A Platinum Open Access Journal
for Organic Chemistry

Paper

Free to Authors and Readers

DOAJ Seal

Arkivoc **2022**, part vi, 0-0
to be inserted by editorial office

One-pot synthesis of indenobenzofurans via tandem Michael addition-elimination and palladium-catalysed C-H activation

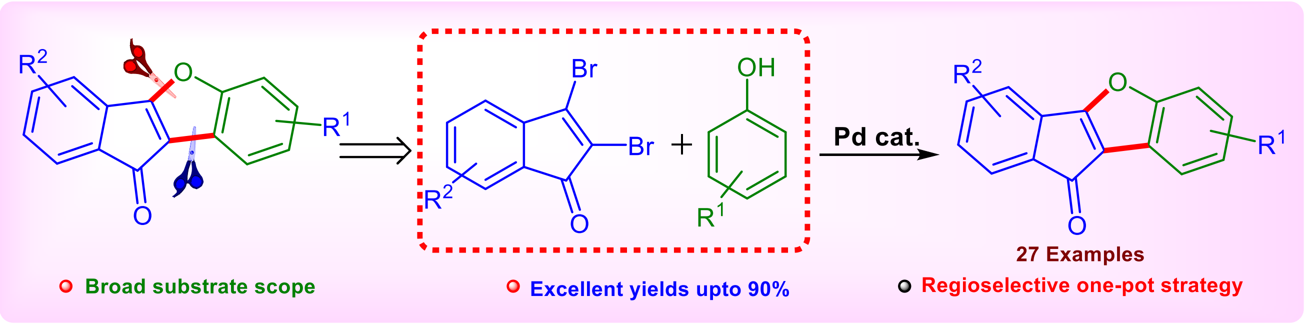
Vijaykumar Naik and Faiz Ahmed Khan*

Department of Chemistry, Indian Institute of Technology Hyderabad, Kandi, Sangareddy, 502285, India
e-mail: *faiz@chy.iith.ac.in*

Received 09-02-2022 **Accepted Manuscript** 10-23-2022 **Published on line** 11-10-2022

Abstract

A tandem, one-pot reaction of 2,3-dibromoindenone with phenols is reported, which provides a straightforward approach to accomplish structurally diverse indenobenzofurans in excellent yields. Besides, the control experiments revealed that reaction proceeds through a two-step sequence *via* an intermolecular Michael addition-elimination reaction, which enables the C–O bond formation, followed by palladium-catalyzed intramolecular C–C bond formation through C–H activation. Significantly, this protocol offers a convenient approach to synthesize the diverse tetracyclic indenobenzofurans.



Broad substrate scope

Excellent yields upto 90%

Regioselective one-pot strategy

Keywords: Indenones, Michael addition-elimination, C–H activation, indenobenzofurans

DOI: https://doi.org/10.24820/ark.5550190.p011.870

Introduction

Indenone core structure is omnipresent in various important natural products and pharmaceuticals.[1,2] For instance, natural products such as onychnine,[3] euplectin,[4] neo-lignin,[5] and indotecan (LMP400)[6] contain the indanone core moiety (Fig. 1). The synthetic molecules endowed with an indenone framework have a wide range of biological activities such as anti-HIV,[7] cytotoxicity,[8] phosphodiesterase inhibition,[9] anti-inflammatory,[10] and adenosine A2A receptor antagonists.[11] Besides, indenone fused heterocyclic substructures are attractive pharmacomodulations where *O*-containing heterocycles such as furans and benzofurans play an important role in the architecture of polycyclic heterocyclic frames, such as the tricyclic indenofurans, which are key substructures for natural product solanacol,[12] ramelteon,[13] and (-)-galiellalactone.[14] Specifically, tetracyclic indenobenzofurans received considerable attention from a synthetic and biological standpoint due to their outstanding pharmacological properties.[15-18] Due to their importance, a considerable number of synthetic models have been developed for the synthesis of indenone derivatives.[19-28] These indenone fused heterocycles drew our attention because of their importance as privileged scaffolds in drug discovery. Therefore, we have become fascinated by their extensive properties, as a result, we have reported the synthesis and biological applications of indanones,[29-32] which encouraged us to further develop in the indenone core skeletoned heterocycles.

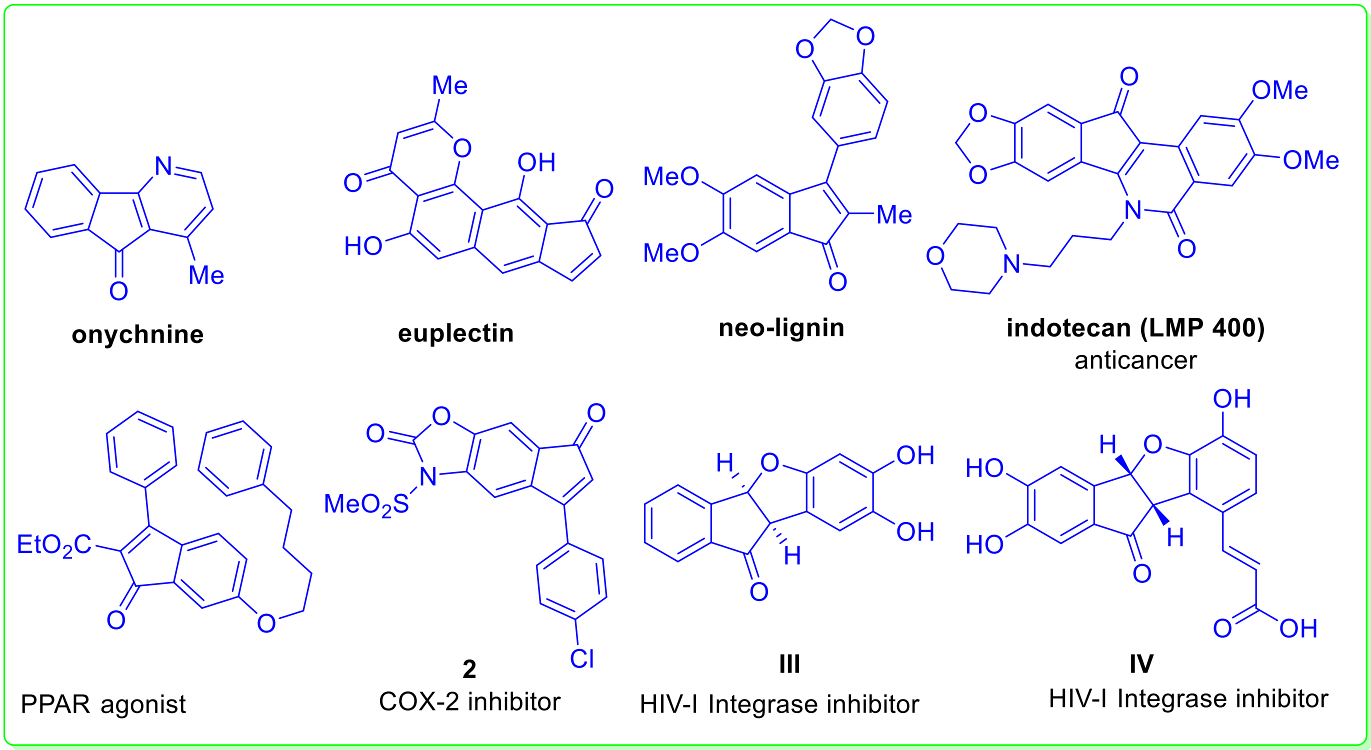

onychnine
euplectin
neo-lignin
indotecan (LMP 400)
anticancer
PPAR agonist
2
COX-2 inhibitor
III
HIV-I Integrase inhibitor
IV
HIV-I Integrase inhibitor

Figure 1. Selective indenone-containing natural products and biologically active molecules.

The significance of palladium-catalyzed C–H activation has been demonstrated in many classical organic transformations in the formation of C–C bonds.[33] To the best of our knowledge, threre are no reports which involve the synthesis of indenobenzofurans via the palladium catalyzed C–H activation as a key sequence. However, only a few methods were reported to synthesize indenobenzofuran derivatives using various strategies.[34-42] In this context, herein, we have developed a convenient method to furnish benzofuran fused indenone heterocycles using 2,3-dibromoindenones and phenols.

Our synthetic strategy involved Michael addition-elimination followed by C–H activation in a one pot protocol. In general, 2,3-dibromoindenone is a good Michael acceptor wherein the β-position is electron-deficient to facilitate nucleophilic addition. Therefore, initially a base promoted Michael addition-elimination between 2,3-dibromoindenone and phenol is anticipated. Subsequently, the palladium-catalyzed *ortho*-C–H activation of the phenolic ring accompanied by cyclization to get indenobenzofurans is planned in a one-pot fashion.

