Chapter-III

An expedient synthesis of enantioenriched substituted (benzofuran-yl)-aryl and heteroaryl carbinols via Rap-Stoermer reaction / Asymmetric transfer hydrogenation.
Chapter 3: An expedient synthesis of enantioenriched substituted (benzofuran-yl)-aryl and heteroaryl carbinols via Rap-Stoermer reaction / Asymmetric transfer hydrogenation.

Introduction

The development of general methods for the synthesis of chiral compounds having biological activity has long constituted challenge for synthetic organic chemists. In general, chiral compounds that contain heteroaromatic functionality, in particular benzofuran motif possessing biologically active natural products are special interest for synthetic organic chemists.\(^1,2\) On the other hand, benzofuran-containing entities may constitute important target for pharmaceutical researches, including the possibility of being mentioned as drug candidates in clinical and preclinical studies.

(Benzofuran-2-yl) carbinols are important intermediates and structural motifs in medicinal chemistry. Such derivatives were investigated as antibacterial\(^3\) or antifungal agents.\(^4,5\) Moreover, optically active 2-(2-tert-butylamino-1-hydroxyethyl)-benzofurans were investigated as \(\beta\)-blockers.\(^5\) Many illustrative examples of this kind are 2-substituted benzofuran drugs such as Amiodarone (cardiac anti-arrythmic)\(^6,7\) and Benziodarone (coronary vasodilator).\(^8\) 2-Substituted benzofurans can also inhibit the HIV-1 reverse transcriptase\(^9\) or act as antiageing compounds.\(^10\) However, many 2-substituted benzofurans are well known to exhibit a broad range of biological activities, and therefore, the search for new biologically active compounds in this series is of interest. From this point of view, synthetic methods may be very useful in the production of specific structures characterized by given pharmacological qualities.

In furtherance of our research to develop new methodologies leads to synthesis of biologically active small molecules, we directed our attention on the development of general methods for the synthesis of various enatioenriched (benzofuran-2-yl) carbinols. In this context we described an approach to synthesis of optically active benzofuran scaffolds starting from simple and achiral starting materials.
Biologically relevant 2-substituted benzofurans:

Oxazolidine 1 was displayed exceptional potency in the ob/ob mouse and the modification in the oxazolidinedione series also led to very potent compounds.\textsuperscript{11a} Similarly, the racemic carbinol 2 was patented as anti-diabetic and hypoglicemic agent (Figure 1).\textsuperscript{11b}

![Figure 1](image1.png)

1 R = H  
2 R = OH

Thiophene 3 has analgesic activity (Figure 2).\textsuperscript{12}

![Figure 2](image2.png)

The triazole 4 was found to act as a plant growth regulator of summer rapes,\textsuperscript{13} while compound 5 is a natural insecticide that is found in derris root (Figure 3).\textsuperscript{14} Analogues of compound 5 have been found to have analgesic activity in addition to insecticidal one.\textsuperscript{15}

![Figure 3](image3.png)

Coumazoline 6 is a peripheral vasoconstrictor useful as a nasal decongestant,\textsuperscript{16} while prifuroline 7 is an antiarrhythmic with low toxicity.\textsuperscript{17} Biclonazole 8 is antimycotic and
antibiotic with activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Figure 4).¹⁸

![Figure 4](image1.png)

Many carboxylic acid derivatives of 2-benzofuranyl carbinols have important activity: the hemisuccinate 9, for example, was reported as cardiotonic and vasodilator (Figure 5).¹⁹

![Figure 5](image2.png)

Furacrinic acid 10 is antihypertensive²⁰ and its pyridinyl derivative 11 (Figure 6) is an inhibitor of thromboxane synthetase.²¹

![Figure 6](image3.png)

Molecules containing the benzofuran scaffold also find use as antioxidants and brightening agents, and in agriculture. The benzofuran group has also been joined to other scaffolds to form molecules that inhibit tubulin (antimitotic activity), EP₃ prostanoid receptors, and show
antipsychotic activity. Moreover, they are active as antifungals, K-selective opioid receptor analgesics, angiotensin II antagonists (hypertension), and inhibitors of platelet aggregation through fibrinogen receptor antagonism such as the amidinobenzofuran 12 (Figure 7).\(^{23}\)

![Figure 7](image)

Cloridarol 13 (Figure 8) was used in for treatment of lipidemia and as an anticoagulant.\(^{24}\) Racemates of 2-benzofuranyl carbinols like 14 have been shown to display antifungal and aromatase inhibiting activities. These carbinols were prepared in racemic form in good yields and recently synthesis of aryl 2-benzofuranyl in high enantiomer purity was reported.\(^{25}\)

![Figure 8](image)

The racemic triazine 15 is an herbicide useful in protecting rice paddies,\(^{26}\) while compound 16 (Figure 9) gave complete control of several weeds without crop damage.\(^{27}\)

![Figure 9](image)
Medical applications of a series of amine benzofuran derivatives have been explored. Etofuradine 17 is an antitussive and antihistamine agent (Figure 10).

![Image 17]

**Figure 10**

Furaprofen (α-methyl-3-phenyl-7-benzofuranacetic acid) 29 has a similar activity than the well-known Ibuprofen (2- [4-(2-methylpropyl)phenyl] propanoic acid). Trioxsalen 18 (Figure 11) is a synthetic psoralen that offers skin protection against UVB erythema and is an orally active tanning and pigmentation agent useful in the treatment of vitiligo.

![Image 18]

**Figure 11**

An optically active benzofuran derivative was isolated from the sponge *Dysidea frondosa* along with other derivatives such as frondosins A-D, each of them inhibiting the binding of IL-8 to its receptor in the low micromolar range. 31 Frondosin B 19 (Figure 12) is isolated in an enantiomeric form and a more recent paper reported the total synthesis and determination of the absolute configuration of Frondosin B. 32
Liphagal 20 is a more potent inhibitor of P13K α, and shows significant *in vitro* cytotoxicity against a small panel of human tumor cell lines, making it a promising lead structure for the development of a new class of P13K inhibitors.

![Figure 13](image1)

Bufuralol 21, the most studied compound of this class, proved effective for treatment of hypertension, is a potent non selective β-adrenergic receptor antagonist, an inhibitor of testosterone 6β-hydroxylase, and is widely used in studies of cytochrome P450. 1-(3-Phenethylbenzofuran-2-yl)-2-propylaminoethanol 22, a propafenone 23 (Figure 14) analogue, shows antiarrhythmic activity, but in contrast to 3 lacks β-adrenoacceptor blocking activity. (R)-Bufuralol is a commonly used marker of hepatic CYP 2D6 activity.

![Figure 14](image2)

The benzofuran derivatives 24a-b are intermediates in the synthesis of chiral azoles 25a-b (Figure 15). Compounds 25a-b were initially examined as antifungal agents and have been found to be powerful nonsteroidal aromatase inhibitors. They are used in the treatment of hormone-dependent breast cancer.
A series of methoxysubstituted 2-(3', 4', 5'-trimethoxybenzoyl)-benzo[b]furan derivatives with an amino or dimethylamino substituent at the 3-position of the benzo[b]furan skeleton 27, 28 and 29 were identified as a new class of antimitotic agents. The presence of a methoxy group at the 6-position contributed to maximal activity. Compound 26 evaluated for their in vitro inhibition of tubulin polymerization and for their inhibitory effects on the binding of [3H] colchicine to tubulin with IC₅₀ values of 0.70, 0.55, 0.43 and 0.57 μM.
Previous approaches for the synthesis of 2-sustituted benzofurans and achiral, chiral benzofuranyl carbinols:

Numerous efforts have been directed for developing synthetic strategies for this privileged structure, and recently combinatorial approaches to this class of compounds have also been an active research area.\textsuperscript{41}

General synthetic methodologies are described\textsuperscript{42} that may involve the condensation reactions between ketones (or aldehydes) and a number of different forms of nucleophiles, under acidic or basic conditions.\textsuperscript{43} For instance, condensation of salicylaldehyde and its derivatives \textbf{30a} with various esters of chloroacetic acids in the presence of tetrabutylammonium bromide (TBAB) leads to the synthesis of benzo[b]furans \textbf{31}. The solventless phasetransfer catalytic (PTC) reaction is carried out under microwave irradiation (Scheme 1) by the use of a domestic oven.\textsuperscript{44}

![Scheme 1](image)

Using an analogue procedure and utilizing ethylbromoacetate a benzofuran scaffold containing molecule was synthesized which exhibits antifungal activity against \textit{C. albicans in vitro} was as well as found to be a potent, selective CaNmt inhibitor (RO-09-4609), (Scheme 2).\textsuperscript{45}

![Scheme 2](image)
The substituted benzofuran scaffold were synthesized starting from 2-allylphenol 34. Epoxidation of 2-allylphenol 34 with \( m \)-chloroperbenzoic acid (MCPBA) followed by oxidation of the dihydrobenzofuran intermediate 35 with excess DDQ (dichloro dicyano quinone) led to the required product moderate to good yields (Scheme 3).

![Scheme 3](image)

In another method, the palladium catalyzed Sonagashira–Stevens coupling reaction was readily applied to the synthesis of 2-hydroxyethylbenzofurans in high yields (Scheme 4).

