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Enantioselective enzymatic desymmetrization of prochiral 1,3-diols and enzymatic resolution of monoprotected 1,3-diols based on α-tetralone and related multifunctional scaffolds

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ABSTRACT

Novel multifunctional chemotypes based on α-tetralone, α-indanone, and chromanone have been synthesized by a chemo-enzymatic approach by applying an enzymatic irreversible transesterification strategy. The scaffolds synthesized can be further elaborated with subsequent enzymatic as well as chemical transformations for the generation of new sets of structurally related organic molecules.

1. Introduction

In recent years, much of the pharmaceutical industry has moved away from natural products research, focusing instead on increasingly narrow regions of chemical structure space which correspond to existing orally bioavailable synthetic drugs. The quest for natural products such as molecules with drug-like libraries is increasing day by day. These natural product-like molecules offer the advantages of easy synthesis and access to analogues, however, the library members are skeletally diverse, structurally complex, stereochemically rich, and densely functionalized. The Diversity-Oriented Synthesis (DOS) has emerged as a powerful approach to obtain complex molecules for biological studies.[1] The utility of DOS relies on the development of chemical methodologies for the synthesis of novel structural types with high levels of skeletal and stereochemical complexity.[2] Polyketide and terpenoid natural products possess a broad range of biological activities and both stereochemical and skeletal diversity, and have served as an inspiration for complex chemical library design.[3] Combinatorial biocatalysis is one of the tools of Diversity-Oriented Synthesis (DOS), which uses enzymes as efficient catalyst for the generation of a small molecule library based on a small molecular scaffold.[4] Although biotransformations have become an established method in organic chemical synthesis,[5] biocatalysis could, from organic chemist's perspective, have a much bigger impact in this area.

In our combinatorial biocatalysis project, we need to design and synthesize various small molecular multifunctional scaffolds which will lead us to a natural product-like library after biocatalytic modification. We choose chromanone and α-tetralone-based scaffolds as there are already many natural products based on chromanone (flavonoids and homoisoflavonoids) and α-tetralone.[6] We have designed and synthesized the α,α-bishydroxymethylated derivative of α-tetralone and chromanone mainly due to the following reasons: (a) the bishydroxymethyl group was chosen mainly to adopt a EED (enzymatic enantioselective desymmetrization) strategy to generate a quaternary stereocenter adjacent to the keto functionality; (b) the keto functionality can be further converted to numerous functionalities by an array of biocatalytic transformations (ketoreduction, transamination, and hydrocynation to name a few); and (c) finally, the existing aromatic ring can undergo a biocatalytic oxidation reaction with arene di-oxygenase type enzymes to generate further diversity (Scheme 1).

2. Results and discussion

2.1. Synthesis of bishydroxymethylated tetralone and chromanones

The bishydroxymethyl group was introduced via base-catalyzed condensation reaction with formalin and the parent tetralone or chromanone. When a methanolic solution of the parent tetralone and chromanone was treated with K_2CO_3 and excess formalin, the required bishydroxymethylated compounds were obtained in excellent yields (80–94% yield).[7] Commercially available tetralones are used, whereas chromanones are synthesized as follows: Properly substituted phenols are alkylated with 3-bromopropionic acid in the presence of NaH in DMF to afford the acids in moderate yield.[8] Acids were treated with oxalyl chloride in DCM to yield the acid chlorides, the acid chlorides were then subjected to ring closure on treatment with $SnCl_4$ to afford the required chromanones in good yield (Scheme 2).[9]

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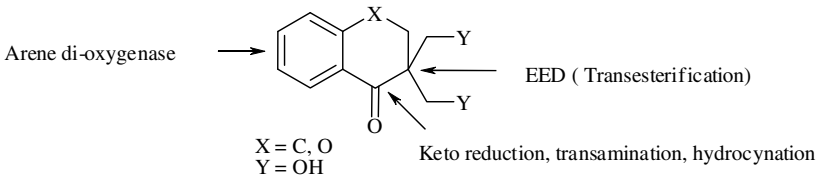
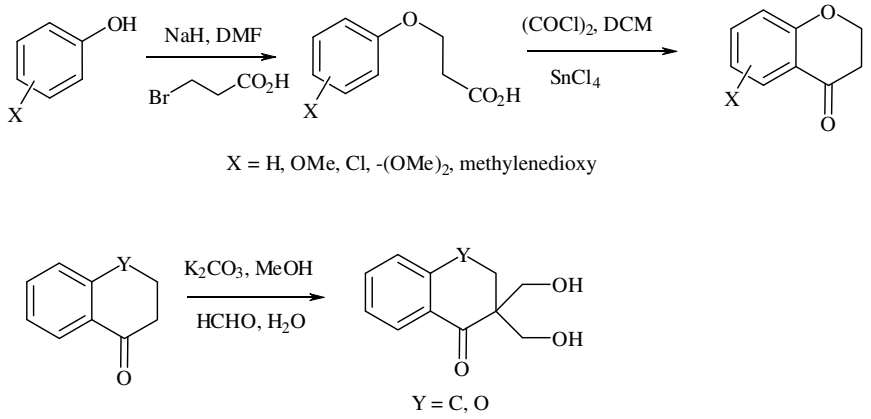


Scheme 1. Multifunctional small molecular scaffolds based on tetralone and chromanone.



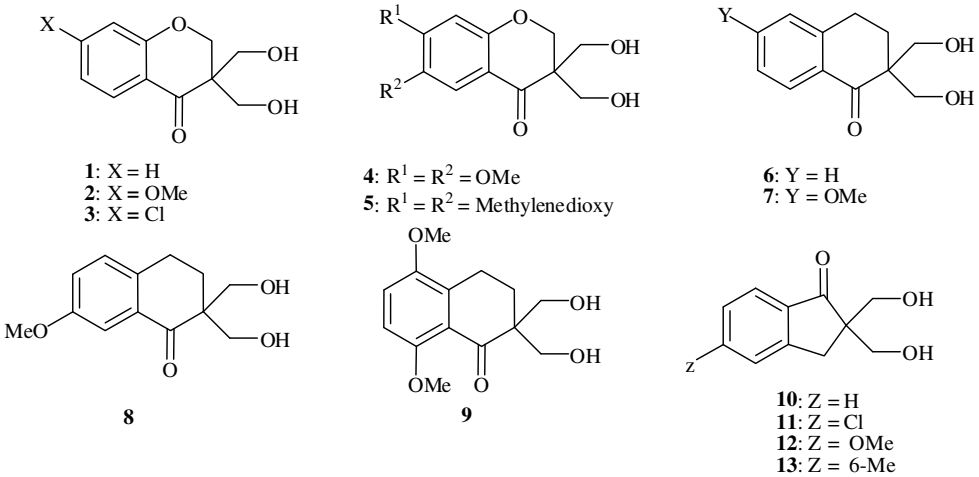
Scheme 2. Synthesis of chromanones and bishydroxymethylated derivative of chromanone and tetralone.

We have also taken four commercially available 1-indanones and synthesized the respective bishydroxymethyl derivatives to access more chemotypes based on the indanone scaffold.

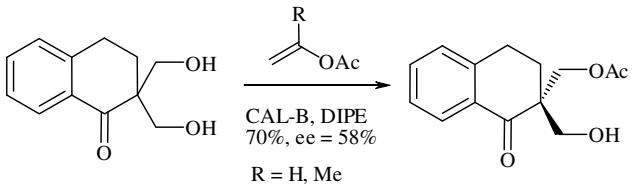
2.2. Enantioselective enzymatic desymmetrization (EED) of compounds 1–13

Enantioselective enzymatic desymmetrizations (EEDs) belong to the field of asymmetric synthesis, and accordingly, a maximum yield of 100% can be attained. For this reason, they constitute a very interesting alternative to kinetic resolutions for the preparation of optically active compounds, which is reflected in the increasing number of enzymatic desymmetrizations applied to organic synthesis recently published in the literature.[10] We initially planned to carry out EEDs on compounds **1**–**13** by an irreversible acylation reaction (transesterification) with a suitable acyl donor in organic solvent. When a trial run was conducted with compound **6** by using CAL-B lipase and vinyl acetate and isopropenyl acetate as the acyl donors, the corresponding monoacetate was obtained in good yield with moderate enantioselectivity (Schemes 3 and 4).

The EED of 2,2-disubstituted propane-1,3-diols using well-known acyl donors, that is, vinyl and isopropenyl acetates, is a well-established process that generates a quaternary stereocenter with excellent asymmetric control. Although it has proven to be successful, it usually suffers from low reactivity in few cases, the reason being that racemization of the products via acyl group migration occurs under different reaction conditions such as acidic or hydrogenolytic ones. Furthermore, this migration has also been observed for the products of the transesterification of other polyhydroxylated compounds such as different *meso* 1,2-diols.[11] Our initial attempts to generate quaternary stereocenters by applying EED strategy on a tetralone-based small scaffold yielded mixed



Scheme 3. Bishydroxymethyl derivatives of chromanone, 1-tetralone, and 1-indanone.



Scheme 4. EED of 2,2-bis-hydroxymethyl-3,4-dihydro-2*H*-naphthalen-1-one.

success. The reaction yield and enantioselectivity were moderate, and the reaction suffers from some side product formation in the form of diacetates. We presume that acyl migration may be responsible for the low enantioselectivity. Hence, we have chosen vinyl benzoate as a transesterification agent and carried out the same reaction with compound **6**. We thought that as vinyl ester is linked to an aromatic moiety, acyl migrations are hampered since the formation of the corresponding ortho ester intermediate involves a greater loss in resonance energy as compared to the case of aliphatic acyl chains.[12] But the observed enantioselectivity is not so encouraging to carry out same reaction with other substrates (Scheme 5).

It should be noted that only one enantiomer can be generated by employing this strategy, whereas the other enantiomer seems to be virtually inaccessible by this method. At this stage we thought to desymmetrize the prochiral diols **1**–**13** at the beginning by selective monoprotection at one of the alcohol functionalities. The monoprotected diols serve as precursor for enzymatic kinetic resolution by applying an irreversible transesterification strategy. The fast reacting enantiomer of the monoprotected diols **1**–**13** will undergo enzymatic acylation, whereas the slow reacting enantiomer will remain intact, hence making both enantiomers accessible with excellent stereocontrol. The diols are monoprotected as their silyl ethers when treated with imidazole and corresponding silyl chloride (1.5 equiv each) in DCM. All the monoprotected silyl ethers are well characterized by ^{1}H and ^{13}C NMR techniques.

2.3. Enzymatic kinetic resolutions of monoprotected silyl ethers

The monoprotected silyl ethers were subjected to a lipase-catalyzed irreversible transesterification reaction with a suitable acyl donor in organic solvents as depicted in Scheme 6.