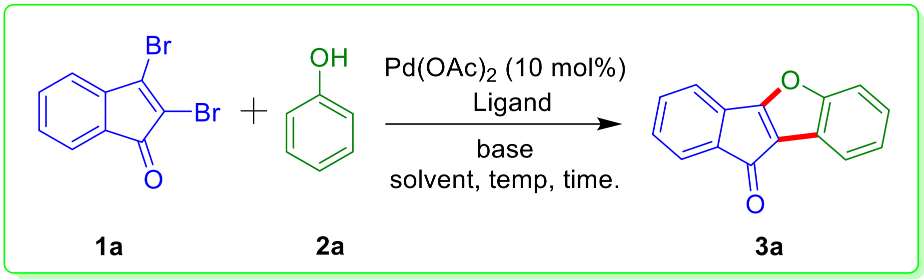
Results and Discussion

We initiated our preliminary investigation with 2,3-dibromoindenone **1a** (0.1736 m.mol), and phenol **2a** (0.1736 m.mol) as model substrates and carried out the reaction in the presence of K_2CO_3 (1 equiv.), $Pd(OAc)_2$ (10 mol%), PPh_3 (20 mol%), in DMF at room temperature (entry 1, Table 1). However, the desired product **3a** was not obtained; instead, we ended up isolating the intermediate **4a** in 87% yield. Next, the reaction is carried out at a higher temperature of 80 °C with K_2CO_3 and Cs_2CO_3 (entries 2-3, Table 1) for 24 h. Pleasingly, the expected product indenobenzofuran **3a** was isolated, though in a poor yield of 23% and 19%, respectively.

The formation of **3a** indicated that the reaction was proceeding via Michael addition-elimination followed by an intramolecular C–C bond formation *via* C–H activation of phenolic *ortho* position, therefore, we have screened various reaction conditions to get this effective transformation in better yield.

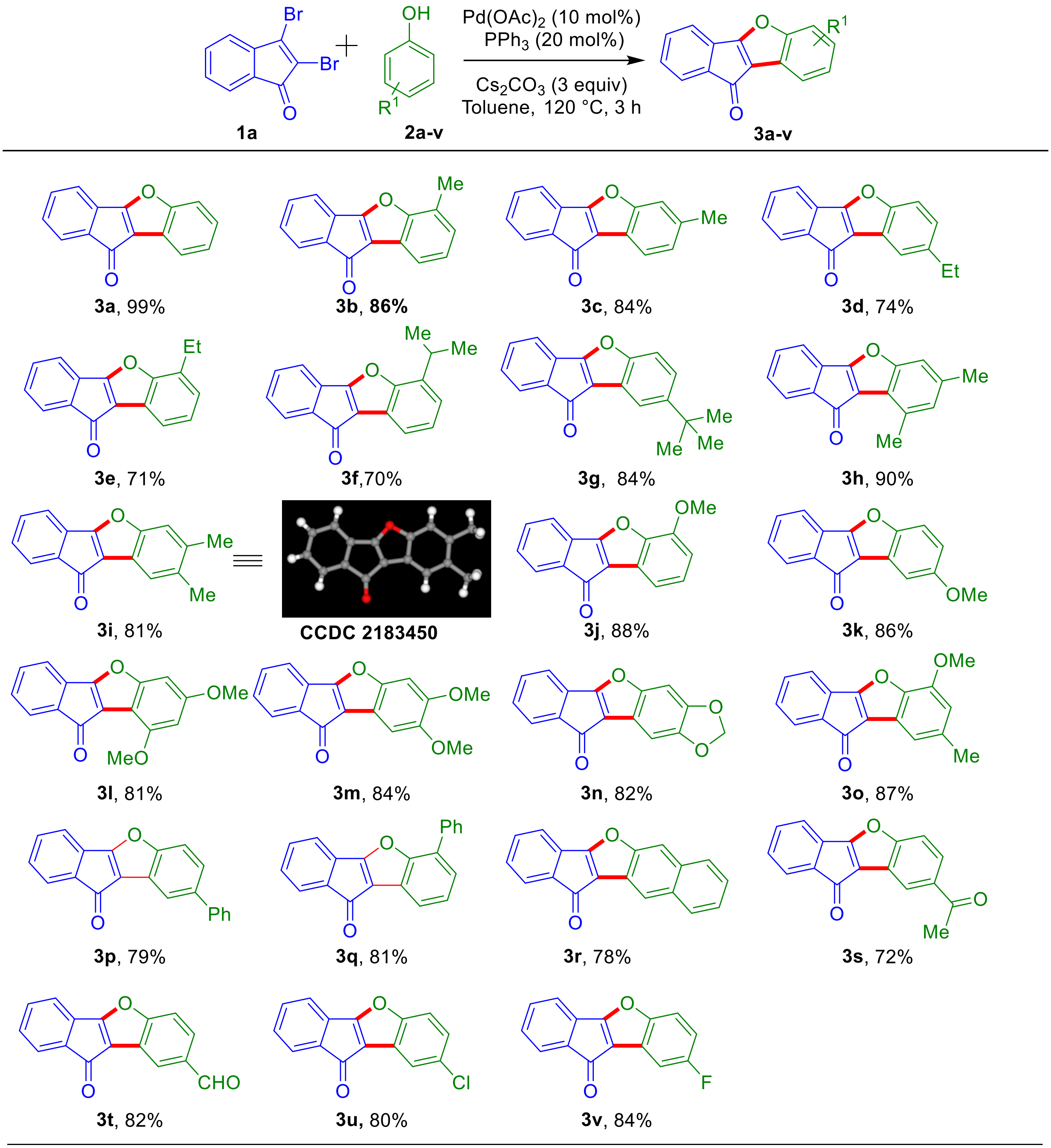
Next, the reaction is performed at an elevated temperature of 120 °C, in different solvents such as DMF, DMA, and toluene by taking K_2CO_3 as a base (entries 4-6, Table 1). It was found that toluene furnished the expected product **3a** in a moderate yield of 60%, therefore, further optimization studies were carried out in toluene as solvent (entry 6, Table 1). In addition, altering the quantity of base from 1 to 3 equivalents has further improved the yield of the tetracyclic product **3a** up to 72% (entry 7, Table 1). Subsequently, we have screened various bases such as KOAc, DBU, NaH, K_3PO_4 and Cs_2CO_3 (entries 8-12, Table 1). Delightfully, the reaction with 3 equivalents of Cs_2CO_3 as a base at 120 °C has provided the highest yield of the requisite product **3a** in 90%, under the short reaction time of 3 h. Besides, the reaction was checked with 1.5 equivalents of Cs_2CO_3 (entry 13, Table 1), where the yield of **3a** was isolated in 65%. Next, the reaction was attempted at the elevated temperature 140 °C in toluene and xylene as solvents. However, the yield is not improved and has furnished the final product **3a** in 25 and 10% (entries 14-15, Table 1). Further decreasing the catalyst loading $Pd(OAc)_2$ to 5 mol% has caused the reaction to be sluggish, as a result, the reaction time is increased from 3 h to 16 h to complete the reaction and has offered the tetracyclic product **3a** in 86% of yield (entry 16, Table 1).

Table 1. Optimization of reaction conditions[a]



Entry	Ligand	Base (equiv)	Solvent	Temp	Time (h)	Yield (%)[c]
1	PPh_3	K_2CO_3 (1)	DMF	rt	24	Nd (87%)[d]
2	PPh_3	K_2CO_3 (1)	DMF	80 °C	24	23
3	PPh_3	Cs_2CO_3 (1)	DMF	80 °C	12	19
4	PPh_3	K_2CO_3 (1)	DMF	120 °C	24	40
5	PPh_3	K_2CO_3 (1)	DMA	120 °C	24	46
6	PPh_3	K_2CO_3 (1)	toluene	120 °C	24	60
7	PPh_3	K_2CO_3(3)	toluene	120 °C	24	72
8	PPh_3	KOAc (3)	toluene	120 °C	24	13
9	PPh_3	DBU (3)	toluene	120 °C	24	27
10	PPh_3	NaH (3)	toluene	120 °C	24	45
11	PPh_3	K_3PO_4 (3)	toluene	120 °C	24	52
12	**PPh_3**	**Cs_2CO_3 (3)**	**toluene**	**120 °C**	**3**	**90**
13	PPh_3	Cs_2CO_3 (1.5)	toluene	120 °C	24	65
14	PPh_3	Cs_2CO_3 (1.5)	toluene	140 °C	24	25
15	PPh_3	Cs_2CO_3 (1.5)	xylene	140 °C	24	10
16[b]	PPh_3	Cs_2CO_3 (3)	toluene	120 °C	16	86

[a]Reaction conditions: **1a** (0.17 mmol), **2a** (0.17 mmol), $Pd(OAc)_2$ (10 mol%), PPh_3 (20 mol%), base (equiv), solvent (1 mL) under N_2 atmosphere. [b]$Pd(OAc)_2$ (5 mol%), PPh_3 (10 mol%). [c]Isolated yields. [d]Yields in the parenthesis represent the intermediate **4a**.

