M+H]^+$: 291.1955; found 291.1955.

Methyl 2-hexanoyl-5-methylbenzoate (3fm): GP-1 was carried out with aryl iodide **1f** (110.0 mg, 0.40 mmol), aromatic alcohol **2m** (245.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 23 h. The progress of the product **3fm** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 98:02 to 97:03) furnished the product **3fm** (61.5 mg, 62%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1f**)=0.80, R_f(**3fm**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2953, 2864, 1718, 1669, 1585, 1452, 1261, 1126, 1080, 927, 727 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.61 (s, 1H, Ar-H), 7.33-7.28 (m, 2H, Ar-H), 3.85 (s, 3H, OCH_3), 2.76 (t, 2H, J=7.8 Hz, CH_2), 2.38 (s, 3H, CH_3), 1.73–1.65 (m, 2H, CH_2), 1.34–1.30 (m, 4H, CH_2), 0.89–0.86 (m, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=205.1 (s, C=O), 167.8 (s, O–C=O), 140.4 (s, Ar-C), 139.6 (s, Ar-C), 132.2 (d, Ar-CH), 130.1 (d, Ar-CH), 129.3 (s, Ar-C), 126.7 (d, Ar-CH), 52.4 (q, CH_3), 42.2 (t, CH_2), 31.3 (t, CH_2), 23.8 (t, CH_2), 22.4 (t, CH_2), 21.1 (q, CH_3), 13.9 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{15}H_{20}O_3]^+$=$[M]^+$: 248.1412; found 248.1438.

1-(2-(4-Methoxybenzoyl)phenyl)butan-1-one (3nk): GP-1 was carried out with aryl iodide **1n** (135.0 mg, 0.40 mmol), aromatic alcohal **2k** (177.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 24 h. The progress of the product **3nk** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 95:05 to 94:06) furnished the product **3nk** (64.3 mg, 57%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10), R_f(**1n**)=0.90, R_f(**3nk**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2926, 1662, 1593, 1507, 1455, 1252, 1151, 1025, 930, 844, 757, 605 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.82 (dd, 1H, J=7.3 and 0.9 Hz, Ar-H), 7.73–7.70 (m, 2H, Ar-H), 7.59–7.52 (m, 2H, Ar-H), 7.38–7.36 (m, 1H, Ar-H), 6.90–6.87 (m, 2H, Ar-H), 3.84 (s, 3H, OCH_3), 2.83 (t, 2H, J=7.0 Hz, CH_2), 1.67–1.58 (m, 2H, CH_2), 0.88 (t, 3H, J=7.3 Hz, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=201.4 (s, C=O), 196.4 (s, C=O), 163.4 (s, Ar-C), 140.9 (s, Ar-C), 138.2 (s, Ar-C), 131.8 (d, 2C, 2 × Ar-CH), 131.5 (d, Ar-CH), 130.3 (s, Ar-C), 129.4 (d, Ar-CH), 128.5 (d, Ar-CH), 128.3 (d, Ar-CH), 113.7 (d, 2C, 2 × Ar-CH), 55.4 (q, CH_3), 41.8 (t, CH_2), 17.5 (t, CH_2), 13.7 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{18}H_{19}O_3]^+$=$[M+H]^+$: 283.1329; found 283.1326.