![Scheme 4](image)

An interesting tandem Pd-assisted cyclization-coupling reaction was reported for the synthesis of 2-functionalized benzofuran 39 (Scheme 5) from readily available \( o \)-(2,2-dibromovinyl)-phenol 39 using a 1,1′-bis(diphenylphosphino)-palladium complex, formed in situ.

![Scheme 5](image)
The reaction of phenoxyacetates with $N,N$-dimethylformamide dimethyl acetal (DMFDMA) at 90 °C for 24 h or by MW irradiation within 2 h followed by Lewis acid mediated cyclization of the corresponding 2-aryloxy-3-dimethylaminopropenoates provided benzofurans 40 (Scheme 6).

![Scheme 6](image)

The synthesis of functionalized benzofurans by sequential Suzuki and BBr$_3$ reaction was reported (Scheme 7).$^{50}$ The Pd(PPh$_3$)$_4$ (3 mol %) catalyzed reaction of methyl 2-bromo-2-(dihydrofuran-2(3H)-ylidene)acetate with (2-methoxyphenyl)boronic acids resulted in 2-alkylenetetrahydrofuran with excellent $E$-diastereoselectivity. On further treatment of this compound with BBr$_3$ afforded the benzofuran 41 through a domino “ring-cleavage deprotection- cyclization” reaction sequence.

![Scheme 7](image)
A general synthesis of 2-benzofuran-2-ylacetamides 42 starting from 1-(2-allyloxyaryl)-2-yn-1-ols, amines, and CO in the presence of catalytic amount of PdI₂ in combination with PPh₃ and KI, has been reported. It was based on the “sequential homobimetallic catalysis” concept (Scheme 8). This is a process in which two different complexes of the same metal, but in two different oxidation states promote two catalytic cycles in sequence.⁵¹

In general, the benzofurylaryl ketones were synthesized by a Rap-Stormer reaction and subsequent reduction with sodium borohydride gave the corresponding racemic carbinol 43 (Scheme 9).⁵²

Later on, a modified procedure was described for the synthesis of 2-alkyl/aryl substituted benzo[b]furan carbinols employing catalytic amount of palladium. Thus, the reaction of o-iodophenol with 2-methyl-3-butyn-2-ol in the presence of catalytic amount of palladium and CuI followed by (S)-prolinol in water at 80 °C (Scheme 10) led to a cyclized product 44.⁵³
Chiral 1-(benzofuran-2-yl)-arylamines \( 45 \) have been developed by Botta et. al., and the resulting derivatives were screened for treatment of fungal skin infections. Enantiomerically pure amines were used as starting material for the synthesis of the target compounds. \((R)-\) and \((S)-\)benzofuran-2-yl (phenyl)-methanamines were prepared from corresponding \((S)-\) and \((R)-\)1-phenyl-2- propynylamine by hetero-annulation with 2-iodophenol (Scheme 11) in the presence of \( \text{PdCl}_2(\text{PPh}_3)_2, \text{CuI}, \) and tetramethylguanidine (TMG) in DMF.\(^{54} \)

\[
\begin{align*}
\text{NH}_2 & \quad \text{I} \quad \text{HO} \\
\text{NH}_2 & \quad \text{PdCl}_2(\text{PPh}_3)_2 \\
\text{CuI, TMG, DMF} & \quad 45
\end{align*}
\]

**Scheme 11**

A Rh(I)-catalyzed demethylation-cyclization sequence for a direct transformation of \( o-\)anisolesubstituted ynamides to benzofurans was described. The procedure utilized both rhodium and silver complexes. The Ag salt functions synergistically with Rh(I) for the key demethylation step of the \( o-\)anisyl amides (Scheme 12).\(^{55} \) A series of chiral 2-amido benzofurans \( 46 \) were synthesized.

\[
\begin{align*}
\text{MeMeO} & \quad \text{Bn} \quad \text{O} \\
\text{N} & \quad \text{Bn} \quad \text{Me} \\
\text{Cat. RhCl(PPh)_3} & \quad \text{Cat. AgBF}_4 \\
46
\end{align*}
\]

**Scheme 12**

*En route* to the total synthesis of Kendomycin, a procedure for the preparation of a chiral 2-substituted benzofuran derivative was disclosed by Lee et. al.,. The synthesis of the benzofuranyl compound \( 47 \) was accomplished using a two-step sequence in which a phenolic phosphonium bromide was coupled through a Wittig process with the chiral non racemic 5-benzyloxy-2,4-dimethylpentanoic acid and ensuing cyclization (Scheme13)\(^{56} \).
Scheme 13

The benzofuranyldiazoacetate was synthesized from p-methoxyphenol and subjected with trans-piperylene in the presence of catalytic amount of Rh$_2$(R-DOSP)$_4$ resulted in the [4 + 3] cycloadduct which was hydrogenated to produce compound 48 (Scheme 14). This is a intermediate for the synthesis of Frondosin B.$^{57}$

Scheme 14

Enantiotopic selective reduction of 2-acetoxy-1-(benzofuran-2-yl)ethanones by Baker’s yeast furnished enantioenriched (benzofuran-2-yl)carbinols 49 (Scheme 15).$^{58}$ Through this protocol several derivatives were synthesized.

Scheme 15

The kinetic resolution of racemic 1-(benzofuran-2-yl)ethanols was attempted employing Lipase/vinylacetate. This process showed (R)-enantiomeric preference yielding (1R)-1-acetoxy-1- (benzo-furan-2-yl)-ethanes (R)-51 and (1S)-1-(benzofuran-2-yl)ethanols (S)-50 (Scheme 16).$^{59}$
Scheme 16

The asymmetric transfer hydrogenation of dialkylaminomethyl ketones also reported with high enantioselectivity. Thus, the synthesis of \((S)\text{-}(\text{-}1\text{-}(\text{benzofuran}\text{-}2\text{-}yI)\text{-}2\text{-}(\text{dimethylamino})\text{ethanol})\) \(52\) was achieved via transfer hydrogenation using formic acid–triethylamine and \(\text{RuCl}(\text{R,R}\text{-TsDPEN})(\text{p-cymene})\) catalyst using \((\text{benzofuran}\text{-}2\text{-}yI)\text{-}2\text{-}(\text{dimethylamino})\text{ethanone}\) which in turn was generated from 2-benzofuryl methyl ketone by bromination with pyridinium perbromide followed by treatment with dimethylamine. (Scheme 17).

\[
\begin{align*}
\text{Scheme 17} & \\
\text{ArylalkylZinc or dialkylZinc addition in the presence of aminoalcohol, (-)-MIB in combination with 0.8 equiv TEEDA (N,N,N',N'-Tetraethylethylene diamine) to benzofuryl aldehyde generated corresponding carbinol (S)-43, in 90% enantioselectivity (Scheme 18).}
\end{align*}
\]
In a similar fashion, the 1,2-addition of phenylboronic acid to aldehyde using 1.0 mol % of catalyst which is generated in situ from thioether-imidazolinium chloride L and [Pd(allyl)Cl]₂ in the presence of cesium fluoride in toluene at 80 °C for 3 h provided cabinol 43 (Scheme 19).

\[
\begin{align*}
&\text{Ph} = \text{Ph} \\
&\text{H} = \text{H} \\
&\text{Cl} = \text{Cl} \\
&\text{PhS} = \text{PhS} \\
&\text{L} = \text{L} \\
\end{align*}
\]

Scheme 19

Asymmetric transfer hydrogenation of α-tosyloxy heteroaryl ketones catalyzed by Cp*RhCl[(S,S)- TsDPEN] using an azeotropic mixture of formic acid/triethylamine afforded the corresponding diol-2-monic sulfonates 53 in good yield with appreciable enantioselectivity (Scheme 20).

\[
\begin{align*}
&\text{Ph} = \text{Ph} \\
&\text{H} = \text{H} \\
&\text{Cl} = \text{Cl} \\
&\text{PhS} = \text{PhS} \\
&\text{L} = \text{L} \\
\end{align*}
\]

Scheme 20

PRESENT WORK

Benzofuran structural moiety is present in numerous biologically active natural products. These privileged pharmacophore containing molecules exhibit therapeutic properties over a wide range of targets. Owing to their prevalence in natural products as well as pharmaceuticals has stimulated significant interest in the synthesis of benzofuran containing heterocycles. A flurry of synthetic methods has been appeared in the literature for the synthesis of benzofuran and their derivatives (vide infra). Among them, Rap-Stoermer reaction is appears to be a versatile straightforward approach for the synthesis of functionally varied benzofuran scaffolds. It was observed that the racemic substituted (benzofuran-yl)-
phenylcarbinols and related compounds reduced blood lipids in both laboratory animals\(^68\) and patients.\(^69\)

The increasing awareness of the importance of chirality in the context of biological activity has stimulated a growing demand for efficient methods for the preparation of optically active compounds. Therefore, when a biologically active chiral compound, such as a drug, interacts with a receptor site which is chiral itself, it should come as no surprise that the two enantiomers of the drug interact differently and may lead to different effects. For many chiral compounds the two enantiomers have quite distinct biological activities. In this context the direct syntheses of chiral substituted benzofuran scaffolds assume a great value as potential drug candidates.