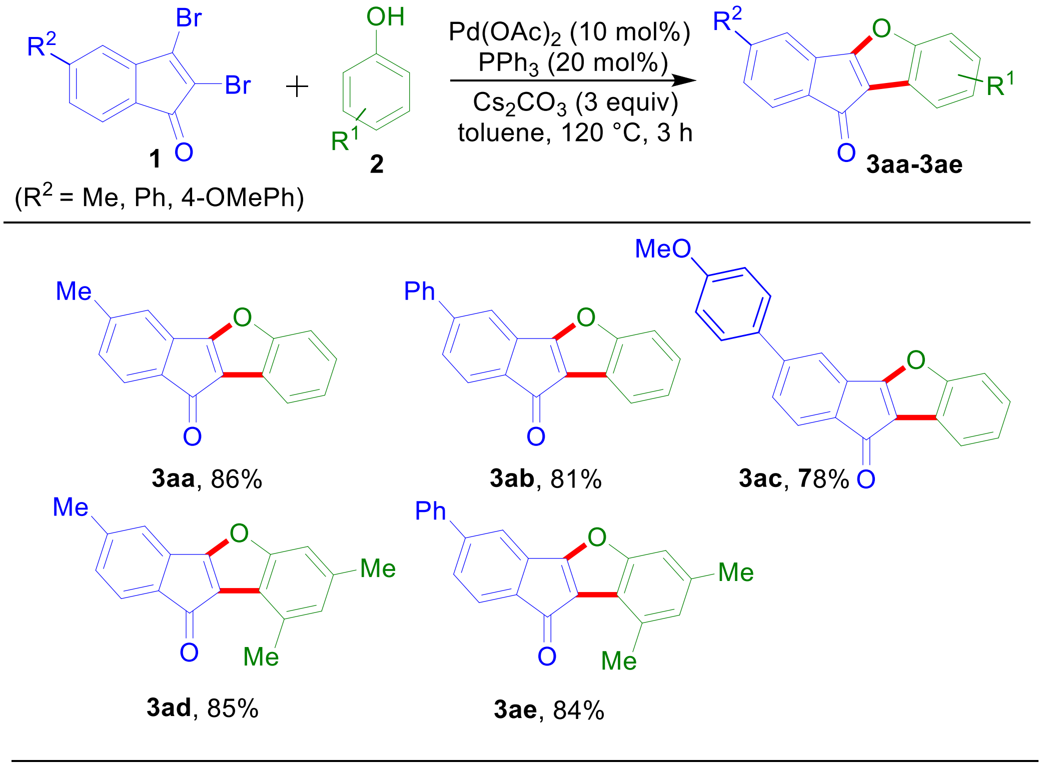


Reaction conditions: 2,3-dibromoindenone (**1**, 0.17 equiv), phenol (**2**, 0.17 mmol), Pd(OAc)$_2$ (10 mol %), PPh$_3$ (20 mol %) toluene (1 mL) under N$_2$ atmosphere, isolated yields.

Scheme 1. Substrate scope of phenols for the synthesis of indenobenzofurans **3a-v**.

After having an optimized reaction condition, the scope of the reaction was explored through which various indenobenzofurans have been synthesized by treating 2,3-dibromoindenone with various phenols

(Scheme 1). All the synthesized indenobenzofurans were obtained in good to excellent yields. Besides, the unambiguous confirmation of **3i** was achieved by using single crystal X-ray data analysis.



Scheme 2. Synthesis of indenobenzofurans **3aa-3ae**.

As anticipated, strong electron-withdrawing substrates like 4-nitrophenol and 2-nitrophenol could not yield the expected tetracyclic moiety but rather afforded an addition product. However, phenolic substrates containing electron-withdrawing groups like -CHO, -$COCH_3$, F, and Cl gave good yields. Also, the substrate scope was checked using different substituted 2,3-dibromoindenones which also gave good yields (Scheme 2).

Interestingly, the compounds **3c**, **3i**, **3m**, **3n**, and **3r** were obtained as a single regioisomer, although there is a possibility of formation of one more regioisomers in each of these cases. The structural assignment for these compounds was done based on the internal consistency in the ^{1}H NMR as depicted in Figure 2. Appearence of a diagnostic singlet at 7.24 ppm (s, H^A) in **3c** and two singlets in **3i** at 7.25 ppm (s H^A) and 7.46 ppm (s, H^B) strongly supportive of their structures which was further corroborated by the unambiguous structural assignment by single crystal x-ray data of **3i**. The same diagnostic pattern was observed for **3m**, showing two singlets at 7.03 ppm (s, H^A) and 7.13 ppm (s, H^B). In the case of **3n**, two singlets were detected at 7.01 ppm (s, H^A) and 7.11 ppm (s, H^B). Similarly, for the compound **3r** two singlets were observed at 7.93 ppm (s, H^A) and 8.19 ppm (s, H^B). Generally, 2-naphthol is know to react at C1 and hence there is a possibility of the formation of the other isomer **3r'**. However, we found only a single regioisomer **3r**, which is further correlated with two singlets in the parent naphtho[2,3-*b*]furan **5a**[44], whereas in the regioisomeric naphtho[2,1-*b*]furan **5b**[45] two doublets were observed (Fig. 2).

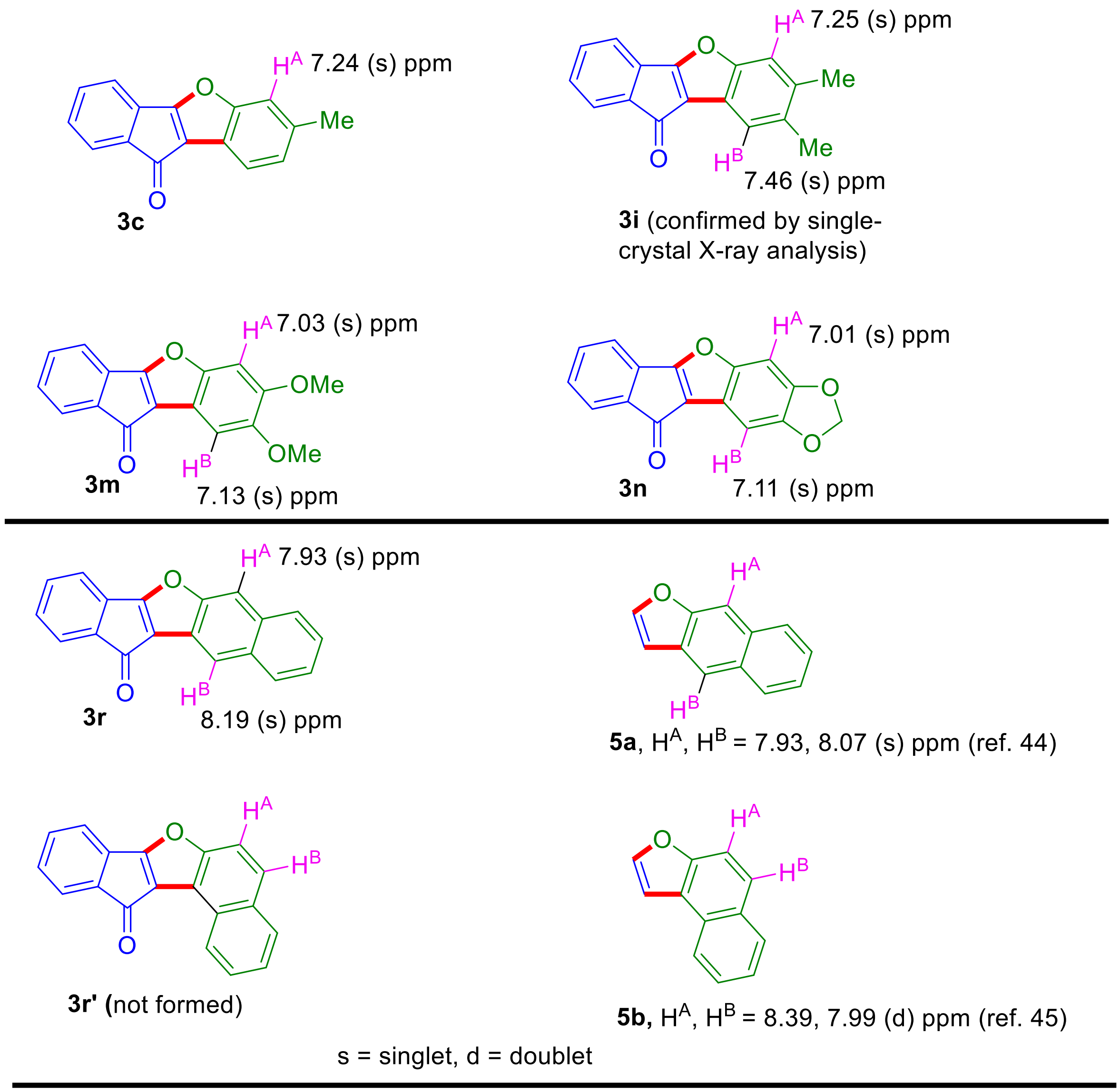
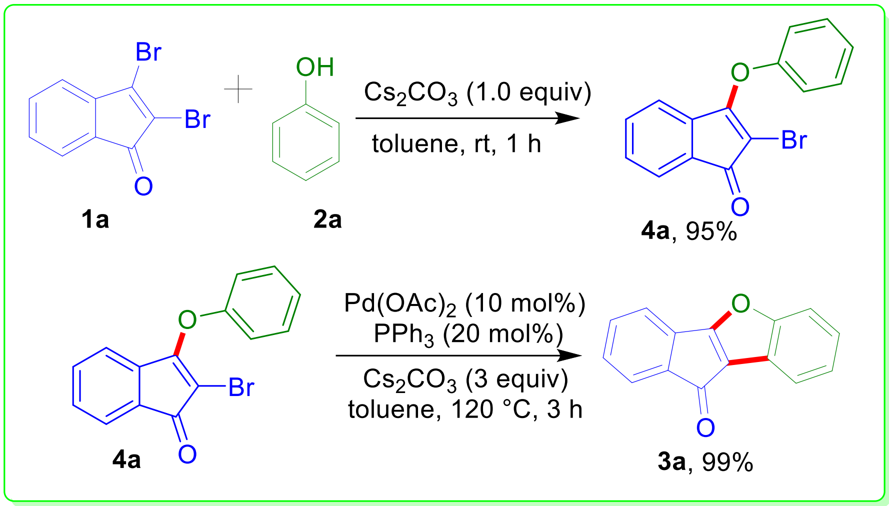


