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SnCl4 or TiCl4: Highly efficient catalysts for detetrahydropyranylation and demethoxymethylation of phenolic ethers and sequel one-pot asymmetric synthesis of 3-aryl-2-hydroxy-2,3-dihydroindan-1-ones from chalcone epoxides

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ARTICLE

$SnCl_4$ or $TiCl_4$: Highly efficient catalysts for detetrahydropyranylation and demethoxymethylation of phenolic ethers and sequel one-pot asymmetric synthesis of 3-aryl-2-hydroxy-2,3-dihydroindan-1-ones from chalcone epoxides

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Abstract: *$SnCl_4$ or $TiCl_4$ catalysts provided a rapid and efficient detetrahydropyranylation and demethoxymethylation of phenolic ethers and sequel one-pot intramolecular Friedel-Crafts alkylation of chalcone epoxides under mild reaction conditions. The reaction took 2-3 min to give the phenols and 1-indanones in excellent yield (90-98%) at 0 °C without affecting other functional groups. With these catalysts, our protocol gave regioselective products as trans-3-aryl-2-hydroxy-1-indanones in excellent yield (76-98%) and enantiomeric excess up to 99.9% under the same conditions.*

Introduction

Protection and deprotection of functional groups are the most frequently used strategies in the multi-step organic synthesis. In particular, the protection and deprotection of the hydroxyl group is extremely important because of its enormous demand for the synthesis of a number of compounds of biological and synthetic interest such as carbohydrates, macrolides, peptides, steroids, nucleotides and polyethers.[1] Protection of the hydroxyl group with 3,4-dihydro-2*H*-pyran (DHP) and methoxymethyl chloride (MOMCl) is the most frequently used method due to the stability of the resulting 2-tetrahydropyranyl ethers (THPEs) and the methoxymethyl ethers (MOMEs) respectively in the presence of strong bases or nucleophiles such as Grignard reagents, organolithium compounds, metal hydrides, catalytic hydrogenation, alkylating and acylating agents.[2,3]

Conversely, the deprotection of THP and MOM ethers required efficient methods to avoid decomposition and/or loss of other functional groups in the product under harsh reaction conditions. Therefore, many catalysts are explored for the detetrahydropyranylation of alcohols and phenols include protic acids,[4] Lewis acids such as BF_3-etherate,[5] LiBr,[6] $LiBF_4$,[7] LiOTf,[8] $LiClO_4$,[9] $Sc(OTf)_3$,[10] $In(OTf)_3$,[11] I_2,[12] $InCl_3$,[13] $ZrCl_4$,[14] $CuCl_2$,[15] and salt NH_4Cl,[16] expansive graphite,[17] clay materials,[18] silica-supported sulfuric acid,[19] and other miscellaneous catalysts.[20-26] Similarly, many catalysts are used for the demethoxymethylation of alcohols and phenols; these catalysts include HCl, BBr_3, pyridinium *p*-toluene sulphonate under strong acidic condition, mild Lewis acids $ZnBr_2$, and $TiCl_4$ in aprotic conditions and BBr_3 derivatives like Me_2BBr, and $(i\text{-PrS})_2BBr$.[27] Most of these methods have different drawbacks such as long reaction time, low yields, reflux at high temperature and tedious workup procedures. Hence, there is still scope to develop more straightforward and efficient methods in the deprotection of tetrahydropyranyl and methoxymethyl ethers.

Indan-1-one and indan-2-one derivatives are important moieties in the core structures of many natural products, agrochemicals and medicines[28] including indacrinone,[28a-c] indanoyl isoleucine conjugates,[28d] indanocines,[28e] quadranglularin A,[28f,g] parthenocissin A,[28h,i] (+)-pauciflorol F,[29] norditerpene taiwaniaquinol B,[30] sulindac, NSAID,[31a-c] NMDA receptor antagonists,[31d] benzodiazepines,[31e] melatonin precursor,[31f,g] and neoflavonoids[32,33] (Figure 1). They are also reported from higher plants such as *Uvaria afzelii roots*,[34] *Pteridium aquilinum*[34c] and *Equisetum arvense*[34d] and screened for various biological activities including cancer and Alzheimer's diseases. 2-(Alkoxycarbonyl)- and 2-acetyl-1-indanones are present in cytotoxic natural compound pterosines,[28,29] a potent and selective COX-2 inhibitor flosulide,[30,32] and the acetylcholinesterase inhibitor donepezil hydrochloride.[30] They are approved by US-FDA for the treatment of mild to moderate Alzheimer's disease.[29] Similarly, the enantiomerically pure derivative, 1-amino-2-indanol is a key precursor of the chiral ligand and the chiral auxiliary for asymmetric synthesis of indinavir, a potent inhibitor of the protease of human immunodeficiency virus (HIV)[35] and Detrol LA (tolterodine tartrate), a muscarine receptor antagonist used for the treatment of urinary bladder disorder.[36a,b]