1-(2-(4-Methoxybenzoyl)phenyl)pentan-1-one (3nl): GP-1 was carried out with aryl iodide **1n** (135.0 mg, 0.40 mmol), aromatic alcohal **2l** (211.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 23 h. The progress of the product **3nl** formation was monitored by TLC till the reaction was completed. Purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 95:05 to 94:06) furnished the product **3nl** (72.3 mg, 61%) as a colourless viscous liquid. [TLC control (petroleum ether/ethyl acetate 90:10), R_f(**1n**)=0.90, R_f(**3nl**)=0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2926, 1662, 1593, 1507, 1455, 1252, 1149, 1025, 930, 843, 756, 604 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.82 (dd, 1H, *J*=7.3 and 0.9 Hz, Ar-H), 7.72–7.69 (m, 2H, Ar-H), 7.56–7.51 (m, 2H, Ar-H), 7.38–7.36 (m, 1H, Ar-H), 6.89–6.87 (m, 2H, Ar-H), 3.83 (s, 3H, O*CH*$_3$), 2.84 (t, 2H, *J*=7.3 Hz, *CH*$_2$), 1.61–1.53 (m, 2H, *CH*$_2$), 1.31–1.23 (m, 2H, *CH*$_2$), 0.85 (t, 3H, *J*=7.3 Hz, *CH*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=201.5 (s, C=O), 196.4 (s, C=O), 163.4 (s, Ar-C), 140.9 (s, Ar-C), 138.2 (s, Ar-C), 131.7 (d, 2C, 2 × Ar-CH), 131.5 (d, Ar-CH), 130.2 (s, Ar-C), 129.4 (d, Ar-CH), 128.4 (d, Ar-CH), 128.2 (d, Ar-CH), 113.6 (d, 2C, 2 × Ar-CH), 55.4 (q, CH_3), 39.6 (t, CH_2), 26.1 (t, CH_2), 22.2 (t, CH_2), 13.8 (q, CH_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{19}H_{21}O_3]^+=[M+H]^+$: 297.1485; found 297.1485.

3-(4-Hydroxy-3-methoxyphenyl)-2-methyl-1*H*-inden-1-one (5ji): GP-3 was carried out with *ortho*-iodoketone **1j** (104.0 mg, 0.40 mmol) and alcohol **2i** (370.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol) and allowed the reaction mixture to stir at 120 °C for 20 h then Then reaction mixture was removed from oil bath and allow to reach room temperature and then added conc. H_2SO_4 (0.1 mL, 2.0 mmol) and allowed the reaction mixture stirred at room temperature for 10 minute for the product **5ji** formation**.** Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 97:03 to 95:05) furnished the product **5ji** (48.0 mg, 45%) as a yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 96:04), R_f(**1j**)=0.50, R_f(**5ji**)=0.80, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=3233, 2961, 1696, 1651, 1584, 1516, 1443, 1365, 1295, 1199, 992, 752 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.45 (d, 1H, *J*=7.3 Hz, Ar-H), 7.29 (td, 1H, *J*=7.2 and *J*=1.2 Hz, Ar-H), 7.20-7.16 (m, 1H, Ar-H), 7.10 (d, 1H, *J*=7.3 Hz, Ar-H), 7.06-7.03 (m, 2H, Ar-H), 6.98 (s, 1H, Ar-H), 5.90 (s, 1H, Ar-OH), 3.93 (s, 3H, -O*CH*$_3$), 1.93 (s, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=198.3 (s, C=O), 154.8 (s, C=C), 146.6 (s, Ar-C), 146.6 (s, Ar-C), 145.7 (s, Ar-C), 133.0 (d, Ar-CH), 131.4 (s, Ar-C), 130.1 (s, Ar-C), 128.0 (d, Ar-CH),

124.8 (s, C=C), 122.3 (d, Ar-CH), 121.9 (d, Ar-CH), 120.3 (d, Ar-CH), 114.7 (d, Ar-CH), 110.5 (d, Ar-CH), 56.1 (q, O*C*H$_3$), 8.7 (q, *C*H$_3$) ppm. HR-MS (ESI$^+$) m/z calculated for [$C_{17}H_{15}O_3$]$^+$=[M+H]$^+$: 267.1016; found 267.1021.