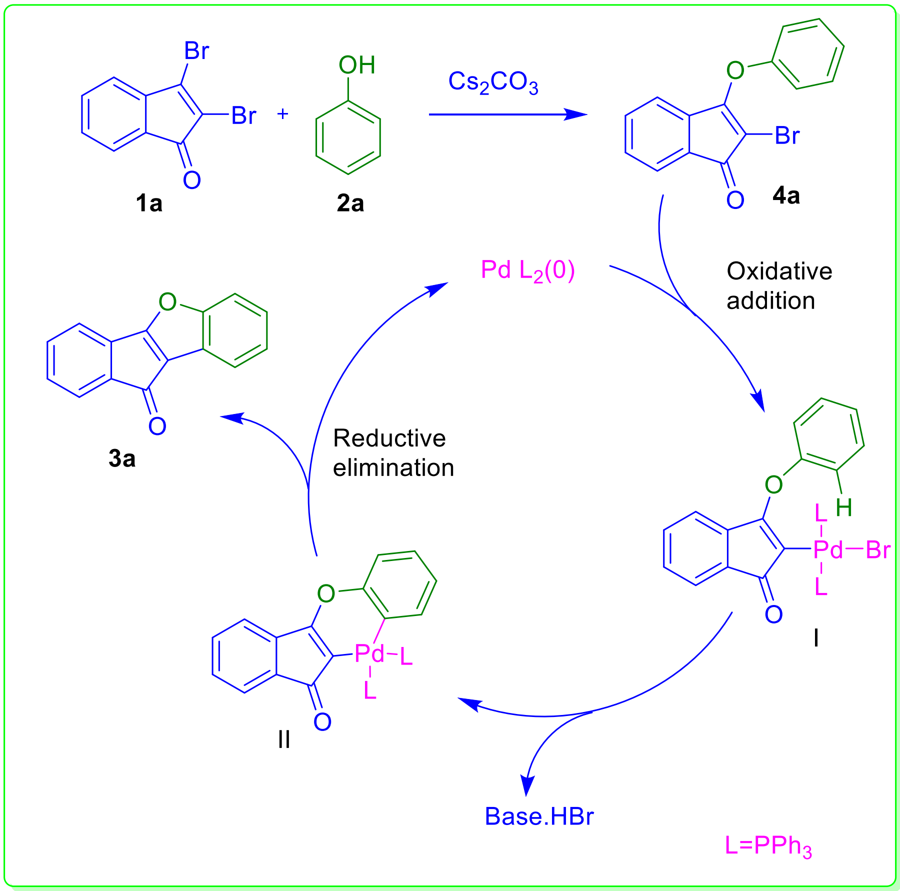
Figure 2. Spectral discussion of **3c**, **3i**, **3m**, **3n** and **3r**.

To gain insight into the reaction mechanism, a few control experiments were performed to identify the pathway of the reaction mechanism. Initially, in presence of base phenoxide nucleophile attacks at the β-position of the 2,3-dibromoindenone which acts as Michael acceptor where the β-position is found to be the electron-deficient center and in a later stage the bromine gets eliminated as a leaving group. By this addition elimination reaction, we isolated compound **4a** in good yield (Scheme 3), which was further treated under the standard condition which involves intramolecular C–H activation to form C–C bond to get the cyclized product, which was obtained with an excellent yield of 99% (Scheme 3).



Scheme 3. Control experiments.

This confirms that the reaction involving Michael addition elimination reaction is the first step. Next, the palladium would play a key role in the subsequent intramolecular C–C bond formation (Scheme 4). Initially, substrate **4** would undergo oxidative addition to deliver the intermediate (I), which then forms the six-membered palladacycle (II) by C–H activation at the *ortho* position of the phenolic ring. In the final step, the desired compound **3a** was obtained through reductive elimination.



Scheme 4. Plausible reaction mechanism.

Conclusions

An efficient route to synthesize indenobenzofurans has been developed using easily accessible starting materials which involve C–O bond formation *via* Michael addition-elimination reaction and C–C bond formation by intramolecular C–H activation strategy, in a one-pot fashion. Also, a plausible mechanism is proposed and supported based on the control experiments.

Experimental Section

General. IR spectra were recorded on an FTIR spectrophotometer. ^{1}H NMR spectra were recorded on a 400 MHz Bruker spectrometer in $CDCl_3$; chemical shifts (δ ppm) and coupling constants (Hz) are reported in a standard fashion about either internal standard tetramethylsilane (TMS) (δ_H 0.00 ppm) or $CHCl_3$ (δ_H 7.26 ppm). ^{13}C NMR spectra were recorded on a 100 MHz spectrometer in $CDCl_3$; chemical shifts (δ ppm) are reported relative to $CHCl_3$ [δ_C 77.00 ppm (central line of triplet)]. In the ^{1}H NMR, the following abbreviations were used throughout: s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, dd = doublet of doublets, m = multiplet and br.s. = broad singlet. The assignment of signals was confirmed by ^{1}H, ^{13}C, and DEPT spectra. High-resolution mass spectra (HR-MS) were recorded using electron spray ionization (ESI); Melting points were determined on an electrothermal melting point apparatus. Phenols were purchased from commercially, 2,3-dibromoindenone was prepared using known protocaol[29,43]. All reactions were performed in oven-dried apparatus under an N_2 atmosphere. Commercial grade solvents were distilled before use. all reactions were monitored by thin-layer chromatography (TLC) on microscopic slides coated with silica gel and visualization of spots was accomplished by exposure to UV radiation or iodine vapor. Compounds were purified using flash chromatography.

General procedure for the synthesis of compound 3. To the solution of **1a** 2,3-dibromo-1*H*-inden-1-one (50 mg 0.17 mmol) in toluene was added **2a** phenol (17 mg 0.17 mmol), Cs_2CO_3 (3.0 equiv.), palladium acetate (4 mg 10 mol%) and triphenylphosphine (20 mol%) under N_2 atmosphere. Then degassed and the mixture was stirred at 120 °C for 3 h. (reaction monitored by TLC). After the complete conversion of intermediate compound **4a**, the reaction was diluted with water (5 mL), and the aqueous layer was extracted with ethyl acetate (3×10 mL). The organic layer was washed with saturated brine then dried over Na_2SO_4 and solvent was evaporated at reduced pressure. The product was isolated by using flash column chromatography (300-400 mesh) using petroleum ether/ethyl acetate as eluent to afford the pure products **3a**.

