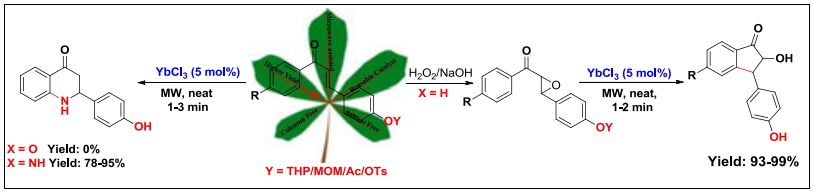
A Green, Solvent-Free, Microwave-Assisted, High-Yielding $YbCl_3$ Catalyzed Deprotection of THP/MOM/Ac/Ts Ethers of Chalcone Epoxide and 2′-Aminochalcone and Their Sequel Cyclization

Sumit Kumar,* Nishant Verma, Iram Parveen, and Naseem Ahmed*

Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee 247 667, India
*E-mail: sumitdcy@iitr.ac.in; nasemfcy@iitr.ac.in

Additional Supporting Information may be found in the online version of this article.
Received May 6, 2015
DOI 10.1002/jhet.2517
Published online 00 Month 2015 in Wiley Online Library (wileyonlinelibrary.com).



Under microwave and solvent-free conditions, $YbCl_3$ efficiently catalyzed the deprotection of tetrahydropyran-2-yl, methoxymethyl (MOM), acetyl, and tosyl groups and sequel cyclization of chalcone epoxide to 2-hydroxyindanone and 2′-aminochalcone to aza-flavanone. The reaction afforded the products in excellent yield (78–99%) at 850 W microwave heating within 1–5 min under eco-friendly conditions. The merits of the presented protocol include high yield, use of microwave irradiation, solvent-free condition, catalyst reusability, and no need for purification with column chromatography. The present method is very much milder but more advanced than those reported earlier.

INTRODUCTION

Protection and deprotection of hydroxyl groups have fundamental importance in the multi-steps organic syntheses. Among the various methods for protecting hydroxy groups, the formation of tetrahydropyranyl ethers is the most commonly employed method due to its easy formation and inertness to various reaction conditions like strong bases such as Grignard reagents, organolithium compounds, metal hydrides, catalytic hydrogenation, and alkylating and acylating conditions [1]. Likewise, methoxymethyl chloride (MOMCl), acetyl chloride/acetic anhydride (CH_3COCl/Ac_2O), and tosyl chloride (TsCl) are also important reagents for the alcoholic and phenolic groups protection. To avoid the product decomposition and loss of other functional groups during the reaction, efficient methods of deprotection are needed. Various methods have been reported for the deprotection of tetrahydropyranyl ethers that include protic acids [2a–d], $SnCl_4$ [2e], LiOTf [2f], $In(OTf)_3$ [2g], I_2 [2h], $InCl_3$ [2i], $ZrCl_3$ [2j], $CuCl_2$ [2k], NH_4Cl [2l], and other catalysts [2m–r]. Many catalysts have been used to remove the MOM group under acidic conditions such as using protic acids [3a], Lewis acids [3b], Lewis acid-thiol [3c], boron halides [3d], and other reagents in protic media or aprotic media [3e], CBr_4-PPh_3 [3f], $ZnBr_2$ [3g], and silica-supported $NaHSO_4$ [3h] and TMSOTf (TESOTf)-2,2′-bipyridyl [3i]. Several catalysts have been reported for the deacetylation and detosylation of alcohols and phenols under acidic and basic conditions including NaOMe [4a], micelles [4b], Zn-MeOH [4c], cyclodextrin [4d], enzymes [4e], metallo-enzyme [4f], metal complexes [4g], antibodies [4h], montmorillonite k-10 [4i], I_2 [4j], $NaBO_3$ [4k], and trifluoroacetic acid [4l]. These methods however have drawbacks such as long reaction time, low yields, high temperature, and excess amounts of reagents and tedious workup procedures. Hence, there is still scope to develop a milder and efficient method in the detetrahydropyranylation, demethoxymethylation, deacetylation, and detosylation of alcohols and phenols.

Our interest in protection–deprotection chemistry encouraged us to study the catalytic activity of rare earth metals in the deprotection functional groups. The utilization of $YbCl_3$ as deprotecting agent is rare, but it was used in a number of organic reactions such as in aldol reaction [5], Pictet–Spengler reaction [6], esterification [7], acetalisation [8], and Biginelli-type reaction in the synthesis of pyrimidinone [9].

Various reagents and reaction conditions have been previously employed for the cyclization of chalcones to aza-flavanones such as acids [10a], bases [10b–d], silica gel [10e–g], light [10h], electrolysis [10i], nanocrystalline MgO [10j], zeolites [10k], L-Proline [10l], $Yb(OTf)_3$ [10m,n], silica gel-supported $TaBr_5$ [10o], alumina supported-$CeCl_3.7H_2O$-NaI [10p], and microwave [10q,r]. Most of these procedures however have drawbacks; for example, in the preparation of aza-flavanones, low yield was obtained, and harsh reaction conditions were required. Therefore, $YbCl_3$ was screened as a catalyst for the deprotection of different functional groups and also the concomitant cyclization of chalcone epoxide to 2-hydroxyindanone

and 2′-aminochalcone to aza-flavanone under solvent-free microwave condition. Herein, we report a simple and efficient deprotection method for tetrahydropyran-2-yl (THP), MOM, Ac, and Ts groups in alcohol and phenol and sequel cyclization of chalcone epoxide to 2-hydroxyindanone and 2′-aminochalcone to aza-flavanone using $YbCl_3$ as catalyst under eco-friendly conditions.

RESULTS AND DISCUSSION

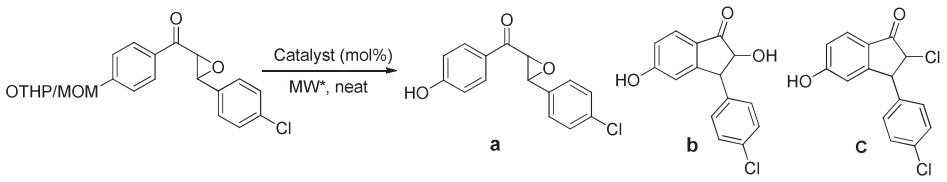
Initially, the catalytic efficiency of different metal halides was screened (Table 1). The metal halides (Table 1, entries 2–4, 6, 11, and 12) exhibited poor to moderate catalytic activity. $CeCl_3$ (Table 1, entry 12) was found to be a good catalyst at 10 mol% catalyst loading, which gave 75% yield of product **b** within 4 min. $CuCl_2$ and CuI_2 at 10 mol% catalyst loading yield 40–80% of product **a** without cyclization in 5–10 min (Table 1, entries 1 and 2). $InCl_3$ (Table 1, entry 11) at 10 mol% catalyst loading furnished moderate yield (67%) of product **b**. Other used metal halides failed to catalyze the reaction even prolonging the reaction time (Table 1). Then, catalyst optimization was achieved for the $YbCl_3$ catalyst. To optimize the catalyst loading, the reactions were carried out in 1, 2, and 5 mol% catalyst loadings under microwave irradiation (Table 1, entries 13–15). The reaction proceeded slowly with $YbCl_3$ at 1 mol% catalyst loading but, at 5 mol% loading, gave 99% yield of product **b** with deprotection of the THP and MOM ethers within 1 min (Table 1, entry 15). We also applied $CdCl_2$, $CoCl_2$, $FeCl_3$, and $ZnCl_2$ in 10 mol% catalysts loading, where we got the product **c** in 90–94% yields in 2 min.

