CHAPTER-II

Radical cyclization routes for the formal synthesis of ethisolide, iso-avenaciolide and cis-fused bicyclic systems
CHAPTER-II

SECTION-A

Radical mediated formal synthesis of ethisolide and
iso-avenaciolide from diacetone glucose
Introduction:

In the preceding chapter, the synthesis of bis-butyro-lactone class of natural products by 5-exo-dig radical cyclization reactions has been extensively discussed. It has also been well demonstrated that the failure in realization of molecules with long alkyl side chains, resulted in a study on the effect of side chains on radical cyclization reaction to realize this class of natural products. Such an impact of side chain was amply evident in the systems derived from L-arabinose, while D-xylose derived systems were compatible for such cyclizations. From the studies presented in the first Chapter, it is evidently indicated that: a) long alkyl side chain from L-Ara configuration inhibit radical cyclization, b) short side chains like ethyl, methyl have no impact or very less impact and c) synthesis of natural product such as iso-avenaciolide can’t be attempted by 5-exo-dig radical cyclization route (Scheme 1).

Scheme 1

\[
\begin{align*}
R = & C_2H_5 \text{ Yes} \\
R = & n-C_8H_{17} \text{ No}
\end{align*}
\]

Hence, alternatively it was felt to develop a general synthetic strategy, whereby, instead of starting the synthesis of related natural products from L-Ara furanoside, it is proposed to start from D-Xylo furanoside and bring in inversion during the radical cyclization reaction to introduce the appropriate stereochemical structure (Scheme 2).

Scheme 2

Based on the above observations and findings, it was felt to adopt the proposed protocol on the inversion of stereocentre during radical cyclization for the synthesis of ethisolide \(^1\) and iso-avenaciolide \(^2\) (Figure 1).
Ethisolide 1 and iso-avenaciolide 2 (Figure 1) are two naturally occurring secondary metabolites, which are structurally related to 4-epi-ethisolide 3 and (-)-avenaciolide 4 (Figure 1), isolated from cultures of Asperigillus and Pencillium species. The interesting bis-lactonic structure with α-methylene group along with their potent biological activity resulted in a great deal of attention from researches, leading to numerous syntheses. These antifungal metabolites exhibit weak antibacterial activities, while iso-avenaciolide 2 was also found to inhibit glutamate transport in rat liver mitochondria.

Figure 1

2,7-Dioxabicyclo[3.3.0]octane skeleton, bearing tetrahydrofuran and/or γ-butyrolactone structures as subunits, are widely distributed in biologically active compounds, for example, 3’-C-branched chain nucleosides such as 5 and plagiogrin A (6) (Figure 1). Although these molecules are structurally small in size, yet they bearing at least three consecutive asymmetric centres in their structures, besides bis-lactone and exo-methylene moieties.

The structural similarity of this class of butyro-lactones with monosacharides in their furanoside form, make them appropriate chiral starting materials. All the asymmetric carbons in these molecules are located on ring forming carbons, while two of them are at the bridged carbons. Thus, the carbohydrates, well placed with diverse stereocentres, are suitably functionalized for ring closure. The advantage on the use of carbohydrates for the synthesis of this class of compounds lies in their functionally well defined ends, beside the absolute stereochemistry, which is predefined.

Several synthetic methods were developed for the successful synthesis of 2, few approaches for 1, which are reviewed below. Three of them are carbohydrate based approaches, while others are non-carbohydrate approaches.
Fraser-Reid et al. approach: \(^{10}\)

The total synthesis of \(2\) (Scheme 3) was achieved from DAG \(7\). Firstly, the C-4 stereocentre was epimerized to get \(9\), which on the side chain \((n-C_8H_{17})\) extension gave \(11\). Acetate side chain on \(11\) was introduced at C-3 to give \(12\), while the exo-methylene was introduced by Mannich reaction, enroute to \(2\).

![Scheme 3]

Burke et al. approach: \(^{11}\)

Burke et al. approach (Scheme 4) was based on the stereocontrolled construction of lactones \(16\alpha\) and \(16\beta\) by the condensation of \(14\) and \(15\). Butenolide \(17\) on Claisen rearrangement gave \(18\), which on sequential treatment with sodium phenylthiolate, diazomethane and BF\(_3\).Et\(_2\)O gave \(19\). Trans-esterification of \(19\) gave bis-lactonic sulphide \(20\), which was finally converted into \(2\).

![Scheme 4]
Martin et al. approach:\textsuperscript{12}

Martin et al. approach (Scheme 5) utilized the alkylation of 21 with MeI and hydroxylation of acetate side chain to afford 22. Heating of 22 with a catalytic amount of CSA in toluene gave bis-lactone 23, which on oxidation with \textit{m}-CPBA afforded sulfoxide 24. Finally, heating of 24 in toluene at reflux afforded 2.

\textbf{Scheme 5}

Dugger et al. approach:\textsuperscript{13}

Dugger et al. described a formal total synthesis of known precursor of 2, starting from D-ribose 25 (Scheme 6). Furanoside obtained from 25 was converted into glycol 27. Alkylation of alcohol 27 afforded radical precursor 28, which on cyclization gave the bicyclic lactol 29. The bicyclic system 29 was further converted into 2.

\textbf{Scheme 6}
Wee et al. approach:¹⁴

Wee et al. adopted a similar strategy like Dugger et al. from D-ribose for the synthesis of *iso-avenaciolide* (Scheme 7). The glycol ester 30 on alkylation afforded radical precursor 31, which on cyclization gave bicyclic system 32. The introduction of C2 and C8 alkyl side chains in bicyclic system 32 by Grignard approach gave 33 and 34, which on oxidation was converted into *bis*-lactone 37. Finally, *exo*-methylene was introduced by Mannich method to give 1 and 2.

**Scheme 7**

Damon et al. approach:¹⁵

Damon et al. described the synthesis of known precursor of *iso-avenaciolide* 2, key step
being the conjugate addition of the latent carbonyl anion 38 to the butenolide 39 (Scheme 8).

**Katsuki et al. approach:**

Katsuki et al. described a new synthetic methodology for the synthesis of the condensed bis-lactone 13 using enantiospecific ring expansion of oxetane 43 as a key step (Scheme 9) leading to the synthesis of known precursor of (-)-iso-avenaciolide 2.

**Scheme 9**

**Cossy et al. approach**

Cossy et al. described a short total synthesis of ethisolide 1 and iso-avenaciolide 2 starting from racemic oxanorbornenone 48, which on further transformation generated radical precursor 49 (Scheme 10). Radical cyclization of 49 and further reactions gave the bicyclic systems 50 and 51. The bicyclic systems 50 and 51 on oxidation gave 52 and 53, further
converted into bis-lactones 1 and 2 (Scheme 10).

**Burke et al. approach:**

Burke et al. synthesized known precursor 13 of *iso*-avenaciolide 2 from homopropargylic alcohol 54, employing radical mediated cyclization approach (Scheme 11).

**Scheme 11**

![Chemical diagram showing the synthesis of bis-lactones 1 and 2](image)

**Metzner et al. approach:**

Metzner et al. achieved an asymmetric synthesis of analogs of 1 and 2 by using two σ[3,3] rearrangements as key steps stereocontrolled by a sulfinyl group.

**Scheme 12**

![Chemical diagram showing the asymmetric synthesis of bis-lactones 1 and 2](image)
Present work

From the above discussions, it is amply evident that, in most of the cases the requisite exo-methylene was introduced by tedious and low yielding Mannich reaction. In many cases, the system utilized appropriate side chain stereochemistry, while, in couple of cases through radical approaches the side chain stereochemistry was introduced. Hence, in the present approach it was proposed not only to introduce the appropriate side chain stereochemistry through radical cyclization reaction, but also to introduce the exo-methylene group by a 5-exo-dig\textsuperscript{20} mode in an efficient way, for the synthesis of 1 and 2.