Despite the availability of several methods for the synthesis of 2-substituted benzofurans, surprisingly not too much attention has been focused on the developments of general methods and strategies for the synthesis of chirally substituted benzofuran derivatives. Though if enantiomerically pure 2-substituted benzofurans might constitute starting materials for the production of biologically active compounds and considering the real tendency directed toward the development of enantiomerically pure drugs, there is actually a limited number of papers related to the preparation of enantiomers of benzofuran derivatives, either by stereoselective synthesis or enantiomeric separation. In particular, only a few examples of enantiopure benzofuran derivatives having the heterocyclic moiety directly linked to the stereogenic center have as yet been reported, most likely because of difficulties in their preparation. This prompted us to initiate a programme for the synthesis of enantioenriched substituted (benzofuran-yl)-phenylcarbinols in substantial amount.

**Results and Discussions:**

Initially, we have evaluated base mediated reaction of salicylaldehyde 30a with \(\alpha\)-haloacyl \(N\)-methoxy-\(N\)-methylketone 54a employing solvent,\(^{67a}\) solvent-free\(^{67a}\) and microwave-assisted conditions.\(^{67b}\) The desired product (benzofuran-yl)-\(N\)-methoxy-\(N\)-methylketone 55a was obtained in poor yield. Additionally, the reaction mixture tlc analysis showed multiple spots. Hence, we performed a reaction between salicylaldehyde 30a and \(\alpha\)-haloacyl \(N\)-methoxy-\(N\)-methylketone 54a employing acetonitrile as a solvent in presence of \(\text{Cs}_2\text{CO}_3\) for 6h stirring at ambient temperature, the desired product 55a was obtained in 95% isolated yield (Scheme 21).
The compound 55a was characterised by $^1$H NMR. The N-attached methyl protons appeared at $\delta$ 3.34 as a singlet integrating for three protons. The NO-attached methyl protons appeared as a singlet at $\delta$ 3.78 integrating for three protons. A singlet was appeared at $\delta$ 7.40 indicating for the presence of a proton at 3-position of benzofuran moiety. The aromatic protons show two doublets at $\delta$ 7.58, 7.51 integrating for one proton each, and two triplets at $\delta$ 7.34, 7.20 integrating for one proton each indicating for the product formation.

The IR spectrum shows a sharp peak at 1647 cm$^{-1}$ characteristic for amide carbonyl group. The mass spectrum showing a peak at $m/z$ 206 [M + H]$^+$ also proved the assigned product structure formation.

In Rap-Stoermer reaction, the choice of base and solvent was found to be critical; hence we screened a number of bases (NaOAc, KOAc, K$_2$CO$_3$, K$_3$PO$_4$, CsOH.H$_2$O, Cs$_2$CO$_3$) and solvents (toluene, CH$_2$Cl$_2$, CHCl$_3$, DMF, EtOAc, CH$_3$CN), but found that Cs$_2$CO$_3$ and acetonitrile gave the desired product 55a (Scheme 21). The Cs$_2$CO$_3$ and EtOAc system also resulted in the desired product 3a but slightly less yield (90%).

The generality and scope of this protocol were evaluated using above optimized conditions and the results are shown in Scheme 22.
From the Scheme 22, it appears that the nature of acyl substitution has no effect on coupling reaction; hence the benzofuryl derivative products were obtained with excellent yields (55b, 55c and 55e). The characteristic spectral data (\( ^1\text{H}, \ ^{13}\text{C}, \text{IR and mass} \)) of these compounds are given in experimental section.

Remarkably, thioaldehyde 30b with N-methoxy N-methyl α-bromoacetamide 54a underwent coupling and the corresponding product 55d furnished 92% indicating the efficiency of this protocol. The compound 55d \(^1\text{H} \) NMR spectra show the \( N \)-attached methyl protons appeared as a singlet at \( \delta \ 3.41 \) integrating for three protons. The NO-attached methyl protons appeared at \( \delta \ 3.83 \) as singlet integrating for three protons. The characteristic heterocyclic –CH appears at \( \delta \ 8.17 \) as singlet indicating for the presence of a proton at 3-position of benzothiofuran moiety. The aromatic protons show doublet of doublet at \( \delta \ 7.84 \) integrating for two protons, and a multiplet at \( \delta \ 7.41-7.34 \) integrating for two protons. The IR spectrum shows a sharp peak at 1680 cm\(^{-1} \) characteristic for amide carbonyl group. The mass spectrum showing peak at \( m/z \ 222 \) [M + H]\(^+ \). Based on the above spectral data the product could be assigned as \( N \)-Methoxy-N-methylbenzo[b]thiophene-2-carboxamide 55d.
As can be seen from scheme 22, we further extrapolated the scope of this protocol with different substituted salicylaldehydes and various α-haloaryl ketones.

The reaction between salicylaldehyde 30a and α-bromacylphenylketone 54e employing acetonitrile as a solvent in presence of Cs₂CO₃ stirring at ambient temperature for 6h, the desired product 55e was obtained in 96% isolated yield (Scheme 23). The reaction of 2,6-dihydroxy benzaldehyde 30c and bromo compound 54e gave the product 55f in 93% yield. The highly substituted benzaldehydes 30d and 30e reacted with α-bromacyl 4-OBn-phenylketone 54f afforded the products 55g and 55h in 86%, 78% yield respectively. The reaction between salicylaldehyde 30a and α-bromacyl 4-OBn, 3-OMe-phenylketone 54g gave the product 55i in 89% yield (Scheme 23).

The compound 55e was identified with ^1H NMR, IR and mass spectral data. In ^1H NMR, a doublet integrating for two protons at δ 8.06 (J = 8.1 Hz) and a triplet appeared at δ 7.70 (J = 8.1 Hz) integrating for two protons indicating the presence of keto group directly attached to a phenyl ring. The characteristic heterocyclic –CH appears as singlet at δ 7.53 integrating for one proton indicating the presence of a proton at 3-position of benzofuran moiety. The aromatic protons show a multiplet at δ 7.54-7.45 integrating for three protons and doublet of doublet at δ 7.29 integrating for one proton. The IR spectrum shows a sharp stretch at 1641 cm⁻¹ characteristic for unsaturated carbonyl group. The mass spectrum showing a peak at m/z 223 [M + H]^+. Based on the above spectral data the product could be assigned as benzofuran-2-yl(phenyl)methanone 55e. The characteristic analytical data (^1H, ^13C, IR and mass) of 55f, 55g, 55h, and 55i are given in experimental section.
Similarly, salicylaldehyde 30a reacted with α-bromacylthiophen-2-ylketone 54h resulted in the product 55j in 91% yield. o-vaniline 30f reacted with α-bromacylthiophen-2-ylketone 54h gave the product 55k in 90% yield. The reaction between salicylaldehyde 30a and α-bromacylfuran-2-ylketone 54i obtained the product 55l in 87% yield. 2-Hydroxy-1-naphthal 30g reacted with α-bromacylphenylketone 54e under standard protocol furnished the product 55m in 92% yield (Scheme 24).
Scheme 24

The compound \(55j\) was identified by its \(^1\)H NMR spectral data. The \(-CH\) adjacent to sulfur atom appeared as doublet at \(\delta 8.34\) \((J = 3.9\text{ Hz})\) integrating for one proton. The aromatic protons show multiplet at \(\delta 7.74-7.69\) integrating for three protons. The characteristic heterocyclic proton appears as singlet at \(\delta 7.61\) indicating the presence of a proton at 3-position of benzofuran moiety. The IR spectrum shows a sharp peak at 1648 cm\(^{-1}\) characteristic for unsaturated carbonyl group. The mass spectrum showing a peak at \(m/z 229\) \([M + H]^+\). Based on the above spectral data the product identified as benzofuran-2-yl(thiophen-2-yl)methanone \(55j\). Likewise, the compounds \(55k, 55l,\) and \(55m\) were also fully characterized and their analytical data is represented in experimental section.