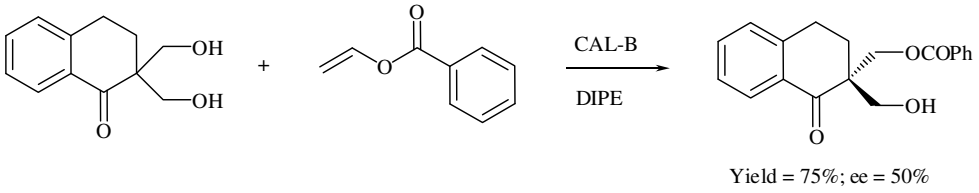
We have first chosen two substrates **19** (TBS protected) and **32** (TBDPS protected), and carried out CAL-B-catalyzed kinetic resolution with vinyl acetate as acyl donor in organic solvent (DIPE). The substrate **19** shows low enantioselectivity when compared with substrate **32**. The respective acetate obtained from compound **32** showed excellent enantioselectivity (ee: approx. 96%), whereas the slow reacting enantiomer of **32** shows 42% ee. In the case of

Table 1
CAL-B-catalyzed transesterification of compounds **27**–**39**

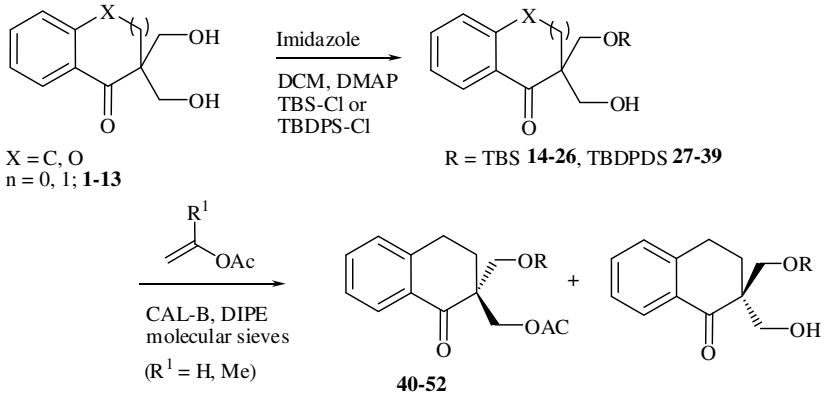
Entry	Substrate	Conversion(c)	ee_s[a] (%)	ee_p[a] (%)	E[b]
1	**27**	29.5	41	98	148
2	**28**	30.1	40	93	41
3	**29**	26.7	32	88	21.4
4	**30**	37.3	56	94	57
5	**31**	34.5	50	95	64.2
6	**32**	30.0	42	98	150
7	**33**	31.4	44	96	76
8	**34**	33.3	48	96	79
9	**35**	39.2	60	93	51
10	**36**	36.4	56	98	174
11	**37**	35.1	52	96	82.4
12	**38**	35.9	52	93	46.3
13	**39**	32.9	48	98	160

[a] Ee_s were calculated by chiral HPLC (Diacel, Chiral AS-H column, hexane–isopropanol, 98:2, flow rate: 0.8 ml/min).

[b] Enantioselectivities of the reactions (E)[14] were determined from the following equation: $E = \ln[1 - c(1 + ee_p)]/\ln[1 - c(1 - ee_p)]$, where ee_p = product ee, ee_s = substrate ee; $c = ee_s/(ee_s + ee_p)$%. Enantioselectivities of the reaction (E) were determined using the 'SELECTIVITY' program developed by Faber, K.; Hönig, H.; Kleewein, A. (http://www.cis.TUGraz.at/orgc/).



Scheme 5. EED reaction of compound **6** with vinyl benzoate.



Scheme 6. Lipase-catalyzed kinetic resolution of monosilyl-protected alcohols.

compound **19**, both the respective acetate and the alcohol were obtained in low enantiomeric excess (30%). The reason behind the observation is not clear to us, but we assume that in the case of **19**, the TBS group as well as the α-tetralone group is similar in size hence causing poor binding in the enzyme active site as predicted by the Kazlauskas empirical rule for enantiopreference of certain lipases toward primary alcohols.[13] Subsequently we have used compounds **27**–**39** for CAL-B-catalyzed irreversible acylation reaction to generate quaternary stereocenters. The results are summarized in Table 1. From Table 1 it is noticed that substrates **27**–**39** yield the respective acetate with good enantioselectivity (88–98%), whereas the slow reacting enantiomeric alcohols are obtained with poor enantioselectivity (32–60%).

2.4. Determination of absolute configuration of the product acetate

Absolute configuration of the product acetate was confirmed by X-ray crystal analysis of the acetate obtained from compound **32** after enzymatic transesterification. The X-ray crystal structure of compound **45** is given in Figure 1, and it is clearly evident from the ORTEP diagram that the newly generated stereocenter has (*S*)-configuration. The stereochemical assignment was further confirmed by chemical transformation of compound **45** to (*R*)-2-hydroxymethyl-2-methyl-3,4-dihydro-2*H*-naphthalen-1-one (**59**, Scheme 7) and by comparing its optical rotation value and HPLC retention time with that of the known compound reported in the literature.[15]

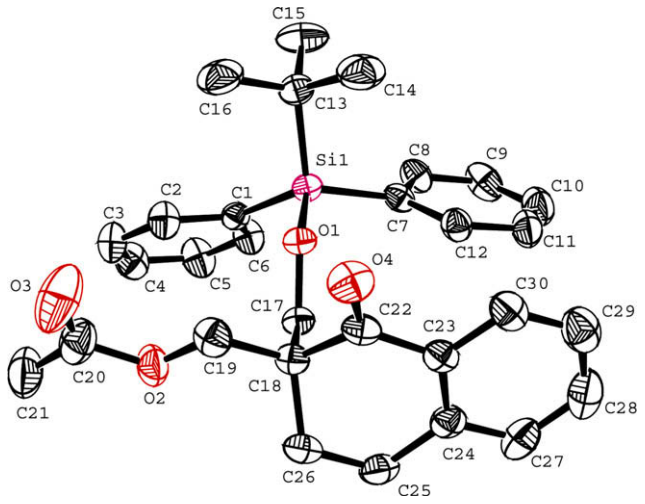


Figure 1. ORTEP diagram of compound **45**.

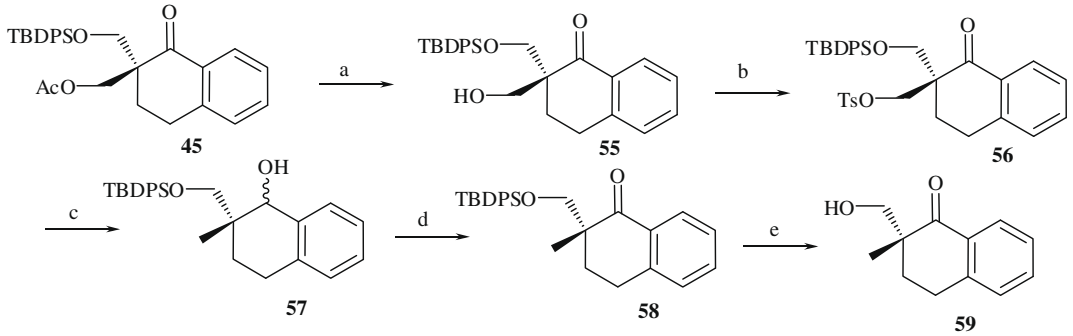
The acetate group in **45** was deprotected with K_2CO_3/MeOH to afford compound **55**. The alcohol functionality in **55** was protected as its *p*-toluenesulfonate ester **56** by treatment with Ts-Cl, Et_3N, and DMAP (cat). Reductive deoxygenation of the *p*-toluenesulfonate ester and ketone reduction were achieved by treatment of **56** with LAH to afford **57** in good yield. Oxidation of **57** under Swern conditions afforded compound **58**. Removal of the TBDPS group was achieved by treating **58** with TBAF to yield the known compound (*R*)-**59**.

3. Conclusion

In conclusion, we have described an efficient enzymatic resolution strategy for 2,2-disubstituted 1,3-propanediols based on 1-tetralone, 1-indanone, and chroman-4-one scaffolds. The enzymatic irreversible transesterification protocol generates a quaternary stereocenter adjacent to the carbonyl group of 1-tetralone and related scaffolds. Further biocatalytic transformation of the carbonyl functionality to create more diversity is currently ongoing in our group.

4. Experimental

Unless otherwise stated, materials were obtained from commercial suppliers and used without further purification. THF and diethyl ether were distilled from sodium benzophenone ketyl. Dichloromethane (DCM), dimethylformamide (DMF), and dimethylsulfoxide (DMSO) were distilled from calcium hydride. Diisopropyl ether (DIPE) was refluxed over P_2O_5 and distilled prior to use. Vinyl acetate and isopropenyl acetate were freshly distilled prior to use. Lipase (from *Candida rugosa*, type VII, 1440 μg of protein), lipase (from *Porcine pancreas*, type II, 6 μg of protein), lipase (from *Rhizopus niveus*), lipase (from wheat germ, type I, 8.2 μg of protein), and CAL-B (immobilized on acrylic resin) were obtained from Sigma and used as obtained. Lipase AK (from *Pseudomonas fluorescens*) and lipase PS (from *Burkholderia cepacia*) were obtained from Wako pure chemicals, Japan. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel plates (Merck) with UV light, ethanolic anisaldehyde, and phosphomolybdic acid/heat as developing agents. Silicagel 100–200 mesh was used for column chromatography. Yields refer to chromatographically and spectroscopically homogeneous materials unless otherwise stated. NMR spectra were recorded on Bruker 400 MHz spectrometers at 25 °C in $CDCl_3$ using TMS as the internal standard. Chemical shifts are shown in δ. ^{13}C NMR spectra were recorded with a complete proton decoupling environment. The chemical shift value is listed as δ_H and δ_C for ^1H and ^{13}C, respectively. Mass spectroscopic analysis was performed in the Central Research Facility (CRF), IIT-Kharagpur. Optical rotations were measured on a JASCO Dip 360 digital polarimeter. Chiral HPLC was performed using Chiral AS-H, OJ-H, and OD-H columns (0.46 × 25 cm, Daicel



Scheme 7. Reagents and conditions: (a) K_2CO_3, MEOH; rt; (b) Ts-Cl, Et_3N, DMAP; (c) LAH/THF, reflux; (d) $(COCl)_2$, Me_2SO, Et_3N, −78 °C; (e) TBAF-THF, rt.

industries) with Shimadzu ProminenceLC-20AT chromatograph coupled with UV–vis detector (254 nm). Eluting solvent used had different ratios of hexane and 2-propanol.

4.1. 3,3-Bis-hydroxymethyl-chroman-4-one 1

Chroman-4-one (250 mg, 1.68 mmol) was taken in MeOH (10 ml) and K_2CO_3 (466 mg, 3.38 mmol), and water (10 ml) was added to it at once. Formalin solution (37%, 0.56 ml, 6.75 mmol) was added to the reaction mixture and it was heated at 50 °C for 2–3 h. After completion of the reaction, as indicated by TLC, MeOH was evaporated under reduced pressure. The residue was taken in ethyl acetate, and washed successively with water and brine. The organic layer was dried with $MgSO_4$ and evaporated under reduced pressure. The product was purified by flash chromatography to afford (g) of diol. δ_H: 7.86 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.53 (t, *J* = 8.0 Hz, 1H, *ArH*), 7.1 (t, *J* = 8.0 Hz, 1H, *ArH*), 7.0 (d, *J* = 8.0 Hz, 1H, *ArH*), 4.4 (s, 2H, –OC*H*$_2$), 3.96 (d, *J* = 10.0 Hz, 2H, –C*H*$_2$OH), 3.87 (d, *J* = 10.0 Hz, 2H, –C*H*$_2$OH). δ_C: 195.7 (*C*=O), 161.36, 153.4, 136.5, 127.47, 121.64, 117.9, 70.04 (*C*2), 61.6 (–*C*H$_2$OH), 60.9 (–*C*H$_2$OH), 51.9 (*C*3).

4.2. 7-Methoxy-3,3-bis-hydroxymethyl-chroman-4-one 2

The diol was prepared from 7-methoxy-chroman-4-one as described earlier. δ_H: 7.78 (d, *J* = 8.4 Hz, 1H, *ArH*), 6.6 (d, *J* = 8.4 Hz, 1H, *ArH*), 6.4 (s, 1H, *ArH*), 4.38 (s, 2H, –OC*H*$_2$), 3.9 (d, *J* = 11.2 Hz, 2H, –C*H*$_2$OH), 3.85 (s, 3H, –O*Me*), 3.82 (d, *J* = 11.2 Hz, 2H, –C*H*$_2$OH). δ_C: 194.97 (*C*=O), 166.57, 163.46, 129.0, 110.65, 100.51, 69.14 (*C*2), 62.12 (–*C*H$_2$OH), 62.00 (–*C*H$_2$OH), 55.68 (–O*Me*), 50.8 (*C*3).