The \(\alpha\)-methylene-\(\gamma\)-butyrolactone system was found to impart biological activity to the natural products of this group. A synthetic protocol was undertaken for the stereoselective synthesis of 1 and 2 starting from ‘diacetone glucose’ by chiron approach using radical protocol. Synthetic application of free radical cyclizations\textsuperscript{21} for C-C bond formation is a versatile protocol for the construction of carbon frameworks, particularly cis-fused bicyclic systems. A suitably substituted 5-vinyl radical usually undergoes a highly regioselective ring closure by a 5-exo-dig mode preferentially. Such a protocol was earlier utilized by our group for the successful synthesis of several natural products containing the bis-butyrolactone moieties.

![Figure 2](image.png)

Ethisolide 1, iso-avenaciolide 2 and avenaciolide 4 are three bis-lactones secondary mold metabolites isolated from broths of *Aspergillus avenaceus* and *Penicillium* species, and have been reported to possess antifungal and antibacterial activities. These bis-lactones have attracted numerous synthetic efforts\textsuperscript{5} that are notable for their strategic diversity. Ethisolide 1 has similar structural features like iso-avenaciolide 2, except for a C2 side chain and thus both of them differ only at the C-4 substitution. Hence, a common synthetic strategy was proposed to arrive at the synthesis of 1 and 2.
The retrosynthetic strategies for 1 and 2 as depicted in Scheme 13 indicate that the bicyclic systems 68 and 69 are the respective late stage intermediates. These bicyclic systems could be realized from glycols 70 and 71 respectively by radical cyclization protocol. The glycols 70 and 71 in turn could be generated from the appropriately substituted triflate derivatives 72 and 73 respectively, derived from diacetone glucose (DAG) 7. Thus, the main synthetic strategy is: a) to generate the C-3/C-4 glycol, b) to utilize a vinyl radical for the radical cyclization to invert the C-4 stereocentre, while creating the cis-fused bicyclic system.

**Scheme 13**

Utilization of easily obtainable furanoid derivative such as DAG offered unique operational advantages, for it allowed regiospecific chain branching at C-3 via a radical cyclization and provided the opportunity to control stereochemistry at that carbon while introducing second cyclic system along with the incorporation of the important exo-methylene group. Thus, the radial reaction here would perform three very important functions at one go: (i) introduction of second cyclic system with cis-stereochemistry (ii) introduction of exo-methylene group and (iii) control the induction of the required stereochemistry at C-3 during the C-C bond formation.
Accordingly, DAG 7 on reaction with PMBBr in the presence of NaH in THF at 0 °C to room temperature for 4 h furnished PMB ether 74 in 77% yield (Scheme 14). Further, acid mediated deprotection of acetonide group in 74 with 60% AcOH at room temperature for 18 h afforded diol 75 in 83% yield (Scheme 14).

**Scheme 14**

Reaction of diol 75 with Ph₃P, imidazole and I₂ in CH₂Cl₂ at 0 °C to room temperature for 2 h furnished olefin 76 in 82% yield (Scheme 15). In ¹H NMR spectrum, the olefinic protons resonated at δ 5.33 and 5.91 as two multiplets, while rest of the protons appeared at the expected chemical shifts. HRMS showed m/z 329.1375 for C₁₇H₂₂O₃Na (M+Na)⁺ further confirming the product.

**Scheme 15**

In order to introduce the ethyl side chain, olefin 76 was treated with PtO₂ in EtOAc under hydrogen pressure (40 psi) for 2 h to afford 77 in 97% yield (Scheme 15). In the ¹H NMR of 77, the corresponding olefinic protons disappeared, while, the methylene protons resonated at δ 1.69 as multiplet and terminal methyl protons at δ 0.88 (J = 7.3 Hz) as a triplet corresponding to ethyl group, while rest of the protons resonated at the expected chemical shifts.
Similarly, to introduce the C8 side chain, diol 75 was treated with sodium metaperiodide and aq. NaHCO$_3$ in CH$_2$Cl$_2$ at 0 °C to room temperature for 3 h to furnish the known aldehyde 78 (93%), which on Grignard reaction with $n$-heptylmagnesium bromide in dry THF at 0 °C for 3 h afforded diastereomeric mixture of alcohol 79 in 80% yield (Scheme 16).

The $^1$H NMR of 79 indicated the disappearance of proton signals corresponding to aldehyde, while the newly introduced alkyl chain protons resonated at $\delta$ 1.13-1.56 as multiplet and terminal methyl protons at $\delta$ 0.87 ($J = 6.8$ Hz) as a triplet confirming the structure. HRMS showed $m/z$ 431.2422 for C$_{23}$H$_{36}$NaO$_6$ (M+Na)$^+$ further confirming the product.

The diastereomeric mixture of alcohols 79 on reaction with NaH and CS$_2$ followed by MeI in THF at 0 °C for 2 h gave the xanthate ester 80 in 85% yield (Scheme 17). In $^1$H NMR spectrum of 80, the methylthio group resonated at $\delta$ 2.53 as a singlet and H-5 proton resonated at $\delta$ 6.05 ($J = 6.5$ Hz) as quintate, clearly indicated the formation of the xanthate ester. HRMS showed $m/z$ 521.2013 for C$_{25}$H$_{38}$O$_6$S$_2$Na (M+Na)$^+$ further confirming the product.

Xanthate ester 80 was subjected to deoxygenation with $n$-Bu$_3$SnH in the presence of catalytic amount of AIBN in dry benzene at reflux for 12 h to give 81 in 89% yield (Scheme 17). In its $^1$H NMR spectrum, proton signals corresponding to xanthate were absent, clearly indicating the formation of deoxygenated product. HRMS showed $m/z$ 415.2475 for C$_{23}$H$_{36}$O$_5$Na (M+Na)$^+$ further confirming the structure.
Having introduced the requisite C2 and C8 side chain, next it was aimed at the introduction of vinyl bromide at C-2 position for the generation of vinyl radical for cyclization. Accordingly, methanolysis of 77 with 2 to 3 drops of conc. HCl in methanol at 0 °C to room temperature for 7 h afforded methyl glycosides 82a and 82b as a separable mixture of α, β-anomers in 1:1.5 ratio (Scheme 18). In the 1H NMR spectrum of 82a (α-anomer), H-2 proton resonated at δ 4.88 (J = 4.5 Hz) as a doublet and -OCH3 proton at δ 3.45 as a singlet. In the 1H NMR spectrum of 82b (β-anomer), H-2 proton resonated at δ 4.70 as a singlet and -OCH3 protons at δ 3.39 as a singlet. HRMS showed m/z 305.1356 and 305.1366 for C13H22O5Na (M+Na)+ further confirming the assigned structures of 82a and 82b. The optical rotation values were recorded as [α]D = +76.5 (c 0.8) for 82a and [α]D = -37.5 (c 1.2) for 82b in chloroform.

Scheme 18

Similarly, 81 on reaction with conc. HCl in MeOH at room temperature for 7 h as described for 80 gave the separable mixture of 83a and 83b in 1:2.3 ratio. In the 1H NMR spectra of 83a (α-anomer), H-2 proton appeared at δ 4.88 (J = 4.6 Hz) as a doublet, while OCH3 protons resonated at δ 3.44 as a singlet. Likewise, for 83b (β-anomer) H-2 appeared at δ 4.65 as a singlet and -OCH3 protons at δ 3.35 as a singlet. HRMS showed m/z 389.2311 and 389.2313 for C21H34O5Na (M+Na)+, further confirming the assigned structures of 83a and 83b. The optical rotation values recorded as [α]D = +39.6 (c 2.5) for compound 83a and [α]D = -41.5 (c 2.4) for compound 83b in chloroform.