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Electronic supplementary information (ESI) available:[details of any supplementary information should be available here]. Experimental procedures, characterization data and ^1H, ^{13}C NMR spectra associated with this article are available

The Indan-1-one bearing carboxylate scaffold is also used a peroxisome proliferator activated receptor γ (PPARγ) agonist in the treatment of type-2 diabetes.[36c]

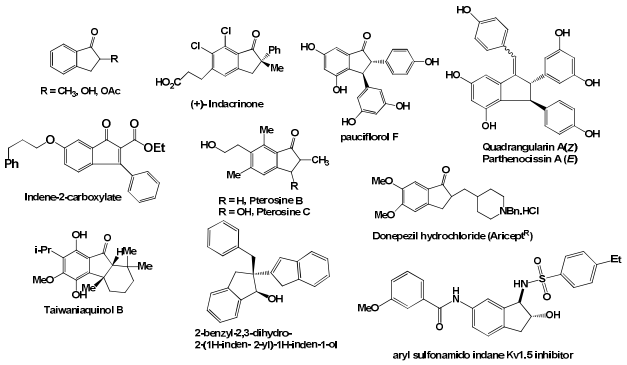


Figure 1. Bioactive indan-1-one derivatives.

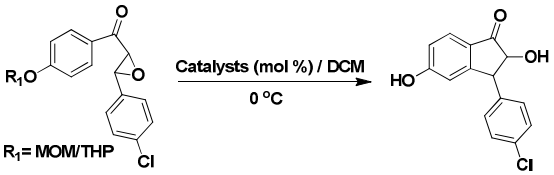
Therefore, a number of synthetic methods have been reported that include intramolecular Friedel-Crafts alkylation,[37] Nazarov cyclization,[38,39] tandem Knoevenagel condensation-cycloalkylation,[40] Heck & Negishi coupling,[41] Larock annulations[42] and ring-closing metathesis[43] reactions under different Lewis acids such as SbF_5,[44a] $AlCl_3$,[44b] and $TiCl_4$.[45-51] The Friedel-Crafts reactions were carried out at high temperature and in strong acidic conditions. Similarly, enantioselective indanones synthesis required multi-step reaction and high catalyst loading for the 3-substituted indanone derivatives.[32]

In continuation of our interest to developed a novel methodologies by using different Lewis acid catalysts.[53] Herein, we report an efficient deprotection method of THP and MOM ethers and sequel Friedel-Crafts alkylation reaction in the stereoselective synthesis of functionalized 3-aryl 2-hydroxy-1-indanone derivatives catalyzed by a highly efficient $SnCl_4$ catalyst at 0 ^oC (Table 1). In comparison with other methods, our protocol gave high yields (76-98%) with excellent regioselective products (up to 99.9% ee) in short reaction time (2-3 min).

Results and Discussion

Inspection of table 1 reveals the catalytic efficiency of different metal halides. The metal halides (Table 1, entries 1-6) exhibited poor to moderate catalytic activity. However, $InCl_3$ (Table 1, entry 7) has shown better activity at 10 mol% catalyst loading, which gave the cyclized products in 90% yield without deprotecting the THP and the MOM ethers. However, $SnCl_4$ and $TiCl_4$ (Table 1, entry 10,12) were found to be the most efficient catalysts at 10 mol% catalyst loading and gave the products in 90-98% yield along with deprotection of the THP and the MOM ethers in one-pot reaction within 2-3 min under the same conditions (Table 1, entry 10, 12). We also used SnI_4 and $SnBr_4$ in 5, 10, and 20 mol% catalysts loading during the deprotection of the THP and the MOM ethers however gave the products in 5-10% yield after stirring for 2-6 h at *0 ^oC* (Table 1).

Table 1. Optimization of catalysts in the synthesis of indanones via one-pot deprotection and cyclization reaction



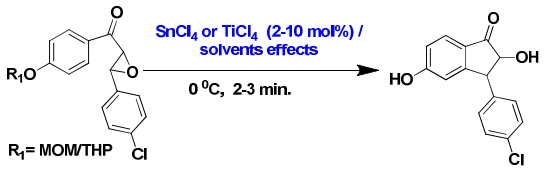
Entry	Catalyst	Loading (mol%)	Rxn.Time	Yield (%)
1	$SbCl_3$	10	20-24 h	28 [a]
2	$SbCl_5$	10	20-24 h	20 [a]
3	$MgCl_2$	10	18-24 h	18 [a]
4	$ZrCl_4$	10	10-15 h	10 [a]
5	$SnBr_4$	10	6 h	10[b]
6	SnI_4	10	6 h	7 [b]
7	**$InCl_3$**	**10**	**4-5 h**	**90[a]**
8	$SnCl_4$	2	30 min	45 [b]
9	$SnCl_4$	5	15 min	65 [b]
10	**$SnCl_4$**	**10**	**2 min**	**98** [b]
11	$InCl_3$	20	1 min	70+20[c]
12	**$TiCl_4$**	**10**	**2 min**	**98** [d]

[a]Gave only cyclization product. [b,d] Gave both THP & MOM ethers deprotection and sequel cyclization, [c] Side product as 3-(4-chlorophenyl)-2-chloro-2,3-dihydro indan-1-one (20%).