4.3. 7-Chloro-3,3-bis-hydroxymethyl-chroman-4-one 3

The diol was prepared from 7-chloro-chroman-4-one as described earlier. δ_H: 7.78 (d, *J* = 6.0 Hz, 1H, *ArH*), 7.0 (2H, *ArH*), 4.4 (s, 2H, –OC*H*$_2$), 3.94 (d, *J* = 10.0 Hz, 2H, –C*H*$_2$OH), 3.83 (d, *J* = 10.0 Hz, 2H, –C*H*$_2$OH). δ_C: 195.14 (*C*=O), 161.88, 142.72, 128.61, 125.26, 122.7, 118.12, 69.39 (*C*2), 62.26 (–CH$_2$OH), 62.06 (–*C*H$_2$OH), 51.53 (*C*3).

4.4. 6,7-Dimethoxy-3,3-bis-hydroxymethyl-chroman-4-one 4

The diol was prepared from 6,7-dimethoxy-chroman-4-one as described earlier. δ_H: 7.22 (s, 1H, *ArH*), 6.43 (s, 1H, *ArH*), 4.5 (s, 2H, –OC*H*$_2$), 4.0–3.8 (10H). δ_C: 195.0 (*C*=O), 158.13, 157.01, 144.95, 112.25, 106.47, 99.88, 69.4 (*C*2), 62.19 (–*C*H$_2$OH), 56.31 (–O*Me*), 56.13 (–O*Me*), 50.64 (*C*3).

4.5. 7,7-Bis-hydroxymethyl-6,7-dihydro-[1,3]dioxolo[4,5-g]chromen-8-one 5

The diol was prepared from 6,7-dihydro-[1,3]dioxolo[4,5-g]chromen-8-one as described earlier. δ_H: 7.13 (s, 1H, *ArH*), 6.43 (s, 1H, *ArH*), 6.0 (s, 2H, –O–C*H*$_2$–O–), 4.33 (s, 2H, –OC*H*$_2$), 3.91 (d, *J* = 11.0 Hz, 2H, –C*H*$_2$OH), 3.80 (d, *J* = 11.0 Hz, 2H, –C*H*$_2$OH). δ_C: 194. 94 (*C*=O), 160.6, 155.9, 128.4, 126.22, 103.8, 102.13, 98.2 (–O–*C*H$_2$–O), 69.3 (*C*2), 62.07 (–*C*H$_2$OH), 50.58 (*C*3).

4.6. 2,2-Bis-hydroxymethyl-3,4-dihydro-2*H*-naphthalen-1-one 6

α-Tetralone (250 mg, 1.71 mmol) was taken in MeOH (10 ml) and K_2CO_3 (447 mg, 3.42 mmol), and water (10 ml) was added to it at once. Formalin solution (37%, 0.542 ml, 6.84 mmol) was added to the reaction mixture and then heated at 50 °C for 2–3 h. After completion of the reaction, as indicated by TLC, MeOH was evaporated under reduced pressure. The residue was taken in ethyl acetate, and washed successively with water and brine. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The product was purified by flash chromatography to afford (g) of diol. δ_H: 8.0 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.5 (t, *J* = 8.0 Hz, 1H, *ArH*), 7.35 (t, *J* = 8.0 Hz, 1H, *ArH*), 7.2 (d, *J* = 8.0 Hz, 1H, *ArH*), 4.0 (d, *J* = 12.0 Hz, 2H, –C*H*$_2$OH), 3.8 (d, *J* = 12.0 Hz, 2H, –C*H*$_2$OH), 3.0 (t, *J* = 6.5 Hz, 2H, C4–*H*), 2.0 (t, *J* = 6.5 Hz, 2H, C3–*H*). δ_C: 202.7 (*C*=O), 143.82, 133.9, 131.8, 128.85, 127.56, 126.65, 64.6 (–*C*H$_2$OH), 63.55 (–*C*H$_2$OH), 51.4 (*C*2), 26.32 (*C*4), 25.0 (*C*3).

4.7. 2,2-Bis-hydroxymethyl-6-methoxy-3,4-dihydro-2*H*-naphthalen-1-one 7

The diol was prepared from 6-methoxy-α-tetralone as described earlier. δ_H: 7.95 (d, *J* = 8.0 Hz, 1H, *ArH*), 6.95 (d, *J* = 8.0 Hz, 1H, *ArH*), 6.65 (s, 1H, *ArH*), 4.0 (d, *J* = 12.0 Hz, 2H, –C*H*$_2$OH), 3.85 (s, 3H, –O*Me*), 3.8 (d, *J* = 12.0 Hz, 2H, –C*H*$_2$OH), 3.0 (t, *J* = 6.5 Hz, 2H, C4–*H*), 2.0 (t, *J* = 6.5 Hz, 2H, C3–*H*). δ_C: 201.5 (*C*=O), 164.0, 146.5, 130.05, 125.2, 113.54, 112.3, 64.6 (–*C*H$_2$OH), 63.6 (–*C*H$_2$OH), 55.4 (–O*Me*), 50.9 (*C*2), 26.24 (*C*4), 25.21 (*C*3).

4.8. 2,2-Bis-hydroxymethyl-7-methoxy-3,4-dihydro-2*H*-naphthalen-1-one 8

The diol was prepared from 7-methoxy-α-tetralone as described earlier. δ_H: 7.5 (d, *J* = 2.8 Hz, 1H, *ArH*), 7.2 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.1 (dd, *J* = 8.0 Hz, 2.8 Hz, 1H, *ArH*), 4.0 (d, *J* = 12.0 Hz, 2H, –C*H*$_2$OH), 3.85 (s, 3H, –O*Me*), 3.8 (d, *J* = 12.0 Hz, 2H, –C*H*$_2$OH), 3.0 (t, *J* = 6.5 Hz, 2H, C4–*H*), 2.0 (t, *J* = 6.5 Hz, 2H, C3–*H*). δ_C: 202.8 (*C*=O), 158.2, 136.35, 132.25, 130.5, 122.45, 109.44, 64.5 (–*C*H$_2$OH), 63.7 (–*C*H$_2$OH), 55.3 (O*Me*), 51.02 (*C*2), 26.44 (*C*4), 24.07 (*C*3).

4.9. 2,2-Bis-hydroxymethyl-5,8-dimethoxy-3,4-dihydro-2*H*-naphthalen-1-one 9

The diol was prepared from 5,8-dimethoxy-α-tetralone as described earlier. δ_H: 7.0 (d, *J* = 9.2 Hz, 1H, *ArH*), 6.8 (d, *J* = 9.2 Hz, 1H, *ArH*), 4.0 (d, *J* = 12.0 Hz, 2H, –C*H*$_2$OH), 3.85 (s, 6H, –O*Me*), 3.8 (d, *J* = 12.0 Hz, 2H, –C*H*$_2$OH), 2.9 (t, *J* = 6.4 Hz, 2H, C4–*H*), 1.8 (t, *J* = 6.4 Hz, 2H, C3–*H*). δ_C: 203.12 (*C*=O), 154.24, 150.06, 134.1, 121.68, 115.8, 109.98, 65.2 (–*C*H$_2$OH), 65.0 (–*C*H$_2$OH), 56.2 (–O*Me*), 55.8 (–O*Me*), 51.7 (*C*2), 25.35 (*C*4), 19.38 (*C*3).

4.10. 2,2-Bis-hydroxymethyl-indan-1-one 10

The diol was prepared from 1-indanone as described earlier. δ_H: 7.6 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.55 (t, *J* = 6.4 Hz, 1H, *ArH*), 7.45 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.34 (t, *J* = 6.4 Hz, 1H, *ArH*), 3.8 (s, 4H, –C*H*$_2$OH), 3.0 (s, 2H, C3–*H*). δ_C: 209.9 (*C*=O), 153.9, 135.5, 135.1, 127.57, 126.4, 123.6, 64.95 (–*C*H$_2$OH), 64.75 (–*C*H$_2$OH), 56.4 (*C*2), 33.9 (*C*3).

4.11. 5-Chloro-2,2-bis-hydroxymethyl-indan-1-one 11

The diol was prepared from 5-chloro-1-indanone as described earlier. δ_H: 7.6 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.45 (s, 1H, *ArH*), 7.27 (d, *J* = 8.0 Hz, 1H, *ArH*), 3.8 (s, 4H, –C*H*$_2$OH), 3.1 (s, 2H, C3–*H*). δ_C: 208.48 (*C*=O), 155.53, 142.11, 134.5, 128.37, 126.9, 125.06, 64.66 (–*C*H$_2$OH), 64.42 (–*C*H$_2$OH), 57.04 (*C*2), 33.79 (*C*3).

4.12. 2,2-Bis-hydroxymethyl-5-methoxy-indan-1-one 12

The diol was prepared from 5-methoxy-1-indanone as described earlier. δ_H: 7.7 (d, *J* = 5.6 Hz, 1H, *ArH*), 6.9 (m, 2H, *ArH*), 3.92 (s, 4H, –C*H*$_2$OH), 3.86 (s, 3H, –O*Me*), 3.03 (s, 2H, C3–*H*). δ_C:

209.46 (*C*=O), 154.28, 146.37, 137.29, 136.71, 126.34, 124.48, 64.32 (–CH_2OH), 64.24 (–CH_2OH), 56.88 (*C*2), 55.86 (*OMe*), 32.46 (*C*3).

4.13. 2,2-Bis-hydroxymethyl-6-methyl-indan-1-one 13

The diol was prepared from 6-methoxy-1-indanone as described earlier. δ_H: 7.5–7.32 (m, 3H, *ArH*), 3.83 (s, 2H, –CH_2OH), 3.81 (s, 2H, –CH_2OH), 3.1 (s, 2H, C3–*H*), 2.36 (s, 3H, –*Me*). δ_C: 210.0 (*C*=O), 151.37, 137.54, 136.81, 136.14, 126.36, 123.90, 64.84 (–*C*H_2OH), 64.66 (–*C*H_2OH), 56.71 (*C*2), 33.45 (*C*3), 20.97 (*Me*).

4.14. 3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-3-hydroxymethyl-chroman-4-one 14

δ_H: 7.86 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.5 (t, *J* = 8.0 Hz, 1H, *ArH*), 7.0 (m, 2H, *ArH*), 4.56 (d, *J* = 11.6 Hz, 1H, –O–CH_2), 4.46 (d, *J* = 11.6 Hz, 1H, –O–CH_2), 3.95–3.84 (m, 4H, –CH_2OH and –CH_2OTBDMS), 0.88 (s, 9H, –Si–*tBu*), 0.06 (s, 6H, Si–Me_2). δ_C: 194.94 (*C*=O), 161.54, 136.27, 127.27, 121.49, 120.15, 117.88, 69.36 (*C*2), 62.75 (–*C*H_2OTBDMS), 62.2 (–*C*H_2OH), 51.9 (*C*3), 25.7, 18.13, −5.73, −5.78.

4.15. 3-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3-hydroxymethyl-chroman-4-one 27

δ_H: 7.7 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.6(m, 4H, *ArH*), 7.5–7.3 (m, 7H, *ArH*), 7.0 (m, 2H, *ArH*), 4.68 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 4.52 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 4.0 (d, *J* = 12.0 Hz, 1H), 3.9–3.8 (m, 3H), 1.05 (s, 9H, Si–*tBu*). δ_C: 194.9 (*C*=O), 161.45, 136.2, 135.8, 134.75, 132.45, 129.84, 127.77, 121.53, 119.8, 117.8, 69.7 (*C*2), 62.5 (–*C*H_2OTBDPS), 62.3 (–*C*H_2OH), 52.27 (*C*3), 26.62, 19.23.