We also screened solvents like CH_2Cl_2, $CHCl_3$, acetone, THF, dimethylformamide, 1,2-dimethoxy ethane, dimethyl sulfoxide, ethanol, and acetonitrile where CH_2Cl_2 gave the maximum yield (Table 2, entry 8). However, neat condition was found to give even better results with quantitative conversion (99%) under microwave condition. Despite the excellent results, we further explored other reaction conditions for the previous reaction in order to target the optimum protocol for the transformation. For example, neat grinding of substrate and $YbCl_3$ for 10 min at room temperature was carried out, but it resulted in non-detectable yield of the product (Table 2, entry 11). The reaction was also subjected to conventional heating; however, it resulted in 81% yield of the product (Table 2, entry 12).

Under optimized reaction conditions, the deprotection of THP/MOM, acetyl, and tosyl ethers was achieved

Table 1

Scope of different catalysts in deprotection of the tetrahydropyran-2-yl and MOM phenolic chalcone epoxide and sequel cyclization of 2-hydroxyindanone.

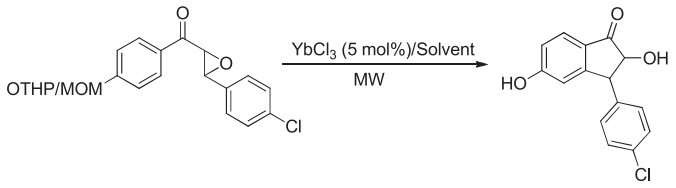


Entry	Catalyst	Mol%	Time (min)	Yield (%)[a] a	b	c
1	$CuCl_2$	10	10	84	—	—
2	CuI_2	10	5	40	20	—
3	NH_4Cl	10	10	55	5	—
4	$SnCl_2.2H_2O$	10	10	—	58	—
5	$SrCl_2$	10	10	—	—	—
6	$HgCl_2$	10	5	—	55	—
7	$CdCl_2$	10	2	—	—	90
8	$CoCl_2$	10	2	—	—	94
9	$FeCl_3$	10	2	—	—	93
10	$ZnCl_2$	10	2	—	—	91
11	$InCl_3$	10	5	10	67	20
12	$CeCl_3$	5	4	—	75	—
13	$YbCl_3$	1	2	—	69	—
14	$YbCl_3$	2	1	—	84	—
15	$YbCl_3$	5	1	—	99	—

General condition: substrate (1 mmol), $YbCl_3$, Anton Paar Monowave-300 reactor. Irradiation power: 850 W; ramp time: 1 min 70°C; holding temp: 120°C.
[a]Isolated yield.

Table 2

Scope of solvents on yields in deprotection of the tetrahydropyran-2-yl, MOM, Ac, and Ts ethers and sequel cyclization reaction.



Entry	Solvent	Condition	Time (min)	Yield (%)[b]
1	THF	MW[a]	2	57
2	Ethanol	MW[a]	5	5
3	Acetonitrile	MW[a]	3	30
4	Acetone	MW[a]	2	51
5	DMF	MW[a]	3	45
6	DME	MW[a]	3	42
7	DMSO	MW[a]	3	48
8	DCM	MW[a]	1	91
9	$CHCl_3$	MW[a]	1	86
10	Neat	MW[a]	1	99
11	Neat	Grinding	10	—
12	Neat	CH	6	81

General condition: substrate (1 mmol), $YbCl_3$ (5 mol%). THF, tetrahydrofuran; DMF, dimethylformamide; DME, 1,2-dimethoxy ethane; DMSO, dimethyl sulfoxide; CH, conventional heating; MW, microwave.
[a]Anton Paar Monowave-300 reactor. Irradiation power: 850 W; ramp time: 1 min 70°C; holding temp: 120°C.
[b]Isolated yield.

using 5 mol% of $YbCl_3$ within 1–5 min in excellent yields (82–99%) without interfering with the other functional groups present. In case of chalcones (Table 3, entries 5–14), only deprotection of THP/MOM was observed without cyclization. Interestingly, the deprotection of THP/MOM ethers followed by the Friedel–Crafts alkylation was observed for the chalcone epoxides (Table 3, entries 15–21) giving the corresponding 2-hydroxyindanones in excellent yields (91–99%) within 1–2 min. We also subjected tetrahydropyranyl tosylates to the same reaction protocol, which resulted in good yields (84–91%) in 4–5 min (Table 3, entries 22–26). All products were characterized by comparing their physical and spectral data with the available literature values [2e,4l].

The scope of $YbCl_3$ as catalyst was also tested for the cyclization of 2′-aminochalcone to their corresponding aza-flavanone. Under optimal reaction conditions, $YbCl_3$ catalyzed the isomerization of 2′-aminochalcones to the corresponding aza-flavanones in excellent yields (78–95%) within 1–3 min (Table 4).

In addition, the scope of the reaction was studied with 2′-aminochalcones bearing substituents on B ring from electron-donating to electron-withdrawing groups. As anticipated, electron-donating groups enhanced the cyclization to give the corresponding aza-flavanone in good yield while electron-withdrawing groups slow down the cyclization leading to moderate yield of aza-flavanone. In case of cyclization of 2′-hydroxychalcones to their corresponding flavanones, reaction did not proceed, and this might be due to poor nucleophilicity of the hydroxyl group under similar reaction conditions.

All the isolated products were confirmed by their IR, ^{1}H-NMR spectral analysis, and available literature data [10o,p]. For example, the ^{1}H-NMR spectra of *2-(3,4-dimethoxyphenyl)-2,3-dihydroquinolin-4(1H)-one* shows a doublet of doublets at 5.43 ppm due to –CH proton at 2-position and 2 doublet of doublets at 2.88–3.13 ppm due to CH_2 proton at 3-position, which is the characteristic of flavanone and peak of 1*H* at 12.17 ppm due to –NH in agreement with cyclization of 2′-aminochalcone to flavanone.