3-(4-Fluorophenyl)-5,6-dimethoxy-2-methyl-1*H*-inden-1-one (**5kc**)**:** GP-3 was carried out with *ortho*-iodoketone **1k** (128.0 mg, 0.40 mmol) and alcohol **2c** (302.0 mg, 2.4 mmol), Pd(OAc)$_2$ (5.0 mg, 5 mol%), Ag$_2$O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol) and allowed the reaction mixture to stir at 120 °C for 24 h then Then reaction mixture was removed from oil bath and allow to reach room temperature and then added conc. H_2SO_4 (0.1 mL, 2.0 mmol) and allowed the reaction mixture stirred at room temperature for 10 minute for the product **5kc** formation**.** Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 85:15) furnished the product **5kc** (62.0 mg, 52%) as a yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 85:15), R_f(**1k**)=0.50, R_f(**5kc**)=0.70, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2925, 1705, 1601, 1464, 1385, 1269, 1096, 1034, 934, 807, 743 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.46 (dd, 2H, *J*=8.8 and *J*=5.3 Hz, Ar-H), 7.25-7.20 (m, 2H, Ar-H), 7.13 (s, 1H, Ar-H), 6.58 (s, 1H, Ar-H), 3.90 (s, 3H, OC*H*$_3$), 3.87 (s, 3H, OC*H*$_3$), 1.87 (s, 3H, CH$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=197.5 (s, C=O), 164.1 (d, *J*=249 Hz, Ar-CF), 152.4 (s, C=C), 152.1 (s, Ar-C), 148.4 (s, Ar-C), 140.0 (s, Ar-C), 129.9 (s, Ar-C), 129.9 (d, Ar-CH), 129.8 (d, Ar-CH), 123.2 (s, C=C), 116.1 (d, Ar-CH), 115.8 (d, Ar-CH), 114.5 (s, Ar-C), 107.6 (d, Ar-CH), 105.2 (d, Ar-CH), 56.3 (q, Ar-O*C*H$_3$), 56.3 (q, Ar-O*C*H$_3$), 8.6 (q, *C*H$_3$) ppm. HR-MS (ESI$^+$) m/z calculated for [$C_{18}H_{16}FO_3$]$^+$=[M+H]$^+$: 299.1078; found 299.1078.

4,5,6-Trimethoxy-2-methyl-3-phenyl-1*H*-inden-1-one (**5la**)**:** GP-3 was carried out with *ortho*-iodoketone **1l** (140.0 mg, 0.40 mmol) and alcohol **2a** (259.0 mg, 2.4 mmol), Pd(OAc)$_2$ (5.0 mg, 5 mol%), Ag$_2$O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol) and allowed the reaction mixture to stir at 120 °C for 24 h then Then reaction mixture was removed from oil bath and allow to reach room temperature and then added conc. H_2SO_4 (0.1 mL, 2.0 mmol) and allowed the reaction mixture stirred at room temperature for 5 minute for the product **5la** formation**.** Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 90:10 to 75:25) furnished the product **5la** (64.5 mg, 52%) as a yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 75:25), R_f(**1l**)=0.30, R_f(**5la**)=0.80, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2924, 1705, 1602, 1463, 1384, 1266, 1185, 1091, 1032, 936, 807, 739 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.45-7.36 (m, 5H, Ar-

H), 6.98 (s, 1H, Ar-H), 3.87 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.28 (s, 3H, OCH_3), 1.75 (s, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=197.2 (s, C=O), 155.4 (s, Ar-C), 153.5 (s, C=C), 148.4 (s, Ar-C), 147.3 (s, Ar-C), 134.2 (s, Ar-C), 130.7 (s, Ar-C), 129.3 (s, Ar-C), 128.4 (d, Ar-CH), 128.0 (d, 2C, 2 × Ar-CH), 127.7 (d, 2C, 2 × Ar-CH), 127.1 (s, C=C), 104.7 (d, Ar-CH), 61.1 (q, Ar-OCH_3), 61.0 (q, Ar-OCH_3), 56.4 (q, Ar-OCH_3), 8.3 (q, CH_3) ppm. HR-MS (ESI$^+$) m/z calculated for $[C_{19}H_{19}O_4]^+$=$[M+H]^+$: 311.1278; found 311.1275.