Having prepared the C-2 hydroxy compounds 82a/82b and 83a/83b, it was next aimed to introduce the bromide side chain. The requisite 2,3-dibromopropene was prepared in two steps from allyl bromide by a known method.22 Accordingly, bromination of allyl bromide with Br2 in 1,4-dioxane at room temperature for 10 min gave 1,2,3-tribromo propane 85 in 82% yield. Base mediated dehydrobromination of tribromide 85 with aq. NaOH and Cetyl pyridinium chloride at 120 °C for 2 h gave the vinyl bromide 86 in 89% yield (Scheme 19).
Alkylation of both the α-anomers and β-anomers 82a/83a and 82b/83b independently on reaction with 2,3-dibromopropene 86 in the presence of NaH in THF at 0 °C to room temperature for 3 h furnished the vinyl bromo derivatives 87a/88a and 87b/88b respectively (Scheme 20).

In the \(^1\)H NMR spectrum of 87a, the olefinic protons appeared at δ 5.60 and 5.91 as a two singlets and -OCH\(_2\) resonated at δ 4.07 as a multiplet. \(^1\)H NMR spectrum of 87b showed olefinic protons resonating at δ 5.62 and 5.96 as a two singlets and -OCH\(_2\) resonating at δ 4.00 as a multiplet. HRMS showed \(m/z\) 423.0774 and 423.0765 for C\(_{18}\)H\(_{25}\)O\(_3\)BrNa (M+Na)\(^+\) further confirmed the assigned structures of 87a and 87b. The optical rotation values for 87a and 87b in chloroform were [\(\alpha\)]\(_D\) = +41.8 (c 0.6) and [\(\alpha\)]\(_D\) = -30.5 (c 1.7) respectively.

Likewise, in \(^1\)H NMR spectrum of 88a, olefinic protons appeared at δ 5.61 and 5.95 as two singlets and -OCH\(_2\) resonated at δ 4.04 as a multiplet. \(^1\)H NMR spectrum of 88b showed the olefinic protons at δ 5.59 and 5.89 as two singlets and -OCH\(_2\) resonating at δ 4.05 as a multiplet.
HRMS showed \( m/z \) 507.1732 and 507.1737 for \( \text{C}_2\text{H}_7\text{O}_5\text{BrNa} \) (M+Na)\(^+ \) further confirming the assigned structures of 88a and 88b. The optical rotation values for 88a and 88b in chloroform were [\( \alpha \)]\( \text{D} \) = 42.9 (c 0.7) and [\( \alpha \)]\( \text{D} \) = -22.5 (c 1.1) respectively.

Having made the vinyl bromo derivatives 87a/87b and 88a/88b, it was next aimed at the conversion into C-3/C-4 glycol by a three step sequence. Accordingly, \( \alpha \)-anomers 87a/88a and \( \beta \)-anomers 87b/88b were independently subjected to reaction with DDQ in aq. \( \text{CH}_2\text{Cl}_2 \) at room temperature for 2 h to give alcohols 89a (72%)/90a (65%) and 89b (75%)/90b (82%) respectively (Scheme 21).

\[ \text{Scheme 21} \]

\[ \begin{align*}
\text{87a} & \quad \text{R} = \text{C}_2\text{H}_5 \\
\text{88a} & \quad \text{R} = \text{n-C}_8\text{H}_{17} \\
\text{87b} & \quad \text{R} = \text{C}_2\text{H}_5 \\
\text{88b} & \quad \text{R} = \text{n-C}_8\text{H}_{17} \\
\end{align*} \]

\( ^1 \)H NMR spectra of 89a and 89b showed the absence of the resonances due to the PMB group, while, rest of the protons appeared at the expected chemical shifts. HRMS showed \( m/z \) 303.0208 and 303.0204 for \( \text{C}_{10}\text{H}_{17}\text{O}_4\text{BrNa} \) (M+Na)\(^+ \) further confirming the assigned structures of 89a and 89b. The optical rotation values for 89a and 89b in chloroform were [\( \alpha \)]\( \text{D} \) = +112.5 (c 0.2) and [\( \alpha \)]\( \text{D} \) = -51.6 (c 0.6) respectively.

The \( ^1 \)H NMR of 90a and 90b also revealed the absence of signals corresponding to the PMB group, which was further supported from their HRMS data. The optical rotation values for 90a and 90b in chloroform were [\( \alpha \)]\( \text{D} \) = +84.5 (c 0.2, \( \text{CHCl}_3 \)) and [\( \alpha \)]\( \text{D} \) = -176.2 (c 0.23) respectively, further confirmed the structures.
The above obtained alcohols 89a/90a and 89b/90b independently on reaction with Tf₂O and pyridine in dry CH₂Cl₂ at -20 °C temperature for 30 min furnished corresponding triflates 72a (88%)/73a (81%) and 72b (95%)/73b (93%) respectively (Scheme 22).

**Scheme 22**

The thus obtained triflates 72a/73a and 72b/73b were subjected to reaction with DBU in dry DMSO at 0 °C to room temperature for 12 h to furnish the respective 3,4-glycols 91a/92a and 91b/92b (Scheme 23).

**Scheme 23**
Having prepared the radical precursors, the glycols 91a/92a and 91b/92b, the stage was set for radical cyclization reactions. Accordingly, the α- and β-anomers 91a/92a and 91b/92b, were subjected to radical cyclization reaction with n-Bu3SnH in the presence of catalytic amount of AIBN in dry benzene at reflux for 12 h to give bicyclic systems 68a/69a and 68b/69b (Scheme 23). The structures of all the compounds were confirmed unambiguously from the corresponding spectral data.

For 68a, H-3a proton shifted towards upfield appeared at δ 3.26 (J = 7.3 Hz) as triplet, while newly formed exo-methylene protons appeared as singlets at δ 4.91 and 5.06. Similarly, in 1H NMR spectrum of 69a the H-3a proton resonated at δ 3.23 (J = 6.8 Hz) as a triplet, while the exo-methylene protons resonated at δ 4.90 and 5.07 as a singlets. Similarly 1H NMR spectrum of 68b the H-3a proton resonated at δ 3.19 (J = 7.1 Hz) as a triplet, while the exo-methylene protons resonated at δ 4.92 (J = 1.7 Hz) and 5.06 (J = 1.5 Hz) as a quintets. Similarly, in 1H NMR spectrum of 69b the H-3a proton resonated at δ 3.17 (J = 6.8 Hz) as a triplet, while the exo-methylene protons resonated at δ 4.92 and 5.06 as two singlets.

Thus, by the vinyl radical cyclization approach on the C-3/C-4 glycol successfully derived the cis-fused bicyclic systems with: a) inversion of stereocenter at the side chain carbon and b) introduction of the exo-methylene group simultaneously. Further, conversion of these bicyclic systems 68b and 69b into ethisolide 1 and iso-avenaciolide 2 is since reported,17 this work constitutes the formal synthesis of 1 and 2.
Experimental Section:

(3aR,5R,6S,6aR)-6-(4-Methoxybenzylloxy)-tetrahydro-2,2-dimethyl-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)furo[2,3-d][1,3]dioxole (74): A stirred suspension of NaH (2.30 g, 96.15 mmol) in dry THF (30 mL) under N₂ atmosphere was treated with a solution of 7 (10.0 g, 38.46 mmol) in THF (50 mL) at 0 °C and stirred for 30 min. PMBBr (9.23 mL, 46.15 mmol) in THF (20 ml) was added to the reaction mixture at 0 °C and stirred at room temperature for 4 h. Reaction mixture was quenched with aq. NH₄Cl solution (30 mL) and extracted with EtOAc (2 x 200 mL). Organic layer was washed with water (100 mL), brine (100 mL), dried (Na₂SO₄) and evaporated. Purification of residue by column chromatography (60-120 Silica gel, ethyl acetate: pet. ether, 1.5:8.5) afforded 74 (9.0 g, 77%) as a colourless liquid; IR (Neat): 3451, 3069, 2934, 2859, 1723, 1612, 1513, 1464, 1249, 1214, 1107, 1030, 820, 704 cm⁻¹; ¹H NMR: (300 MHz, CDCl₃): δ 1.28 (s, H, CH₃), 1.35 (s, 3H, CH₃), 1.40 (s, 3H, CH₃), 1.46 (s, 3H, CH₃), 3.79 (s, 3H, OCH₃), 3.93 (m, 2H, CH₂), 4.01-4.06 (m, 2H, H-5, H-6), 4.26 (q, 1H, J = 6.0, 12.0 Hz, H-5), 4.48 (d, 2H, J = 3.7 Hz, H-6a), 4.55 (d, 2H, J = 3.0 Hz, OCH₂), 5.79 (d, 1H, J = 3.4 Hz, H-3a), 6.80 (d, 2H, J = 8.6 Hz, Ar-H), 7.20 (d, 2H, J = 8.6 Hz, Ar-H); ¹³C NMR (CDCl₃, 150 MHz): δ 159.1, 129.4, 129.0 (2C), 113.5 (2C), 105.0, 82.4, 81.0, 72.3, 71.7, 67.0, 54.8, 26.5 (2C), 25.9, 25.1.