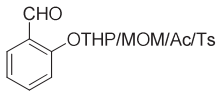
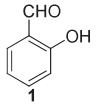
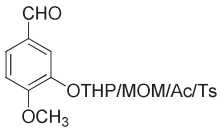
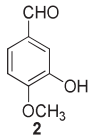
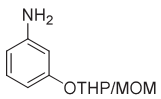
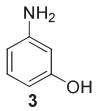
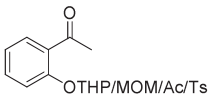
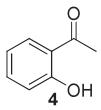
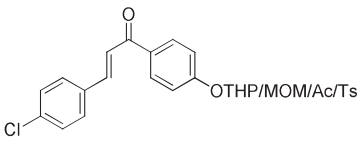
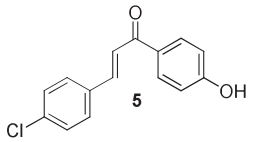
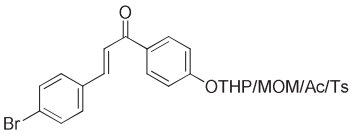
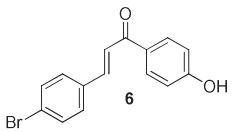
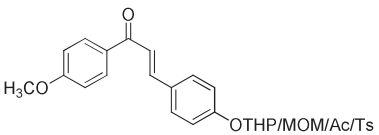
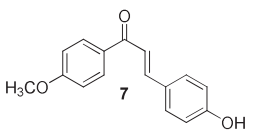
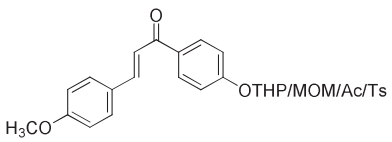
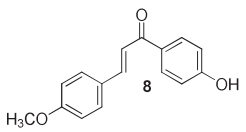
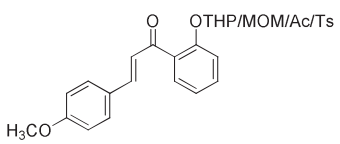
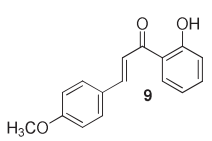
Recyclability of the catalyst in the reaction was also examined (Table 5). $YbCl_3$ was recovered by simple filtration from the reaction mixture, rinsed by CH_2Cl_2 and reused. The recycling of the catalysts was studied in *(E)-1-(2-aminophenyl)-3-phenylprop-2-en-1-one*. The recycled $YbCl_3$ showed good catalytic activity as the product **1a** obtained in 94%, 91%, 84%, 78%, and 71% yield in five successive runs, respectively.

A plausible reaction mechanism for the MOM ether deprotection and the simultaneous intramolecular Friedel–Crafts alkylation is depicted in Scheme 1 where $YbCl_3$ acts as a Lewis acid [11].

The coordination of $YbCl_3$ with MOM oxygen resulted in the removal of the methyl (methylene) oxonium group followed by Cl^- attack and the removal of MOMCl. At the same time, ligation of $YbCl_3$ took place with the

Table 3

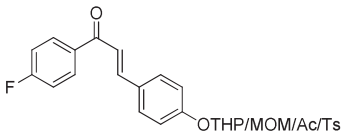
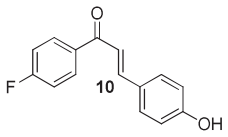
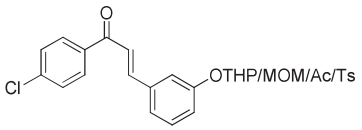
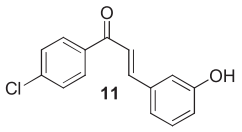
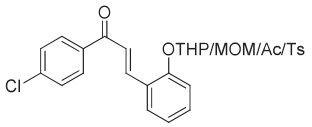
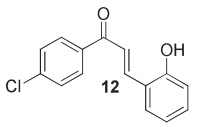
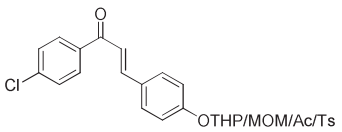
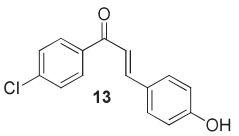
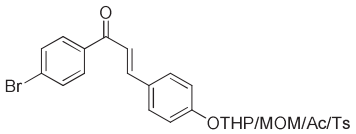
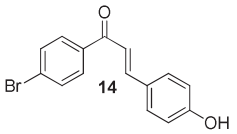
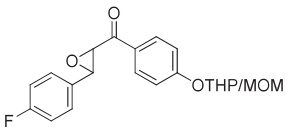
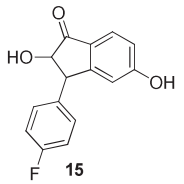
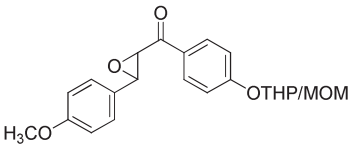
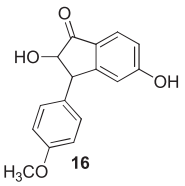
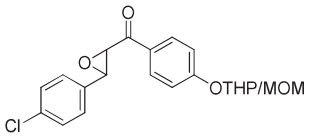
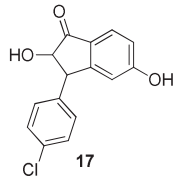
Substrate scope for deprotection and sequel cyclization of chalcone epoxides.

Entry	Substrate	Product	Time (min)	Yields (%)			
				a[a]	**b**[b]	**c**[c]	**d**[d]
1			1	98	97	99	97
2			1	94	95	98	96
3			1	95	93	—	—
4			1	93	92	98	91
5			2	95	94	97	92
6			1	92	95	98	97
7			1.5	93	96	94	95
8			1.5	94	96	94	94
9			2	94	94	97	95

(*Continued*)

Table 3

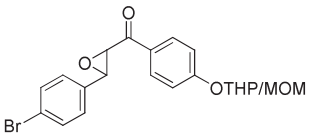
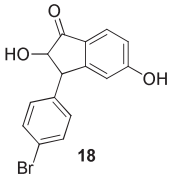
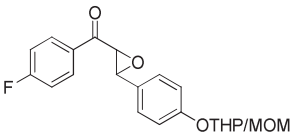
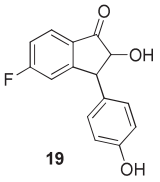
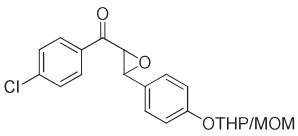
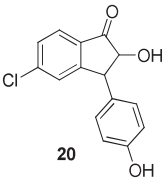
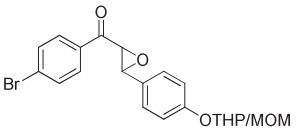
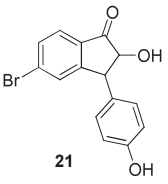
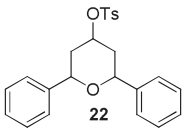
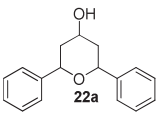
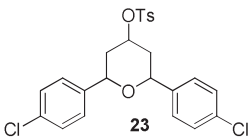
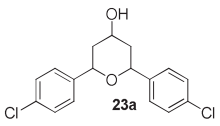
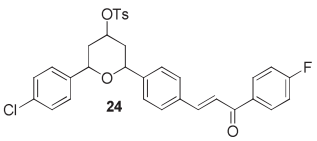
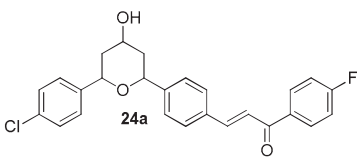
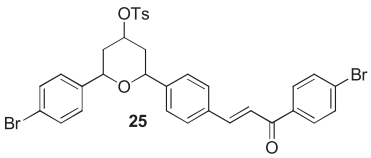
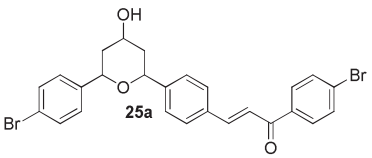
(*Continued*)