Having realized optimum conditions for synthesis of benzofuryl derivative; further, we envisaged to generate optically active carbinols via a Rap-Stoermer reaction / catalytic asymmetric transfer hydrogenation (ATH).\(^7\) At the outset, we have selected salicylaldehyde \(30a\) and \(54e\) as a test substrates and carried out the reaction under standard protocol \((\text{vide infra})\). After 6h, the reaction mixture was filtered and the filtrate was evaporated. To the
resulting residue, 2-propanol was added followed by 2 mol% of \( R,R \)-diamine-Ru catalyst A and heated to 60 °C for 10 h (Scheme 25).

```
\[ \text{Cat. A} \]
\[
\begin{align*}
\text{Cat. B}
\end{align*}
\]
```

Scheme 25

The anticipated product 43a was not observed. While, the same reaction with \( \text{Et}_3\text{N.HCOOH} \) azeotropic mixture (5:2) as hydrogen source, in EtOAc at rt for 3 h resulted in the desired carbinol 43a in 96% yield with 82% enantiomeric ratio. Further, enantioenrichment of 43a was achieved under similar conditions using 1 mol% of \( R,R \)-diamine-Rh catalyst B in place of catalyst A. Fortunately, employing EtOAc as solvent in both reactions (i.e. Rap-Stoermer reaction and ATH reaction) and \( R,R \)-diamine-Rh (Cat. B)\textsuperscript{71} as a catalyst under otherwise identical conditions were furnished the required product 43a in 93% yield with 99%ee (Scheme 25). It was observed that less than 1 mol% loading of catalyst, led to a decreased yield and ee. The Enantiomeric excess was analyzed by HPLC on chiral column OD-H (250 x 4.6mm, 5 μm, UV\textsubscript{254nm}, Hexane:2-propanol (80:20), tr (1) = 27.1 min, tr (2) = 31.4 min using recemates for comparison. The absolute configuration of new stereogenic center was assigned as R by comparison of sign of rotation \( \{[\alpha]^{23}_D = -7.9^\circ (c = 3.0, \text{CHCl}_3); \text{lit.}^{72} [\alpha]^{23}_D = + 3.5^\circ (c = 0.041, \text{CHCl}_3 \text{ for opposite isomer}) \} \) which is also in agreement with Noyori’s protocol\textsuperscript{73} i.e. \( R,R \)-diamine-Rh induces R-configuration, while \( S,S \)-diamine-Rh generates S-configuration. Absolute configuration of remaining was assigned by analogy.

The compound (\textit{R})-43a was characterised by \(^1\text{H} \text{NMR}. \) The aromatic protons show three sets of multiplets at \( \delta \) 7.51-7.42 integrating for three protons, at \( \delta \) 7.41-7.30 integrating for four protons, and at \( \delta \) 7.24-7.12 for two protons. The characteristic heterocyclic proton appears as singlet at \( \delta \) 6.46 indicating the presence of a proton at 3-position of benzofuran moiety and hydroxyl group attached proton appears as singlet at \( \delta \) 5.90. The IR spectrum shows a
prominent stretch at 3404 cm\(^{-1}\) characteristic for hydroxyl group. The mass spectrum showing peak at \(m/z\) 247 [M + Na]\(^+\). Based on the above spectral data the product could be assigned as \((R)\)-benzofuran-2-yl(phenyl)methanol \((R)-43a\).

To test the generality and efficiency of this methodology, we subjected various substituted salicylaldehydes with \(\alpha\)-bromoaryl ketones and our results are shown in Table 1.

A series of different \(\alpha\)-haloaryl ketones and various salicylaldehydes were subjected to this protocol. We were pleased to see that the reaction between \(o\)-vaniline \(30f\) and \(\alpha\)-bromoarylketone \(54e\) afforded the product \((R)-43b\) in 96% yield and with 99% enantiomeric excess. Similarly \(o\)-vaniline \(30f\) reacted with \(\alpha\)-bromoarylketone \(54j\) afforded the product \((R)-43c\) in 91% yield and with excellent ee (99%). The reaction between \(o\)-vaniline \(30f\) and \(\alpha\)-bromoarylketone \(54k\) afforded the product \((R)-43d\) in 87% yield and with 95% enantiomeric excess. While, \(p\)-fluoro aryl keto substrate \(54l\) (Table 1, entry 4) gave the product \((R)-43e\) in moderate ee (80%) and yield. In the case of \(p\)-OBn- aryl keto substrate \(54m\) (Table 1, entry 5) obtained the product \((R)-43f\) in 92% yield with 82% ee. It was observed that the reaction of salicylaldehyde \(30a\) and 2’,4’-dimethoxy aryl keto substrate \(54n\) gave the product \((R)-43g\) in 91% yield with excellent (99%) ee.
Table 1: Synthesis of enantioenriched substituted (benzofuran-yl)-phenylcarbinols.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>α-haloketone</th>
<th>Product</th>
<th>% yield</th>
<th>% ee</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>30f</td>
<td>54e</td>
<td><img src="image1" alt="Product image" /></td>
<td>96</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>30f</td>
<td>54j</td>
<td><img src="image2" alt="Product image" /></td>
<td>91</td>
<td>99</td>
</tr>
<tr>
<td>3</td>
<td>30f</td>
<td>54k</td>
<td><img src="image3" alt="Product image" /></td>
<td>87</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><img src="image4" alt="Product image" /></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4  30f

(R)-43g

84  80

5  30f

92  82

91  99

6  30a
The product (R)-43b was identified by $^1$H NMR data. The aromatic protons show two sets of multiplets at $\delta$ 7.50-7.43 integrating for two protons, and at $\delta$ 7.39-7.29 for two protons. A singlet was appeared at $\delta$ 7.24. Another multiplet at $\delta$ 7.07-7.03 integrates one proton and a doublet of doublet was appeared at $\delta$ 6.71 ($J = 2.2, 6.4$ Hz) integrating for one proton. The characteristic heterocyclic proton appears as singlet at $\delta$ 6.40 and hydroxyl group attached proton appears as singlet at $\delta$ 5.91. The O-attached methyl protons appeared at $\delta$ 3.97 as singlet. The IR spectrum shows a peak at 3433 cm$^{-1}$ characteristic for hydroxyl group. The mass spectrum showing a peak at $m/z$ 277 [M + Na]$^+$. Based on the above spectral data the product identified as (7-methoxybenzofuran-2-yl)(phenyl)methanol (R)-43b.

Further, we performed the reactions under standard conditions with sterically and electronically differentiated salicylaldehydes and $\alpha$-bromoarylketone 54e and the results are shown in Table 2.

The reaction between di-OBn-aldehyde 30h and $\alpha$-bromoarylketone 54e afforded the product (R)-43h in 89% yield with 85% ee. The 5-$^3$Bu-salicylaldehyde 30i and 3,5-di-$^3$Bu-salicylaldehyde 30j reacted with $\alpha$-bromoarylketone 54e gave the products (R)-43i and (R)-43j with 86% yield, 94% ee and 78% yield, 90% ee respectively. Similarly the reaction between 5-bromo salicylaldehyde 30k and $\alpha$-bromoarylketone 54e furnished the product (R)-43k with high yield and enantioselectivity.
Table 2: Synthesis of enantioenriched substituted (benzofuran-yl)-phenylcarbinols.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Aldehyde</th>
<th>α-haloketone</th>
<th>Product</th>
<th>% yield</th>
<th>% ee</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Structure" /></td>
<td>54e</td>
<td><img src="image2" alt="Structure" /></td>
<td>89</td>
<td>85</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="Structure" /></td>
<td>54e</td>
<td><img src="image4" alt="Structure" /></td>
<td>86</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="Structure" /></td>
<td>54e</td>
<td><img src="image6" alt="Structure" /></td>
<td>78</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>54e</td>
<td></td>
<td></td>
<td>92</td>
<td>88</td>
</tr>
</tbody>
</table>
The product \((R)-43i\) confirmed by \(^1\)H NMR data. A singlet at \(\delta\) 1.34 integrates for nine protons correspond to \(t\)-Butyl group. A broad singlet appeared at \(\delta\) 2.48 indicated for hydroxyl proton. Another singlet integrates for one proton at \(\delta\) 5.85 relates to hydroxyl group attached carbon proton. The characteristic heterocyclic proton appears as singlet at \(\delta\) 6.41. The aromatic protons show two sets of multiplets at \(\delta\) 7.44-7.40 integrating for three protons, and at \(\delta\) 7.36-7.24 for five protons. The IR spectrum shows a peak at 3412 cm\(^{-1}\) characteristic for hydroxyl group. The mass spectrum showing peak at \(m/z\) 281 [M + H]\(^+\). Based on the above spectral data the product could be assigned as \((R)-(5\text{-}\text{tert-butylbenzofuran}-2\text{-}y\text{l})(\text{phenyl})\text{methanol} (R)-43i\).

Likewise, \((R)-43h\), \((R)-43j\), and \((R)-43k\) were fully characterized by \(^1\)H NMR, IR and mass. The complete analytical data was given in the experimental section.

\[
\begin{align*}
30g & \quad + \quad \text{Br-} & 54e & \quad \xrightarrow{\text{a) \(\text{Cs}_2\text{CO}_3\) (1 equiv.)} \quad \text{EtOAc, rt, 6h} \quad \text{b) 1 mol% cat. B} \quad \text{Et}_3\text{N-HCO}_2\text{H (5:2)} \quad \text{rt, 3h}} & \quad \xrightarrow{(R)-43i} \\
30a & \quad + \quad \text{Br-} & 54h & \quad \xrightarrow{\text{a) \(\text{Cs}_2\text{CO}_3\) (1 equiv.)} \quad \text{EtOAc, rt, 6h} \quad \text{b) 1 mol% cat. B} \quad \text{Et}_3\text{N-HCO}_2\text{H (5:2)} \quad \text{rt, 3h}} & \quad \xrightarrow{(R)-43m} \\
30f & \quad + \quad 54h & \quad \xrightarrow{\text{a) \(\text{Cs}_2\text{CO}_3\) (1 equiv.)} \quad \text{EtOAc, rt, 6h} \quad \text{b) 1 mol% cat. B} \quad \text{Et}_3\text{N-HCO}_2\text{H (5:2)} \quad \text{rt, 3h}} & \quad \xrightarrow{(R)-43n} \\
30a & \quad + \quad \text{Br-} & 54i & \quad \xrightarrow{\text{a) \(\text{Cs}_2\text{CO}_3\) (1 equiv.)} \quad \text{EtOAc, rt, 6h} \quad \text{b) 1 mol% cat. B} \quad \text{Et}_3\text{N-HCO}_2\text{H (5:2)} \quad \text{rt, 3h}} & \quad \xrightarrow{(R)-43o} \\
\end{align*}
\]

Scheme 26
Additionally, we envisaged applying this protocol to various α-bromoheteroarylketones 54h-i and aldehydes 30a and 30f and the results are shown in scheme 26. The reaction between 2-hydroxy-1-naphthal 30g and α-bromoarylketone 54e resulted in the product (R)-43l in 90% yield with 99% ee. The reaction of α-bromothiofuryl ketone 54h with 3-methoxy salicylaldehyde 30f and 30a led to the expected products (R)-43m, (R)-43n with high ee and yield. In the similar vein, α-bromofuryl ketone 54i with 30a also furnished the product (R)-43o in 85% yield and with 87% ee (Scheme 26).