(R)-1-((3aR,5R,6S,6aR)-6-(4-Methoxybenzylloxy)-tetrahydro-2,2-dimethylfuro[2,3-d][1,3]dioxol-5-yl)ethane-1,2-diol (75): A solution of 74 (7.80 g, 20.52 mmol) in 60% aq. CH₃COOH (40 mL) was stirred at room temperature for 18 h. The reaction mixture was neutralized with solid NaHCO₃ (110 g) and crude residue was extracted with EtOAc (3 x 200 mL) and dried (Na₂SO₄). Solvent was evaporated under reduced pressure and purified the residue by column chromatography (60-120 Silica gel, ethyl acetate: pet. ether, 5:5) to afford diol 75 (5.8 g, 83%) as a colourless syrup; [α]D = -42.2 (c 0.30, CHCl₃); IR (neat): 3434, 2935, 1613, 1514, 1377, 1248, 1170, 1126, 1025, 876, 824, 758 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.29 (s, 3H, CH₃), 1.45 (s, 3H, CH₃), 1.70 (m, 1H, H-5), 3.79 (s, 3H, OCH₃), 3.92 (m, 1H, H-6), 4.01 (m2H, CH₂), 4.44-4.64 (m, 3H, OCH₂ & H-6a), 5.85 (d, 1H, J = 3.7 Hz, H-3a), 6.83 (d, 2H, J = 8.5 Hz, Ar-H), 7.21 (d, 2H, J = 8.5 Hz, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 159.3, 129.4 (2C), 129.1, 113.9 (2C), 111.6, 104.9, 71.7, 69.0, 64.1, 55.1, 26.5, 26.0; HRMS (ESI): calculated for C₁₇H₂₄O₇ (M⁺+Na) 363.1419; found 363.1413.
(3aR,5R,6S,6aR)-6-(4-Methoxybenzyloxy)-tetrahydro-2,2-dimethyl-5-vinylfuro[2,3-d][1,3]dioxole (76): To a mixture of 75 (8.0 g, 23.52 mmol), Ph3P (24.65 g, 94.11 mmol) and imidazole (6.39 g, 94.11 mmol) in CH2Cl2 (60 mL), I2 (17.78 g, 70.58 mmol) was added at 0 °C and stirred at room temperature for 3 h. Sat. aq. NaOH solution (15 mL) was added to the reaction mixture and extracted with CHCl3 (100 mL). Organic layers were washed with sat. aq. hypo (40 mL), brine (40 mL) and dried (Na2SO4). Solvent was removed under reduced pressure and purified the residue by column chromatography (60-120 Silica gel, ethyl acetate: pet. ether, 0.5:9.5) to afford olefin 76 (5.9 g, 82%) as a colourless syrup; [α]D = -67.5 (c 0.43, CHCl3); IR (neat): 2987, 2934, 1613, 1513, 1375, 1248, 823, 768 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 1.28 (m, 3H, CH3), 1.46 (m, 3H, CH3), 3.78 (m, 4H, OCH3 and H-6), 4.47 (m, 4H, OCH2, H-6a and H-5), 5.33 (m, 2H, =CH2), 5.91 (m, 2H, =CH & H-3a), 6.80 (d, 2H, J = 8.6 Hz, Ar-H), 7.19 (d, 2H, J = 8.6 Hz, Ar-H); 13C NMR (CDCl3, 75 MHz): δ 159.0, 132.2, 129.5, 129.1 (2C), 118.8, 113.7 (2C), 111.4, 104.7, 82.8, 81.4, 71.7, 55.1, 26.6, 26.1; HRMS (ESI): m/z calculated for C17H25O5Na (M⁺+Na) 329.1364; found 329.1375.

(3aR,5R,6S,6aR)-6-(4-Methoxybenzyloxy)-5-ethyl-tetrahydro-2,2-dimethylfuro[2,3-d][1,3]dioxole (77): A solution of 76 (3.70 g, 12.09 mmol) in dry EtOAc (20 mL) was treated with catalytic amount of PtO2 (0.04 g) under H2 atmosphere and stirred at room temperature for 2 h. It was filtered, solvent was removed and purified the residue by column chromatography (60-120 Silica gel, ethyl acetate: pet. ether, 0.7:9.3) to afford 77 (3.60 g, 97%) as a colourless liquid; [α]D = -55.73 (c 3.52, CHCl3); IR (Neat): 2941, 1450, 1100, 720 cm⁻¹; 1H NMR (300 MHz, CDCl3): δ 0.88 (t, 3H, J = 7.3 Hz, CH3), 1.29 (s, 3H, CH3), 1.45 (s, 3H, CH3), 1.69 (m, 2H, allylic-CH2), 3.69 (d, 1H, J = 3.0 Hz, H-6), 3.78 (s, 3H, OCH3), 3.96 (dt, 1H, J = 3.0, 8.4 Hz, H-5), 4.35-4.62 (m, 3H, H-6a, OCH2), 5.83 (d, 1H, J = 3.8 Hz, H-3a), 6.80 (d, 2H, J = 8.5 Hz, Ar-H), 7.19 (d, 2H, J = 8.5 Hz, Ar-H); 13C NMR (CDCl3, 75 MHz): δ 159.2, 131.7, 129.2 (2C), 113.7 (2C), 110.9, 104.5, 82.0, 81.7, 81.0, 71.2, 55.0, 26.6, 26.1, 20.9, 10.3; HRMS (ESI): m/z calculated for C17H24NaO5 (M⁺+Na) 331.1624, found 331.1627.

1-((3aR,5R,6S,6aR)-6-(4-Methoxybenzyloxy)-tetrahydro-2,2-dimethylfuro[2,3-d][1,3]dioxol-5-yl)octan-1-ol (79): To a solution of diol 75 (2.0 g, 5.91 mmol) in CH2Cl2 (5 mL), NaIO4 (1.90
g, 8.87 mmol) was added and stirred at 0 °C to room temperature for 3 h. Solvent was evaporated and the residue extracted with CH₂Cl₂ (3 x 20 mL), dried (Na₂SO₄) and evaporated to give aldehyde 78 as a yellow liquid, which was used as such for the next reaction.