Entry	Substrate	Product	Time (min)	Yields (%)			
				a[a]	**b**[b]	**c**[c]	**d**[d]
10			1	91	92	95	93
11			1	95	94	96	92
12			1	96	91	93	97
13			1	93	97	94	96
14			1	97	98	96	92
15			2	98	95	—	—
16			1.25	92	92	—	—
17			1	99	97	—	—

(*Continued*)

Table 3

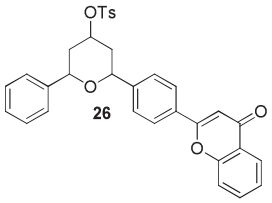
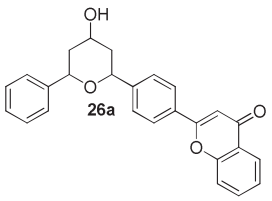
(*Continued*)

Entry	Substrate	Product	Time (min)	Yields (%)			
				a[a]	**b**[b]	**c**[c]	**d**[d]
18		 **18**	1	93	93	—	—
19		 **19**	1.5	94	91	—	—
20		 **20**	1	96	93	—	—
21		 **21**	1	99	95	—	—
22	 **22**	 **22a**	2	—	—	—	90
23	 **23**	 **23a**	4	—	—	—	88
24	 **24**	 **24a**	5	—	—	—	84
25	 **25**	 **25a**	5	—	—	—	85

(*Continued*)

Table 3

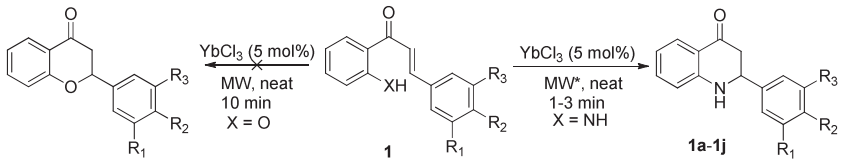
(*Continued*)

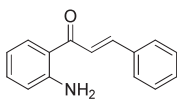
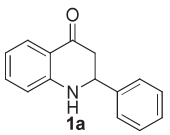
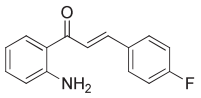
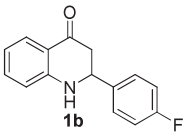
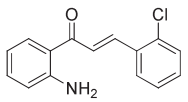
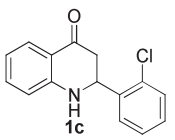
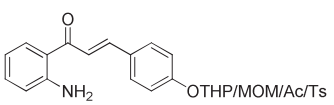
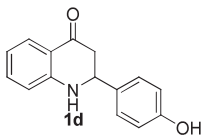
Entry	Substrate	Product	Time (min)	Yields (%)			
				a[a]	**b**[b]	**c**[c]	**d**[d]
26	 **26**	 **26a**	4.5	—	—	—	91

[a]Isolated yields from OTHP.
[b]Isolated yields from OMOM.
[c]Isolated yields from OAc.
[d]Isolated yields from OTs.

Table 4

$YbCl_3$ mediated oxidative cyclization of 2′-aminochalcones under solvent-free MW condition.

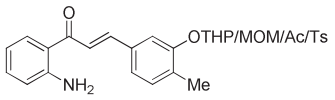
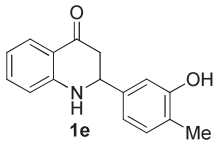
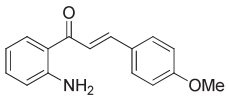
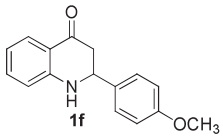
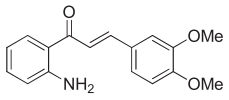
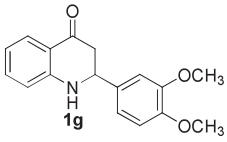
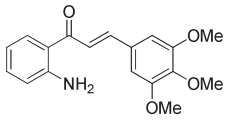
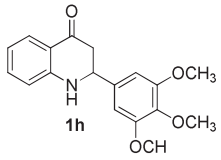
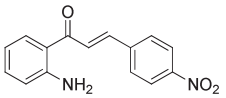
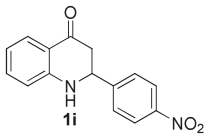
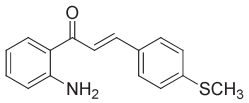
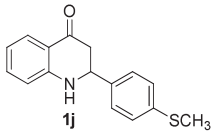


Entry	Substrate	Product	Time (min)	Yield (%)[a]
1		 **1a**	1.5	94
2		 **1b**	2	89
3		 **1c**	2	90
4		 **1d**	2.5	92,[b] 91,[c] 95,[d] 90[e]

(*Continued*)

Table 4

(*Continued*)

Entry	Substrate	Product	Time (min)	Yield (%)[a]
5			2	88,[b] 90,[c] 94,[d] 91[e]
6			1	95
7			0.75	93
8			1	91
9			2	78
10			1.5	88

General condition: substrate (1 mmol), $YbCl_3$ (5 mol%).
Anton Paar Monowave-300 reactor. Irradiation power: 850 W; ramp time: 1 min 70°C; holding temp: 120°C.
[a]Isolated yield.
[b]Yields from OTHP.
[c]Yields from OMOM.
[d]Yields from OAc.
[e]Yields from OTs.

epoxide oxygen, which resulted in faster epoxide ring opening from β-carbon due to considerable electron-deficient character at this particular position resulting in a five-membered ring that on hydrolysis gave the desired product.

CONCLUSIONS

In conclusion, we have devised a highly efficient protocol for the deprotection of THP, MOM, acetyl, and tosyl ethers in alcohols and phenols and sequel cyclization of chalcone epoxide to 2-hydroxyindanone and 2′-aminochalcone to aza-flavanone. The reaction gave the products in excellent yield (78–99%) at 850 W within 1–5 min. The catalyst can be recycled and reused in the same reaction efficiently. Some important features of the method include high yields, shorter reaction time, avoidance of use of organic solvents, reusability of $YbCl_3$ catalyst, easy workup, and eco-friendliness.

Scheme 1. A plausible mechanism for the MOM ether deprotection and sequel cyclization mediated by $YbCl_3$.

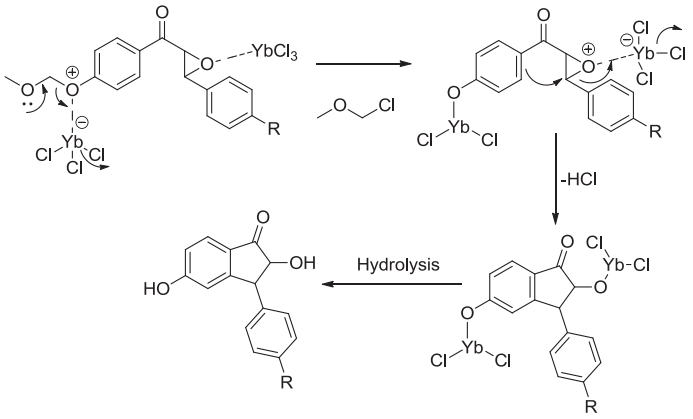


Table 5

Recycling and reusability of the catalyst.