4.16. 3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-3-hydroxymethyl-7-methoxy-chroman-4-one 15

δ_H: 7.78 (d, *J* = 8.8 Hz, 1H, *ArH*), 6.58 (dd, *J* = 8.8, 2.4 Hz, 1H, *ArH*), 6.4 (d, *J* = 2.4 Hz, 1H, *ArH*), 4.56 (d, *J* = 11.2 Hz, 1H, –OCH_2), 4.42 (d, *J* = 11.2 Hz, 1H, –OCH_2), 3.9 (d, *J* = 10.0 Hz, 2H), 3.85–3.80 (m, 5H), 0.9 (s, 9H, –Si–*tBu*), 0.06 (s, 6H, Si–Me_2). δ_C: 193.58 (*C*=O), 166.28, 163.61, 128.97, 114.04, 110.35, 100.48, 69.6 (*C*2), 62.86 (–*C*H_2OTBDMS), 62.22 (–*C*H_2OH), 55.6 (–O*Me*), 51.4 (*C*3), 25.7, 18.13, −5.72, −5.77.

4.17. 3-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3-hydroxymethyl-7-methoxy-chroman-4-one 28

δ_H: 7.78 (d, *J* = 8.8 Hz, 1H, *ArH*), 7.65 (m, 4H, *ArH*), 7.4–7.3 (m, 6H, *ArH*), 6.58 (dd, *J* = 8.8, 2.0 Hz, 1H, *ArH*), 6.4 (d, *J* = 2.0 Hz, 1H, *ArH*), 4.66 (d, *J* = 11.2 Hz, 1H, –OCH_2), 4.48 (d, *J* = 11.2 Hz, 1H, –OCH_2), 4.1–3.8 (m, 7H), 1.05 (s, 9H, Si–*tBu*). δ_C: 193.56 (*C*=O), 166.26, 163.515, 135.54,132.56, 129.82, 128.98, 127.73, 114.1, 110.22, 100.5, 69.76 (*C*2), 62.47 (–*C*H_2OTBDPS), 62.45 (–*C*H_2OH), 55.61 (–O*Me*), 51.77 (*C*3), 26.69, 19.25.

4.18. 3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-7-chloro-3-hydroxymethyl-chroman-4-one 16

δ_H: 7.78 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.0 (m, 2H, *ArH*), 4.59 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 4.48 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 3.96–3.82 (m, 4H, –CH_2OH and –CH_2OTBDMS), 2.6 (br s, 1H), 0.9 (s, 9H, Si–*tBu*), 0.06 (s, 6H, –SiMe_2). δ_C: 193.84 (*C*=O), 161.86, 142.19, 134.94, 128.52, 122.35, 117.95, 69.78 (*C*2), 62.8 (–*C*H_2OTBDMS), 62.14 (–*C*H_2OH), 51.94 (*C*3), 29.64, 18.11, −5.74, −5.79.

4.19. 3-(*tert*-Butyl-diphenyl-silanyloxymethyl)-7-chloro-3-hydroxymethyl-chroman-4-one 29

δ_H: 7.77 (d, *J* = 8.2 Hz, 1H, *ArH*), 7.74–7.65 (m, 4H, *ArH*), 7.59–7.25 (m, 6H, *ArH*), 7.0 (m, 2H, *ArH*), 4.65 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 4.55 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 4.2–3.8 (m, 4H, –CH_2OH and –CH_2OTBDMS), 1.0 (s, 9H, –Si–*tBu*). δ_C: 193.84 (*C*=O), 161.82, 142.20, 135.58, 134.97,132.40, 129.98, 128.59, 124.88, 122.38, 117.98, 70.04 (*C*2), 62.63 (–*C*H_2OTBDPS), 62.26 (–*C*H_2OH), 52.8 (*C*3), 26.74, 19.29.

4.20. 3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-3-hydroxymethyl-6,7-dimethoxy-chroman-4-one 17

δ_H: 7.21 (s, 1H, *ArH*), 6.43 (s, 1H, *ArH*), 4.52 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 4.40 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 3.9–3.82 (10H), 0.9 (s, 9H, –Si–*tBu*), 0.07 (s, 6H, –SiMe_2). δ_C: 193.54 (*C*=O), 158.2, 156.49, 144.65, 112.37, 106.52, 99.88, 69.8 (*C*2), 62.99 (–*C*H_2OTBDMS), 62.32 (–*C*H_2OH), 56.27 (–O*Me*), 56.12 (–O*Me*), 51.19 (*C*3), 25.71, 18.14, −5.70, −5.75.

4.21. 3-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3-hydroxymethyl-6,7-dimethoxy-chroman-4-one 30

δ_H: 7.67–7.61 (m, 4H, *ArH*), 7.43–7.34 (m, 6H, *ArH*), 7.18 (s, 1H, *ArH*), 6.39 (s, 1H, *ArH*), 4.63 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 4.46 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 4.0–3.83 (10H), 0.9 (s, 9H, –Si–*tBu*). δ_C: 193.52 (*C*=O), 158.2, 156.6, 144.76, 135.59, 132.72, 129.89, 127.81, 112.57, 106.78, 99.91, 70.11 (*C*2), 62.72 (–*C*H_2OTBDPS), 62.65 (–*C*H_2OH), 56.31 (–*OMe*), 56.21 (O*Me*), 51.71 (*C*3), 26.80, 19.34.

4.22. 7-(*tert*-Butyl-dimethyl-silanyloxymethyl)-7-hydroxymethyl-6,7-dihydro-[1,3]dioxolo[4,5-*g*]chromen-8-one 18

δ_H: 7.2 (s, 1H, *ArH*), 6.4 (s, 1H, *ArH*), 5.9 (s, 2H, –O–CH_2–O–), 4.51 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 4. 37 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 3.9–3.8 (m, 4H, –CH_2OTBDMS and –CH_2OH), 0.8 (s, 9H, –Si–*tBu*), 0.02 (s, 6H, –SiMe_2). δ_C: 193.17 (*C*=O), 159.76, 154.60, 149.69, 128.72, 103.94, 102.1, 98.17 (–O–*C*H_2–O–), 69.82 (*C*2), 62.80 (–*C*H_2OTBDMS), 62.23 (–*C*H_2OH), 51.17 (*C*3), 25.69, 19.68, −5.73, −5.78.

4.23. 7-(*tert*-Butyl-diphenyl-silanyloxymethyl)-7-hydroxymethyl-6,7-dihydro-[1,3]dioxolo[4,5-*g*]chromen-8-one 31

δ_H: 7.67–7.6 (m, 4H, *ArH*), 7.44–7.2 (m, 6H, *ArH*), 7.1 (s, 1H, *ArH*), 6.4 (s, 1H, *ArH*), 5.96 (s, 2H, –O–CH_2–O), 4.63 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 4.44 (d, *J* = 12.0 Hz, 1H, –O–CH_2), 4.0–3.84 (m, 4H, –CH_2OTBDPS and –CH_2OH), 1.0 (s, 9H, –Si–*tBu*). δ_C: 193.22 (*C*=O), 159.71, 154.62, 143.21, 135.55, 132.51, 129.85, 127.76, 113.77, 103.96, 102.01, 98.1 (–O–*C*H_2–O–), 69.92 (*C*2), 62.45 (–*C*H_2OTBDPS), 62.42 (–*C*H_2OH), 51.53 (*C*3), 26.7, 19.2.

4.24. 2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-2-hydroxymethyl-3,4-dihydro-2*H*-naphthalen-1-one 19

Diol **6** (250 mg, 1.21 mmol) was dissolved in anhydrous DCM (10 ml) and cooled to 0 °C. Imidazole (100 mg, 1.5 mmol) and DMAP (catalytic) were added to the reaction mixture followed by addition of TBS-Cl (220 mg, 1.5 mmol). The reaction mixture was allowed to warm at room temperature for 6 h, after which water was added to it and the organic layer was washed with brine and dried over $MgSO_4$. Evaporation and purification yielded the mono TBS protected alcohol in 80% yield. δ_H: 7.97 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.47 (t, *J* = 8.0 Hz, 1H, *ArH*), 7.3 (t, *J* = 8.0 Hz, 1H, *ArH*), 7.24

(d, *J* = 8.0 Hz, 1H, *ArH*), 4.0 (d, *J* = 10.0 Hz, 1H), 3.8 (m, 3H), 3.1–3.0 (m, 2H, –C4–*H*), 2.17–2.1 (m, 2H, C3–*H*), 0.86 (s, 9H, –Si–*tBu*), 0.058 (s, 3H, –Si–*Me*), 0.028 (s, 3H, –Si–*Me*). δ_C: 201.76 (*C*=O), 144.04, 133.69, 131.94, 128.77, 127.455, 126.59, 65.6 (–*C*H$_2$OTBDMS), 64.38 (–*C*H$_2$OH), 51.5 (*C*2), 26.78 (*C*4), 25.68 (*C*3), 25.11, 18.06, −5.69, −5.77.

4.25. 2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-hydroxymethyl-3,4-dihydro-2*H*-naphthalen-1-one 32

Diol **6** (250 mg, 1.21 mmol) was taken in anhydrous DCM (10 ml) and cooled to 0 °C. Imidazole (100 mg, 1.5 mmol) and DMAP (catalytic) were added to the reaction mixture followed by the addition of TBDPS-Cl (400 mg, 1.5 mmol). The reaction mixture was allowed to warm at room temperature for 6 h, after which water was added to it and the organic layer was washed with brine and dried over $MgSO_4$. Evaporation and purification yielded the mono TBDPS-protected alcohol in 80% yield. δ_H: 7.98 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.6–7.4 (m, 10H, *ArH*), 7.3–7.19 (m, 3H, *ArH*), 4.0 (d, *J* = 10.4 Hz, 1H, –C*H*$_2$OTBDPS), 3.93 (d, *J* = 10.0 Hz, 2H, –C*H*$_2$OH), 3.82 (d, *J* = 10.4 Hz, 1H, –C*H*$_2$OTBDPS), 3.0 (m, 2H, –C4–*H*), 2.22 (m, 2H, C3–*H*), 1.0 (s, 9H, –Si–*tBu*). δ_C: 201.68 (*C*=O), 143.9, 135.58, 135.564, 134.75, 133.68, 132.05, 129.8, 128.72, 127.72, 126.61, 65.6 (–*C*H$_2$OTBDPS), 64.5 (–*C*H$_2$OH), 51.9 (*C*2), 26.94 (*C*4), 26.5 (*C*3), 25.03, 19.24.

4.26. 2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-2-hydroxymethyl-7-methoxy-3,4-dihydro-2*H*-naphthalen-1-one 20

δ_H: 7.4 (d, *J* = 2.8 Hz, 1H, *ArH*), 7.16 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.05 (dd, *J* = 8.0, 2.8 Hz, 1H, *ArH*), 4.0 (d, *J* = 10.0 Hz, 1H), 3.81–3.76 (m, 6H), 3.0 (m, 1H, –C4–*H*), 2.94 (m, 1H, –C4–*H*), 2.12(m, 2H, –C3–*H*), 0.86 (s, 9H, –Si–*tBu*), 0.06 (s, 3H, –Si*Me*), 0.03 (s, 3H, –Si*Me*). δ_C: 201.6 (*C*=O), 158.26, 136.65, 132.62, 129.9, 122.2, 109.2, 65.64 (–*C*H$_2$OTBDMS), 64.32 (–*C*H$_2$OH), 55.43 (–O*Me*), 51.36 (*C*2), 26.94 (*C*4), 25.69 (*C*3), 24.28, 18.07, −5.67, −5.75.

4.27. 2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-hydroxymethyl-7-methoxy-3,4-dihydro-2*H*-naphthalen-1-one 33

δ_H: 7.7–7.6 (m, 5H, *ArH*), 7.44–7.35 (m, 6H, *ArH*), 7.1–7.0 (m, 2H, *ArH*), 4.0 (d, *J* = 10.0 Hz, 1H, –C*H*$_2$OTBDPS), 3.93 (d, *J* = 10.0 Hz, 1H, –C*H*$_2$OTBDPS), 3.84–3.80 (m, 5H), 2.92 (m, 2H, –C4–*H*), 2.2 (m, 2H, C3–*H*), 1.04 (s, 9H, –Si–*tBu*). δ_C: 201.62 (*C*=O), 158.26, 136.52, 135.6, 134.75, 132.71, 129.81, 127.72, 127.6, 122.25, 109.15, 65.61 (–*C*H$_2$OTBDPS), 64.4 (–*C*H$_2$OH), 55.43 (–O*Me*), 51.76 (*C*2), 27.08 (*C*4), 26.74 (*C*3), 24.2, 19.26.