2-Ethyl-3-(4-methoxyphenyl)-1*H*-inden-1-one (5nk): GP-3 was carried out with *ortho*-iodoketone **1n** (135.0 mg, 0.40 mmol) and alcohol **2k** (177.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol) and allowed the reaction mixture to stir at 120 °C for 20 h then Then reaction mixture was removed from oil bath and allow to reach room temperature and then added conc. H_2SO_4 (0.1 mL, 2.0 mmol) and allowed the reaction mixture stirred at room temperature for 20 minute for the product **5nk** formation**.** Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 97:03 to 95:05) furnished the product **5nk** (53.9 mg, 51%) as a yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 95:05), R_f(**1n**)=0.30, R_f(**5nk**)=0.50, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2947, 2864, 1717, 1675, 1586, 1468, 1395, 1271, 1134, 1086, 930, 844, 732 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.46-7.41 (m, 3H, Ar-H), 7.28 (t, 1H, *J*=7.3 Hz, Ar-H), 7.18 (t, 1H, *J*=7.3Hz, Ar-H), 7.04 (d, 3H, *J*=8.3 Hz, Ar-H), 3.88 (s, 3H, OCH_3), 2.35 (q, 2H, *J*=7.6 Hz, -C$H_2$$CH_3$), 1.12 (t, 3H, *J*=7.6 Hz, -CH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=198.2 (s, C=O), 160.3 (s, Ar-C), 154.4 (s, C=C), 145.8 (s, Ar-C), 135.8 (s, Ar-C), 132.9 (d, Ar-CH), 131.3 (s, Ar-C), 129.3 (d, 2C, 2 × Ar-CH), 128.1 (d, Ar-CH), 125.0 (s, C=C), 122.2 (d, Ar-CH), 120.5 (d, Ar-CH), 114.2 (d, 2C, 2 × Ar-CH), 55.3 (q, Ar-OCH_3), 16.7 (t, -$CH_2$$CH_3$), 13.9 (q, -$CH_2$$CH_3$) ppm. HR-MS (ESI$^+$) m/z calculated for $[C_{18}H_{17}O_2]^+$=$[M+H]^+$: 265.1223; found 265.1219.

2-Ethyl-3-(thiophen-2-yl)-1H-inden-1-one (5pk): GP-3 was carried out with *ortho*-iodoketone **1p** (125.0 mg, 0.40 mmol) and alcohol **2k** (177.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol) and allowed the reaction mixture to stir at 120 °C for 20 h then Then reaction mixture was removed from oil bath and allow to reach room temperature and then added conc. H_2SO_4 (0.1 mL, 2.0 mmol) and allowed the reaction mixture stirred at room temperature for 15 minute for the product **5pk** formation**.** Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 97:03 to 95:05) furnished the product **5pk** (48.0 mg, 50%) as a yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 96:04), R_f(**1p**)=0.50, R_f(**5pk**)=0.80, UV detection].

IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2924, 2857, 1720, 1593, 1453, 1284, 1133, 1087, 928, 755 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.57 (dd, 1H, *J*=5.1 and *J*=1.2 Hz, Ar-H), 7.50-7.49 (m, 2H, Ar-H), 7.44 (d, 1H, *J*=7.3 Hz, Ar-H), 7.36 (td, 1H, *J*=6.3 and *J*=1.4 Hz, Ar-H), 7.26-7.21 (m, 2H, Ar-H), 2.56 (q, 2H, *J*=7.5 Hz, Ar-H), 1.17 (t, 3H, *J*=7.5 Hz, Ar-H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=197.3 (s, C=O), 146.8 (s, Ar-C), 144.9 (s, C=C), 136.3 (s, Ar-C), 134.2 (s, C=C), 133.1 (d, Ar-CH), 131.2 (s, C=C), 128.6 (d, Ar-CH), 128.3 (d, Ar-CH), 128.1 (d, Ar-CH), 127.8 (d, Ar-CH), 122.4 (d, Ar-CH), 120.8 (d, Ar-CH), 17.0 (t, -*C*$H_2$$CH_3$), 13.7 (q, -$CH_2$*C*$H_3$) ppm. HR-MS ($ESI^+$) m/z calculated for $[C_{15}H_{13}OS]^+$=$[M+H]^+$: 241.0682; found 241.0680.