Entry	Run	Time (min)	Yield (%)[a]
1	First	1.5	94
2	Second	1.5	91
3	Third	1.5	84
4	Fourth	1.5	78
5	Fifth	1.5	71

[a]Isolated yields.

EXPERIMENTAL

Unless otherwise noted, chemicals were purchased from commercial suppliers at the highest purity grade available and were used without further purification. Solvents were distilled by standard methods. Thin layer chromatography was performed on Merck (Germany) precoated 0.25 mm silica gel plates (60 F-254) using UV light as visualizing agent and/or iodine as developing agent. Silica gel (100–200 mesh) was used for column chromatography. IR spectra were recorded on Fourier transform IR spectrometer and expressed as wavenumbers (cm^{-1}). ^{1}H- and ^{13}C-NMR spectra were recorded on a Brüker (500 and 125 MHz; Bruker Avance, Fallanden, Switzerland) and Jeol (400 and 100 MHz; JEOL ECX, Japan) spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm) or with tetramethylsilane (δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from tetramethylsilane. ^{13}C-NMR spectra were referenced to $CDCl_3$ (δ 77.23 ppm, the middle peak). Coupling constants are expressed in hertz. The following abbreviations are used to explain the multiplicities: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; m, multiplet; br, broad. High-resolution mass spectra (HRMS) were obtained on a Brüker micrOTOF-Q II mass spectrometer (ESIMS).

Microwave irradiation experiment. All microwave experiments were carried out in a dedicated Anton Paar Monowave-300 reactor (Gaas, Austria), operating at a frequency of 2.455 GHz with continuous irradiation power of 0 to 850 W. The reactions were performed in a G-4 Borosilicate glass vial sealed with Teflon septum and placed in a microwave cavity. Initially, microwave of required power was used, and temperature was being ramped from room temperature to a desired temperature. Once this temperature was attained, the process vial was held at this temperature for required time. The reactions were continuously stirred. Temperature was measured by an IR sensor. After the experiments, a cooling jet cooled the reaction vessel to ambient temperature.

General procedure for the microwave-assisted deprotection of THP, MOM, acetyl, and tosyl ethers and sequel cyclization of chalcone epoxide and 2′-aminochalcone. Substrate (1 mmol) and $YbCl_3$ (14 mg, 5 mol%) were mixed well in a G-4 process vial capped with Teflon septum. After a pre-stirring for 1 min, the vial was subjected to microwave irradiation with the initial ramp time of 1 min at 70°C. The temperature was then raised to 120°C with the holding time of 1–5 min. The reaction was brought to room temperature, then crude product was dissolved in CH_2Cl_2 (10 mL), and the catalyst was filtered off and washed with CH_2Cl_2 (2 × 5 mL). The filtrate was washed with water (10 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. This, in most of the cases, was pure enough for spectral elucidation by ^{1}H-NMR and ^{13}C-NMR except in few cases (**24a**, **25a**, and **1i**).

Characterization data for representative compounds. ***(E)-3-(4-Chlorophenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one (5).*** ^{1}H-NMR ($CDCl_3$, 500 MHz, ppm) δ 7.99 (d, J = 8 Hz, 2H), 7.77 (d, J = 15.5 Hz, 1H), 7.63 (t, J = 8 Hz, 2H), 7.46 (d, J = 15.5 Hz, 1H), 7.10 (t, J = 8.5 Hz, 2H), 6.95 (d, J = 8 Hz, 2H), 5.38 (s, 1H, D_2O exchangeable). ^{13}C-NMR ($CDCl_3$, 125 MHz, ppm) δ 186.88, 162.05, 141.32, 131.41, 130.90, 130.83, 128.92, 121.85, 115.81, 115.21. IR (KBr,

ν_{max} = cm^{-1}): 3410, 2926, 2875, 1686, 1599, 1265, 1078, 862, 730. Gas chromatography/mass spectrometry (GC–MS) (*m/z*): 302 [$M^{+\cdot}$, $C_{15}H_{11}BrO_2$], 304 [M + 2].

(E)-3-(4-Bromophenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one (6). ^{1}H-NMR ($CDCl_3$, 500 MHz, ppm) δ 7.99 (d, *J* = 8 Hz, 2H), 7.77 (d, *J* = 15.5 Hz, 1H), 7.63 (t, *J* = 8 Hz, 2H), 7.46 (d, *J* = 15.5 Hz, 1H), 7.10 (t, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8 Hz, 2H), 5.48 (s, 1H, D_2O exchangeable). ^{13}C-NMR ($CDCl_3$, 125 MHz, ppm) δ 186.88, 162.05, 141.32, 131.41, 130.90, 130.83, 128.92, 121.85, 115.81, 115.21. IR (KBr, ν_{max} = cm^{-1}): 3410, 2926, 2875, 1686, 1599, 1265, 1078, 862, 730. GC–MS (*m/z*): 302 [$M^{+\cdot}$, $C_{15}H_{11}BrO_2$], 304 [M + 2].

(E)-3-(4-Hydroxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (7). ^{1}H-NMR ($CDCl_3$, 500 MHz, ppm) δ 8.03 (d, *J* = 8 Hz, 2H), 7.74 (d, *J* = 15.5 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 16 Hz, 1H), 7.38 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 9 Hz, 2H), 5.48 (s, 1H, D_2O exchangeable), 3.89 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz, ppm) δ 188.2, 163.9, 142.7, 131.4, 131.3, 130.1, 121.5, 116.8, 116.6, 114.2, 55.1. IR ν_{max} (KBr, cm^{-1}): 3410, 2928, 2880, 1684, 1599, 1265. GC–MS (*m/z*): 254 [M^+, $C_{16}H_{14}O_3$].

(E)-1-(4-Hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (8). ^{1}H-NMR ($CDCl_3$, 500 MHz, ppm) δ 8.03 (d, *J* = 8 Hz, 2H), 7.77 (d, *J* = 16 Hz, 1H), 7.55 (d, *J* = 8 Hz, 2H), 7.42 (d, *J* = 15.5 Hz, 1H), 6.98 (d, *J* = 8 Hz, 2H), 6.89 (d, *J* = 8 Hz, 2H), 5.82 (s, 1H, D_2O exchangeable), 3.89 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz, ppm) δ 188.7, 163.6, 142.8, 131.2, 131.0, 130.4, 121.7, 116.3, 116.2, 114.0, 55.7. IR (KBr, ν_{max} = cm^{-1}): 3410, 2926, 2875, 1686, 1599, 1265. GC–MS (*m/z*): 254 [M^+, $C_{16}H_{14}O_3$].

(E)-1-(2-Hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (9). ^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ 7.91–7.86 (m, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 15.6 Hz, 1H), 7.49–7.45 (m, 2H), 7.00 (dd, *J* = 1.2, 8.8 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 2H), 3.84 (s, 3H), 1.68 (s, 1H, D_2O exchangeable). ^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ 193.8, 163.7, 162.1, 145.5, 136.3, 130.7, 129.7, 127.4, 120.2, 118.9, 118.7, 117.7, 114.6, 55.6. IR (KBr, ν_{max} = cm^{-1}): 3410, 2926, 2875, 1686, 1599, 1265. GC–MS (*m/z*): 254 [M^+, $C_{16}H_{14}O_3$].