A stirred suspension of Mg metal (1.24 g, 51.94 mmol) in dry THF (35 mL) under N₂ atmosphere was treated with 1-bromoheptane (9.24 g, 51.94 mmol). The thus generated Grignard reagent in THF was treated with a solution of 78 (8.0 g, 25.97 mmol) in THF (30 mL) at 0 °C and stirred at room temperature for 3 h. The reaction mixture was quenched with aq. NH₄Cl solution (30 mL) and extracted with EtOAc (3 x 100 mL). Organic layers were washed with water (50 mL), brine (50 mL) and dried over Na₂SO₄. Solvent was evaporated and purified the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.5:8.5) to afford 79 (8.5 g, 80%) as syrup; [α]D = -72.6 (c 1.7, CHCl₃); IR (neat): 3448, 2921, 2851, 1724, 1460, 1250, 1071, 771 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.87 (t, 3H, J = 6.8 Hz, CH₃), 1.13-1.56 (m, 12H, 6CH₂), 2.50 (s, 1H, -OH), 3.70-3.92 (m, 6H, H-5, H-6, H-7 and Ar-OCH₃), 4.42-4.65 (m, 3H, OCH₂ and H-6a), 5.89 (d, 1H, J = 3.5 Hz, H-3a), 6.83 and 7.20 (2d, 4H, J = 8.3 Hz, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 159.5, 129.6 (2C), 128.7, 113.9 (2C), 111.5, 104.7, 96.1, 82.9, 82.3, 81.8, 71.3, 69.7, 54.9 (2C), 32.7 (2C), 31.9, 29.6, 29.3, 26.8, 26.4, 25.5, 22.6, 14.2; HRMS (ESI): m/z calculated for C₂₃H₃₆NaO₆ (M⁺+Na) 431.2409, found 431.2422.

**O-1-((3aR,5R,6R,6aR)-6-(4-Methoxybenzylxoy)-tetrahydro-2,2-dimethylfuro[2,3-d][1,3]dioxol-5-yloctyl S-methyl carbonodithioate (80):** A stirred suspension of NaH (0.68 g, 28.43 mmol) in dry THF (15 mL) under N₂ atmosphere was treated with a solution of 79 (5.80 g, 14.21 mmol) in THF (15 mL) at 0 °C and stirred at room temperature for 30 min. CS₂ (1.29 mL, 21.32 mmol) was added at 0 °C and stirred at room temperature for 30 min. MeI (1.33 mL, 21.32 mmol) was added at 0 °C and stirred at room temperature for 2 h. The reaction mixture was quenched with aq. NH₄Cl solution (20 mL) and extracted with EtOAc (2 x 100 mL). Organic layer was washed with water (50 mL), brine (50 mL), dried (Na₂SO₄) and evaporated. Purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1:9) afforded 80 (6.0 g, 85%) as light yellow liquid; [α]D = -55.7 (c 0.8, CHCl₃); IR (neat): 3448, 2921, 2851, 1724, 1460, 1250, 1071, 771 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 0.87 (t, 3H, J = 6.8 Hz, CH₃), 1.13-1.56 (m, 12H, 6xCH₂), 2.53 (s, 3H, SCH₃), 3.79 (s, 3H, Ar-OCH₃), 3.84 (d, 1H, J = 2.9 Hz, H-6), 4.22 (m, 1H, H-5), 4.32-4.61 (m, 3H, OCH₂ and H-6a), 5.88 (d, 1H, J =
3.4 Hz, H-3a), 6.05 (q, 1H, J = 6.5 Hz, H-5’), 6.82 and 7.21 (2d, 4H, J = 8.3 Hz, Ar-H); 13C NMR (CDCl3, 75 MHz): δ 216.0, 159.4, 129.8 (2C), 128.8, 113.8 (2C), 111.6, 105.0, 81.9, 81.7, 81.2, 80.8, 71.1, 55.2, 31.7, 30.4, 29.5, 29.0, 26.8, 26.3, 24.7, 22.5, 18.9, 14.0; HRMS (ESI): m/z calculated for C25H36NaO5S2 (M\(^+\)+Na) 521.2007, found 521.2013.

(3aR,5R,6S,6aR)-6-(4-Methoxybenzyloxy)-tetrahydro-2,2-dimethyl-5-octylfuro[2,3-d][1,3]dioxole (81): A solution of 80 (5.90 g, 11.84 mmol) in dry benzene (50 mL) under N\(_2\) atmosphere was treated with n-Bu\(_3\)SnH (6.36 mL, 23.69 mmol) at room temperature and heated at reflux for 30 min. After 30 min, catalytic amount of AIBN was added at reflux and continued reflux for 12 h. The reaction mixture was cooled to room temperature, evaporated solvent under reduced pressure and purified the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1:9) to afford 81 (4.1 g, 89\%) as a colourless liquid; [α]\(_D\) = -51.45 (c 1.0, CHCl3); IR (neat): 3448, 2921, 2851, 1724, 1460, 1250, 1071, 771 cm\(^{-1}\); 1H NMR (300 MHz, CDCl3): δ 0.88 (t, 3H, J = 6.8 Hz, CH3), 1.13-1.68 (m, 12H, 6xCH2), 3.66 (d, 1H, J = 3.0 Hz, H-6), 3.78 (s, 3H, Ar-OCH3), 4.01 (m, 1H, H-5), 4.34-4.52 (m, 3H, OCH2 and H-6a), 5.81 (d, 1H, J = 3.9 Hz, H-3a), 6.82 and 7.18 (2d, 4H, J = 8.4 Hz, Ar-H); 13C NMR (CDCl3, 75 MHz): δ 159.3, 129.6, 129.3 (2C), 128.3, 113.7 (2C), 111.0, 104.5, 82.1, 81.2, 80.4, 71.2, 55.2, 31.8, 29.7, 29.4, 29.1, 27.7, 26.6, 26.1, 25.9, 22.6, 14.0; HRMS (ESI): m/z calculated for C25H36NaO5 (M\(^+\)+Na) 415.2460, found 415.2475.

**Hydrolysis of 77**

To a solution of 77 (1.80 g, 5.84 mmol) in MeOH (25 mL) under N\(_2\) atmosphere, 3 drops of conc. HCl was added at 0 °C and stirred for 6 h. The reaction mixture was cooled to 0 °C and neutralized with solid NaHCO\(_3\) (0.4 g) at 0 °C. It was filtered, evaporated solvent and purified the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.8:8.2). First eluted was α-anomer 82a (0.56 g, 34\%) in 1:1.5 ratio as a liquid; [α]\(_D\) = +76.5 (c 0.8, CHCl3); IR (neat): 3448, 3282, 1720, 1636, 771, 600 cm\(^{-1}\); 1H NMR (300 MHz, CDCl3): δ 0.89 (t, 3H, J = 7.3 Hz, CH3), 1.62 (m, 2H, CH2), 3.45 (s, 3H, anomeric OCH3), 3.74 (m, 4H, H-4 and Ar-OCH3), 3.96 (q, 1H, J = 6.8, 12.1 Hz, H-5), 4.13 (q, 1H, J = 3.0, 4.1 Hz, H-3), 4.40-4.65 (dd, 2H, J = 11.0 Hz, OCH2), 4.88 (d, 1H, J = 4.5 Hz, H-2), 6.79 (d, 2H, J = 8.6 Hz, Ar-H), 7.19 (d, 2H, J = 8.3 Hz, Ar-H); 13C NMR (CDCl3, 75 MHz): δ 159.2, 131.9, 129.3 (2), 113.6 (2C), 109.2,
101.4, 95.5, 83.1, 79.4, 71.6, 55.1, 23.2, 10.5; HRMS (ESI): m/z calculated for C_{15}H_{22}NaO_5(M^+Na) 305.1364, found 305.1356.

Second eluted was β-anomer 82b (0.84 g, 51%) as colourless liquid; [α]_D = -37.5 (c 1.2, CHCl_3); IR (neat): 3590, 3500, 2237, 1724, 1256, 867,793 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl_3): δ 0.97 (t, 3H, J = 7.4 Hz, CH_3), 1.65 (m, 2H, CH_2), 3.39 (s, 3H, anomeric OCH_3), 3.79 (m, 4H, H-4 and Ar-OCH_3), 4.03 (q, 1H, J = 6.5, 12.1 Hz, H-5), 4.14 (s, 1H, H-3), 4.40-4.59 (dd, 2H, J = 11.4 Hz, OCH_2), 4.70 (s, 1H, H-2), 6.83 (d, 2H, J = 7.9 Hz, Ar-H), 7.23 (d, 2H, J = 7.9 Hz, Ar-H); \(^1^3\)C NMR (CDCl_3, 75 MHz): δ 159.1, 131.7, 129.3 (2C), 113.6 (2C), 109.2, 101.4, 95.5, 83.2, 80.1, 71.1, 55.1, 22.0, 10.2; HRMS (ESI): m/z calculated for C_{15}H_{22}NaO_5 (M^+Na) 305.1364, found 305.1366.