10*H*-Indeno[1,2-*b*]benzofuran-10-one (3a).[41] orange solid (34 mg, 90%); mp 158-160 °C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.76 - 7.72 (m, 1H), 7.54 - 7.48 (m, 2H), 7.38 - 7.31 (m, 2H), 7.31 - 7.27 (m, 2H), 7.27 - 7.24 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.0, 178.4, 160.8, 138.7, 133.6, 132.9, 130.4, 125.3, 125.1, 123.6, 122.2, 121.0, 118.5, 118.3, 112.6 ppm. IR ν_{max} (KBr): 3069, 1722, 1597, 1537, 1436, 1404, 1051, 915, 856; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{15}H_9O_2$ 221.0597, found: 221.0584.

6-Methyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3b). Red solid (35 mg, 86%); mp 118-120 °C**;** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* 7.3 Hz, 1H), 7.47 (d, *J* 7.3 Hz, 1H), 7.37 - 7.31 (m, 1H), 7.28 - 7.23 (m, 2H), 7.20 (t, *J* 7.6 Hz, 1H), 7.08 (d, *J* 6.8 Hz, 1H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.1, 178.0, 159.9, 138.7, 133.7, 132.8, 130.3, 126.3, 125.2, 123.5, 122.8, 121.8, 118.8, 118.4, 118.2, 15.0; IR ν_{max} (KBr): 2926, 1709, 1594,1542, 1408, 1137, 895, 760 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]+ calcd for $C_{16}H_{11}O_2$ 235.0754, found: 235.0753.

7-Methyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3c). Red solid (34 mg, 84%); mp 112-113 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.54 (d, *J* 7.8 Hz, 1H), 7.42 (d, *J* 6.8 Hz, 1H), 7.31 - 7.26 (m, 1H), 7.24 (s, 1H), 7.23 - 7.18 (m, 1H), 7.14 (d, *J* 6.8 Hz, 1H), 7.08 (d, *J* 7.8 Hz, 1H), 2.42 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ 184.9, 177.8, 161.2, 138.6, 135.6, 133.7, 132.7, 130.1, 126.5, 123.4, 120.3, 119.6, 118.5, 118.0, 112.7, 21.7 ppm; IR ν_{max} (KBr): 2921, 1712, 1597, 1461, 1049, 905, 755 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]+ calcd for $C_{16}H_{11}O_2$ 235.0754, found: 235.0742.

8-Ethyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3d). Red solid (32 mg, 74%); mp 104-106 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.54 (s, 1H), 7.46 (d, *J* 6.8 Hz, 1H), 7.38 (dd, *J* 2.7, 8.6 Hz, 1H), 7.34 - 7.28 (m, 1H), 7.25 -7.17 (m, 2H), 7.09 (d, *J* 8.3 Hz, 1H), 2.71 (q, *J* 7.8 Hz, 2H), 1.27 (t, *J* 7.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ 185.0, 178.4, 159.4, 141.6, 138.7, 133.7, 132.8, 130.2, 125.2, 123.5, 122.2, 119.8, 118.4, 118.2, 112.0, 28.8, 16.0 ppm; IR ν_{max} (KBr) : 2960, 2931, 1710, 1598, 1460, 1401, 1045, 875, 718 cm^{-1}. HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{17}H_{13}O_2$ 249.0910, found: 249.0902.

6-Ethyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3e). Red solid (30 mg, 71%); mp 102-104 °C; ^{1}H NMR (400MHz, CDCl$_3$): δ 7.55 (d, *J* 7.3 Hz, 1H), 7.50 - 7.46 (m, 1H), 7.36 - 7.31 (m, 1H), 7.28 - 7.24 (m, 2H), 7.24 - 7.19 (m, 1H), 7.11 (d, *J* 7.3 Hz, 1H), 2.95 (q, *J* 7.8 Hz, 2H), 1.37 (t, *J* 7.6 Hz, 3H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ 185.1, 178.0, 159.4, 138.8, 133.7, 132.7, 130.3, 129.1, 125.4, 124.6, 123.5, 121.9, 118.8, 118.5, 118.2, 22.8, 14.2 ppm; IR ν_{max} (KBr): 3019, 2972, 1708, 1599, 1487, 1462, 1215, 1136 cm^{-1}. HRMS (ESI-TOF) m/z: [M+H]$^+$ calcd for $C_{17}H_{13}O_2$ 249.0910, found: 249.899.

6-Isopropyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3f). Red solid (32 mg, 70%); mp 149-151 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.48 (dd, *J* 7.8 Hz, 1H), 7.40 (d, *J* 6.8 Hz, 1H), 7.29 - 7.23 (m, 1H), 7.21 - 7.14 (m, 4H), 7.08 (d, *J* 7.3 Hz, 1H), 3.41 (td, *J* 6.9 Hz, 1H), 1.33 (d, *J* 6.8 Hz, 6H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ 185.1, 177.9, 158.9, 138.8, 133.8, 133.7, 132.7, 130.3, 125.5, 123.5, 122.3, 122.0, 118.8, 118.4, 118.2, 28.5, 22.7 ppm. IR ν_{max} (KBr): 2965, 1712, 1595, 1460, 1409, 1135, 987, 720 cm^{-1}. HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{18}H_{15}O_2$ 263.1067, found: 263.1059.

8-(tert-Butyl)-10*H*-indeno[1,2-*b*]benzofuran-10-one (3g). Red solid (40 mg, 84%). mp 142-144 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.73 (d, *J* 2.0 Hz, 1H), 7.46 (d, *J* 7.3 Hz, 1H), 7.42 - 7.38 (m, 1H), 7.35 - 7.28 (m, 2H), 7.27 - 7.23 (m, 1H), 7.22 - 7.17 (m, 1H), 1.37 (s, 9H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ 185.2, 178.6, 159.0, 148.7, 138.7, 133.7, 132.8, 130.2, 123.5, 122.9, 121.9, 118.6, 118.1, 117.5, 111.7, 35.0, 31.7. IR ν_{max} (KBr): 2964, 1715, 1599, 1445, 1407, 1045, 880, 721 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+K]$^+$ calcd for $C_{19}H_{16}KO_2$ 315.0782, found: 315.0767.

7,9-Dimethyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3h). Red solid (39 mg, 90%). mp 133-135 °C**;** ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.48 (d, *J* 6.8 Hz, 1H), 7.37 - 7.31 (m, 1H), 7.28 - 7.23 (m, 1H), 7.21 (d, *J* 6.8 Hz, 1H), 7.13 (s, 1H), 6.94 (s, 1H), 2.68 (s, 3H), 2.44 (s, 3H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$) δ 184.7, 177.4, 161.1, 138.5, 135.9, 133.9, 132.7, 131.7, 130.0, 127.1, 123.4, 120.6, 119.1, 117.8, 109.8, 21.7, 20.4 ppm; IR ν_{max} (KBr): 3012, 1709, 1600, 1538, 1403, 907, 756 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{17}H_{13}O_2$ 249.0910, found: 249.0895.

7,8-Dimethyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3i). Red solid (35 mg, 81%); mp 169-171 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.46 (s, 1H), 7.44 (d, *J* 6.8 Hz, 1H), 7.32 - 7.27 (m, 1H), 7.25 (s, 1H), 7.24 - 7.19 (m, 1H), 7.17 (d, *J* 7.3 Hz, 1H), 2.33 (s, 3H), 2.30 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ 185.1, 177.7, 159.8, 138.7, 134.4, 134.1, 133.9, 132.7, 130.0, 123.4, 121.1, 119.9, 118.4, 117.9, 112.8, 20.5, 19.9 ppm; IR ν_{max} (KBr) 2924, 1713, 1597, 1475, 1446, 906, 756 cm^{-1}. HRMS (ESI-TOF) *m/z*: [M+H]$^+$ calcd for $C_{17}H_{13}O_2$ 249.0910, found: 249.0900.

6-Methoxy-10*H*-indeno[1,2-*b*]benzofuran-10-one (3j). Red solid (38 mg, 88%); mp 146-148 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.40 (d, *J* 6.8 Hz, 1H), 7.26 - 7.21 (m, 2H), 7.19 (dd, *J* 2.4, 7.3 Hz, 2H), 7.16 - 7.11 (m, 1H), 6.73 (d, *J* 7.8 Hz, 1H), 3.94 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ 184.8, 178.1, 149.6, 145.7, 138.7, 133.4, 132.9, 130.3, 126.0, 123.7, 123.6, 118.9, 118.5, 113.2, 107.6, 56.1, ppm; IR ν_{max} (KBr) 3055, 2925, 1715, 1586, 1488, 1138, 889, 776 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+Na]$^{+}$ calcd for $C_{16}H_{10}NaO_3$ 273.0522, found: 273.0511.