The compound (R)-43l was identified with 1H NMR, IR and mass spectral data. In 1H NMR, a broad singlet appeared at δ 2.62 indicates the hydroxyl proton. The hydroxyl attached carbon proton appeared as singlet at δ 5.97 integrating for one proton. The characteristic heterocyclic proton appears as singlet at δ 6.92. The aromatic protons show two sets of doublets at δ 7.98 (J = 8.1 Hz) integrating for one proton, and at δ 7.85 (J = 7.9 Hz) for one proton. A multiplet appeared at δ 7.68-7.61 integrating for one proton. Another doublet appeared at δ 7.55 (J = 8.8 Hz) integrates for one proton and the other protons appeared at their respective positions. The IR spectrum shows a peak at 3422 cm⁻¹ characteristic for hydroxyl group. The mass spectrum showing a peak at m/z 275 [M + H]^+. Based on the above spectral data the product could be assigned as (R)-naphtho[2,1-b]furan-2-yl(phenyl)methanol (R)-43l.

The compound (R)-43m was characterized by 1H NMR. The hydroxyl attached carbon proton appeared at δ 6.05 as a broad singlet integrating for one proton. The characteristic heterocyclic proton appears as singlet at δ 6.57. The aromatic protons showed a multiplet at δ 7.24-7.13 integrating for three protons. Two sets of doublets appeared at δ 7.45 (J = 7.5 Hz) and at δ 7.38 (J = 8.3 Hz) for one proton each. Another doublet appears at δ 6.99 (J = 3.0 Hz) integrating for one proton indicates product formation. The IR spectrum shows a peak at 3426 cm⁻¹ characteristic for hydroxyl group. The mass spectrum showing a peak at m/z 275 [M + H]^+. Based on the above spectral data the product could be assigned as (R)-benzofuran-2-yl(thiophen-2-yl)methanol (R)-43m.

In conclusion, we have developed an expedient synthesis of enantioenriched substituted (benzofuran-yl)-phenyl-carbinols with high optical and chemical yields. A key feature of this protocol is synthesis of functionally varied benzofuran scaffolds via a Rap-Stoermer reaction / catalytic asymmetric transfer hydrogenation (ATH) using substituted salicylaldehyde and α-haloaryl ketones. This protocol in turn could be facilitates to synthesis of numerous
biologically important new compounds with varying substitutions in the salicylaldehyde and α-bromoarylketones, which could be screened for biological activity.
EXPERIMENTAL SECTION

Typical experimental procedure for synthesis of bezofuran:

To a stirred solution of bromo compound (1.0 mmol) in CH$_3$CN (10 mL) was added Cs$_2$CO$_3$ (1.0 mmol) under N$_2$ atmosphere, after stirred the reaction mixture for 10 min the aldehyde (1.0 mmol) was added and the resulting reaction mixture was stirred for 6 h at room temperature. The reaction mixture was filtered through a pad of celite and the filtrate was concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography.

*N*-Methoxy-*N*-methylbenzofuran-2-carboxamide (55a):

General procedure was applied for the preparation of 55a. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 90/10).

Yield : 797 mg, 95%

$^1$H NMR (500 MHz, CDCl$_3$) : $\delta$ 7.58 (d, $J = 7.8$ Hz, 1H), 7.51 (d, $J = 8.2$ Hz, 1H), 7.40 (s, 1H), 7.34 (t, $J = 7.3$ Hz, 1H), 7.20 (t, $J = 7.3$ Hz, 1H), 3.78 (s, 3H), 3.34 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 159.3, 154.7, 146.4, 127.4, 127.1, 123.4, 122.6, 113.7, 112.2, 61.4, 33.2.

MS (ESI) : $m/z$ 206 (M+H)$^+$.  

HRMS (ESI) : $m/z$ 206.0815 (calcd for C$_{11}$H$_{12}$NO$_3$: 206.0817).

IR (neat) : 2935, 1647, 1552, 1417, 1184, 983, 744 cm$^{-1}$.  

Benzofuran-2-yl(morpholino) methanone (55b):

General procedure was applied for the preparation of 55b. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 85/15).

Yield : 897 mg, 95%

$^1$H NMR (300 MHz, CDCl$_3$) : δ 7.63 (d, $J$ = 7.9 Hz, 1H), 7.48 (d, $J$ = 8.3, 1H), 7.38 (dd,

$J$ = 1.1, 7.1 Hz, 1H), 7.34 ( s, 1H), 7.27 ( t, $J$ = 7.1 Hz,

1H), 3.89-3.83 (m, 4H), 3.75 ( t, $J$ = 4.9 Hz, 4H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : δ 159.6, 154.6, 148.7, 126.5, 123.6, 122.2, 112.4, 111.8,

66.9.

MS (ESI) : $m/z$ 232 (M+H)$^+$.  

HRMS (ESI) : $m/z$ 232.0980 (calcd for C$_{13}$H$_{14}$NO$_3$: 232.0973). 

IR (neat) : 2987, 2867, 1668, 1600, 1433, 1243, 1113, 1028,

765 cm$^{-1}$.

tert-Butyl 4-(benzofuran-2-carbonyl) piperazine-1-carboxylate (55c):

$^{1}$H NMR (300 MHz, CDCl$_3$) : δ 2.07 ( s, 2H), 1.29 ( t, $J$ = 7.3 Hz, 3H), 1.07 ( t, $J$ = 7.3 Hz, 4H), 0.90 ( t, $J$ = 7.3 Hz, 4H), 0.90 ( t, $J$ = 7.3 Hz, 4H). 

$^{13}$C NMR (75 MHz, CDCl$_3$) : δ 159.6, 154.6, 148.7, 126.5, 123.6, 122.2, 112.4, 111.8, 

66.9.

MS (ESI) : $m/z$ 352 (M+H)$^+$.  

HRMS (ESI) : $m/z$ 352.1260 (calcd for C$_{15}$H$_{18}$NO$_5$: 352.1268). 

IR (neat) : 2987, 2867, 1668, 1600, 1433, 1243, 1113, 1028,

765 cm$^{-1}$.
General procedure was applied for the preparation of 55c. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 85/15).

Yield : 1.24 g, 93%

$^1$H NMR (300 MHz, CDCl$_3$) : $\delta$ 7.63 (d, $J = 7.5$ Hz, 1H), 7.48 (d, $J = 8.3$, 1H), 7.39 (m, 1H), 7.34 (s, 1H), 7.28 (m, 1H), 3.87-3.78 (m, 4H), 3.56-3.52 (m, 4H), 1.48 (s, 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 159.9, 154.6, 148.8, 126.5, 123.6, 122.2, 112.5, 111.7, 80.3, 43.8, 43.5, 28.3.

MS (ESI) : $m/z$ 331 (M+H)$^+$. 

IR (neat) : 2975, 2863, 1691, 1563, 1411, 1006, 742 cm$^{-1}$.

$N$-Methoxy-$N$-methylbenzo[b]thiophene-2-carboxamide (55d):

\[
\begin{array}{c}
\text{H}_2\text{CO} \\
\text{N-CH}_3 \\
\text{O} \\
\end{array}
\]

General procedure was applied for the preparation of 55d. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 90/10).

Yield : 830 mg, 92%

$^1$H NMR (300 MHz, CDCl$_3$) : $\delta$ 8.17 (s, 1H), 7.84 (dd, $J = 7.8$, 17.5 Hz, 2H), 7.41-7.34 (m, 2H), 3.83 (s, 3H), 3.41 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 162.3, 142.5, 137.9, 133.1, 131.2, 126.4, 125.1, 124.5, 122.2, 61.7, 33.1.
MS (ESI) : \textit{m/z} 222 (M+H)$^+$. 

HRMS (ESI) : \textit{m/z} 222.0578 (calcd for C$_{11}$H$_{12}$NO$_2$S: 222.0588).