**Hydrolysis of 81**

To a solution of 81 (1.70 g, 4.33 mmol) in dry MeOH (25 mL) under N\(_2\) atmosphere 3 drops of conc. HCl was added at 0 °C and stirred for 6 h. Worked up as described for 82a and purified the residue by column chromatography (60-120 Silica gel, ethyl acetate: pet. ether, 1.8:8.2). First eluted was 83a (0.39 g, 25%) as a colourless liquid; [α]_D = +39.6 (c 2.5, CHCl_3); IR (neat): 3500, 3590, 1765, 879 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl_3): δ 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.26 (s, 12H, 6xCH_2), 1.56 (m, 2H, CH_2), 2.70 (d, 1H, J = 6.2 Hz, OH), 3.44 (s, 3H, anomic OCH_3), 3.70 (q, 1H, J = 2.6, 4.6 Hz, H-4), 3.77 (s, 3H, Ar-OCH_3), 4.01 (q, 1H, J = 6.2, 11.9 Hz, H-5), 4.13 (p, 1H, J = 2.6, 6.7 Hz, H-3), 4.40-4.64 (dd, 2H, J = 11.9 Hz, OCH_2), 4.88 (d, 1H, J = 4.6 Hz, H-2), 6.81 (d, 2H, J = 8.3 Hz, Ar-H), 7.19 (d, 2H, J = 8.3 Hz, Ar-H); \(^1^3\)C NMR (CDCl_3, 125 MHz): δ 159.1, 130.0, 129.1 (2C), 113.6, 101.4, 83.4, 78.8, 76.7, 70.9, 55.5, 55.1, 31.7, 29.6, 29.4, 29.2, 28.8, 25.9, 22.6, 14.0; HRMS (ESI): m/z calculated for C_{21}H_{34}NaO_5 (M^+Na) 389.2303, found 389.2311.

Second eluted was 83b (0.90 g, 57%) as a liquid; [α]_D = -41.5 (c 2.4, CHCl_3); IR (neat): 3500, 3590, 1765, 879 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl_3): δ 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.26 (s, 12H, 6xCH_2), 1.57 (m, 2H, CH_2), 2.84 (bs, 1H, OH), 3.35 (s, 3H, anomeric OCH_3), 3.75 (m, 4H, H-4 and Ar-OCH_3), 4.04-4.10 (m, 2H, H-4 and H-3), 4.36-4.56 (dd, 2H, J = 11.0 Hz, OCH_2), 4.65 (s, 1H, H-2), 6.80 (d, 2H, J = 8.3 Hz, Ar-H), 7.19 (d, 2H, J = 8.3 Hz, Ar-H); \(^1^3\)C NMR (CDCl_3, 75 MHz): δ 159.2, 129.8, 129.4 (2C), 113.7, 109.2, 83.1, 81.0, 79.6, 71.6, 55.6,
(2S,3R,4S,5R)-3-(2-Bromoallyloxy)-4-(4-methoxybenzylloxy)-5-ethyl-tetrahydro-2-methoxyfuran (87a): A stirred suspension of NaH (0.09 g, 3.77 mmol) in THF (4 mL) under N₂ atmosphere was treated with a solution of 82a (0.43 g, 1.52 mmol) in THF (4 mL) at 0 °C and stirred for 15 min. A solution of 2,3-dibromopropene (0.20 mL, 1.67 mmol) in THF (2 mL) was added to the reaction mixture at 0 °C and stirred at room temperature for 3 h. Reaction mixture was quenched with aq. NH₄Cl solution (3 mL) and extracted with EtOAc (2 x 20 mL). Organic layers were washed with water (10 mL), brine (10 mL) and dried over Na₂SO₄. Solvent was evaporated and purified the residue by column chromatography (60-120 Silica gel, ethyl acetate: pet. ether, 1.8:8.2) to give 87a (0.44 g, 72%) as colourless liquid; [α]D = +41.8 (c 0.6, CHCl₃); IR (neat): 3448, 3282, 1720, 1636, 771, 600 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.93 (t, 3H, J = 7.3 Hz, CH₃), 1.52 (m, 2H, CH₂), 3.39 (s, 3H, anomeric OCH₃), 3.79 (s, 3H, Ar-OCH₃), 3.84-4.08 (m, 4H, H-5, H-4 and OCH₂), 4.21 (m, 1H, H-3), 4.44-4.62 (dd, 2H, J = 11.7 Hz, OCH₂), 4.84 (d, 1H, J = 4.1 Hz, H-2), 5.62 (s, 1H, olefinic), 5.96 (s, 1H, olefinic), 6.82 (d, 2H, J = 8.5 Hz, Ar-H), 7.21 (d, 2H, J = 8.5 Hz, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 159.2, 131.7, 129.3 (2C), 128.9, 118.4, 113.7 (2C), 100.4, 84.3, 81.4, 79.0, 74.4, 71.8, 55.2, 55.1, 22.7, 10.3; HRMS (ESI): m/z calculated for C₁₈H₂₅NaO₅Br (M⁺+Na) 423.0783, found 423.0774.

(2R,3R,4S,5R)-3-(2-Bromoallyloxy)-4-(4-methoxybenzylloxy)-5-ethyl-tetrahydro-2-methoxyfuran (87b): A stirred suspension of NaH (0.29 g, 12.41 mmol) in dry THF (5 mL) under N₂ atmosphere was treated with a solution of 82b (1.40 g, 4.96 mmol) in THF (8 mL) at 0 °C and stirred for 15 min. A solution of 2,3-dibromopropene (0.66 mL, 5.46 mmol) in THF (2 mL) was added and stirred for 3 h. Workup as described for 77a and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.2:8.8) afforded 87b (1.54 g, 78%) as a liquid; [α]D = -30.5 (c 1.7, CHCl₃); IR (neat): 3451, 3282, 2924, 1720, 1611, 1513, 1248, 1100, 1065, 1050, 943, 771 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.94 (t, 3H, J = 7.3 Hz, CH₃), 1.63 (p, 2H, J = 7.3, 14.7 Hz, CH₂), 3.38 (s, 3H, anomeric OCH₃), 3.79 (s, 3H, Ar-OCH₃), 3.84-3.99 (m, 3H, H-5, H-4 and H-3), 4.07 (m, 2H, OCH₂), 4.41-4.57 (dd, 2H, J = 11.7 Hz, OCH₂), 4.75 (s, 1H, H-2), 5.60 (s, 1H, olefinic), 5.91 (s, 1H, olefinic), 6.81 (d, 2H, J = 8.5 Hz, Ar-H).
Hz, Ar-H), 7.23 (d, 2H, J = 8.5 Hz, Ar-H); $^{13}$C NMR (CDCl$_3$, 75 MHz): δ 159.2, 129.8, 129.4 (2C), 128.5, 118.1, 113.7 (2C), 107.6, 86.9, 82.5, 81.2, 73.7, 71.7, 55.6, 55.2, 23.2, 10.6; HRMS (ESI): m/z calculated for C$_{18}$H$_{25}$NaO$_3$Br (M$^+$+Na) 423.0783, found 423.0765.