4.28. 2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-2-hydroxymethyl-6-methoxy-3,4-dihydro-2*H*-naphthalen-1-one 21

δ_H: 7.93 (d, *J* = 8.8 Hz, 1H, *ArH*), 6.8 (d, *J* = 8.8 Hz, 1H, *ArH*), 6.67 (s, 1H, *ArH*), 4.0 (d, *J* = 10.0 Hz, 1H, –C*H*$_2$OTBDMS), 3.84 (s, 3H, –O*Me*), 3.76 (m, 3H), 3.02 (m, 1H, C4–*H*), 2.9 (m, 1H, C4–*H*), 2.1 (t, *J* = 6.0 Hz, 2H, C3–*H*), 0.8 (s, 9H, –Si–*tBu*), 0.05 (s, 3H, –Si*Me*), 0.02 (s, 3H, –Si*Me*). δ_C: 200.5 (*C*=O), 163.84, 146.63, 129.92, 125.54, 113.35, 112.32, 65.71 (–*C*H$_2$OTBDMS), 64.24 (–*C*H$_2$OH), 55.39 (–O*Me*), 51.01 (*C*2), 26.78 (*C*4), 25.69 (*C*3), 25.55, 18.07, −5.67, −5.76.

4.29. 2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-hydroxymethyl-6-methoxy-3,4-dihydro-2*H*-naphthalen-1-one 34

δ_H: 7.94 (d, *J* = 8.8 Hz, 1H, *ArH*), 7.64 (m, 4H, *ArH*), 7.40 (m, 6H, *ArH*), 6.80 (d, *J* = 8.8 Hz, 1H, *ArH*), 6.64 (s, 1H, *ArH*), 4.0 (d, *J* = 10.0 Hz, 1H, –C*H*$_2$OTBDPS), 3.91 (d, *J* = 10.0 Hz, 1H, –C*H*$_2$OTBDPS), 3.88–3.79 (m, 5H), 2.9 (m, 2H, C4–*H*), 2.2 (m, 2H, C3–*H*), 1.0 (s, 9H, Si–*tBu*). δ_C: 200.42 (*C*=O), 163.86, 146.5, 135.58, 132.94, 129.9, 127.7, 127.6 125.6, 113.3, 112.4, 65.7 (–*C*H$_2$OTBDPS), 64.3 (–*C*H$_2$OH), 55.4 (–O*Me*), 51.4 (*C*2), 26.95 (*C*4), 26.76 (*C*3), 25.47, 19.26.

4.30. 2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-2-hydroxymethyl-5,8-dimethoxy-3,4-dihydro-2*H*-naphthalen-1-one 22

δ_H: 6.98 (d, *J* = 8.2 Hz, 1H, *ArH*), 6.76 (d, *J* = 8.2 Hz, 1H, *ArH*), 3.94 (d, *J* = 10.0 Hz, 1H), 3.81 (s, 3H, –O*Me*), 3.80 (s, 3H, –O*Me*), 3.75–3.70 (m, 3H), 2.89 (m, 2H, C4–*H*), 2.0 (m, 2H, C3–*H*), 0.85 (s, 9H, Si–*tBu*), 0.02 (s, 6H, Si*Me*$_2$). δ_C: 202.05 (*C*=O), 154.18, 149.97, 134.7, 122.17, 115.59, 109.77, 65.62 (–*C*H$_2$OTBDMS), 63.72 (–*C*H$_2$OH), 56.11 (–O*Me*), 55.88 (–O*Me*), 52.38 (*C*2), 25.67 (*C*4), 25.55 (*C*3), 19.41, 18.05, −5.67, −5.76.

4.31. 2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-hydroxymethyl-5,8-dimethoxy-3,4-dihydro-2*H*-naphthalen-1-one 35

δ_H: 7.7–7.5 (m, 4H, *ArH*), 7.48–7.3 (m, 6H, *ArH*), 7.0 (d, *J* = 8.2 Hz, 1H, *ArH*), 6.75 (d, *J* = 8.2 Hz, 1H, *ArH*), 4.0 (d, *J* = 10.0 Hz, 1H), 3.80 (s, 3H, –O*Me*), 3.79 (s, 3H, –O*Me*), 3.78–3.75 (m, 3H), 3.0 (m, 2H, C4–*H*), 2.2 (m, 2H, C3–*H*), 1.0 (s, 9H, Si–*tBu*). δ_C: 201.97 (*C*=O), 154.2, 150.1, 135.64, 134.6, 133.09, 129.75, 127.73, 122.54, 115.72, 109.87, 65.77 (–*C*H$_2$OTBDPS), 64.43 (–*C*H$_2$OH), 56.18 (–O*Me*), 56.03 (–O*Me*), 52.85 (*C*2), 26.78 (*C*4), 25.78, 19.48, 19.32.

4.32. 2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-2-hydroxymethyl-indan-1-one 23

δ_H: 7.60 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.55 (t, *J* = 8.0 Hz, 1H, *ArH*), 7.46 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.28 (t, *J* = 8.0 Hz, 1H, *ArH*), 4.0–3.77 (m, 4H, –C*H*$_2$OTBDMS and –C*H*$_2$OH), 3.26 (d, *J* = 16.0 Hz, 1H, C3–*H*), 3.06 (d, *J* = 16.0 Hz, 1H, C3–*H*), 0.75 (s, 9H, Si–*tBu*), 0.025 (s, 6H, Si*Me*$_2$). δ_C: 209.29 (*C*=O), 154.38, 136.66, 135.18, 127.31, 126.55, 123.85, 66.07 (–*C*H$_2$OTBDMS), 65.34 (–*C*H$_2$OH), 56.99 (*C*2), 33.92 (*C*3), 25.69, 18.0, −5.64, −5.7.

4.33. 2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-hydroxymethyl-indan-1-one 36

δ_H: 7.8 (d, *J* = 8.6 Hz, 1H, *ArH*), 7.6–7.2 (m, 13H, *ArH*), 4.0–3.78 (m, 4H, –C*H*$_2$OTBDPS and –C*H*$_2$OH), 3.33 (d, *J* = 17.2 Hz, 1H, C3–*H*), 3.08 (d, *J* = 17.2 Hz, 1H, C3–*H*), 1.0 (s, 9H, Si–*tBu*). δ_C: 209.44 (*C*=O), 154.32, 136.83, 135.56, 135.15, 132.98, 129.72, 127.68, 127.30, 126.46, 123.81, 66.52 (–*C*H$_2$OTBDPS), 64.88 (–*C*H$_2$OH), 56.94 (*C*2), 34.12 (*C*3), 26.66, 19.14.

4.34. 2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-5-chloro-2-hydroxymethyl-indan-1-one 24

δ_H: 7.65 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.48 (s, 1H, *ArH*), 7.34 (d, *J* = 8.0 Hz, 1H, *ArH*), 3.84–3.78 (m, 4H, –C*H*$_2$OTBDMS and –C*H*$_2$OH), 3.25 (d, *J* = 16.0 Hz, 1H, C3–*H*), 3.08 (d, *J* = 16.0 Hz, 1H, C3–H), 0.75 (s, 9H, Si–*tBu*), 0.003 (s, 6H, Si*Me*$_2$). δ_C: 207.73 (*C*=O), 155.77, 141.75, 135.17, 128.18, 126.75, 124.93, 66.0 (–*C*H$_2$OTBDMS), 65.26 (–*C*H$_2$OH), 57.32 (*C*2), 33.66 (*C*3), 25.59, 18.01, −5.65, −5.71.

4.35. 2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-5-chloro-2-hydroxymethyl-indan-1-one 37

δ_H: 7.7 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.5–7.2 (m, 12H, *ArH*), 4.0–3.75 (m, 4H, –C*H*$_2$OTBDPS and –C*H*$_2$OH), 3.3 (d, *J* = 16.0 Hz, 1H, C3–*H*), 3.1 (d, *J* = 16.0 Hz, 1H, C3–*H*), 0.9 (s, 9H, Si–*tBu*). δ_C: 207.90 (*C*=O), 155.82, 141.74, 135.61, 132.95, 129.86, 128.19, 127.78,

126.72, 124.94, 124.18, 66.51 (–CH_2OTBDPS), 64.78 (–CH_2OH), 57.47 (*C*2), 33.88 (*C*3), 26.63, 19.22.

4.36. 2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-5-methoxy-2-hydroxymethyl-indan-1-one 25

δ_H: 7.82 (d, *J* = 7.8 Hz, 1H, *ArH*), 6.9–6.8 (m, 2H, *ArH*), 4.0–3.77 (m, 7H, –CH_2OTBDMS and –CH_2OH, –O*Me*), 3.32 (d, *J* = 17.2 Hz, 1H, C3–*H*), 3.0 (d, *J* = 17.2 Hz, 1H, C3–*H*), 0.9 (s, 9H, –Si–*tBu*), 0.09 (s, 6H, SiMe_2). δ_C: 207.30 (*C*=O), 166.73, 157.29, 133.54, 133.45, 128.78, 109.56, 65.48 (–CH_2OTBDMS), 65.40 (–CH_2OH), 55.46 (–O*Me*), 55.04 (*C*2), 33.83 (*C*3), 27.53, 19.48, −5.62, −5.64.

4.37. 2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-5-methoxy-2-hydroxymethyl-indan-1-one 38

δ_H: 7.8 (d, *J* = 7.8 Hz, 1H, *ArH*), 7.6–7.3 (m, 10H, *ArH*), 6.88 (m, 2H, *ArH*), 4.0–3.77 (m, 7H, –CH_2OTBDPS and –CH_2OH, –O*Me*), 3.3 (d, *J* = 17.2 Hz, 1H, C3–*H*), 3.0 (d, *J* = 17.2 Hz, 1H, C3–*H*), 0.9 (s, 9H, –Si–*tBu*). δ_C: 207.30 (*C*=O), 165.73, 157.28, 135.56, 133.06, 129.98, 129.69, 127.65, 125.56, 115.46, 109.52, 66.44 (–CH_2OTBDPS), 65.10 (–CH_2OH), 56.96 (–O*Me*), 55.64 (*C*2), 34.13 (*C*3), 26.59, 19.18.

4.38. 2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-6-methyl-2-hydroxymethyl-indan-1-one 26

δ_H: 7.3 (m, 3H, *ArH*), 3.9–3.7 (m, 4H, –CH_2OTBDMS and –CH_2OH), 3.3, (d, *J* = 17.2 Hz, 1H, C3–*H*), 3.06 (d, *J* = 17.2 Hz, 1H, C3–*H*), 2.44 (s, 3H, –*Me*), 0.9 (s, 9H, Si–*tBu*), 0.06 (s, 6H, SiMe_2). δ_C: 207.27 (*C*=O), 152.68, 138.44, 136.38, 132.43, 127.71, 123.92, 67.09 (–CH_2OTBDMS), 65.55 (–CH_2OH), 56.38 (*C*2), 32.71 (*C*3), 27.38 (–*Me*), 21.92, 19.89, −5.12, −5.42.

4.39. 2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-6-methyl-2-hydroxymethyl-indan-1-one 39

δ_H: 7.7–7.3 (m, 13H, *ArH*), 3.9–3.7 (m, 4H, –CH_2OTBDPS and –CH_2OH), 3.3, (d, *J* = 17.2 Hz, 1H, C3–*H*), 3.02 (d, *J* = 17.2 Hz, 1H, C3–*H*), 2.4 (s, 3H, –*Me*), 0.9 (s, 9H, Si–*tBu*). δ_C: 209.47 (*C*=O), 151.67, 137.21, 136.89, 135.56, 135.52, 133.0, 132.84, 129.71, 127.67, 123.72, 66.49 (–CH_2OTBDPS), 65.02 (–CH_2OH), 57.24 (*C*2), 33.74 (*C*3), 29.66 (–*Me*), 21.02, 19.17.