To optimize the reaction conditions, the catalysts ($InCl_3$, $SnCl_4$ and $TiCl_4$) loading were carried out in 2, 5, 10 and 20 mol% (Table 1, entries 8-12) in CH_2Cl_2 .$SnCl_4$ at 2 and 5 mol% loading proceeded slowly, whereas at 20 mol% loading gave the side product as *3-(4-chlorophenyl)-2-chloro-2,3-dihydroindan-1-one* (20%), which was isolated and characterized by GC-MS.

Table 2 shows solvent effects using acetone, chloroform, dichloromethane and tetrahydrofuran where $CHCl_3$ and CH_2Cl_2 were found to be the desired solvents (Table 2, entries 4, 6).

Table 2 Solvent effects on yields in the deprotection of THP and MOM ethers



Entry	Mol%	Solvents	Yield (%)
1	2	Acetone	40[a]
2	5	Acetone	45[a]
3	5	DCM	80[b]
4	**10**	**DCM**	**98[b]**
5	5	$CHCl_3$	85[c]
6	**10**	**$CHCl_3$**	**96[c]**
7	5	THF	52[d]

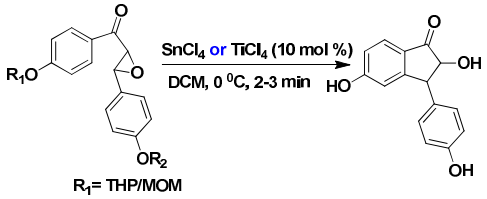
8	10	THF	60[d]

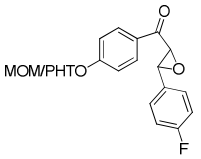
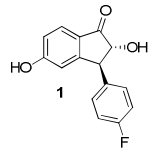
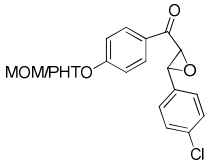
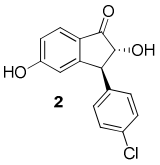
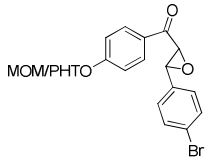
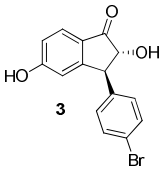
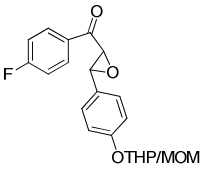
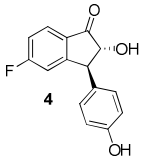
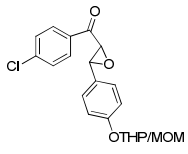
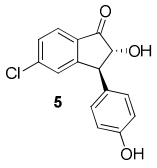
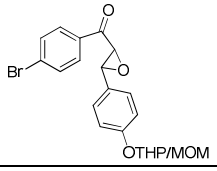
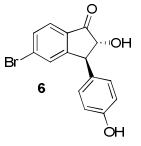
Reaction time: [a]2h, [b,c] 3 min, [d] 3h.

Table 3 reveals that the THP and MOM removal followed by the Friedel-Crafts alkylation was observed for the chalcone epoxides which gave the corresponding indanone derivatives **1- 6** in excellent yield (90-98%) within 2-3 min. at 0 ^{o}C (Table 3, entries 1-6). The products were characterized on the basis of their spectral analysis ^{1}H-, ^{13}C-NMR, GCMS (see supporting information).

One-pot deprotection of the phenolic THP and MOM ethers followed by Friedel-Crafts alkylation reaction gave the indanones in 90-98% yield at 10 mol% catalyst loading ($TiCl_4$ or $SnCl_4$) within 2-3 min at 0 ^{0}C. The presence of other functional groups was fully tolerated under optimized conditions. However, in the alcoholic THP and MOM ethers, 20 mol% catalyst loading gave only 10 and 25% yield respectively (Tables 3, entry 7). However, the chalcones **12**-**19** only THP and MOM removal was observed, but no intramolecular Friedel-Crafts alkylation. The products were characterized by comparing their physical and spectral data with literature value (Table 3, entries 7-19, see supporting information).