2-Butyl-3-(thiophen-2-yl)-1*H*-inden-1-one (**5pm**)**:** GP-3 was carried out with *ortho*-iodoketone **1p** (125.0 mg, 0.40 mmol) and alcohol **2m** (245.0 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol%), Ag_2O (111.0 mg, 0.48 mmol) and TBHP (308.0 mg, 2.4 mmol) and allowed the reaction mixture to stir at 120 °C for 21 h then Then reaction mixture was removed from oil bath and allow to reach room temperature and then added Conc. H_2SO_4 (0.1 mL, 2.0 mmol) and allowed the reaction mixture stirred at room temperature for 15 minute for the product **5pm** formation**.** Purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate, 97:03 to 95:05) furnished the product **5pm** (56.8 mg, 53%) as a yellow viscous liquid. [TLC control (petroleum ether/ethyl acetate 96:04), R_f(**1p**)=0.50, R_f(**5pm**)=0.80, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max}=2924, 2857, 1716, 1448, 1281, 1128, 1085, 939, 749 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ=7.58 (dd, 1H, *J*=4.8 and *J*=0.9 Hz, Ar-H), 7.50-7.48 (m, 2H, Ar-H), 7.44 (d, 1H, *J*=7.3 Hz, Ar-H), 7.37 (td, 1H, *J*=7.8 and *J*=1.4 Hz, Ar-H), 7.26-7.22 (m, 2H, Ar-H), 2.54 (t, 2H, *J*=7.3 Hz, -CH_2*C*H_2CH_2 CH_2CH_3), 1.55-1.50 (m, 2H, -CH_2CH_2*C*$H_2CH_2CH_3$), 1.45-1.38 (m, 2H, -$CH_2CH_2CH_2$*C*H_2CH_3), 0.93 (t, 3H, *J*=7.3 Hz, -$CH_2CH_2CH_2$*C*H_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=197.5 (s, C=O), 147.0 (s, C=C), 144.9 (s, Ar-C), 135.2 (s, Ar-C), 134.3 (s, Ar-C), 133.0 (d, Ar-CH), 131.2 (s, C=C), 128.6 (d, Ar-CH), 128.3 (d, Ar-CH), 128.1 (d, Ar-CH), 127.8 (d, Ar-CH), 122.4 (d, Ar-CH), 120.8 (d, Ar-CH), 31.3 (t, -*C*H_2CH_2 CH_2CH_3), 23.5 (t, -CH_2*C*$H_2CH_2CH_3$), 23.0 (t, -CH_2CH_2*C*H_2CH_3), 13.9 (q, -$CH_2CH_2CH_2$*C*H_3) ppm. HR-MS (ESI^+) m/z calculated for $[C_{17}H_{17}OS]^+$=$[M+H]^+$: 269.0995; found 269.1001.

2,2,6,6-Tetramethylpiperidin-1-yl benzoate (7aa): To an oven dried Schlenk tube, were added **1a** (104 mg, 0.4 mmol), alcohol **2a** (259 mg, 2.4 mmol), TEMPO (374 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111 mg, 0.48 mmol), and TBHP (151 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 20 h. Progress of the reaction was monitored by TLC until the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with

saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 55:45−50:50) furnished the product **7aa** (596 mg, 95%) as white solid. [TLC control (petroleum ether/ethyl acetate 50:50), Rf (**2a**) = 0.99, Rf (**7aa**) = 0.50, UV detection].