4.40. Acetic acid (*S*)-3-(*tert*-butyl-diphenyl-silanyloxymethyl)-4-oxo-chroman-3-ylmethyl ester 40

In a typical resolution experiment, a solution of **27**–**39** (50 mg) in anhydrous diisopropyl ether (5 ml) was stirred with vinyl acetate (20 equiv) and powdered molecular sieves (25 mg, 4 Å) followed by the addition of CAL-B (50 mg). The reaction mixture was stirred in an orbit shaker (250 rpm) at room temperature for 12–36 h. After 50% conversion (by TLC analysis), the reaction mixture was filtered through a pad of Celite and evaporated to dryness. The alcohols and their acetates **40**–**52** were isolated by flash chromatography. δ_H: 7.8 (d, *J* = 7.2 Hz, 1H, *ArH*), 7.7–7.5 (m, 4H, *ArH*), 7.5–7.3 (m, 7H, *ArH*), 7.0 (m, 2H, *ArH*), 4.6–4.4 (m, 4H, –OCH_2– and –CH_2–OAc)), 3.8 (m, 2H, –CH_2–OTBDPS), 2.0 (s, 3H, OCO*Me*), 1.0 (s, 9H, Si*tBu*) δ_C: 191.89 (*C*=O), 170.84 (–CH_2–O–*C*OMe), 136.01, 135.53, 135.46, 129.81, 127.72, 127.68, 127.53, 127.61, 120.98, 117.75, 69.87 (*C*2), 62.49 (*C*H_2–OCOMe), 61.93 (–*C*H_2–OTBDPS), 50.87 (*C*3), 26.58 (–OCO*Me*), 20.69, 19.21. $[\alpha]_D^{28} = +11.0$ (*c* 0.2, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 4.25 min (minor, assumed *R*), t_R = 5.05 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 511.1911; calculated 511.1921 for $C_{29}H_{32}O_5Si$.

4.41. Acetic acid (*S*)-3-(*tert*-butyl-diphenyl-silanyloxymethyl)-7-methoxy-4-oxo-chroman-3-ylmethyl ester 41

δ_H: 7.75 (d, *J* = 8.8 Hz, 1H, *ArH*), 7.7–7.5 (m, 4H *ArH*), 7.5–7.4 (m, 6H, *ArH*), 6.6 (dd, *J* = 8.8 Hz, 2.4 Hz, 1H, *ArH*), 6.38 (d, *J* = 2.4 Hz, 1H, *ArH*), 4.66–4.4 (m, 4H), 3.9–3.76 (m, 5H), 1.98 (s, 3H, –OCO*Me*), 1.03 (s, 9H, OSi*tBu*). δ_C: 190.42 (*C*=O), 170.56 (–OCOMe), 166.01, 163.13, 135.54, 132.59, 129.78, 129.75, 127.69, 114.18, 110.21, 100.54, 70.16(*C*2), 62.64 (*C*H_2–OCOMe), 62.15 (–*C*H_2–OTBDPS), 55.59 (–O*Me*), 50.52 (*C*3), 26.67 (–OCO*Me*), 20.67, 19.22. $[\alpha]_D^{28} = +14.2$ (*c* 0.1, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 6.32 min (minor, assumed *R*), t_R = 6.78 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 541.2010; calculated 541.2017 for $C_{30}H_{34}O_6Si$

4.42. Acetic acid (*S*)-3-(*tert*-butyl-diphenyl-silanyloxymethyl)-7-chloro-4-oxo-chroman-3-ylmethyl ester 42

δ_H: 7.80 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.7–7.4 (m, 10H, *ArH*), 7.0 (m, 2H, *ArH*), 4.6 (d, *J* = 11.2 Hz, 1H, –O*C*H_2), 4.52 (dd, *J* = 11.2, 1.6 Hz, 2H, –*C*H_2OAc), 4.4 (d, *J* = 11.2 Hz, 1H, –O*C*H_2), 3.88 (d, *J* = 10.4 Hz, 1H, –*C*H_2OTBDPS), 3.8 (d, *J* = 10.4 Hz, 1H, –*C*H_2OTBDPS), 1.98 (s, 3H, –OCO*Me*), 1.06 (s, 9H, OSi*tBu*). δ_C: 190.91 (*C*=O), 170.48 (–O*C*OMe), 161.43, 141.91, 135.50, 134.72, 132.37, 129.87, 128.76, 127.74, 122.45, 117.86, 70.28 (*C*2), 62.32 (*C*H_2–OCOMe), 61.94 (–*C*H_2–OTBDPS), 50.84 (*C*3), 26.63(–OCO*Me*), 20.64, 19.20. $[\alpha]_D^{28} = +12.8$ (*c* 1.0, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 3.42 min (minor, assumed *R*), t_R = 4.31 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 545.1514; calculated 545.1521 for $C_{29}H_{31}ClO_5Si$.

4.43. Acetic acid (*S*)-3-(*tert*-butyl-diphenyl-silanyloxymethyl)-6,7-dimethoxy-4-oxo-chroman-3-ylmethyl ester 43

δ_H: 7.6–7.5 (m, 4H, *ArH*), 7.5–7.3 (m, 6H, *ArH*), 7.23 (s, 1H, *ArH*), 6.39 (s, 1H, *ArH*), 4.6 (d, *J* = 11.2 Hz, 1H, –O*C*H_2), 4.5 (q, *J* = 11.2 Hz, 2H, –*C*H_2–OAc), 4.42 (d, *J* = 11.2 Hz, 1H, –O*C*H_2), 3.93 (d, *J* = 10.4 Hz, 1H, –*C*H_2OTBDPS), 3.91(s, 3H, O*Me*), 3.90 (s, 3H, O*Me*), 3.80 (d, *J* = 10.4 Hz, 1H, –*C*H_2OTBDPS), 1.99 (s, 3H, –OCOMe), 1.04 (s, 9H, OSi*tBu*). δ_C: 190.45 (*C*=O), 170.60 (–O*C*OMe), 157.66, 156.17, 144.67, 135.55, 132.60, 129.79, 112.52, 109.67, 106.90, 99.80, 70.34 (*C*2), 62.72 (*C*H_2–OCOMe), 62.25 (–*C*H_2–OTBDPS), 56.25 (–O*Me*), 56.13 (–O*Me*), 50.39 (*C*3), 26.68 (–OCO*Me*), 20.71, 19.24. $[\alpha]_D^{28} = +3.6$ (*c* 0.18, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 8.54 min (minor, assumed *R*), t_R = 10.12 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 571.2130; calculated 571.2122 for $C_{31}H_{36}O_7Si$.

4.44. Acetic acid (*S*)-7-(*tert*-butyl-diphenyl-silanyloxymethyl)-8-oxo-7,8-dihydro-6*H*-[1,3]dioxolo[4,5-*g*]chromen-7-ylmethyl ester 44

δ_H: 7.7–7.5 (m, 4H, *ArH*), 7.4 (m, 6H, *ArH*), 7.20 (s, 1H, *ArH*), 6.39 (s, 1H, *ArH*), 5.97 (s, 2H, –O–CH_2–O), 4.59 (d, *J* = 11.6 Hz, 1H, –O–CH_2), 4.48 (q, *J* = 11.2 Hz, 2H, –*C*H_2OAc), 3.88 (d, *J* = 10.4 Hz, 1H, –*C*H_2OTBDPS), 3.78 (d, *J* = 10.4 Hz, 1H, –*C*H_2OTBDPS), 1.98 (s, 3H, –OCO*Me*), 1.04 (s, 9H, OSi*tBu*). δ_C: 190.15 (*C*=O), 170.57 (–O*C*OMe), 159.24, 154.33, 143.26, 135.54, 132.54, 129.80, 127.71, 113.90, 104.33, 101.98, 98.08 (–O–*C*H_2–O), 70.31 (*C*2), 62.64 (*C*H_2–OCOMe), 62.12 (–*C*H_2–OTBDPS), 50.31 (*C*3), 26.68 (–OCO*Me*), 20.69, 19.23. $[\alpha]_D^{28} = +3.90$ (*c* 0.36, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 9.27 min (minor, assumed *R*), t_R = 12.24 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 555.1813; calculated 555.1809 for $C_{30}H_{32}O_7Si$.

4.45. Acetic acid (*S*)-2-(*tert*-butyl-diphenyl-silanyloxymethyl)-1-oxo-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl ester 45

δ_H: 8.0 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.78–7.6 (m, 4H, *ArH*), 7.5–7.1 (m, 9H, *ArH*), 4.51 (d, *J* = 10.8 Hz, 1H, –C*H*$_2$–OAc), 4.38 (d, *J* = 10.8 Hz, 1H, –C*H*$_2$–OAc), 3.84 (m, 2H, –C*H*$_2$OTBDPS), 2.9 (m, 2H, *C*4), 2.3 (m, 2H, *C*3), 1.97 (s, 3H, –OCO*Me*), 1.07 (s, 9H, OSi*tBu*). δ_C: 197.81 (*C*1), 170.79 (–OCOMe), 143.15, 135.56, 134.72, 132.85, 129.72, 129.59, 128.65, 127.66, 127.63, 126.64, 65.59 (–*C*H$_2$–OCOMe), 64.35 (–*C*H$_2$–OTBDPS), 50.87 (*C*2), 27.09 (*C*4), 26.66 (–OCO*Me*), 24.91 (*C*3), 20.77, 19.21. $[\alpha]_D^{28} = +6.7$ (*c* 0.2, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 4.57 min (minor, assumed *R*), t_R = 5.45 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 509.2115; calculated 509.2118 for $C_{30}H_{34}O_4Si$.

4.46. Acetic acid (*S*)-2-(*tert*-butyl-diphenyl-silanyloxymethyl)-7-methoxy-1-oxo-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl ester 46

δ_H: 7.78 (m, 1H, *ArH*), 7.6–7.5 (m, 4H, *ArH*), 7.5–7.0 (m, 8H, *ArH*), 4.54 (d, *J* = 11.0 Hz, 1H, –C*H*$_2$–OAc), 4.42 (d, *J* = 11.0 Hz, 1H, –C*H*$_2$–OAc), 3.86 (m, 5H), 2.9 (t, *J* = 6.2 Hz, 2H, C4), 2.3 (m, 2H, C3), 2.02 (s, 3H, –OCO*Me*), 1.09 (s, 9H, OSi*tBu*). δ_C: 197.75 (C1), 170.82 (–OCOMe), 158.31, 135.76, 134.73, 132.868,, 132.77, 129.89, 129.73, 127.66, 121.96, 109.41, 65.59 (–*C*H$_2$–OCOMe), 64.27 (–*C*H$_2$–OTBDPS), 55.44 (–O*Me*), 50.74 (*C*2), 27.27 (*C*4), 26.67 (–OCO*Me*), 24.10 (*C*3), 20.79, 19.23. $[\alpha]_D^{28} = +23.8$ (*c* 0.2, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 5.67 min (minor, assumed *R*), t_R = 6.45 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 539.2216; calculated 539.2224 for $C_{31}H_{36}O_5Si$.