IR (neat) : 2938, 1680, 1629, 1383, 1176, 1001, 754 cm$^{-1}$.

**Ethyl benzofuran-2-carboxylate (31):**

![Ethyl benzofuran-2-carboxylate](image)

General procedure was applied for the preparation of 31. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 95/5). 

**Yield** : 738 mg, 95%

$^1$H NMR (300 MHz, CDCl$_3$) : $\delta$ 7.63 (d, $J = 7.5$ Hz, 1H), 7.56 (d, $J = 8.3$ Hz, 1H), 7.47 (s, 1H), 7.40 (td, $J = 1.5$, 7.1 Hz, 1H), 7.25 (t, $J = 7.9$ Hz, 1H), 4.41 (q, $J = 6.7$ Hz, 2H), 1.43 (t, $J = 7.1$ Hz, 3H). MS (ESI) : \textit{m/z} 191 (M+H)$^+$. 

**Benzofuran-2-yl(phenyl)methanone (55e):**

![Benzofuran-2-yl(phenyl)methanone](image)

General procedure was applied for the preparation of 55e. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 95/5).

**Yield** : 870 mg, 96%

$^1$H NMR (300 MHz, CDCl$_3$) : $\delta$ 8.06 (d, $J = 8.1$ Hz, 2H), 7.70 (d, $J = 7.9$ Hz, 1H), 7.61 (t, $J = 8.1$ Hz, 2H), 7.53 (s, 1H), 7.54-7.45 (m, 3H), 7.29 (dd, $J = 7.3$, 15.1 Hz, 1H).
\[ ^{13}C \text{ NMR (75 MHz, CDCl}_3) \quad : \delta 184.4, 155.7, 152.2, 137.1, 132.8, 128.7, 128.2, 127.0, 124.0, 123.3, 116.5, 112.5. \]

MS (ESI) : \( m/z \) 223 (M+H)^+.  

HRMS (ESI) : \( m/z \) 223.0753 (calcd for C\(_{15}\)H\(_{11}\)O\(_2\): 223.0759).  

IR (neat) : 3140, 3056, 1641, 1543, 1329, 1215, 970, 744, 692 cm\(^{-1}\).  

(4-hydroxybenzofuran-2-yl)(phenyl)Methanone (55f):

\[ \begin{array}{c}
\text{OH} \\
\text{O} \\
\text{O}
\end{array} \]

\[ \begin{array}{c}
\text{HO} \\
\text{O} \\
\text{O}
\end{array} \]

General procedure was applied for the preparation of 55f. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 90/10).

Yield : 800 mg, 93%  

\[ ^1H \text{ NMR (300 MHz, CDCl}_3 + \text{DMSO}) \quad : \delta 9.88 \text{ (s, } 1\text{H}), 8.00 \text{ (d, } J = 6.9 \text{ Hz, } 2\text{H}), 7.71 \text{ (s, } 1\text{H)}, 7.66-7.48 \text{ (m, } 4\text{H}), 7.03 \text{ (d, } J = 8.4 \text{ Hz, } 1\text{H}), 6.66 \text{ (d, } J = 7.7 \text{ Hz, } 1\text{H}). \]

\[ ^{13}C \text{ NMR (75 MHz, CDCl}_3 + \text{DMSO}) \quad : \delta 180.4, 161.2, 153.6, 150.9, 133.3, 130.4, 126.2, 125.2, 122.2, 121.5, 114.1, 113.6, 110.6. \]

MS (ESI) : \( m/z \) 239 (M+H)^+.  

HRMS (ESI) : \( m/z \) 261.0539 (calcd for C\(_{15}\)H\(_{10}\)O\(_3\): 261.0527).  

IR (neat) : 3277, 2935, 2363, 1647, 1597, 1484, 1254, 971, 730 cm\(^{-1}\).
(4-(benzyloxy)Phenyl)(5,7-bis(benzyloxy)Benzofuran-2-yl)methanone (55g):

General procedure was applied for the preparation of 55g. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 85/15).

Yield : 277 mg, 86%

$^1$H NMR (300 MHz, CDCl$_3$) : $\delta$ 8.01 (d, $J = 8.6$ Hz, 2H), 7.54 (s, 1H), 7.46-7.32 (m, 15H), 7.06 (d, $J = 8.6$ Hz, 2H), 6.79 (s, 1H), 6.51 (s, 1H), 5.15 (s, 4H), 5.10 (s, 2H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 179.4, 162.4, 161.4, 157.9, 154.1, 150.9, 136.1, 131.8, 131.5, 128.6, 128.2, 127.5, 127.4, 127.3, 114.5, 114.2, 96.9, 89.5, 70.7, 70.4, 70.1.

MS (ESI) : $m/z$ 541 (M+H)$^+$. IR (neat) : 2922, 2854, 2366, 1708, 1597, 1499, 1156, 1023 cm$^{-1}$.

(4-(benzyloxy)Phenyl)(5,7-dihydroxybenzofuran-2-yl)Methanone (55h):

General procedure was applied for the preparation of 55h. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 80/20).

Yield : 904 mg, 78%
^1^H NMR (300 MHz, CDCl$_3$) : δ 7.99 (d, J = 8.6 Hz, 2H), 7.60 (s, 1H), 7.44-7.23 (m, 5H), 7.05 (d, J = 8.6 Hz, 2H), 6.61 (s, 1H), 6.57 (s, 1H), 5.17 (s, 2H).

MS (ESI) : m/z 361 (M+H)$^+$.  

Benzofuran-2-yl(4-(benzyloxy)-3-methoxyphenyl) methanone (55i):

General procedure was applied for the preparation of 55i. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 90/10).

Yield : 485 mg, 89%

^1^H NMR (300 MHz, CDCl$_3$) : δ 7.75 (dd, J = 2.2, 8.6 Hz, 2H), 7.62 (dd, J = 1.8, 9.4 Hz, 2H), 7.51 (s, 1H), 7.45 (s, 1H), 6.97 (d, J = 8.6 Hz, 1H), 5.27 (s, 2H), 3.97 (s, 3H).

IR (neat) : 2922, 2850, 1642, 1546, 1269, 997, 746 cm$^{-1}$.

Benzofuran-2-yl(thiophen-2-yl)methanone (55j):

General procedure was applied for the preparation of 55j. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 90/10).

Yield : 849 mg, 91%

^1^H NMR (300 MHz, CDCl$_3$) : δ 8.34 (d, J = 3.9 Hz, 1H), 7.74-7.69 (m, 3H), 7.61 (s, 1H), 7.47 (t, J = 7.1 Hz, 1H), 7.31 (t, J = 7.1 Hz, 1H), 7.23 (t, J
3.9 Hz, 1H).

MS (ESI) : m/z 229 (M+H)+.

(7-methoxybenzofuran-2-yl)(thiophen-2-yl)methanone (55k):

\[
\begin{align*}
\text{MeO} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\text{S} & \\
\end{align*}
\]

General procedure was applied for the preparation of 55k. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 85/15).

Yield : 849 mg, 90%

\[\begin{align*}
^{1}H \text{ NMR (300 MHz, CDCl}_3\text{)} & : \delta 8.43 (d, J = 3.7 \text{ Hz, 1H}), 7.73 (d, J = 4.9 \text{ Hz, 1H}), 7.67 \\
& \quad (s, 1H), 7.17-7.04 (m, 2H), 6.92-6.87 (m, 2H), 4.06 (s, 3H).
\end{align*}\]

IR (neat) : 3076, 2922, 2845, 1615, 1556, 1274, 967, 723 cm\(^{-1}\).

MS (ESI) : 259 (M+H)+.

Naphtho[2,1-\text{b}]furan-2-yl(phenyl)methanone (55m):

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O} \\
\text{S} & \quad \text{O} \\
\end{align*}
\]

General procedure was applied for the preparation of 55m. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 90/10).

Yield : 834 mg, 92%

\[\begin{align*}
^{1}H \text{ NMR (300 MHz, CDCl}_3\text{)} & : \delta 8.13 (s, 1H), 8.09 (d, J = 8.3 \text{ Hz, 2H}), 7.96 (s, 1H), 7.90 \\
& \quad (d, J = 8.3 \text{ Hz, 1H}), 7.85 (d, J = 9.0 \text{ Hz, 1H}), 7.68 (d, J =
\end{align*}\]
9.0 Hz, 1H), 7.60 (d, J = 8.3 Hz, 2H), 7.52 (t, J = 3.0, 9.8 Hz, 3H).

**MS (ESI)**: m/z 295 (M+Na)^+.

**IR (neat)**: 3038, 2924, 1638, 1538, 1329, 1175, 971, 806 cm⁻¹.

**Typical experimental procedure for one pot reduction:**

To a stirred solution of bromo compound (1.0 mmol) in EtOAc (5 mL) was added Cs₂CO₃ (1.0 mmol) under N₂ atmosphere. After stirred the reaction mixture for 10 min, salicylaldehyde (1.0 mmol) was added and the resulting reaction mixture was stirred at room temperature. After 6 h, the reaction mixture was filtered through a pad of celite and the filtrate was transferred to a round bottom flask under N₂ atmosphere. To this reaction mixture **Cat. B** (1 mol%) was added followed by NEt₃:HCOOH (5:2) azeotropic mixture (0.2 mL). The resulting reaction mixture was stirred for 3 h at room temperature and then filtered through a small pad silica gel, the filtrate was concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography.