Table 3 Examples of the THP and MOM ethers deprotection and sequel cyclization reaction



Entry*	ROTHP/MOM	ROH	Time (min)	Yield (%)[a]	Yield (%)[b]
1			3	96	93
2			2	98	98
3			2	95	94
4			3	96	93
5			3	95	92
6			2	92	92

[a] yield (1-19) from R-OTHP and [b] yield (1-19) from R-OMOM ethers deprotection. *Table 3, entries 7-19, see supporting information.

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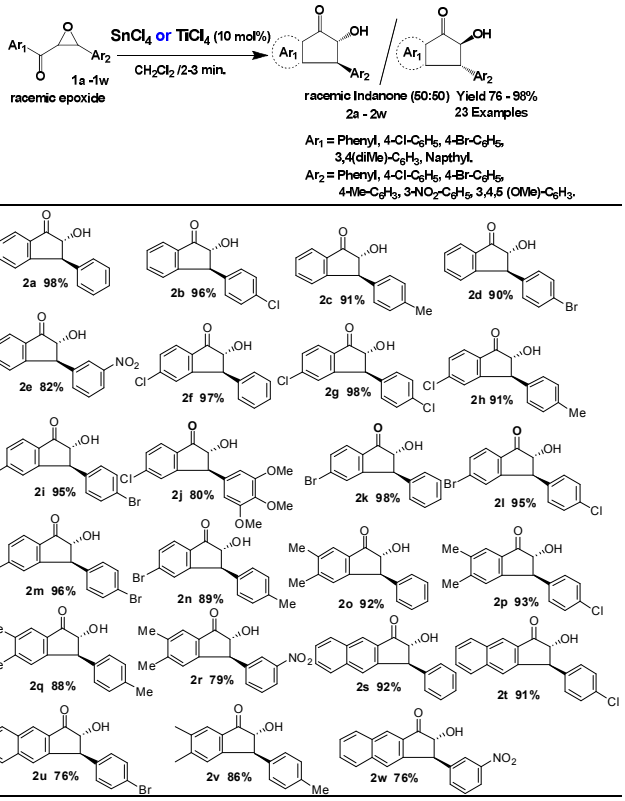
Inspection of Table 4 reveals that in racemic indanone synthesis, following a simple experimental procedure (given in the experimental section), trans-chalcone epoxides **1a-1w** was dissolved in CH_2Cl_2 by stirring and $SnCl_4$ or $TiCl_4$ was added in portion and stirred at 0 ^{0}C for 2-3 min. After usual work up, the trans-3-aryl-2-hydroxy-2, 3-dihydroindan-1-ones **2a-2w** was obtained in 76-98% yields (Table 4).

For example, in the synthesis of racemic indanone **2b** (table 4) chiral HPLC purification gave peaks at 26.9 (50%) and 35.4 (50%) min. for diastereomers (see experimental section).The assigned structures of the chalcone epoxides **1a-1w** and the products **2a-2w** were confirmed on the basis of their spectral analysis (IR, ^{1}H and ^{13}C-NMR, and GC–MS/HRMS) and also compared with the reported data in the literature. The *trans*-stereochemistry of epoxides **1a-1w** were confirmed by the coupling constants of the α- & β-protons. For example, (*4-chlorophenyl)-3-(4-bromophenyl)oxiran-2-yl-methanone* (**1i**), the ^{1}H NMR (500 MHz) δ (ppm): 4.07 (d, *J* = 2.0 Hz, β-*H*, 1H), 4.21 (d, *J* = 2.0 Hz, α-*H*, 1H), in which the *J*-values (2.0 Hz) indicate a *trans*-substituted epoxide. Similarly, the *trans*-configuration of 2-hydroxy-2,3-dihydro indan-1-ones **2a-2w** were confirmed by the coupling constants of the α-& β-protons. For example, *trans-3-(4-bromophenyl)-5-chloro-2-hydroxy-2,3-dihydroindan-1-one* (**2i**), the ^{1}H NMR (500 MHz) δ (ppm) at 5.15 (d, *J* = 2.0 Hz, β-*H,* 1H), 5.31 (d, *J* = 2.0 Hz, α-*H,* 1H), in which the *J*-values (2.0 Hz) indicate a *trans*-configuration (Lee et al., 2011). In the case of electron donating (Table 4, entry **2j**) and electron withdrawing groups on ring-Ar_2 (Table 4, entries **2e**, **2r**, **2w**) the reaction at 0 ^{o}C gave the decomposed products. Therefore, the reactions were carried out by lowering the temperature (-20 ^{o}C) to obtain the desired products.