4.47. Acetic acid (*S*)-2-(*tert*-butyl-diphenyl-silanyloxymethyl)-6-methoxy-1-oxo-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl ester 47

δ_H: 7.95 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.7–7.5 (m, 4H, *ArH*), 7.5–7.3 (m, 6H, *ArH*), 6.9–6.6 (m, 2H, *ArH*), 4.50 (d, *J* = 10.8 Hz, 1H, –C*H*$_2$–OAc), 4.35 (d, *J* = 10.8 Hz, 1H, –C*H*$_2$–OAc), 3.87–3.81 (m, 5H), 2.9 (t, *J* = 6.0 Hz, 2H, C4), 2.28 (m, 2H, C3), 1.99 (s, 3H, –OCO*Me*), 1.01 (s, 9H, OSi*tBu*). δ_C: 196.49 (C1), 170.92 (–OCOMe), 163.63, 145.79, 135.65, 133.00, 130.28, 129.78, 127.70, 125.89, 113.36, 112.37, 65.86 (–*C*H$_2$–OCOMe), 64.51 (–*C*H$_2$–OTBDPS), 55.46 (–O*Me*), 50.74 (*C*2), 27.12 (*C*4), 26.77 (–OCO*Me*), 25.41 (*C*3), 20.89, 19.32. $[\alpha]_D^{28} = +11.10$ (*c* 0.2, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 5.87 min (minor, assumed *R*), t_R = 6.89 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 539.2218 calculated 539.2224 for $C_{31}H_{36}O_5Si$.

4.48. Acetic acid (*S*)-2-(*tert*-butyl-diphenyl-silanyloxymethyl)-5,8-dimethoxy-1-oxo-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl ester 48

δ_H: 7.64–7.5 (m, 4H, *ArH*), 7.5–7.3 (m, 6H, *ArH*), 7.0 (d, *J* = 9.0 Hz, 1H, *ArH*), 6.89 (d, *J* = 9.0 Hz, 1H, *ArH*), 4.46 (d, *J* = 11.2 Hz, 1H, –C*H*$_2$–OAc), 4.40 (d, *J* = 11.2 Hz, 1H, –C*H*$_2$–OAc), 3.9–3.75 (m, 8H), 2.85 (m, 2H, C4), 2.25 (m, 2H, C3), 1.96 (s, 3H, –OCO*Me*), 1.0 (s, 9H, OSi*tBu*). δ_C: 197.92 (C1), 170.87 (–OCOMe), 153.94, 149.92, 135.55, 133.52, 132.95, 129.62, 127.61, 122.69, 115.06, 109.98, 65.66 (–*C*H$_2$–OCOMe), 64.26 (–*C*H$_2$–OTBDPS), 56.18 (–O*Me*), 55.89 (–O*Me*), 51.49 (*C*2), 26.62 (*C*4), 26.22 (–OCO*Me*), 20.83 (*C*3), 19.34, 19.21. $[\alpha]_D^{28} = +13.3$ (*c* 0.4, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 8.31 min (minor, assumed *R*), t_R = 9.49 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 569.2323; calculated 569.2329 for $C_{32}H_{38}O_6Si$.

4.49. Acetic acid (*S*)-2-(*tert*-butyl-diphenyl-silanyloxymethyl)-1-oxo-indan-2-ylmethyl ester 49

δ_H: 7.78 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.7–7.3 (m, 13H, *ArH*), 4.27 (d, *J* = 10.8 Hz, 1H, –C*H*$_2$–OAc), 4.24 (d, *J* = 10.8 Hz, 1H, –C*H*$_2$–OAc), 3.88 (d, *J* = 9.6 Hz, 1H, –*C*H$_2$–OTBDPS), 3.74 (d, *J* = 9.6 Hz, 1H, –*C*H$_2$–OTBDPS), 3.34 (d, *J* = 17.2 Hz, 1H, *C*3), 3.14 (d, *J* = 17.2 Hz, 1H, *C*3), 1.90 (s, 3H, –OCO*Me*), 0.85 (s, 9H, OSi*tBu*). δ_C: 206.24 (C1), 170.76 (–OCOMe), 153.54, 136.83, 135.53, 134.95, 132.91, 129.72, 127.65, 127.29, 126.29, 123.92, 66.02 (–*C*H$_2$–OCOMe), 65.22 (–*C*H$_2$–OTBDPS), 55.21 (*C*2), 34.03 (C3), 26.46 (–OCO*Me*), 20.64, 19.09. $[\alpha]_D^{28} = +15.8$ (*c* 0.24, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 4.67 min (minor, assumed *R*), t_R = 5.32 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 495.1956; calculated 495.1962 for $C_{29}H_{32}O_4Si$.

4.50. Acetic acid (*S*)-2-(*tert*-butyl-diphenyl-silanyloxymethyl)-5-chloro-1-oxo-indan-2-ylmethyl ester 50

δ_H: 7.69 (d, *J* = 6.4 Hz, 1H, *ArH*), 7.6–7.3 (m, 12H, *ArH*), 4.2 (m, 2H, –C*H*$_2$–OAc), 3.87 (d, *J* = 9.6 Hz, 1H, –*C*H$_2$–OTBDPS), 3.70 (d, J = 9.6 Hz, 1H, –*C*H$_2$–OTBDPS), 3.26 (d, *J* = 17.2 Hz, 1H, *C*3), 3.15 (d, *J* = 17.2 Hz, 1H, *C*3), 1.90 (s, 3H, –OCO*Me*), 0.9 (s, 9H, OSi*tBu*). δ_C: 204.85 (C1), 170.65 (–OCOMe), 155.01, 141.49, 135.51, 132.76, 130.83, 129.79, 128.74, 127.69, 126.50, 124.98, 65.95 (–*C*H$_2$–OCOMe), 65.03 (–*C*H$_2$–OTBDPS), 55.50 (*C*2), 33.73 (*C*3), 26.47 (–OCO*Me*), 20.62, 19.10. $[\alpha]_D^{28} = +13.1$ (*c* 0.2, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 4.04 min (minor, assumed *R*), t_R = 4.60 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 529.1578; calculated 529.1572 for $C_{29}H_{31}ClO_4Si$.

4.51. Acetic acid (*S*)-2-(*tert*-butyl-diphenyl-silanyloxymethyl)-5-methoxy-1-oxo-indan-2-ylmethyl ester 51

δ_H: 7.72 (d, *J* = 8.0 Hz, 1H, *ArH*), 7.6 (m, 4H, *ArH*), 7.5–7.3 (m, 6H, *ArH*), 6.9 (m, 2H, *ArH*), 4.30 (d, *J* = 10.8 Hz, 1H, –C*H*$_2$–OAc), 4.23 (d, *J* = 10.8 Hz, 1H, –C*H*$_2$–OAc), 3.99 (s, 3H, –O*Me*), 3.8 (m, 2H, –C*H*$_2$–OTBDPS), 3.29 (d, *J* = 17.2 Hz, 1H, C3–*H*), 3.07 (d, *J* = 17.2 Hz, 1H, C3–*H*), 1.91 (s, 3H, –OCO*Me*), 0.92 (s, 9H, OSi*tBu*). δ_C: 204.13 (C1), 170.86 (–OCOMe), 165.64, 156.53, 135.64, 133.13, 130.23, 129.78, 127.73, 125.73, 115.36, 109.57, 66.09 (*C*H$_2$–OCOMe), 65.47 (–*C*H$_2$–OTBDPS), 34.07 (C3), 26.62 (–OCO*Me*), 20.75, 19.24. $[\alpha]_D^{28} = +18.3$ (*c* 0.4, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 6.15 min (minor, assumed *R*), t_R = 7.29 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 525.2073; calculated 525.2067 for $C_{30}H_{34}O_5Si$.

4.52. Acetic acid (*S*)-2-(*tert*-butyl-diphenyl-silanyloxymethyl)-6-methyl-1-oxo-indan-2-ylmethyl ester 52

δ_H: 7.6–7.4 (m, 13H, *ArH*), 4.30 (d, *J* = 11.0 Hz, 1H, –C*H*$_2$–OAc), 4.24 (d, *J* = 11.0 Hz, 1H, –C*H*$_2$–OAc), 3.86 (d, *J* = 9.4 Hz, 1H, –C*H*$_2$–OTBDPS), 3.75 (d, *J* = 9.4 Hz, 1H, –C*H*$_2$–OTBDPS), 3.28 (d, *J* = 17.2 Hz, 1H, C3–*H*), 3.07 (d, *J* = 17.2 Hz, 1H, C3–*H*), 2.6 (s, 3H, –*Me*), 1.90 (s, 3H, –OCO*Me*), 0.88 (s, 9H, OSi*tBu*). δ_C: 206.19 (C1), 170.79 (–OCOMe), 150.90, 137.26, 136.27, 135.58, 132.88, 133.08, 129.76, 127.71, 126.05, 123.92, 66.12 (*C*H$_2$–OCOMe), 65.39 (–*C*H$_2$–OTBDPS), 55.66 (C2), 33.73 (C3), 26.61 (–OCO*Me*), 21.06 (–Ar–*C*H$_3$), 20.69, 19.22. $[\alpha]_D^{28} = +10.6$ (*c* 0.4, MeOH). HPLC (Daicel Chiralcel AS-H, hexane/*i*-PrOH = 49:1, flow rate = 0.8 ml/min) t_R = 4.42 min (minor, assumed *R*), t_R = 5.14 min (major, assumed *S*). HRMS *m/z* [M+Na]$^+$ found 509.2113; calculated 509.2118 for $C_{30}H_{34}O_4Si$.

4.53. Acetic acid 2-hydroxymethyl-1-oxo-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl ester 53

In a typical EED reaction, diol **6** (50 mg, 0.24 mmol) was taken in 2 ml of anhydrous DIPE, followed by the addition of CAL-B (30 mg), vinyl acetate (20 equiv) and molecular sieves (4 Å). The reaction mixture was kept under an argon atmosphere until an appreciable amount of conversion was achieved (as measured by TLC). The reaction mixture was filtered, and the solvent was evaporated in vacuo. The product was purified by preparative TLC (hexane/EtOAc, 3:1). δ_H: 7.99 (d, J = 8.0 Hz, 1H, *ArH*), 7.49 (t, J = 7.6 Hz, 1H, *ArH*), 7.31 (t, J = 7.6 Hz, 1H, *ArH*), 7.24 (d, J = 8.0 Hz, 1H, *ArH*), 4.41 (d, J = 11.2 Hz, 1H, –C*H*$_2$OAc), 4.31 (d, J = 11.2 Hz, 1H, –C*H*$_2$OAc), 3.77 (s, 2H, –C*H*$_2$OH), 3.0 (m, 2H, C4–*H*), 2.5 (br, 1H, –*OH*), 2.12 (t, J = 6.4 Hz, 2H, C3–*H*), 2.02 (s, 3H, –OCO*Me*). δ_C: 200.52 (*C*=O), 170.99 (–OCOMe), 144.82, 133.94, 130.84, 128.45, 127.26, 126.46, 64.68 (–*C*H$_2$OAc), 63.06 (–*C*H$_2$OH), 50.68 (*C*2), 29.63 (*C*4), 25.80 (*C*3), 20.78 (–OCO*Me*). HPLC (Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 9:1, flow rate = 1.0 ml/min) t_R = 15.08 min (major), t_R = 16.17 min (minor).

4.54. Benzoic acid 2-hydroxymethyl-1-oxo-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl ester 54

In a typical EED reaction, diol **6** (50 mg, 0.24 mmol) was dissolved in 2 ml of anhyd DIPE, followed by the addition of CAL-B (30 mg), vinyl benzoate (20 equiv), and molecular sieve (4 Å). The reaction mixture was kept under an argon atmosphere until an appreciable amount of conversion was achieved (as measured by TLC). The reaction mixture was filtered, and the solvent was evaporated in vacuo. The product was purified by preparative TLC (hexane/EtOAc, 3:1). δ_H: 8.03 (d, J = 8.0 Hz, 1H, *ArH*), 7.98 (d, J = 7.8 Hz, 2H, *ArH*), and 7.6–7.2 (m, 6H, *ArH*), 4.7 (d, J = 11.2 Hz, 1H, –C*H*$_2$OCOPh), 4.58 (d, J = 11.2 Hz, 1H, –C*H*$_2$OCOPh), 3.9 (m, 2H, –C*H*$_2$OH), 3.0 (m, 2H, C4–*H*), 2.2 (m, 2H, C3–*H*). δ_C: 200.68 (C=O), 171.56 (–OCOPh), 134.48, 132.27, 130.46, 129.76, 129.54, 129.28, 128.76, 128.43, 127.68, 127.25, 69.83, 65.44, 49.2 (*C*2), 29.78 (*C*4), 26.57 (*C*3). HPLC (Daicel Chiralcel OJ-H, hexane/*i*-PrOH = 9:1, flow rate = 1.0 ml/min) t_R = 17.18 min (major), t_R = 19.53 min (minor).