(2S,3R,4S,5R)-3-(2-Bromoallyloxy)-4-(4-methoxybenzyloxy)-tetrahydro-2-methoxy-5-octylfuran (88a): A stirred suspension of NaH (0.078 g, 3.27 mmol) in dry THF (3 mL) under N$_2$ atmosphere was treated with a solution of 83a (0.48 g, 1.31 mmol) in THF (5 mL) at 0 °C and stirred for 15 min. A solution of 2,3-dibromo propene (0.36 mL, 1.44 mmol) in THF (2 mL) was added and stirred for 3 h. Workup as described for 87a and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1:9) afforded 88a (0.41 g, 65%) as a liquid; [α]$_D$ = +42.9 (c 0.7, CHCl$_3$); IR (neat): 3500, 3590, 1765, 879 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): δ 0.88 (t, 3H, J = 6.3 Hz, CH$_3$), 1.26 (s, 12H, 6xCH$_2$), 1.53 (m, 2H, CH$_2$), 3.39 (s, 3H, anomeric OCH$_3$), 3.78 (s, 3H, Ar-OCH$_3$), 3.93 (t, 1H, J = 4.3 Hz, H-4), 4.01-4.07 (m, 3H, H-5 and OCH$_2$), 4.20 (d, 1H, J = 14.1 Hz, H-3), 4.44-4.60 (dd, 2H, J = 11.2 Hz, OCH$_2$), 4.82 (d, 1H, J = 3.9 Hz, H-2), 5.61 (s, 1H, olefinic), 5.95 (s, 1H, olefinic), 6.80 (d, 2H, J = 8.3 Hz, Ar-H), 7.19 (d, 2H, J = 8.3 Hz, Ar-H); $^{13}$C NMR (CDCl$_3$, 75 MHz): δ 159.1, 130.0, 129.4 (2C), 129.2, 118.3, 118.0, 113.6 (2C), 107.6, 100.3, 86.8, 84.2, 81.4, 81.2, 81.0, 77.5, 74.3, 73.6, 71.7, 71.6, 55.6, 55.1 (2C), 31.7, 29.8, 29.6, 29.5, 29.4 (2C), 29.1, 26.0, 25.9, 22.5, 14.0; HRMS (ESI): m/z calculated for C$_{24}$H$_{37}$NaO$_3$Br (M$^+$+Na) 507.1722, found 507.1726.

(2R,3R,4S,5R)-3-(2-Bromoallyloxy)-4-(4-methoxybenzyloxy)-tetrahydro-2-methoxy-5-octylfuran (88b): A stirred suspension of NaH (0.07 g, 3.27 mmol) in dry THF (3 mL) under N$_2$ atmosphere was treated with a solution of 83b (0.48 g, 1.31 mmol) in THF (4 mL) at 0 °C and stirred for 15 min. 2,3-dibromo propene (0.36 mL, 1.44 mmol) in THF (2 mL) was added and stirred for 3 h. Workup as described for 87a and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1:9) afforded 88b (0.40 g, 64%) as a liquid; [α]$_D$ = -22.5 (c 1.10, CHCl$_3$); IR (neat): 3500, 3590, 1765, 879 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): δ 0.88 (t, 3H, J = 6.3 Hz, CH$_3$), 1.27 (s, 12H, 6xCH$_2$), 1.57 (m, 2H, CH$_2$), 3.37 (s, 3H, anomeric OCH$_3$), 3.78 (s, 3H, Ar-OCH$_3$), 3.82-3.90 (m, 2H, H-4 and H-5), 3.98-4.12 (m, 3H, H-3 and OCH$_2$), 4.40-4.56 (dd, 2H, J = 11.2 Hz, OCH$_2$), 4.74 (s, 1H, H-2), 5.59 (s, 1H, olefinic), 5.89 (s, 1H, olefinic), 6.80 (d, 2H, J = 8.5 Hz, Ar-H), 7.20 (d, 2H, J = 8.5 Hz, Ar-H); $^{13}$C NMR
(CDCl₃, 75 MHz): δ 159.2, 129.5, 129.3 (2C), 118.4, 118.1, 113.7 (2C), 107.6, 100.4, 86.9, 84.3, 81.5, 81.2, 81.0, 77.6, 74.4, 73.7, 71.6, 55.6, 55.2, 55.1, 31.8, 29.9, 29.6, 29.5 (3C), 29.2, 26.1, 25.9, 22.6, 14.0; HRMS (ESI): m/z calculated for C₂₉H₂₇NaO₃Br (M⁺+Na) 507.1722, found 507.1728.

(2R,3S,4R,5S)-4-(2-Bromoallyloxy)-2-ethyl-tetrahydro-5-methoxyfuran-3-ol (89a): A solution of 87a (0.15 g, 0.37 mmol) in aq. CH₂Cl₂ (1:19, H₂O:CH₂Cl₂, 10 mL) was treated with DDQ (0.17 g, 0.75 mmol) at 0 °C and stirred for 2 h. The reaction mixture was quenched with aq. NaHCO₃ solution (2 mL) and extracted with CH₂Cl₂ (2x10 mL). Organic layer was washed with aq. NaHCO₃ solution (5 mL), water (5 mL), brine (5 mL) and dried (Na₂SO₄). Evaporation of the solvent and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1:2:8.8) afforded 89a (0.07 g, 72%) as a liquid; [α]D = +112.5 (c 0.2, CHCl₃); IR (neat): 3448, 3282, 1720, 1636, 771, 600 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.0 (t, 3H, J = 6.1 Hz, CH₃), 1.49-1.68 (m, 2H, CH₂), 2.56 (d, 1H, J = 11.5 Hz, OH), 3.40 (s, 3H, anemic OCH₃), 3.81 (t, 1H, J = 4.5 Hz, H-3), 4.0 (m, 1H, H-2), 4.08-4.28 (m, 3H, H-4 and OCH₂), 4.84 (d, 1H, J = 4.0 Hz, H-5), 5.62 (s, 1H, olefinic), 5.99 (s, 1H, olefinic); ¹³C NMR (CDCl₃, 75 MHz): δ 128.4, 118.3, 105.9, 86.4, 85.6, 73.7, 73.5, 54.8, 23.0, 10.2; HRMS (ESI): m/z calculated for C₁₀H₁₇NaO₄Br (M⁺+Na) 303.0207, found 303.0208.

(2R,3S,4R,5R)-4-(2-Bromoallyloxy)-2-ethyl-tetrahydro-5-methoxyfuran-3-ol (89b): A solution of 87b (0.90 g, 2.25 mmol) in aq. CH₂Cl₂ (1:19, H₂O:CH₂Cl₂, 10 mL) was treated with DDQ (1.03 g, 4.50 mmol) at 0 °C and stirred for 2 h. Work up as described for 89a and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1:2:8.8) afforded 89b (0.43 g, 75%) as a liquid; [α]D = -51.6 (c 0.6, CHCl₃); IR (neat): 3500, 3590, 1765, 879 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.01 (t, 3H, J = 7.4 Hz, CH₃), 1.67 (p, 2H, J = 7.3, 14.5 Hz, CH₂), 2.48 (d, 1H, J = 11.7 Hz, OH), 3.36 (s, 3H, anemic OCH₃), 3.86 (s, 1H, H-3), 3.93 (dd, H, J = 3.5, 11.7 Hz, H-2), 4.07 (m, 1H, H-4), 4.16 (s, 2H, OCH₂), 4.81 (s, 1H, H-5), 5.62 (s, 1H, olefinic), 5.93 (s, 1H, olefinic); ¹³C NMR (CDCl₃, 75 MHz): δ 128.5, 118.3, 106.0, 86.5, 85.1, 73.8, 73.6, 54.8, 23.1, 10.3; HRMS (ESI): m/z calculated for C₁₀H₁₇NaO₄Br (M⁺+Na) 303.0207, found 303.0204.
(2R,3S,4R,5S)-4-(2-Bromoallyloxy)-tetrahydro-5-methoxy-2-octylfuran-3-ol (90a): A solution of 88a (0.26 g, 0.53 mmol) in aq. CH₂Cl₂ (1:19, H₂O:CH₂Cl₂, 10 mL) was treated with DDQ (0.24 g, 1.07 mmol) at 0 °C and stirred for 2 h. Work up as described for 89a and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.4:8.6) afforded 90a (0.13 g, 65%) as a liquid; [α]D = +84.5 (c 0.2, CHCl₃); IR (neat): 3456, 3272, 1744, 1686, 757, 623 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.88 (t, 3H, J = 4.1 Hz, CH₃), 1.27 (s, 14H, 7xCH₂), 3.40 (s, 3H, anomeric OCH₃), 3.80 (m, 2H, H-3 and H-2), 4.07 (m, 2H, OCH₂), 4.27 (m, 1H, H-4), 4.83 (d, 1H, J = 4.1 Hz, H-5), 5.62 (s, 1H, olefinic), 5.98 (s, 1H, olefinic).