8-Methoxy-10*H*-indeno[1,2-*b*]benzofuran-10-one (3k). Red solid (37 mg, 86%); mp 110-112 °C**;** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, *J* 6.8 Hz, 1H), 7.37 (d, *J* 9.3 Hz, 1H), 7.35-7.30 (m, 1H), 7.28-7.24 (m, 1H), 7.24 - 7.19 (m, 1H), 7.16 (d, *J* 2.9 Hz, 1H), 6.84 (dd, *J* 2.7, 9.0 Hz, 1H), 3.85 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.0, 178.8, 157.7, 155.6, 138.7, 133.6, 132.9, 130.3, 123.6, 122.8, 118.6, 118.2, 113.8, 113.0, 103.2, 55.9 ppm; IR ν_{max} (KBr);2957, 1713, 1617, 1480, 1404, 1167,887,759 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^{+}$ calcd for $C_{16}H_{11}O_3$ 251.0703, found: 251.0691.

7,9-Dimethoxy-10*H*-indeno[1,2-*b*]benzofuran-10-one (l).). Red solid (39 mg, 81%); mp 150-152 °C**;** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* 6.8 Hz, 1H), 7.30 - 7.24 (m, 1H), 7.18 (t, *J* 7.1 Hz, 1H), 7.13 - 7.07 (m, 2H), 7.01 (s, 1H), 3.92 (d, *J* 3.9 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.2, 177.0, 155.3, 148.1, 138.4, 133.9, 132.8, 129.6, 123.4, 118.9, 117.5, 114.4, 101.9, 96.4, 56.4, 56.3 ppm. IR ν_{max} (KBr) 2929, 1707, 1536, 1490, 1461, 839, 757 cm^{-1}. HRMS (ESI-TOF) *m/z*: [M+Na]$^{+}$ calcd for $C_{17}H_{12}NaO_4$ 303.0628, found: 303.0621.

7,8-Dimethoxy-10*H*-indeno[1,2-*b*]benzofuran-10-one (3m). Red solid (39 mg, 84%); mp 144-146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* 7.3 Hz, 1H), 7.31 - 7.26 (m, 1H), 7.22 - 7.16 (m, 1H), 7.14 - 7.10 (m, 2H), 7.03 (s, 1H), 3.93 (6H) ppm. ^{13}C NMR (100MHz, $CDCl_3$) δ 185.2, 177.1, 155.3, 148.1, 138.4, 134.0, 132.8, 129.7, 123.5, 118.9, 117.5, 114.4, 101.9, 96.4, 56.4, 56.3 ppm. IR ν_{max} (KBr) HRMS (ESI-micrOTOF) *m/z*: [M+H]$^{+}$ calcd for $C_{17}H_{18}NO$ 281.0814, found: 281.0803

10*H*-[1,3]Dioxolo[4,5-*f*]indeno[1,2-*b*]benzofuran-10-one (3n). Red solid (37 mg, 82%); mp 136-138 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J* 6.8 Hz, 1H), 7.34 - 7.28 (m, 1H), 7.23 - 7.18 (m, 1H), 7.15 (d, *J* 7.3 Hz, 1H), 7.11 (s, 1H), 7.01 (s, 1H), 6.02 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.0, 177.2, 155.9, 146.4, 146.3, 138.3, 134.0, 132.9, 129.7, 123.6, 119.0, 117.6, 115.9, 101.8, 99.7, 94.9ppm; IR ν_{max} (KBr): 3056, 1718, 1641, 1471, 1409, 1282, 1023, 906, 750 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^{+}$ calcd for $C_{16}H_9O_4$ 265.0495, found: 265.0479.

6-Methoxy-8-methyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3o). Red solid (40 mg, 87%); mp 173-175 °C**;** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 - 7.45 (m, 1H), 7.35 - 7.30 (m, 1H), 7.28 - 7.21 (m, 2H), 7.12 (s, 1H), 6.64-6.61 (m, 1H), 4.01 (s, 3H), 2.42 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.0, 178.2, 148.1, 145.0, 138.8, 136.3, 133.6, 132.9, 130.2, 123.5, 123.5, 118.7, 118.4, 113.1, 109.0, 56.1, 21.8 ppm. IR ν_{max} (KBr): 2971, 1713, 1596, 1484, 1404, 1133, 889, 759 cm^{-1}; HRMS (ESI-micrOTOF) *m/z*: [M+H]$^{+}$ calcd for $C_{17}H_{13}O_3$ 265.0859, found: 265.0842.

8-Phenyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3p). Red solid (40 mg, 79%); mp 208-210 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, *J* 1.5 Hz, 1H), 7.65 (dd, *J* 1.2, 8.1 Hz, 2H), 7.61 - 7.57 (m, 1H), 7.56 - 7.51 (m, 2H), 7.51 - 7.44 (m, 2H), 7.42 - 7.35 (m, 2H), 7.33 - 7.28 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.9, 178.9, 160.4, 140.7, 139.0, 138.7, 133.5, 132.9, 130.5, 128.8, 127.4, 124.6, 123.7, 122.7, 119.5, 118.6, 118.4, 112.6 ppm; IR ν_{max} (KBr): 3052, 1711, 1590, 1474, 1403, 1136, 879 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^{+}$ calcd for $C_{21}H_{13}O_2$ 297.0910, found: 297.0891.

6-Phenyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3q). Red solid (41 mg, 81%); mp 208-209 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 - 7.72 (m, 2H), 7.66 (dd, *J* 2.0, 6.8 Hz, 1H), 7.51 - 7.43 (m, 3H), 7.40 (d, *J* 7.3 Hz, 1H), 7.37 - 7.32 (m, 2H), 7.28 - 7.22 (m, 1H), 7.22 - 7.18 (m, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.9, 178.4, 158.0, 138.7, 135.6, 133.5, 132.8, 130.4, 128.8, 128.8, 128.2, 127.1, 125.7, 125.1, 123.6, 122.9, 120.0, 118.7, 118.5 ppm; IR ν_{max} (KBr): 3064, 1714, 1588, 1482, 1401, 1144, 886 cm^{-1}; HRMS (ESI-TOF) *m/z*: [M+H]$^{+}$ calcd for $C_{21}H_{13}O_2$ 297.0910, found: 297.0899.

12*H*-Indeno[1,2-*b*]naphtho[2,3-*d*]furan-12-one (3r). Orange solid (36 mg, 78%); mp 210-212 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.19 (s, 1H), 7.96 - 7.89 (m, 3H), 7.55 - 7.53 (d, 1H), 7.50 - 7.46 (m, 2H), 7.40 - 7.37 (m, 1H), 7.35 - 7.31 (m, 2H) ppm; ; ^{13}C NMR (150 MHz, $CDCl_3$): δ 184.7, 181.3, 159.7, 139.0, 133.3, 132.8, 131.7, 131.2, 131.1, 128.3, 128.1, 125.7, 125.4, 123.6, 121.9, 119.2, 118.8, 117.6, 108.7; IR ν_{max} (KBr): 3052, 1715, 1580, 1492, 1408, 1143, 896 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{19}H_{11}$O2 271.0759, found: 271.0741.

8-Acetyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3s). Red solid (33 mg, 72%); mp 174-176 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, *J* 1.5 Hz, 1H), 7.98 (dd, *J* 2.0, 8.8 Hz, 1H), 7.59 (d, *J* 8.8 Hz, 1H), 7.54 (d, *J* 7.3 Hz, 1H), 7.43-7.37 (m, 1H), 7.36-7.32 (m, 1H), 7.32-7.28 (m, 1H), 2.69 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 184.5, 179.6, 162.9, 138.4, 134.7, 133.1, 133.1, 130.9, 125.5, 123.9, 122.3, 122.0, 118.7, 118.5, 112.7, 26.9 ppm; IR ν_{max} (KBr): 3080, 1708, 1679, 1594, 1456, 1399, 1185, 875, 764 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{17}H_{11}O_3$ 263.0703, found: 263.0686.