4.55. Toluene-4-sulfonic acid (*R*)-2-(*tert*-butyl-diphenyl-silanyloxymethyl)-1-oxo-1,2,3,4-tetrahydro-naphthalen-2-ylmethyl ester 56

(*S*)-2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-hydroxymethyl-3,4-dihydro-2*H*-naphthalen-1-one (**32**, 750 mg, 1.7 mmol) was dissolved in anhydrous DCM (10 ml) at 0 °C. Next, Et_3N (0.47 ml, 3.4 mmol) was added to it at the same temperature and the solution was stirred for a further 15 min, after which Ts-Cl (644 mg, 3.4 mmol) and DMAP (0.3 mmol) were added at once. After completion of reaction, as indicated by TLC (12–18 h), water was added to the reaction mixture and it was further extracted with DCM. The organic layer was successively washed with $NaHCO_3$ and brine. Purification after chromatography afforded the compound in 82% yield. δ_H: 7.92 (d, J = 8.0 Hz, 1H, *ArH*), 7.72 (d, J = 8.0 Hz, 2H, *ArH*), 7.52 (d, J = 8.0 Hz, 2H, *ArH*), 7.5–7.2 (m, 13H, *ArH*), 4.37 (d, J = 9.6 Hz, 1H, –C*H*$_2$OTs), 4.34 (d, J = 9.6 Hz, 1H, –C*H*$_2$OTs), 3.79 (d, J = 10.0 Hz, 1H, –C*H*$_2$OTBDPS), 3.67 (d, J = 10.0 Hz, 1H, –C*H*$_2$OTBDPS), 2.86 (m, 2H, C4–*H*), 2.42 (s, 3H, –*Me*), 2.35 (m, 2H, C3–*H*), 0.9 (s, 9H, OSi*tBu*). δ_C: 196.95, 144.69, 142.97, 135.38, 133.54, 132.57, 131.76, 129.78, 129.75, 129.69, 128.68, 127.99, 127.70, 127.62, 126.66, 71.52, 63.66, 51.14 (*C*2), 29.56 (*C*4), 26.53 (–*Me*), 24.63 (*C*3), 21.59, 19.10.

4.56. (*R*)-2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-methyl-3,4-dihydro-2*H*-naphthalen-1-one 58

Oxalyl chloride (0.1 ml, 1.17 mmol) was taken in DCM (15 ml) at −78 °C. To this cold solution, DMSO (0.16 ml, 2.34 mmol) was slowly added and the mixture was kept for 5 min at the same temperature. Alcohol **57** (335 mg, 0.78 mmol) in DCM (3 ml) was added to the solution. The temperature was maintained at −78 °C for a further 1 h. Triethylamine (0.43 ml, 3.17 mmol) was then added and the reaction mixture was allowed to attain room temperature. Water was added to the solution, and the mixture was extracted with DCM. The organic extract was washed successively with aq $NaHCO_3$ and brine and dried over Na_2SO_4. The organic extract was evaporated and purified by column chromatography to afford the ketone **58** in 90% yield. δ_H: 8.0 (d, J = 8.0 Hz, 1H, *ArH*), 7.7–7.1 (m,13H, *ArH*), 3.98 (d, J = 9.8 Hz, 1H, –C*H*$_2$OTBDPS), 3.62 (d, J = 9.8 Hz, 1H, – C*H*$_2$OTBDPS), 2.98 (t, J = 6.8 Hz, 2H, C4–*H*), 2.4 (m, 1H, C3–*H*), 2.0 (m, 1H, C3–*H*), 1.2 (s, 3H, –*Me*), 1.0 (s, 9H). δ_C: 201.19, 143.72, 135.73, 133.56, 133.39, 132.26, 129.61, 128.66, 127.80, 127.65, 126.56, 68.77 (–CH$_2$OTBDPS), 47.51 (*C*2), 31.74 (*C*4), 26.80 (*C*3), 25.51, 19.62, 19.37. $[\alpha]_D^{28} = +21.2$ (*c* 0.9, MeOH).

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References

1. (a) Dai, W.-M.; Shi, J. *Comb. Chem. High Throughput Screening* **2007**, *10*, 837–856; (b) Kubota, H.; Lim, J.; Depew, K. M.; Schreiber, S. L. *Chem. Biol.* **2002**, *9*, 265–276; (c) Sternson, S. M.; Louca, J. B.; Wong, J. C.; Schreiber, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 1740–1747; (d) Reayi, A.; Arya, P. *Curr. Opin. Chem.Biol.* **2005**, *9*, 240–247; (e) Wrenn, S. J.; Weisinger, R. M.; Halpin, D. R.; Harbury, P. B. *J. Am. Chem. Soc.* **2007**, *129*, 13137–13143; (f) Wu, L.; Xiao, D.; Ye, H. *Huaxue Shijie* **2004**, *45*, 603–609.
2. (a) Oikawa, M.; Ikoma, M.; Sasaki, M. *Tetrahedron Lett.* **2005**, *46*, 5863–5866; (b) Pulici, M.; Cervi, G.; Martina, K.; Quartieri, F. *Comb. Chem. High Throughput Screening* **2003**, *6*, 693–727; (c) Weber, L. *Cur. Med. Chem.* **2002**, *9*, 2085–2093; (d) Spring, D. R.; Krishnan, S.; Blackwell, H. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1354–1363.
3. (a) Kuzuyama, T.; Noel, J. P.; Richard, S. B. *Nature* **2005**, *435*, 983–987; (b) Yu, D.; Morris-Natschke, S. L.; Lee, K-Hsiung. *Med. Res. Rev.* **2007**, *27*, 108–132; (c) Alvaro, E.; de la Torre, M. C.; Sierra, M. A. *Chem. Eur. J.* **2006**, *12*, 6403–6411; (d) Hagiwara, H.; Kamat, V. *Recent Res. Dev. Org. Biorg. Chem.* **1997**, *1*, 25–32; (e) Anon *Heterocycles* **2008**, *75*, 2351–2352; (f) Anon *Heterocycles* **2008**, *75*, 2309–2311.
4. (a) Yu, H.-L.; Xu, J.-H.; Wang, Y.-X.; Lu, W.-Y.; Lin, G.-Q. *J. Comb. Chem.* **2008**, *10*, 79–87; (b) Secundo, F.; Carrea, G.; De Amici, M.; Di Ventimiglia, S. J.; Dordick, J. S. *Biotechnol. Bioeng.* **2003**, *81*, 391–396; (c) Rich, J. O.; Michels, P. C.; Khmelnitsky, Y. L. *Curr. Opin. Chem. Biol.* **2002**, *6*, 161–167; (d) Krstenansky, J. L.; Khmelnitsky, Y. *Biorg. Med. Chem.* **1999**, *7*, 2157–2162; (e) Altreuter, D. H.; Clark, D. S. *Curr. Opin. Biotechnol.* **1999**, *10*, 130–136; (f) Michels, P. C.; Khmelnitsky, Y. L.; Dordick, J. S.; Clark, D. S. *Trends Biotechnol.* **1998**, *16*, 210–215.
5. (a) Monti, H.; Audran, G. *Mini-Rev. Org. Chem.* **2005**, *2*, 265–281; (b) Faber, K.; Kroutil, W. *Curr. Opin. Chem. Biol.* **2005**, *9*, 181–187; (c) Mueller, M. *Curr. Opin. Biotechnol.* **2004**, *15*, 591–598; (d) Shaw, N. M.; Robins, K. T.; Kiener, A. *Adv. Synth. Catal.* **2003**, *345*, 425–435; (e) Davis, B. G.; Boyer, V. *Nat. Prod. Rep.* **2001**, *18*, 618–640; (f) Whalem, L. J.; Wong, Chi-Huey *Aldrichim. Acta* **2006**, *39*, 63–71.
6. (a) Kesavan, S.; Panek, J. S.; Porko, J. A., Jr. *Org. Lett.* **2007**, *9*, 5203–5206; (b) Gu, W.; Ge, H. M.; Song, Y. C.; Ding, H.; Zhu, H. L.; Zhao, X. A.; Tan, R. X. *J. Nat. Prod.* **2007**, *701*, 114–117; (c) Beugelmans, R.; Chastanet, J.; Ginsburg, H.; Quintero-Cortes, L.; Roussi, G. *J. Org. Chem.* **1985**, *50*, 4933–4938.
7. Wipf, P.; Diana, C. *J. Org. Chem.* **2001**, *66*, 337–343.
8. (a) Vu, An. T.; Campbell, A. N.; Harris, H. A.; Unwalla, R. J.; Manas, E. S.; Mewshaw, R. E. *Biorg. Med. Chem. Lett.* **2007**, *17*, 4053–4056; (b) Siddaiah, V.; Rao, C. V.; Venkateswarlu, S.; Krishnaraju, A. V.; Subbaraju, G. V. *Biorg. Med. Chem.* **2006**, *14*, 2545–2551.

9. Cueva, J. P.; Giorgioni, G.; Grubbs, R. A.; Chemel, B. R.; Watts, V. J.; Nicholad, D. E. *J. Med. Chem.* **2006**, *49*, 6848–6857.
10. Garcia-Urdiales, E.; Alfonso, I.; Gotor, V. *Chem. Rev.* **2005**, *105*, 313–354.
11. (a) Fadel, A.; Arzel, P. *Tetrahedron: Asymmetry* **1997**, *8*, 283; (b) Kirihara, M.; Takuwa, T.; Kawasaki, M.; Kakuda, H.; Hirokami, S.; Takahata, H. *Chem. Lett.* **1999**, 405; (c) Ihara, M.; Suzuki, M.; Fukumoto, K.; Kabuto, C. *J. Am. Chem. Soc.* **1990**, *112*, 1164; (d) Toyooka, N.; Nishino, A.; Momose, T. *Tetrahedron Lett.* **1993**, *34*, 4539; (e) Suemune, H.; Harabe, T.; Xie, Z.-F.; Sakai, K. *Chem. Pharm. Bull.* **1988**, *36*, 4337.
12. (a) Kita, Y.; Takebe, Y.; Murata, K.; Naka, T.; Akai, S. *Tetrahedron Lett.* **1996**, *37*, 7369; (b) Kita, Y.; Naka, T.; Imanishi, M.; Akai, S.; Takebe, Y.; Matsugi, M. *Chem. Commun.* **1998**, 1183; (c) Kita, Y.; Takebe, Y.; Murata, K.; Naka, T.; Akai, S. *J.Org. Chem.* **2000**, *65*, 83.
13. (a) Weissfloch, A. N. E.; Kazlauskas, R. J. *J. Org. Chem.* **1995**, *60*, 6959–6969; (b) Hof, R. P.; Kellogg, M. R. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2051–2060; (c) Chen, S. T.; Fang, G. M. *J. Org. Chem.* **1997**, *62*, 4349–4357.
14. (a) Chen, C. S.; Wu, S. H.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc.* **1982**, *104*, 7294–7299; (b) Chen, C. S.; Wu, S. H.; Girdaukas, G.; Sih, C. J. *J. Am. Chem. Soc.* **1987**, *109*, 2812–2817.
15. (a) Kobayashi, S.; Ogino, T.; Shimizu, H.; Ishikawa, S.; Hamada, T.; Manabe, K. *Org. Lett.* **2005**, *7*, 4729–4731; (b) Ishikawa, S.; Hamada, T.; Manabe, K.; Kobayashi, S. *J. Am. Chem. Soc.* **2004**, *126*, 12236–12237; (c) Mahapatra, T.; Jana, N.; Nanda, S. *Tetrahedron: Asymmetry* **2008**, *19*, 1224–1232.