Table 4. Synthesis of 3-aryl-2-hydroxy-1-indanones from racemic chalcone epoxides[a, b, c]



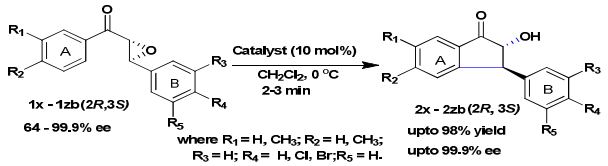
Epoxides and 2-hydroxyindan-1-ones are racemic compounds and are shown as a single enantiomeric derivative (*trans*- configuration). [b] Reaction of **2e**, **2j**, **2r**, **2w** were carried out at – 20 °C and others are at 0 ^{0}C using 10 mol% of $SnCl_4$. [c] Isolated yield of racemic 2-hydroxy indan-1-ones.

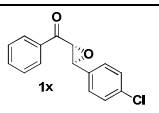
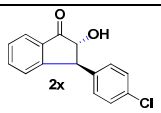
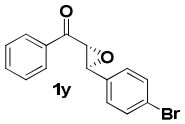
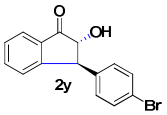
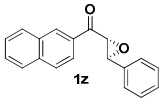
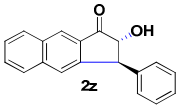
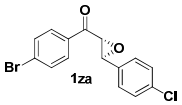
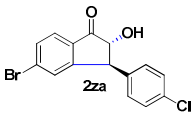
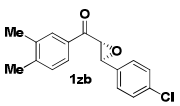
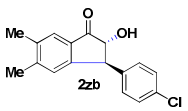
Table 5 clearly shows that during stereoselective synthesis of indanones, first we synthesized diastereoisomerically excess *trans* (2*R*,3S)-chalcone epoxides (**1x-1zb**) from the corresponding chalcone with α,α'-diphenyl-L-prolinol and TBHP in hexane which gave good yield (58%) with 64-99.9% enantiomeric excess. Epoxides were characterized by comparing with the literature values and enantiomeric excess was determined by chiral HPLC column and optical rotation in chloroform[54] (see in supporting information). The epoxide ring opening followed by intramolecular Friedel-Crafts alkylation was performed in the presence of $TiCl_4$ or $SnCl_4$ to obtain the enantiomerically excess *trans* (2*R*, 3S)-indanone derivatives **2x-2zb** (Table 5). The enantiomeric excess of indanones was again determined by chiral HPLC column and optical rotation in chloroform (see in experimental section). In general, indanones were obtained in 90-98% yields with 64-99.9% ee (Table 6, supporting information). It was observed that the ring opening of epoxides in the presence of the metal halides, the configuration at C-2 position is retained while C-3 position is changed due to S_N2-like mechanism to obtain regio- and stereoselective intramolecular Friedel-Crafts alkylation. The protons at C-2 and C-3 positions are in *trans*-orientation which was confirmed by the coupling constant (*J* =

2.0 Hz) in ^{1}H NMR spectrum. Therefore, the absolute configurations at C-2 and C-3 were confirmed as 2*R* and 3*S* respectively.

Table 5 and 6 show that the assigned structures of enantiomerically excess *trans*-chalcone epoxides **1x-1zb** and the products **2x-2zb** were confirmed on the basis of their spectral analysis (^{1}H- & ^{13}C-NMR and chiral HPLC) and also compared with those reported data. For example, *trans-3-(4-chlorophenyl)-2-hydroxy-2,3- dihydroindan-1-one* (**2x**) gave the ^{1}H NMR (500 MHz) δ (ppm) at 5.36 (d, *J* = 2.0 Hz, 1H, -CO-C*H*-) and 5.21 (d, *J* = 2.0 Hz, -C*H*-Ar-,1H), in which the *J*-values indicate a *trans*-configuration. The ^{13}CNMR spectrum gave peaks at δ 197.49 ppm for the characteristic carbonyl carbon, 62.95 ppm for Ar-*CH*-CH, and 75.89 ppm for Ar-CH-*CH*-CO- of indanone ring carbon. Since diastereoselective epoxide **1x** gave peaks at 54.7 min (13%) and 58.7 min (87%), the major peak correlated with the retention time of the reported literature[54]. Therefore, the configuration is confirmed as 2*R* and 3*S*. We also took diastereoselective indanone **2x** (Table 5) which gave peaks at 27.9 min (13.9%) and 36.9 min (86.1%) (HPLC chromatogram in the supporting information). This retention time match those of racemic indanone (**2b**). Similarly, all other compounds **2y**- **2zb** were confirmed on the basis of their analytical data.