(E)-1-(4-Chlorophenyl)-3-(2-hydroxyphenyl)prop-2-en-1-one (11). ^{1}H-NMR ($CDCl_3$, 400 MHz, ppm) δ 7.92–7.84 (m, 2H), 7.64–7.58 (m, 3H), 7.53–7.49 (m, 1H), 7.41 (d, *J* = 8.8 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 7.2 Hz, 2H), 4.84 (s, 1H, D_2O exchangeable). ^{13}C-NMR ($CDCl_3$, 100 MHz, ppm) δ 193.6, 163.8, 144.1, 136.7, 133.2, 131.7, 130.0, 129.8, 129.5, 129.0, 120.7, 119.1, 118.9. IR (KBr, ν_{max} = cm^{-1}): 3410, 2926, 2875, 1686, 1599, 1265. GC–MS (*m/z*): 258 [M^+, $C_{15}H_{11}ClO_2$], 260 $[M + 2]^+$.

2,5-Dihydroxy-3-(4-methoxyphenyl)-2,3-dihydro-1H-inden-1-one (15). ^{1}H-NMR ($CDCl_3$, 500 MHz, ppm) δ 7.92 (dd, *J* = 1.5, 7 Hz, 2H), 7.55–7.52 (m, 2H), 7.07–7.01 (m, 3H), 5.31 (d, *J* = 2 Hz, 1H), 5.22 (d, *J* = 2 Hz, 1H), 4.19 (s, 1H, D_2O exchangeable), 3.91 (s, 3H), 1.61 (s, 1H, D_2O exchangeable). ^{13}C-NMR ($CDCl_3$, 125 MHz, ppm) δ 195.9, 162.6, 162.2, 136.8, 134.8, 131.4, 129.3, 128.9, 125.6, 116.7, 115.8, 75.4, 63.6, 53.7. IR (KBr, ν_{max} = cm^{-1}): 3408, 2925, 2879, 1685, 1595, 1266, 1089, 858, 731. GC–MS (*m/z*): 270 [M^+, $C_{16}H_{14}O_4$].

3-(4-Bromophenyl)-2,5-dihydroxy-2,3-dihydro-1H-inden-1-one (17). ^{1}H-NMR ($CDCl_3$, 500 MHz, ppm) δ 7.93 (m, 2H), 7.70–7.67 (m, 1H), 7.58–7.53 (m, 2H), 7.08–7.04 (m, 2H), 6.10 (s, 1H, D_2O exchangeable), 5.37 (d, *J* = 2 Hz, 1H), 5.22 (d, *J* = 2.5 Hz, 1H), 4.15 (s, 1H, D_2O exchangeable). ^{13}C-NMR ($CDCl_3$, 125 MHz, ppm) δ 195.6, 161.9, 137.4, 132.4, 131.9, 131.5, 130.0, 129.8, 126.0, 123.1, 116.3, 75.4, 63.6. IR (KBr, ν_{max} = cm^{-1}): 3433, 2935, 2877, 1687, 1585, 1266, 1088, 862, 733. GC–MS (*m/z*): 318 [M^+, $C_{15}H_{11}BrO_3$], 320 $[M + 2]^+$.

5-Chloro-2-hydroxy-3-(4-hydroxyphenyl)-2,3-dihydro-1H-inden-1-one (19). ^{1}H-NMR ($CDCl_3$, 500 MHz, ppm) δ 7.92 (m, 2H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.58–7.50 (m, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 5.36 (d, *J* = 1.5 Hz, 1H), 5.19 (d, *J* = 2 Hz, 1H), 4.13 (s, 1H, D_2O exchangeable), 1.81 (s, 1H, D_2O exchangeable). ^{13}C-NMR ($CDCl_3$, 125 MHz, ppm) δ 195.7, 162.4, 161.5, 136.7, 134.7, 131.4, 130.5, 129.4, 128.8, 125.3, 116.2, 75.4, 63.6. IR (KBr, ν_{max} = cm^{-1}): 3417, 2931, 2871, 1681, 1597, 1263, 1081, 860, 737. GC–MS (*m/z*): 274 [M^+, $C_{15}H_{11}ClO_3$], 276 $[M + 2]^+$.

5-Bromo-2-hydroxy-3-(4-hydroxyphenyl)-2,3-dihydro-1H-inden-1-one (20). ^{1}H-NMR ($CDCl_3$, 500 MHz, ppm) δ 7.91 (dd, *J* = 1, 8 Hz, 2H), 7.70–7.67 (m, 1H), 7.58–7.54 (m, 2H), 7.43 (t, *J* = 8.5 Hz, 2H), 6.10 (s, 1H, D_2O exchangeable), 5.38 (d, *J* = 2 Hz, 1H), 5.22 (d, *J* = 2.5 Hz, 1H), 4.15 (s, 1H, D_2O exchangeable). ^{13}C-NMR ($CDCl_3$, 125 MHz, ppm) δ 197.7, 163.9, 161.9, 134.5, 134.2, 133.6, 130.1, 130.0, 129.3, 128.7, 115.7, 76.1, 63.1. IR (KBr, ν_{max} = cm^{-1}): 3427, 2937, 2875, 1685, 1593, 1266, 1083, 864, 727. GC–MS (*m/z*): 318 [M^+, $C_{15}H_{11}BrO_3$], 320 $[M + 2]^+$.

2,6-Diphenyltetrahydro-2H-pyran-4-ol (22a). ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): δ 7.19–7.41 (m, 8H), 4.51–4.43 (m, 2H), 4.07 (tt, *J* = 4.5, 11.5 Hz, 1H), 2.28 (s, br, D_2O exchangeable, 1H, OH), 2.21 (dd, *J* = 4, 11.5 Hz, 2H), 1.53 (q, *J* = 11.5 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$, ppm): δ 131.4, 128.3, 127.5, 125.8, 77.8, 68.6, 42.9. IR (KBr, cm^{-1}): 3433, 2965, 2921, 2852, 1634, 1452, 1382, 1265, 1156, 1065, 900, 760, 700. GC–MS (*m/z*): 410 [M^+, $C_{17}H_{18}O_2$].

2,6-Bis(4-chlorophenyl)tetrahydro-2H-pyran-4-ol (23a). ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): δ 7.29–7.24 (m, 8H), 4.47 (d, *J* = 11.5 Hz, 2H), 4.06 (tt, *J* = 4.5, 11.5 Hz, 1H), 2.19 (dd, *J* = 4, 11.5 Hz, 2H), 1.48 (q, *J* = 11.5 Hz, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$, ppm): δ 139.2, 132.3, 127.5, 126.2, 77.8, 67.4, 41.9. IR (KBr, cm^{-1}): 3447, 2960, 2886, 1652, 1543, 1088, 804. GC–MS (*m/z*): 323 [M^+, $C_{17}H_{16}Cl_2O_2$].