2,2,6,6-Tetramethylpiperidin-1-yl 4-methoxybenzoate: To an oven dried Schlenk tube, were added **1a** (104 mg, 0.4 mmol), alcohol **2g** (331 mg, 2.4 mmol), TEMPO (374 mg, 2.4 mmol), $Pd(OAc)_2$ (5.0 mg, 5 mol %), Ag_2O (111 mg, 0.48 mmol), and TBHP (151 mg, 2.4 mmol). The resulting reaction mixture was stirred at 120 °C for 26 h. Progress of the reaction was monitored by TLC until the reaction was completed. The reaction mixture was quenched by the addition of aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 15 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4) and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica-gel column chromatography (petroleum ether/ethyl acetate, 55:45−50:50) furnished the product **7ag** (649 mg, 93%) as white solid. [TLC control (petroleum ether/ethyl acetate 50:50), **Rf** (**2a**) = 0.99, **Rf** (**7ag**) = 0.50, UV detection]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ=8.01 (d, 2H, *J*=8.9 Hz, Ar-H), 6.92 (d, 2H, *J*=8.9 Hz, Ar-H), 3.84 (s, 3H, Ar-H), 1.80-1.63 (m, 3H), 1.59-1.53 (m, 2H), 1.47-1.38 (m, 1H), 1.24 (s, 6H), 1.09 (s, 6H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ=165.9 (s, O-C=O), 163.0 (s, Ar-C), 131.3 (d, 2C, 2 × Ar-CH), 121.6 (s, Ar-C), 113.4 (d, 2C, 2 × Ar-CH), 60.0 (s, $C(CH_3)_4$), 55.2 (q, Ar-OMe), 38.7 (t, 2 × CH_2), 31.6 (q, 2 × CH_3), 20.6 (q, 2 × CH_3), 16.7 (t, -CH_2) ppm. HR-MS (ESI^+) m/z calculated for $[C_{17}H_{26}NO_3]^+$=$[M+H]^+$: 292.1907; found 292.1909.

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FULL PAPER

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Layout 1:

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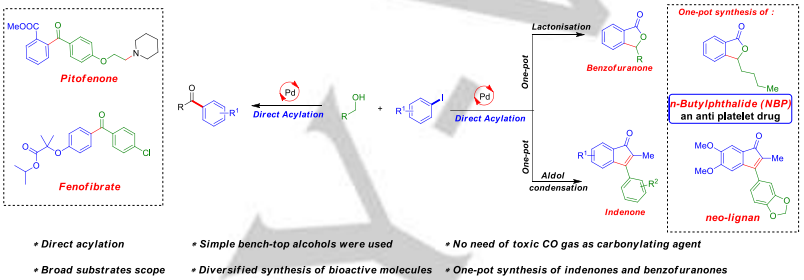
Palladium-catalyzed direct oxidative acylation through cross-dehydrogenative coupling has been demonstrated, for the synthesis of a wide varity of ketones. Readily available primary alcohols have been utilized as acylating sources. Overall, this oxidative coupling proceeds *via* three distinct transformations such as oxidation, radical formation and cross-coupling in one catalytic process. This protocol does not involve the assistance of a directing group or activation of the carbonyl group by any other means. Further, this reaction made use of no toxic CO gas as carbonylating agent; instead, feedstock primary alcohols have been utilized as acylation source. Notably, enabled the synthesis of benzofuranones and indenones. Significantly, this divergent coupling strategy has been applied to the synthesis of *n*-butylphthalide, fenofibrate, pitofenone and neo-lignan.



Key Topic*

Acylation, Indenone, Benzofuranone

Author(s), Corresponding Author(s)*

Basuli Suchard, Chinnabattigalla Sreenivasulu And Gedu Satyanarayana*

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Title

Palladium-Catalyzed Direct Oxidative Coupling of Iodoarenes with Primary Alcohols Leading to Ketones: Application to the Synthesis of Benzofuranones and Indenones

*one or two words that highlight the emphasis of the paper or the field of the study