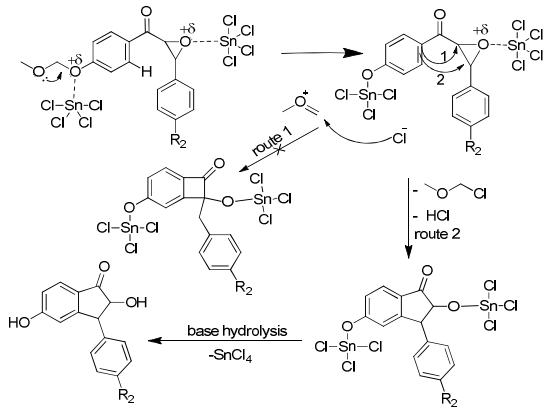
Table 5. Synthesis of Enantioselective 3-aryl-2-hydroxy-1-indanones. [a,b,c]



Entry	Epoxide	Indanone	Yield (%)[b]	ee (%)[a] Confign.
1	 74% ee; (2*R*,3*S*)		98	72.2% (2*R*,3*S*)
2	 77.6% ee; (2*R*,3*S*)		90	75% (2*R*,3*S*)
3	 64.8% ee; (2*R*,3*S*)		92	64.8% (2*R*,3*S*)
4	 >99.9% ee;(2*R*,3*S*)		95	>99.9% (2*R*,3*S*)
5	 66.8% ee; (2*R*,3*S*)		93	66.8% (2*R*,3*S*)

[a] enantiomeric excess (ee) was determined by chiral HPLC column and found to be equivalent to literature data, [b]isolated yields. [c]Reactions are carried out at 0 °C for 2-3 min. HPLC conditions and retention times of racemic and de of the indanonone derivatives is given in Tables 6(supporting information).

Scheme 3 shows the stereoselectivity and high yields for 1-indanones under acidic condition ($TiCl_4$ or $SnCl_4$) might be due to the variable oxidation state and availability of relatively low energy 5d-orbitals on tin. A proposed reaction mechanism is shown in the Scheme 3, where ligation of $SnCl_4$ with the MOM oxygen resulted in the removal of the methyl (methylene) oxonium group followed by its reaction with Cl^- generated the MOMCl. Similarly, epoxide oxygen ligation might change the tetrahedron structure of $SnCl_4$ into trigonal bipyramide/octahedron structure. The geometry changes enhanced the steric hindrance which results in the faster epoxide ring opening from *β*-carbon due to considerable electron deficient character at benzylic position. Therefore, mostly the nucleophile attack took place at β-carbon of carbonyl group. Finally, a base hydrolysis produces $SnCl_4$ which is used in the next catalytic cycle.



Scheme 3: Proposed mechanism for the deprotection of MOM ethers followed by cyclization with $SnCl_4$

Conclusions

In conclusion, we developed a novel and highly efficient catalytic protocol for the detetrahydropyranylation and demethoxymethylation of phenolic ethers and stereoselective synthesis of trans-2-hydroxy-3-aryl-1-indanone derivatives by sequential ring opening of chalcone epoxides and intramolecular Friedel-Crafts alkylation in the presence of $SnCl_4$ or $TiCl_4$. This method has advantages such as (i) mild protocol (ii) excellent yield (up to 98%) with high regio and stereoselectivity (up to 99.9% ee) (iii) short reaction time (2-3 min) and (iv) easy work-up procedure. To the best of our knowledge, $SnCl_4$ and $TiCl_4$ have not been studied in this capacity before and therefore represent a novel subject for investigation.

Experimental Section

General methods

Organic solvents were dried by standard methods; the reagents (chemicals) were purchased from commercial sources, and used withoutfurther purification. All reactions were monitored by TLC using precoated silica gel aluminum plates. Visualization of TLC plates was accomplished with an UV lamp. Column chromatography was performed using silica gel 60–120 mesh size (RANKEM Limited) with EtOAc–hexanes as eluent. Melting points were recorded on

Perfit apparatus and are uncorrected. All products were characterized by NMR, IR and MS spectra. 1H and 13C NMR spectra were recorded in deuterated chloroform ($CDCl_3$) on a 500 MHz and 125 MHz spectrometer (Bruker), respectively. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br).

General Procedure for the deprotection of THP and MOM Ethers in alcohols and phenols followed by cyclization to indanones:

$SnCl_4$ **or** $TiCl_4$ (10 mol %) was added to a stirred solution of **1a -1w** & **THP/MOM** ethers (1 mmol) in CH_2Cl_2 (5 mL) at 0 ^oC. After TLC monitoring, the reaction mixture was poured in 10 % aqueous Na_2CO_3 solution and extracted with CH_2Cl_2. The combined organic layer was washed with brine solution, dried with anhyd. Na_2SO_4 and concentrated in *vacuo* to give the corresponding alcohol or phenol, which was purified by silica gel column chromatography with hexane-EtOAc eluent to obtain the products **2a -2w** & **1 to 19** in excellent yield (80-98%).