**(R)-Benzofuran-2-yl(phenyl)methanol (43a):**

![](image)

General procedure was applied for the preparation of **(R)-43a**. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 90/10).

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Yield</strong></td>
<td>834 mg, 92%</td>
<td></td>
</tr>
<tr>
<td>[α]²³⁻D</td>
<td>-7.9 (c 3.0, CHCl₃)</td>
<td></td>
</tr>
<tr>
<td><strong>¹H NMR (300 MHz, CDCl₃)</strong></td>
<td>δ 7.51-7.42 (m, 3H), 7.41-7.30 (m, 4H), 7.24-7.12 (m, 2H), 6.46 (s, 1H), 5.90 (s, 1H), 2.40 (bs, 1H).</td>
<td></td>
</tr>
<tr>
<td><strong>¹³C NMR (75 MHz, CDCl₃)</strong></td>
<td>δ 158.7, 154.9, 140.2, 128.6, 128.4, 126.8, 124.3, 122.8, 121.1, 111.3, 104.0, 70.6.</td>
<td></td>
</tr>
</tbody>
</table>
General procedure was applied for the preparation of \((R)\)-43b. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 80/20).

Yield : 768 mg, 96%

\([\alpha]^{23}_D\) : +8.1 (c 2.2, CHCl₃).

\(^1\)H NMR (300 MHz, CDCl₃) : \(\delta\) 7.50-7.43 (m, 3H), 7.39-7.29 (m, 2H), 7.24 (s, 1H), 7.07-7.03 (m, 1H), 6.71 (dd, \(J = 2.2, 6.4\) Hz, 1H), 6.40 (s, 1H), 5.91 (s, 1H), 3.97 (s, 3H).

\(^13\)C NMR (75 MHz, CDCl₃) : \(\delta\) 159.1, 145.2, 144.8, 140.2, 128.6, 128.5, 128.3, 126.8, 123.5, 113.7, 106.4, 104.3, 70.5, 56.0.

MS (ESI) : \(m/z\) 277 (M+Na)

HRMS (ESI) : \(m/z\) 277.0852 (calcd for C\(_{16}\)H\(_{14}\)NaO\(_3\): 277.0840).

IR (neat) : 3433, 3022, 2924, 1602, 1498, 1309, 1173, 1017 cm\(^{-1}\).
General procedure was applied for the preparation of (R)-43c. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 75/25).

Yield : 1.14 g, 91%

[$\alpha$]$^{23}_{D}$ : +6.9 (c 1.5, CHCl$_3$).

$^1$H NMR (300 MHz, CDCl$_3$) : δ 7.34 (d, $J = 8.4$ Hz, 2H), 7.08-7.01 (m, 2H), 6.84 (d, $J = 8.6$ Hz, 2H), 6.69 (dd, $J = 2.2$, 6.4 Hz, 1H), 6.40 (s, 1H), 5.84 (s, 1H), 3.95 (s, 3H), 3.78 (s, 3H), 2.65 (bs, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : δ 159.5, 159.2, 145.3, 144.3, 132.4, 129.1, 128.2, 123.5, 114.0, 113.5, 106.4, 104.2, 70.1, 55.9, 55.2.

MS (ESI) : m/z 307 (M+Na)$^+$.  

HRMS (ESI) : m/z 307.0960 (calcd for C$_{17}$H$_{16}$NaO$_4$: 307.0946).

IR (neat) : 3418, 2932, 2841, 1612, 1513, 1248, 1031, 732 cm$^{-1}$.

(R)-(4-chlorophenyl)(7-methoxybenzofuran-2-yl)Methanol (43d):

![Chemical structure of (R)-43d]

General procedure was applied for the preparation of (R)-43d. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 85/15).

Yield : 800 mg, 87%

[$\alpha$]$^{23}_{D}$ : +10.5 (c 4.0, CHCl$_3$).

$^1$H NMR (300 MHz, CDCl$_3$) : δ 7.42 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.4$ Hz, 2H), 7.26 (d, $J = 7.7$ Hz, 2H), 6.73 (dd, $J = 1.7$, 7.1 Hz, 2H),
1H), 6.40 (s, 1H), 5.90 (s, 1H), 3.97 (s, 3H), 2.59 (s, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 158.3, 145.3, 144.2, 138.6, 133.8, 129.5, 128.6, 128.0, 126.7, 123.5, 113.4, 106.5, 104.4, 69.6, 55.8. MS (ESI) : $m/z$ 311 (M+Na)$^+$. 

HRMS (ESI) : $m/z$ 311.0459 (calcd for C$_{16}$H$_{13}$NaO$_3$Cl: 295.0746).

IR (neat) : 3367, 2936, 2842, 1592, 1490, 1270, 1091, 779 cm$^{-1}$.

(R)-(4-fluorophenyl)(7-methoxybenzofuran-2-yl)Methanol (43e):

General procedure was applied for the preparation of (R)-43e. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 85/15).

Yield : 730 mg, 84%

$[^{[\alpha]}]^{23}_D$ : -3.8 (c 3.0, CHCl$_3$).

$^1$H NMR (300 MHz, CDCl$_3$) : $\delta$ 7.33 (dd, $J = 5.4, 8.4$ Hz, 2H), 7.06-6.91 (m, 4H), 6.67 (dd, $J = 1.3, 7.3$ Hz, 1H), 6.32 (s, 1H), 5.81 (s, 1H), 3.87 (s, 3H), 3.52 (bs, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 164.1, 160.8, 158.6, 145.1, 136.0, 135.9, 129.5, 128.6, 128.4, 123.5, 115.4, 115.1, 113.4, 106.4, 104.2, 69.7, 55.8.

MS (ESI) : $m/z$ 295 (M+Na)$^+$. 

HRMS (ESI) : $m/z$ 295.0756 (calcd for C$_{16}$H$_{13}$NaO$_3$F: 295.0746).
**IR (neat)**

\[ \text{3388, 2936, 2844, 1599, 1500, 1222, 1094, 730 \text{ cm}^{-1}.} \]

**(R)-(4-(benzylloxy)phenyl)(7-methoxybenzofuran-2-yl)methanol (43f):**

![Chemical structure](image)

General procedure was applied for the preparation of **(R)-43f**. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 80/20).

**Yield**

\[ 1.05 \text{ g, 92\%} \]

**\([\alpha]^{23}_D\)**

\[ +5.3 \text{ (c 1.5, CHCl}_3\). \]

**\(^1\text{H NMR (300 MHz, CDCl}_3\)**

\[ \delta 7.41-7.24 \text{ (m, 7H), 7.05-7.02 (m, 2H), 6.93 (d, } J = 8.6 \text{ Hz, 2H), 6.71 (dd, } J = 2.4, 6.4 \text{ Hz, 1H), 6.42 (s, 1H), 5.86 (s, 1H), 5.05 (s, 2H), 3.98 (s, 3H), 2.38 (bs, 1H).} \]

**\(^{13}\text{C NMR (75 MHz, CDCl}_3\)**

\[ \delta 159.2, 158.8, 145.3, 144.2, 136.9, 132.6, 129.9, 128.5, 128.2, 127.9, 127.4, 123.4, 114.8, 113.4, 106.2, 104.0, 70.0, 69.9, 55.8. \]

**MS (ESI)**

\[ m/z 383 \text{ (M+Na).} \]

**HRMS (ESI)**

\[ m/z 383.1266 \text{ (calcd for } C_{23}H_{20}NaO_4: 383.1259). \]

**IR (neat)**

\[ 3409, 3034, 2933, 1609, 1502, 1309, 1237, 1173, 1017, 784 \text{ cm}^{-1}. \]
(R)-Benzofuran-2-yl(2,4-dimethoxyphenyl)methanol (43g):

![Chemical structure](image)

General procedure was applied for the preparation of (R)-43g. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 75/25).

Yield : 1.42 g, 91%

$^1$H NMR (300 MHz, CDCl$_3$) : $\delta$ 7.65-7.36 (m, 3H), 7.22-7.11 (m, 2H), 6.55-6.46 (m, 1H), 6.44 (s, 2H), 6.05 (s, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 2.81 (s, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 160.5, 157.7, 156.3, 156.2, 129.1, 127.6, 125.1, 124.7, 123.3, 120.9, 111.5, 110.9, 105.0, 100.6, 66.7, 55.6, 55.4.

MS (ESI) : $m/z$ 307 (M+Na)$^+$.  
HRMS (ESI) : $m/z$ 307.0956 (calcd for C$_{17}$H$_{16}$NaO$_4$: 307.0946).

IR (neat) : 3565, 2932, 2841, 1609, 1459, 1209, 1034, 750 cm$^{-1}$.

(R)-(4,6-bis(benzyloxy)benzofuran-2-yl)(phenyl)methanol (43h):

![Chemical structure](image)

General procedure was applied for the preparation of (R)-43h. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 95/5).
Yield: 580 mg, 89%

$\alpha_{D}^{23}$: $-6.7$ (c 2.3, CHCl$_3$).