(E)-3-(4-(6-(4-Chlorophenyl)-4-hydroxytetrahydro-2H-pyran-2-yl)phenyl)-1-(4-fluorophenyl)prop-2-en-1-one (24a). ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): δ 8.18 (d, *J* = 8 Hz, 1H), 7.95 (d, *J* = 8 Hz, 2H), 7.59 (d, *J* = 9 Hz, 3H), 7.48 (d, *J* = 8 Hz, 2H), 7.41 (d, *J* = 9 Hz, 2H), 7.36 (d, *J* = 8.5 Hz,

2H), 7.01 (d, $J = 9$ Hz, 2H), 4.66 (t, $J = 3$ Hz, 2H), 4.14 (tt, $J = 11$, 3 Hz, 1H), 2.22–2.85 (m, 2H), 2.04 (s, br, D_2O exchangeable, 1H), 1.73–1.84 (m, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$, ppm): δ 188.8, 166.7, 164.6, 144.6, 143.7, 140.8, 134.5, 134.3, 131.2, 130.0, 128.7, 127.7, 126.5, 125.9, 121.6, 115.9, 78.0, 77.7, 69.4, 40.0. IR (KBr, cm^{-1}): 3434, 3010, 2922, 2843, 1734, 1626, 1456, 1256, 1069, 808.8. HRMS (ESIMS): for $C_{26}H_{22}ClFNaO_3$ $(M + Na)^+$ *Anal.* Calcd 459.1139; found 459.1150.

(E)-1-(4-Bromophenyl)-3-(4-(6-(4-bromophenyl)-4-hydroxytetrahydro-2H-pyran-2-yl)phenyl)prop-2-en-1-one (25a). ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): δ 7.88 (d, $J = 8$ Hz, 2H), 7.82 (d, $J = 8.5$ Hz, 2H), 7.78 (s, 1H), 7.61–7.66 (m, 4H), 7.47 (s, 1H), 7.35 (d, $J = 8$ Hz, 2H), 7.31–7.32 (m, 2H), 4.45 (d, $J = 32$, 11.5 Hz, 2H), 4.07 (tt, $J = 10.5$, 3 Hz, 1H), 2.30–2.35 (m, 2H), 2.20 (s, br, D_2O exchangeable, 1H), 1.77–1.86 (m, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$, ppm): δ 189.8, 143.7, 140.7, 135.4, 134.4, 134.1, 129.8, 129.2, 128.5, 128.4, 127.8, 127.5, 126.2, 125.7, 122.0, 77.8, 77.4, 67.2, 39.8. IR (KBr, cm^{-1}): 3454, 2961, 2878, 1651, 1541, 1091, 801. HRMS (ESIMS): for $C_{26}H_{22}Br_2NaO_3$ $(M + Na)^+$ *Anal.* Calcd 562.9833; found 562.9853.

2-(4-(4-Hydroxy-6-phenyltetrahydro-2H-pyran-2-yl)phenyl)-4H-chromen-4-one (26a). ^{1}H-NMR (500 MHz, $CDCl_3$, ppm): δ 7.74 (d, $J = 8$ Hz, 2H), 7.37 (dd, $J = 6$, 3 Hz, 2H), 7.27 (d, $J = 8.5$ Hz, 2H), 7.17–7.21 (m, 3H), 7.15 (d, $J = 8.5$ Hz, 2H), 6.92 (s, 1H), 6.79 (dd, $J = 6.5$, 3 Hz, 2H), 4.40 (t, $J = 11.5$ Hz, 2H), 3.90 (tt, $J = 11$, 3 Hz, 1H), 2.15–2.22 (m, 2H), 1.68–1.77 (m, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$, ppm): δ 190.0, 163.0, 156.0, 139.8, 135.5, 134.1, 131.6, 129.9, 129.3, 128.6, 128.6, 127.6, 127.5, 126.3, 122.2, 121.8, 77.1, 76.9, 65.0, 39.8, 39.7. IR (KBr, cm^{-1}): 3446, 2971, 2880, 1652, 1513, 1208, 799. HRMS (ESIMS): for $C_{26}H_{21}NaO_4$ $(M + Na)^+$ *Anal.* Calcd 421.1416; found 421.1441.

2-(3,4-Dimethoxyphenyl)-2,3-dihydroquinolin-4(1H)-one (1g). ^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 12.17 (s, 1H, D_2O exchangeable), 7.93 (d, $J = 10$ Hz, 1H), 7.51 (t, $J = 10.5$ Hz, 1H), 7.01–7.08 (m, 4H), 6.91 (d, $J = 10$ Hz, 1H), 5.43 (dd, $J = 16.5$, 2.5 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.13 (dd, $J = 21$, 17 Hz, 1H), 2.88 (dd, $J = 21$, 2.5 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 192.2, 161.6, 149.4, 149.3, 136.2, 131.2, 127.1, 120.9, 121.6, 118.8, 118.2, 111.1, 109.4, 79.6, 56.0, 55.9, 44.6. IR (KBr, cm^{-1}): 3110, 2837, 1687, 1598, 1026. GC–MS (*m/z*): 283 [M+, $C_{17}H_{17}NO_3$].

2-(2-Chlorophenyl)-2,3-dihydroquinolin-4(1H)-one (1c). ^{1}H-NMR (500 MHz, $CDCl_3$, ppm) δ 11.34 (s, 1H, D_2O exchangeable), 8.58 (d, $J = 6$ Hz, 1H), 7.87 (dd, $J = 10$, 2.5 Hz, 1H), 7.75–7.79 (m, 1H), 7.59 (d, $J = 10$ Hz, 1H), 7.44–7.48 (m, 1H), 7.26–7.29 (m, 1H), 6.98–7.03 (m, 2H), 5.60 (dd, $J = 13.5$, 6.5 Hz, 1H), 3.06–3.16 (m, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$, ppm) δ 191.2, 160.8, 157.1, 148.4, 138.3, 136.2, 127.1, 123.8, 121.9, 121.4, 121.2, 118.1, 79.1, 42.8. IR (KBr, cm^{-1}): 3164, 2926, 1693, 1606, 1462, 1305, 763. GC–MS (*m/z*): 257 [M^+, $C_{15}H_{12}ClNO$], 259 $[M + 2]^+$ (Supporting Information).

Acknowledgments. Financial support from DST and BRNS and award of JRF to S.K. and N.K. by the CSIR and I.P. by the UGC, New Delhi, India, are gratefully acknowledged.

REFERENCES AND NOTES

[1] Hajipour, A. R.; Kargosha, M.; Ruoho, A. E. Synth Comm 2009, 39, 1084.