2.2.1 Trans-(2R, 3S)-3-(4-Chlorophenyl)-2-hydroxy-2, 3-dihydroindan-1-one (2x): Light yellow solid; Yield: 745 mg (98%); m.p = 188-190°C; IR ν_{max} (KBr, cm^{-1}): 3408 (OH str), 2917 (aromatic C-H str), 1689 (C=O str), 1589 (aromatic, C=C str), 1489, 1415, 1288, 1177, 1091, 1014, 929 and 701; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 7.92 (d, *J* = 7.5 Hz, 2 H, H_{Ar}), 7.69 (d, *J* = 7.0 Hz, 1 H, H_{Ar}), 7.56 (t, *J* = 7.0 Hz, 2 H, H_{Ar}), 7.49 (d, *J*=7.5 Hz, 2 H, H_{Ar}), 7.35 (d, *J* = 7.0 Hz, 1 H, H_{Ar}), 5.36 (d, *J* = 2.0 Hz, 1 H, H2), 5.21 (d, *J* = 2.0 Hz, 1 H, H3), 4.13 (s, br, D_2O exchangeable, 1 H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 197.4 (C=O), 136.6, 134.8, 134.4, 133.5, 129.4, 129.2, 128.7, 128.5, 75.9 (C2), 62.9 (C3); MS (EI, 70eV): m/z (%) = 258(17) [M^+, $C_{15}H_{11}ClO_2$], 242(28), 207(36), 179(43), 165(32), 135(57), 130(61), 105(100), 89(49), 77(61), 75(55) and 51(62);HRMS (ESI-TOF) calcd for $C_{15}H_{11}ClO_2$ 258.0448, found 258.0450;The absolute configuration was determined by comparison with the optical rotation reported for the $[\alpha]_D^{25}$ = -16.4 (c 1.0, $CHCl_3$) and chiral HPLC using Chiralcel OD-H column.

2.2.2 Trans-(2R, 3S)-3-(4-Bromophenyl)-2-hydroxy-2, 3-dihydroindan-1-one (2y): Light yellow solid; Yield: 546 mg (90%); m.p = 183-185°C; IR ν_{max} (KBr, cm^{-1}): 3434 (OH str), 2924 (aromatic C-H str), 1670 (C=O str), 1588 (aromatic, C=C str), 1485, 1413, 1288, 1177, 1071, 930, 703 and 545; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 7.91 (d, *J* = 7.5 Hz, 2 H, H_{Ar}), 7.57 (t, *J* = 7.0 Hz, 1 H, H_{Ar}), 7.50 (d, *J* = 7.0 Hz, 2 H, H_{Ar}), 7.43 (d, *J* = 7.0, 2.0 Hz, 2 H, H_{Ar}), 7.24 (m, 1 H, H_{Ar}), 5.35 (d, *J* = 2.0 Hz, 1 H, H2), 5.19 (d, *J* = 2.0 Hz, 1 H, H3), 4.13 (s, br, D_2O exchangeable, 1 H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ(ppm): 197.3 (C=O), 136.6, 134.6, 134.2, 133.4, 129.3, 129.3, 128.6, 128.4, 76.0 (C2), 62.5 (C3); MS (EI, 70eV): m/z (%) = 302(16) [M^+, $C_{15}H_{11}BrO_2$], 196(55), 169(45), 139(73), 105(100), 89(47), 77(54), 63(49) and 51(66);HRMS (ESI-TOF) calcd for $C_{15}H_{11}BrO_2$ 301.9942, found 301.9940;The absolute configuration was determined by comparison with the optical rotation reported for the $[\alpha]_D^{25}$ = -8.8 (c 1.2, $CHCl_3$) and chiral HPLC using Chiralcel OD-H column.

*2.2.3 Trans-(2R, 3S)-2-Hydroxy-3-phenyl-2, 3-dihydrocyclo penta [b]naphthalen-1-one (2z):*Light yellow solid; Yield: 757 mg (92%); m.p = 114-116°C; IR ν_{max} (KBr, cm^{-1}): 3395 (OH str), 2951, 2848 (aromatic C-H str), 1677 (C=O str), 1580 (aromatic, C=C str), 1247, 1092, 842; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ(ppm): 8.45 (m, 1 H, H_{Ar}), 7.99 (m, 2 H, H_{Ar}), 7.85 (m, 1 H, H_{Ar}), 7. 65 (t, *J* = 7.0 Hz, 1 H, H_{Ar}), 7.60 (m, 3 H, H_{Ar}), 7.39-7.34 (m, 3 H, H_{Ar}), 5.57 (d, *J* = 2.0 Hz, 1 H, H2), 5.32 (d, *J* = 2.0 Hz, 1 H, H3), 4.19 (s, br, D_2O Exchange-able, 1H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 197.7 (C=O), 138.2, 136.0,132.4, 130.9, 130.5, 129.7, 129.3, 129.2, 128.8, 128.6, 128.0, 127.9, 127.3, 123.9, 76.2 (C2), 64.1 (C3); MS (EI, 70eV): m/z (%) = 274 (12) [$M^{+\cdot}$, $C_{19}H_{14}O_2$], 256 (15), 110 (100);HRMS (ESI-TOF) calcd for $C_{19}H_{14}ClO_2$ 274.0994, found 274.0995;The absolute configuration was determined by comparison with the optical rotation reported for the $[\alpha]_D^{25}$ = -3.5 (c 0.12, $CHCl_3$) and chiral HPLC using Chiralcel AD-H column.