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.43-7.26 (m, 15H), 6.59 (s, 1H), 6.48 (s, 1H), 6.36 (s, 1H), 5.80 (s, 1H), 5.05 (s, 2H), 4.98 (s, 2H).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 158.0, 156.7, 156.0, 152.6, 140.3, 136.7, 128.4, 128.0, 127.5, 127.4, 126.7, 101.8, 96.0, 89.8, 70.5, 70.4, 70.1.

MS (ESI): $m/z$ 459 (M+Na)$^+$.  
HRMS (ESI): $m/z$ 459.1588 (calcd for C$_{29}$H$_{24}$NaO$_4$: 459.1572).

IR (neat): 3442, 3032, 2927, 2325, 1615, 1498, 1154, 1030 cm$^{-1}$.

$(R)$-(5-tert-butylbenzofuran-2-yl)(phenyl)methanol (4i):

General procedure was applied for the preparation of $(R)$-43i. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 90/10).

Yield: 675 mg, 86%

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.44-7.40 (m, 3H), 7.36-7.24 (m, 5H), 6.41 (s, 1H), 5.85 (s, 1H), 2.48 (bs, 1H), 1.34 (s, 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 158.5, 153.0, 145.8, 140.3, 128.6, 128.3, 127.6, 126.7, 122.2, 117.2, 110.5, 104.1, 70.7, 34.6, 31.8.

MS (ESI): $m/z$ 281 (M+H)$^+$.  
IR (neat): 3412, 2922, 2838, 1609, 1502, 1248, 1026, 728 cm$^{-1}$. 
(R)-(5,7-di-tert-butylbenzofuran-2-yl)(phenyl)Methanol (43j):

General procedure was applied for the preparation of (R)-43j. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 90/10).

Yield : 559 mg, 78%

$[\alpha]_{D}^{23}$ : -97.5 (c 0.4, CHCl$_3$).

$^1$H NMR (300 MHz, CDCl$_3$) : $\delta$ 7.49-7.45 (m, 2H), 7.37-7.28 (m, 4H), 7.14 (d, $J = 1.8$ Hz, 1H), 6.42 (s, 1H), 5.91 (d, $J = 3.7$ Hz, 1H), 2.31 (d, $J = 4.3$ Hz, 1H), 1.45 (s, 9H), 1.34 (s, 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 157.8, 145.7, 140.7, 133.7, 128.3, 128.1, 126.8, 124.0, 122.5, 118.9, 115.1, 103.8, 70.6, 34.7, 34.3, 31.8, 29.0;

MS (ESI) : $m/z$ 359 (M+Na$^+$).

IR (neat) : 3415, 2924, 2833, 1605, 1499, 1027, 738 cm$^{-1}$.

(R)-(5-bromobenzofuran-2-yl)(phenyl)Methanol (43k):

General Procedure was applied for the preparation of (R)-43k. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 90/10).

Yield : 760 mg, 95%

$[\alpha]_{D}^{23}$ : -7.3 (c 1.5, CHCl$_3$).

$^1$H NMR (300 MHz, CDCl$_3$) : $\delta$ 7.58 (d, $J = 1.8$ Hz, 1H), 7.51 (dd, $J = 1.5$, 5.2 Hz,
1H), 7.46-7.31 (m, 5H), 7.29 (d, $J = 1.8$ Hz, 1H), 6.42 (s, 1H), 5.84 (s, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 160.0, 139.9, 139.7, 129.6, 128.7, 127.1, 126.7, 123.8, 122.9, 112.7, 104.2, 103.3, 70.6.

HRMS (ESI) : $m/z$ 324.9838 (calcd for C$_{15}$H$_{11}$NaO$_2$Br: 324.9840).

IR (neat) : 3432, 3028, 2927, 1611, 1498, 1150, 748 cm$^{-1}$.

(R)-Naphtho[2,1-b]furan-2-yl(phenyl) Methanol (43l):

![Chemical Structure](image)

General Procedure was applied for the preparation of (R)-43l. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 85/15).

Yield : 716 mg, 90%

[$\alpha$]$^{23}$ D : -10.3 (c 2.0, CHCl$_3$).

$^1$H NMR (300 MHz, CDCl$_3$) : $\delta$ 7.98 (d, $J = 8.1$ Hz, 1H), 7.85 (d, $J = 7.9$ Hz, 1H), 7.68-7.61 (m, 1H), 7.55 (d, $J = 8.8$ Hz, 1H), 7.51-7.45 (m, 2H), 7.40-7.23 (m, 5H), 6.92 (s, 1H), 5.97 (s, 1H), 2.62 (bs, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 157.8, 152.6, 140.4, 130.3, 128.7, 128.6, 128.4, 127.7, 126.8, 126.3, 125.3, 124.5, 123.3, 112.4, 103.2, 70.8.
MS (ESI) : $m/z$ 275 (M+H$^+$).

IR (neat) : 3416, 3058, 2924, 1630, 1519, 1257, 804, 745 cm$^{-1}$.

(S)-(7-methoxybenzofuran-2-yl)(thiophen-2-yl)Methanol (43m):

![Chemical Structure Image]

General Procedure was applied for the preparation of (R)-43m. The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 85/15).

Yield : 709 mg, 87%

$[\alpha]_{23}^D$ : +5.0 (c 0.5, CHCl$_3$).

$^1$H NMR (200 MHz, CDCl$_3$) : $\delta$ 7.22 (d, $J = 3.7$ Hz, 1H), 7.05 (d, $J = 2.2$ Hz, 1H) 7.03 (s, 1H), 7.00 (d, $J = 3.0$ Hz, 1H), 6.90 (dd, $J = 3.0$, 4.5 Hz, 1H), 6.69 (dd, $J = 3.7$, 6.0 Hz, 1H), 6.55 (s, 1H), 6.09 (s, 1H), 3.91 (s, 3H), 3.36 (bs, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) : $\delta$ 157.7, 145.2, 143.7, 129.5, 126.6, 125.7, 125.6, 123.5, 113.5, 106.2, 104.2, 66.5, 57.0.

MS (ESI) : $m/z$ 283 (M+Na$^+$).

IR (neat) : 3394, 2924, 2848, 1591, 1491, 1269, 1176, 703 cm$^{-1}$.
(S)-Benzofuran-2-yl(thiophen-2-yl)methanol (43n):

![Chemical Structure]

General Procedure was applied for the preparation of \((R)-43n\). The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 85/15).

Yield : 658 mg, 92%

\([\alpha]^{23}_D\) : +14.3 (c 0.8, CHCl₃).

\(^1\)H NMR (200 MHz, CDCl₃) : \(\delta 7.45 \text{ (d, } J = 7.5 \text{ Hz, 1H)}, 7.38 \text{ (d, } J = 8.3 \text{ Hz, 1H)}, 7.24-7.13 \text{ (m, 3H)}, 6.99 \text{ (d, } J = 3.0 \text{ Hz, 1H)}, 6.92 \text{ (dd, } J = 3.7, 5.2 \text{ Hz, 1H)}, 6.57 \text{ (s, 1H)}, 6.05 \text{ (bs, 1H)}, 3.28 \text{ (bs, 1H)}.\)

\(^{13}\)C NMR (75 MHz, CDCl₃) : \(\delta 157.4, 155.0, 143.8, 127.9, 126.8, 125.9, 124.5, 124.1, 122.9, 111.4, 104.0, 66.7.\)

MS (ESI) : \(m/z 253 \text{ (M+Na)}^+.\)

IR (neat) : 3388, 2923, 2856, 1601, 1453, 1230, 1126, 748 cm\(^{-1}\).

(R)-benzofuran-2-yl(furan-2-yl)methanol (43o):

![Chemical Structure]

General Procedure was applied for the preparation of \((R)-43o\). The crude residue was purified by column chromatography on silica gel (hexanes/EtOAc: 85/15).

Yield : 650 mg, 90%

\([\alpha]^{23}_D\) : -10.6 (c 1.3, CHCl₃).

\(^1\)H NMR (200 MHz, CDCl₃) : \(\delta 7.55 \text{ (d, } J = 7.8 \text{ Hz, 1H)}, 7.47 \text{ (d, } J = 8.8 \text{ Hz, 1H)},\)
7.44 (s, 1H), 7.30-7.20 (m, 2H), 6.70 (s, 1H), 6.39 (s, 2H), 5.96 (s, 1H), 2.68 (bs, H).

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 155.7, 155.0, 152.7, 142.9, 124.5, 122.9, 121.3, 117.8,
111.4, 110.5, 108.2, 104.3, 64.5.

MS (ESI): $m/z$ 237 (M+Na)$^+$. 

IR (neat): 3394, 2923, 2854, 1709, 1458, 1233, 1014, 749 cm$^{-1}$. 
REFERENCES


23. Su, T.; Naughton, M. A. H.; Smyth, M. S.; Rose, J. W.; Arfsten, A. E.; McCowan, J. R.; Jakubowski, J. A.; Wyss, V. L.; Ruterbories, K. J.; Sall, D. J.; Scarborough, R.