10-Oxo-10*H*-indeno[1,2-*b*]benzofuran-8-carbaldehyde (3t). Red solid (35 mg, 82%); mp 206-208 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98 (s, 1H), 8.16 (s, 1H), 7.79 (dd, *J* 1.2, 8.6 Hz, 1H), 7.57 (d, *J* 8.8 Hz, 1H), 7.45 (d, *J* 6.8 Hz, 1 H), 7.37 - 7.29 (m, 1H), 7.28 - 7.17 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2, 183.1, 178.7, 162.6, 137.3, 133.1, 132.1, 131.9, 130.0, 124.8, 123.0, 121.8, 117.7, 117.3, 112.3; IR ν_{max} (KBr) 2851, 1720, 1697, 1461, 1395, 1141, 883, 717 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+NH_4]^+$ calcd for $C_{16}H_{12}NO_3$ 266.0812, found: 266.0806

8-Chloro-10*H*-indeno[1,2-*b*]benzofuran-10-one (3u). Red solid (35 mg, 80%); mp 170-172 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98 (s, 1H), 8.16 (s, 1H), 7.79 (dd, *J* 1.2, 8.6 Hz, 1H), 7.57 (d, *J* 8.8 Hz, 1H), 7.45 (d, *J* 6.8 Hz, 1 H), 7.37 - 7.29 (m, 1H), 7.28 - 7.17 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2, 183.1, 178.7, 162.6, 137.3, 133.1, 132.1, 131.9, 130.0, 124.8, 123.0, 121.8, 117.7, 117.3, 112.3; IR ν_{max} (KBr) 3051, 1720, 1590, 1485, 1402, 1151, 873, 747 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{15}H_8Cl\ O_2$ 255.0213, found: 255.0174.

8-Fluoro-10*H*-indeno[1,2-*b*]benzofuran-10-one (3v). Red solid (34 mg, 84%); mp 180-182 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* 6.8 Hz, 1H), 7.44 (dd, *J* 3.9, 8.8 Hz, 1H), 7.41 - 7.33 (m, 2H), 7.32 - 7.28 (m, 1H), 7.28 - 7.24 (m, 1H), 6.99 (dt, *J* 2.4, 9.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.4, 178.6, 160.7, 158.3, 155.8, 137.5, 132.0, 129.7, 122.7, 117.5, 112.3, 111.7, 111.4, 106.2, 105.9; IR ν_{max} (KBr) 3082, 1720, 1698, 1588, 1490, 1406, 1140, 888, 729 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for C_{15}H8FO_2 239.0508, found: 239.0490.

3-Methyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3aa). Orange solid (33 mg, 86%); mp 154-156 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.71 (td, *J* 0.7, 7.4 Hz, 1H), 7.51 - 7.48 (m, 1H), 7.36 (d, *J* 7.3 Hz, 1H), 7.31 - 7.24 (m, 2H), 7.05 - 7.01 (m, 2 H), 2.35 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 185.0, 178.1, 160.7, 143.7, 136.1, 133.8, 130.2, 125.2, 124.9, 123.6, 122.3, 120.9, 119.6, 118.8, 112.5, 21.9 ppm; IR ν_{max} (KBr): 3056, 2943, 1715, 1587, 1494, 1421, 1280, 1035, 842 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd 235.0759 for $C_{16}H_{11}O_2$, found: 235.0742.

3-Phenyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3ab). Orange solid (40 mg, 81%); mp 185-187 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.76 - 7.72 (m, 1H), 7.63 - 7.59 (m, 2H), 7.56 - 7.51 (m, 2H), 7.50 - 7.45 (m, 4H), 7.44 - 7.39 (m, 1H), 7.34 - 7.27 (m, 2H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 184.8, 160.8, 146.1, 139.7, 137.3, 134.4, 129.0, 128.7, 128.5, 127.0, 125.3, 125.1, 124.0, 122.3, 121.0, 119.2, 117.5, 112.6 ppm; IR ν_{max} (KBr): 3080, 1713, 1609, 1503, 1422, 1266, 1032, 840 cm^{-1}

3-(4-Methoxyphenyl)-10*H*-indeno[1,2-*b*]benzofuran-10-one (3ac). Red solid (42 mg, 78%); mp 166-168 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.77 - 7.74 (m, 1H), 7.58 - 7.55 (m, 2H), 7.55 - 7.52 (m, 2H), 7.46 (d, *J* 1.1 Hz, 1H), 7.43 (dd, *J* 1.5, 7.5 Hz, 1H), 7.34 - 7.28 (m, 2H), 7.02 - 6.99 (m, 2H), 3.87 (s, 3H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 184.9, 177.8, 160.8, 160.1, 145.7, 136.7, 134.4, 132.1, 128.2, 127.9, 125.3, 125.1, 124.1, 122.3, 121.0, 119.2, 117.1, 114.4, 112.6, 55,4 ppm; IR ν_{max} (KBr): 2919, 2854, 1709, 1593, 1488, 1412, 1260, 1021, 832, 772 cm^{-1};

3,7,9-Trimethyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3ad). Red solid (36 mg, 85%); mp 141-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, *J* 7.8 Hz, 1H), 7.11 (s, 1H), 7.03-6.98 (m, 2H), 6.91 (s, 1H), 2.65 (s, 3H), 2.41 (s, 3H), 2.36 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.8, 177.1, 161.0, 143.5, 136.0, 135.7, 134.1, 131.6, 129.7, 127.0, 123.4, 120.7, 119.1, 109.8, 21.9, 21.6, 20.4 ppm; IR ν_{max} (KBr): 2919, 2854, 1709, 1593, 1488, 1412, 1260, 1021, 832, 772 cm^{-1}; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd 263.1073 for $C_{18}H_{15}O_2$, found: 263.1053.

7,9-Dimethyl-3-phenyl-10*H*-indeno[1,2-*b*]benzofuran-10-one (3ae). Orange solid (47 mg, 84%); mp 190-192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 - 7.55 (m, 2H), 7.50 - 7.43 (m, 3H), 7.42 - 7.35 (m, 3H), 7.08 (s, 1H), 6.88 (s, 1H), 2.63 (s, 3H), 2.39 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.4, 176.8, 161.1, 145.9, 139.8, 137.2, 135.9, 134.6, 131.7, 129.0, 128.4, 128.2, 127.1, 127.0, 123.8, 120.6, 119.7, 116.9, 109.8, 21.7, 20.4 ppm. IR ν_{max} (KBr): 3058, 2962, 1715, 1591, 1489, 1405, 1265, 1022, 926, 757 cm$^{-1;}$ HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd 325.1229 for $C_{23}H_{17}O_2$, found: 325.1227.

2-Bromo-3-phenoxy-1*H*-inden-1-one (4a). yellow solid (47 mg, 95%); mp 124-126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 - 7.46 (m, 1H), 7.45 - 7.38 (m, 2H), 7.32 - 7.25 (m, 3H), 7.21 (d, *J* 7.8 Hz, 2H), 6.88 - 6.82 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.2, 169.8, 153.6, 138.9, 133.0, 131.1, 129.9, 129.7, 126.0, 122.3, 120.1, 119.6, 96.0 ppm. IR ν_{max} (KBr): 3044, 1705, 1580, 1489, 1395, 1205, 1032 cm^{-1}

Acknowledgments

We gratefully acknowledge DST and CSIR for financial support. Vijaykumar thanks CSIR for a senior research fellowship.

Supplementary Material

^{1}H NMR and ^{13}C NMR spectra of compounds reported in this article are available as supplementary information.

References

1. Park, C. H.; Siomboing, X.; Yous, S.; Gressier, B.; Luyckx, M.; Chavatte, P. *Eur. J. Med. Chem*. **2002**, *37*, 461. https://doi.org/10.1016/S0223-5234(02)01373-9
2. Park, C. H.; Siomboing, X.; Yous, S.; Gressier, B.; Luyckx, M.; Chavatte, P. *Eur. J. Med. Chem*. **2002**, *37*, 461. https://doi.org/10.1016/S0223-5234(02)01373-9
3. Prachayasittikul, S.; Manam, P.; Chinworrungsee, M.; Ayudhya, M.I.; Ruchirawat, S.; Prachayasittikul, V. *Molecules* **2009**, *14*, 4414 https://doi.org/10.3390/molecules14114414PK
4. Ernst-Russell, M.A.; Chai, C.L.L.; Wardlaw, J.H; John A. Elix. *J. Nat. Prod.* **2000**, *63*, 1, 129 https://doi.org/10.1021/np9903245
5. Harrowven, D.C.; Newman, N. A.; Knight, C. A. *Tetrahedron Lett*. **1998**, *39*, 6757; https://doi.org/10.1016/S0040-4039(98)01419-1
6. Lv, P. C.; Elsayed, M.S.A.; Agama, K.; Marchand, C.; Pommier, Y.; Cushman, M. *J. Med. Chem*. **2016**, *59*, 4890 https://doi.org/10.1021/acs.jmedchem.6b00220