[2] (a) Tamami, B.; Parvanak, K. Tetrahedron Lett 2004, 45, 715; (b) Namboodiri, V. V.; Varma, R. S. Tetrahedron Lett 2002, 43, 1143; (c) Babu, B. S.; Balasubramanian, K. Tetrahedron Lett 1998, 39, 9287; (d) Reddy, P. N.; Sunil, B. K.; Kumar, P. S.; Srinivasulu, N. Y.; Reddy, T.; Rajitha, B. Chem Heterocycl Compd 2005, 41, 11; (e) Ahmed, N.; Pathe, G. K.; Babu, B. V. Tetrahedron Lett 2014, 55, 3683; (f) Karimi, B.; Maleki, J. Tetrahedron Lett 2002, 43, 5353; (g) Mineno, T. Tetrahedron Lett 2002, 43, 7975; (h) Ranu, B. C.; Saha, M. J Org Chem 1994, 59, 8269; (i) Haraldsson, G. G.; Baldwin, J. E. Tetrahedron 1997, 53; (j) Tanemura, K.; Haraguchi, T.; Suzuki, T. Bull Chem Soc Jpn 1992, 65, 304; (k) Kumar, H. M. S.; Reddy, B. V. S.; Reddy, E. J.; Yadav, J. S. Chem Lett 1999, 28, 857; (l) Yadav, J. S.; Srinivas, D.; Reddy, G. S. Synth Commun 1998, 28, 1399; (m) Matthew, K. K.; Waymouth, R. M. Organometallics 2010, 29, 6051; (n) Akai, S.; Tanaka, R.; Hoshi, H.; Sato, K. I. J Org Chem 2013, 78, 8802; (o) Syam, S.; Abdelvahab, S. I.; Mamary, M. A.; Syam, M. Molecule 2012, 17, 6179; (p) Sabhita, G.; Yadav, J. S.; Rajkumar, M.; Babu, R. Org Lett 2001, 3, 1149; (q) Rigby, J. H.; Wilson, J. Z. Tetrahedron Lett 1984, 25, 1429; (r) William, D. R.; Sakdarat, S. Tetrahedron Lett 1983, 24, 3965.

[3] (a) Amano, S.; Takemura, N.; Ohtsuka, M.; Ogawa, S.; Chida, N. Tetrahedron 1999, 55, 3855; (b) Sharma, G. V. M.; Reddy, K. L.; Lakshmi, P. S.; Krishna, P. R. Tetrahedron Lett 2004, 45, 9229; (c) Kieczykowski, G. R.; Schlessinger, R. H. J Am Chem Soc 1978, 100, 1938; (d) Paquette, L. A.; Gao, Z.; Ni, Z.; Smith, G. F. Tetrahedron Lett 1997, 38, 1271; (e) Keith, J. M. Tetrahedron Lett 2004, 45, 2739; (f) Peng, Y.; Ji, C.; Chen, Y.; Huang, C.; Jiang, Y. Synth Commun 2004, 34; (g) Hana, J. H.; Kwona, Y. E.; Sohnb, J.-H.; Ryua, D. H. Tetrahedron 2010, 66, 1673; (h) Ramesh, C.; Ravindranath, N.; Das, B. Org Chem 2003, 68, 7101; (i) Fujioka, H.; Kubo, O.; Senami, K.; Minamitsuji, Y.; Maegawa, T. Chem Comm 2009, 4229.

[4] (a) Otera, J. Chem Rev 1993, 93, 1449; (b) Kunitake, T.; Okahata, Y.; Sakamoto, T. J Am Chem Soc 1976, 98, 7799; (c) Gonzalez, A. G.; Jorge, Z. D.; Dorta, H. L.; Rodriguez, F. L. Tetrahedron Lett 1981, 22, 335; (d) Tee, V. S.; Mazza, C.; Zano-Hemmer, R. L.; Giorgi, I. B. J Org Chem 1994, 59, 7602; (e) Parmer, V. S.; Prasad, A. K.; Sharma, N. K.; Bisht, K. S.; Pati, H. N.; Taneja, P. Bioorg Med Chem Lett 1993, 3, 585; (f) Crampton, M. R.; Holt, K. E.; Perey, J. M. J Chem Soc 1990, 2, 1701; (g) Boisselier, V. L.; Postel, M.; Dunach, E. Tetrahedron Lett 1997, 38, 2981; (h) Guo, J.; Huang, W.; Scanlan, T. S. J Am Chem Soc 1994, 116, 8062; (i) Bandgar, B. P.; Uppalla, L. S.; Sagar, A. D.; Sadavarte, V. S. Tetrahedron Lett 2001, 42, 1163; (j) Das, B.; Banerjee, J.; Ramu, R.; Pal, R.; Ravindranath, N.; Ramesh, C. Tetrahedron Lett 2003, 44, 5465; (k) Bandgar, B. P.; Uppalla, L. S.; Patil, V. S. S. New J Chem 2003, 5, 68; (l) Ahmed, N.; Konduru, N. K.; Ahmad, S.; Owais, M. Eur J Med Chem 2014, 75, 233.

[5] Lou, S.; Westbrook, J. A.; Schaus, S. E. J Am Chem Soc 2004, 126, 11440.

[6] Srinivasan, N.; Ganesan, A. Chem Commun 2003, 916.

[7] Clarke, P. A. Tetrahedron Lett 2002, 43, 4761.

[8] Luche, J.-L.; Gemal, A. L. J Chem Soc, Chem Comm 1978, 22, 976.

[9] Zhang, H.; Zhou, Z.; Yao, Z.; Xu, F.; Shen, Q. Tetrahedron Lett 2009, 50, 1622.

[10] (a) Kulkarni, P.; Wagh, P.; Zubaidha, P. Chem J 2012, 2, 106; (b) Aitmambetov, A.; Kubzheterova, A. Russ J BioorgChem 2002, 28, 165; (c) Tanka, K.; Sugino, T. Green Chem 2001, 3, 133; (d) Mondal, R.; Das Gupta, A.; Mallik, A. K. Tetrahedron Lett 2011, 52, 5020; (e)

Ahmed, N.; Ali, H.; van Lier, J. E. Tetrahedron Lett 2005, 46, 253; (f) Sagrerai, G. J.; Seoane, G. A. J Braz Chem Soc 2005, 16, 851; (g) Li, J. J.; Jin, L. Y.; Yu, C. M.; Su, W. K. J Chem Res 2009, 3, 170; (h) Maki, Y.; Shimada, K.; Sakoand, M.; Hirota, K. Tetrahedron 1988, 44, 3187; (i) Sanicanin, Z.; Tabakovic, I. Tetrahedron Lett 1986, 27, 407; (j) Choudary, B.; Ranganath, K. V. S.; Yadav, J.; Kantam, M. L. Tetrahedron Lett 2005, 46, 1369; (k) Climent, M. J.; Corma, A.; Iborra, S.; Primo, J. J Catal 1995, 151, 60; (l) Chandrasekhar, S.; Vijeender, K.; Reddy, K. V. Tetrahedron Lett 2005, 46, 6991; (m) Rao, V. K.; Rao, M. S.; Kumar, A. J Heterocyclic Chem 2011, 48, 1356; (n) Genovese, S.; Fiorito, S.; Specchiulli, M. C.; Taddeo, V. A.; Epifano, F. Tetrahedron Lett 2015, 56, 847; (o) Ahmed, N.; Van Lier, J. E. Tetrahedron Lett 2006, 47, 2725; (p) Ahmed, N.; van Lier, J. E. Tetrahedron Lett 2007, 48, 13; (q) Patonay, T.; Varma, R. S.; Vass, A.; Levai, A.; Dudas, J. Tetrahedron Lett 2001, 42, 1403; (r) Kabalka, G. W.; Mereddy, A. R. Tetrahedron Lett 2005, 46, 6315.

[11] Murakami, M.; Kadowaki, S.; Fujimoto, A.; Ishibashi, M.; Matsuda, T. Org Lett 2005, 7, 2059.