2.2.4 Trans-(2R, 3S)-3-(4-Chlorophenyl)-5-bromo-2-hydroxy-2,3-dihydroindan-1-one (2za):Light yellow solid; Yield: 641mg (95%); m.p = 205-207°C; IR ν_{max} (KBr, cm^{-1}): 3422 (OH str), 3087 (aromatic C-H str), 1678 (C=O str), 1583 (aromatic, C=C str), 1404, 1278, 1169, 1091, 830, 752 (C-Br, str); ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 7.89 (m, 2 H, H_{Ar}), 7.56-7.50 (m, 3 H, H_{Ar}), 7.41 (m, 2 H, H_{Ar}), 5.31 (d, *J* = 2.0 Hz, 1 H, H2), 5.16, (d, *J* = 2.0 Hz, 1 H, H3), 4.04 (s, br, D_2O exchangeable, 1 H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 196.6 (C=O), 136.3, 134.9, 132.6, 132.3, 129.8, 129.4, 128.8, 75.9 (C2), 62.8 (C3); MS (EI, 70eV): m/z (%) = 336(30) [$M^{+\cdot}$, $C_{15}H_{10}ClBrO_2$], 185(79), 183 (100), 125(49);HRMS (ESI-TOF) calcd for $C_{15}H_{10}BrClO_2$ 335.9553, found 335.9555;The absolute configuration was determined by comparison with the optical rotation reported for the $[\alpha]_D^{25}$ = -10.1 (c 0.26, $CHCl_3$) & chiral HPLC using Chiralcel AD-H column.

2.2.5 Trans-(2R, 3S)-3-(4-Chlorophenyl)-2-hydroxy-5, 6-dimethyl-2,3-dihydroinden-1-one (2zb):Light yellow solid; Yield: 533 mg (93%); m.p =116-118°C; IR ν_{max} (KBr, cm^{-1}): 3412 (OH str), 2952, 2847 (aromatic C-H str), 1675 (C=O str), 1609 (aromatic, C=C str), 1225, 1091, 842, 762; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ (ppm): 7.71 (m, 1 H, H_{Ar}), 7.61 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 7.50 (m, 2 H, H_{Ar}), 7.33 (m, 1 H, H_{Ar}),7.28 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 5.25 (d, *J* = 2.0 Hz, 1 H, H2), 5.14 (d, *J* = 2.0 Hz, 1 H, H3), 4.10 (s, br, D_2O exchangeable, 1 H), 2.36(s, 3H), 2.35 (s, 3H); ^{13}C-NMR ($CDCl_3$, 125 MHz) δ (ppm): 197.1 (C=O), 144.4, 137.9, 136.9, 134.6, 131.1, 130.3, 129.7, 129.4, 128.7, 126.1, 75.6 (C2), 63.2 (C3), 20.2, 19.9; MS (EI, 70eV): m/z (%) = 286(10) [$M^{+\cdot}$, $C_{17}H_{15}ClO_2$], 268 (20), 122 (100); HRMS (ESI-TOF) calcd for $C_{17}H_{15}ClO_2$ 286.0761, found 286.0763;The absolute configuration was determined by comparison with the optical rotation reported for the $[\alpha]_D^{25}$ = -9.5 (c 0.57, $CHCl_3$) and chiral HPLC using Chiralcel AD-H column.

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Keywords: $SnCl_4$ or $TiCl_4$ catalyst/ Chalcone epoxide ring opening/ THP and MOM ethers/ Intramolecular Friedel-Crafts alkylation/ Trans-3-aryl-2-hydroxy-2,3-dihydroindan-1-ones.

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GRAPHICAL ABSTRACT

$SnCl_4$ or $TiCl_4$: Highly efficient catalysts for detetrahydropyranylation and demethoxymethylation of phenolic ethers and sequel one-pot asymmetric synthesis of 3-aryl-2-hydroxy-2,3-dihydroindan-1-ones from chalcone epoxides

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