7. Ahsan, M. J.; Govindasamy, J. A.; Khalilullah, H. A.; Govind Mohan,G. B.; Stables, J. P.; Pannecouque, C.; Clercq, E.D. *Bioorg. Med. Chem. Lett*. **2012**, *22*, 7029 https://doi.org/10.1016/j.bmcl.2012.09.108
8. Miri, R.; Javidnia, K.; Hemmateenejad, B.; Azarpira, A.; Amirghofran, Z. *Bioorg. Med. Chem*. **2004**, *12*, 2529. https://doi.org/10.1016/j.bmc.2004.03.032
9. Heintzelman, G. R.; Averill, K. M.; Dodd, J. H. PCT Int. Appl. WO2002085894 A1 20021031, 2002.
10. Cooper, K.; Fray, M. J.; Cross, P. E.; Richardson, K. Eur. Pat. Appl., EP 299727 A1 19890118, 1989.
11. Shook, B. C.; Rassnick, S.; Wallace, N.; Crooke, J.; Ault,M.; Chakravarty, D.; Barbay, K. *J. Med. Chem*. **2012**, *55*, 3, 1402 https://doi.org/10.1021/jm100971t
12. Xiaonan Xie, X.; Kusumoto, D.; Takeuchi, Y.; Yoneyama , K.; Yamada,Y.; Yoneyama, K. *J. Agric. Food Chem*. **2007**, *55*, 20, 8067 https://doi.org/10.1021/jf0715121
13. Uchikawa, O.; Fukatsu, K.; Tokunoh, R.; Kawada, M.; Matsumoto, K.; Imai, Y.; Hinuma, S.; Kato, K.; Nishikawa, H.; Hirai, K.; Miyamoto, M.; Ohkawa, S. *J. Med. Chem*. **2002**, *45*, 4222. https://doi.org/10.1021/jm0201159
14. Koike, T.; Hoashi, Y.; Takai, T.; Nakayama, M.; Yukuhiro, N.; Ishikawa, T.; Hirai, K.; Uchikawa, O. *J. Med. Chem*. **2011**, *54*, 3436. https://doi.org/10.1021/jm200221q
15. Azuma, T.; Tanaka, Y.; Kikuzaki, H. *Phytochemistry* **2008**, *69*, 2743, https://doi.org/10.1016/j.phytochem.2008.09.001
16. Prabhakar, K. R.; Veerapur, V. P.; Bansal, P.; Vipan, K. P.; Reddy, K. M.; Barik, A.; Reddy, B. K. D.; Reddanna, P.; Priyadarsini, K. I.; Unnikrishnan, M. K. *Bioorg. Med. Chem*. **2006**, *14*, 7113. https://doi.org/10.1016/j.bmc.2006.06.068
17. Review: Singh, K. *Curr. Org. Synth*. **2016**, *13*, 385. https://doi.org/10.2174/1570179412666150817222851
18. Queffélec, C.; Bailly, F.; Mbemba, G.; Mouscadet, J.-F.; Hayes, S.; Debyser, Z.; Witvrouw, M.; Cotelle, P. *Bioorg. Med. Chem. Lett*. **2008**, *18*, 4736. https://doi.org/10.1016/j.bmcl.2008.06.063
19. Hassan, A. A.; Mohamed, N. K.; Aly, A. A.; Tawfeek, H. N.; Brase, S.; Nieger, M. *Mol. Diversity* **2021**, *25*, 99. https://doi.org/10.1007/s11030-019-10027-8
20. Rezvanian, A.; Moradi, F.; Zadsirjan, V.; Mohammadnejad, M.; Heravi, M. M. *Mol. Diversity* **2020**, *24*, 1313. https://doi.org/10.1007/s11030-019-09996-7
21. Khoeiniha, R.; Olyaei, A.; Saraei, M. *Synth. Commun*. 2018, 48, 155. https://doi.org/10.1080/00397911.2017.1388409
22. Vinoth, P.; Vivekanand, T.; Suryavanshi, P. A.; Menendez, J. C.; Sasai, H.; Sridharan, V. *Org. Biomol. Chem*. **2015**, *13*, 5175. https://doi.org/10.1039/C5OB00458F
23. Ahadi, S.; Abaszadeh, M.; Bazgir, A. *Mol. Diversity* **2012**, *16,* 299. https://doi.org/10.1007/s11030-012-9363-4
24. Heravi, M. M.; Baghernejad, B.; Oskooie, H. A. *Mol. Diversity* **2009**, *13,* 385. https://doi.org/10.1007/s11030-009-9122-3
25. Horcajada, R.; Batanero, B.; Barba, F.; Martin, A. *Tetrahedron Lett*. **2007**, *48*, 6437. https://doi.org/10.1016/j.tetlet.2007.07.065

26. Maertens, F.; Toppet, S.; Compernolle, F.; Hoornaert, G. J. *Eur. J. Org. Chem*. **2004**, *12*, 2707 https://doi.org/10.1002/ejoc.200400096
27. Basu, P.; Satam, N.; Namboothiri,I.N. N. *org. Biomol. Chem.* **2020**, *18*, 5677 https://doi.org/10.1039/D0OB01115K
28. Suresh, A.; Baiju, T.V.; Kumar, T.; Namboothiri, I. N. N. *J. Org. Chem.* **2019**, *84*, 3158 https://doi.org/10.1021/acs.joc.8b03039
29. Babu, K. R.; Khan, F. A. *Org. Biomol. Chem*. **2015**, *13*, 299 https://doi.org/10.1039/C4OB01977F
30. Nigam, R.; Babu, K. R.; Ghosh, T.; Kumari, B.; Subha, D. A.; Rath, N.; Das, P.; Roy, A.; Khan, F. A. *Bioorg. Med. Chem*. **2018**, *26*, 4100 https://doi.org/10.1016/j.bmc.2018.06.040
31. Nigam, R.; Babu, K. R.; Ghosh, T.; Kumari, B.; Das, P.; Roy, A.; Khan, F. A. *Chem. Biol. Drug. Des*. **2021**, *97* (6), 1170. https://doi.org/10.1111/cbdd.13839
32. Rollania Negi,R.; Jena,T, K.; Jyoti.; N.K.; Roy, A.; F. A. *Org. Biomol. Chem*. **2022**,*20*, 5820 https://doi.org/10.1039/D2OB00595F
33. Chen, X.; Engle, K.M.; Wang, D.; Yu, J.Q. *Angew. Chem*. **2009**, *48*, 5094 https://doi.org/10.1002/anie.200806273
34. Guillaumel, J.; Boccara, N.; Demerseman, P. *J. Heterocyclic Chem*. **1990**, *27*, (4), 1047 https://doi.org/10.1002/jhet.5570270444
35. Bullinton, J. L.; Dodd, J. H. *J. Org. Chem.* **1993**, *58*, 4833 https://doi.org/10.1021/jo00070a017
36. Moghaddam, S. K.; Shahvelayati, A. S.; Aliahmadi, A. *J. Chem. Health Risks* **2020**, *10*(1), 75. https://doi.org/10.22034/JCHR.2020.671485
37. Campo, M. A.; Larock, R. C. *J. Org. Chem*. **2002**, *67*, 5616 https://doi.org/10.1021/jo020140m
38. Wei, B.; Zhang, D.; Chen, Y.-H.; Lei, A.; Knochel, P. *Angew. Chem. Int. Ed*. **2019**, *58*, 15631 https://doi.org/10.1002/anie.201908046
39. Yamaguchi,S.; Uchiuzoh,Y.; Sanada. K. *J. Heterocyclic Chem*. **1995**, *32*, (2), 419 https://doi.org/10.1002/jhet.5570320207
40. Ameri, M.; Asghari, A.; Amoozadeh, A.; Bakherad, M.; Nematollahi, D. *Tetrahedron Lett*. **2015**, *56,* (17), 2141. https://doi.org/10.1016/j.tetlet.2015.03.049
41. Pandey, G.; Muralikrishna, C.; Bhalerao, U. T. *Tetrahedron Lett*. **1989**, *45,* (21), 6867. https://doi.org/10.1016/S0040-4020(01)89154-7
42. Sha, Q.; Liu, H. *Org. Biomol. Chem*. **2019**, *17*, 7547 https://doi.org/10.1039/C9OB01422E
43. Zinad, D.S; Villinger, A.; Langer, P. *Eur. J. Org. Chem***. 2011**, *22*, 4212 https://doi.org/10.1002/ejoc.201100313
44. Niimi, K.; Mori, M; Miyazaki, E.; Osaka, I.; Kakizoe, H.; Takimiya, K.; Adachi.C. *Chem. Commun*. **2012**, *48*, 5892 https://doi.org/10.1039/C2CC31960H
45. SunPeng, N.; Yifan, H.; Weimin, W.; HuZhenlu, M.B.; Hu, X. *Tetrahedron* **2015**, *71*, 4835 http://dx.doi.org/10.1016/j.tet.2015.05.029