(2R,3S,4R,5R)-4-(2-Bromoallyloxy)-tetrahydro-5-methoxy-2-octylfuran-3-ol (90b): A solution of 88b (0.40 g, 0.82 mmol) in aq. CH₂Cl₂ (1:19, H₂O:CH₂Cl₂, 10 mL) was treated with DDQ (0.37 g, 1.65 mmol) at 0 °C and stirred for 2 h. Work up as described for 89a and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.2:8.8) afforded 90b (0.24 g, 82%) as a liquid; [α]D = -176.2 (c 0.2, CHCl₃); IR (neat): 3448, 3282, 1720, 1636, 771, 600 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.88 (t, 3H, J = 4.1 Hz, CH₃), 1.28 (s, 14H, 7xCH₂), 3.38 (s, 3H, anomeric OCH₃), 3.80 (m, 2H, H-3 and H-5), 4.07-4.32 (m, 3H, OCH₂ and H-4), 4.78 (s, 1H, H-5), 5.62 (s, 1H, olefinic), 5.98 (s, 1H, olefinic); ¹³C NMR (CDCl₃, 75 MHz): δ 129.1, 118.5, 100.7, 85.9, 78.1, 76.2, 74.5, 65.2, 31.7, 29.9, 29.2, 27.1, 22.3, 14.0; HRMS (ESI): m/z calculated for C₁₆H₂₉BrO₄Na (M⁺+Na) 387.1249, found 387.1258.

(3aR,4S,6S,6aR)-4-Ethyl-hexahydro-6-methoxy-3-methylenefuro[3,4-b]furan (68a): To a solution of 89a (0.70 g, 2.50 mmol) and pyridine (0.40 mL, 5.00 mmol) in CH₂Cl₂ (4 mL) at -20 °C, Tf₂O (0.49 mL, 3.00 mmol) was added and stirred for 30 min. It was cooled to room temperature and decanted. Residue was dissolved in aq. NaHCO₃ solution (6 mL) and extracted with CH₂Cl₂ (2 × 10 mL). Combined organic layers were washed with aq. NaHCO₃ solution (5 mL), water (5 mL), 2N aq. HCl (5 mL) and brine (5 mL). It was dried (Na₂SO₄) and evaporated to give 72a (0.90 g, 88%) as a yellow syrup, which was used as such for the next reaction.

To a stirred solution of 72a (0.90 g, 2.18 mmol) in dry DMSO (5 mL), DBU (0.66 ML, 4.36 mmol) was added at 0 °C and stirred for 12 h. Reaction mixture was extracted with EtOAc
(2 x 10 mL) and washed with water (5 mL) and brine (5 mL). It was dried (Na₂SO₄) and evaporated to afford 91a as a liquid, which was used as such for next reaction.

A solution of 91a (0.25 g, 0.95 mmol) in dry benzene (25 mL) was treated with n-Bu₃SnH (0.51 mL, 1.90 mmol), heated to reflux and catalytic amount of AIBN was added at reflux. After 12 h at reflux, the reaction mixture was cooled to room temperature, evaporated under reduced pressure and purified the residue by column chromatography (60-120 Silica gel, ethyl acetate: pet. ether, 0.9:9.1) to give 68a (0.13 g, 71%) as a colourless liquid; [α]D = -285.8 (c 0.23, CHCl₃); IR (neat): 3412, 2891, 2797, 1764, 1176, 1083, 804 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.02 (t, 3H, J = 7.3 Hz, CH₃), 1.55 (m, 2H, CH₂), 3.26 (t, 1H, J = 7.3 Hz, H-3a), 3.51 (s, 3H, OCH₃), 3.74 (m, 1H, H-4), 4.25-4.35 (q, 2H, J = 12.1 Hz, OCH₂), 4.60 (m, 1H, H-6a), 4.67 (d, 1H, J = 3.6 Hz, H-6), 4.91 (s, 1H, olefinic), 5.06 (s, 1H, olefinic); ¹³C NMR (CDCl₃, 75 MHz): δ 146.6, 107.8, 105.1, 83.5, 78.6, 74.0, 57.5, 50.1, 24.9, 11.2; HRMS (EI): m/z calculated for C₁₀H₁₅O₃ (M⁺+H) 185.1177, found 185.1175.

(3aR,4S,6R,6aR)-4-Ethyl-hexahydro-6-methoxy-3-methylenefurano[3,4-b]furan (68b): To a solution of 89b (0.70 g, 2.50 mmol) and pyridine (0.40 mL, 5.00 mmol) in CH₂Cl₂ (4 mL) at -20 °C, Tf₂O (0.49 mL, 3.00 mmol) was added and stirred for 30 min. Work up as described for 72a afforded 72b (0.98 g, 95%) as a yellow syrup, which was used as such for the next reaction.

To a stirred solution of 72b (0.95 g, 2.30 mmol) in dry DMSO (5 mL), DBU (0.70 mL, 4.61 mmol) was added at 0 °C and stirred for 12 h. Work up as described for 91a afforded 91b as a liquid, which was used as such for next reaction.

To a solution of 91b (0.25 g, 0.95 mmol) in dry benzene (25 mL) under N₂ atmosphere was treated with n-Bu₃SnH (0.51 mL, 1.91 mmol) at reflux, AIBN (cat.) was added and heated at reflux for 12 h. Work up as described for 68a and purification of the residue by column chromatography (60-120 Silica gel, ethyl acetate: pet. ether, 0.7:9.3) gave 68b (0.11 g, 60%) as a colourless liquid; [α]D = -49.2 (c 0.23, CHCl₃); IR (neat): 3437, 2926, 2856, 1737, 1219, 1051, 769 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.01 (t, 3H, J = 7.3 Hz, CH₃), 1.49 (m, 2H, CH₂), 3.19 (t, 1H, J = 7.1 Hz, H-3a), 3.29 (s, 3H, OCH₃), 3.94 (m, 1H, H-4), 4.16 (m, 2H, J = 1.7, 3.5 Hz, OCH₂), 4.53 (d, 1H, J = 6.4 Hz, H-6a), 4.81 (s, 1H, H-6), 4.92 (q, 1H, J = 1.7 Hz, olefinic) 5.06 (q, 1H, J = 1.5 Hz, olefinic); ¹³C NMR (CDCl₃, 75 MHz): δ 147.1, 107.7, 96.2, 88.5, 80.9, 72.6,
(3aR,4S,6R,6aR)-Hexahydro-6-methoxy-3-methylene-4-octylfuro[3,4-b]furan (69a): To a solution of 90a (0.80 g, 2.19 mmol) and pyridine (0.35 mL, 4.38 mmol) in CH₂Cl₂ (10 mL) at -20 °C, TfO (0.40 g, 2.63 mmol) was added and stirred for 30 min. Work up as described for 72a gave 73a (0.88 g, 81%) as a yellow syrup, which was used as such for the next reaction.

To a stirred solution of 73a (0.80 g, 1.60 mmol) in DMSO (5 mL), DBU (0.49 mL, 3.21 mmol) was added at 0 °C and stirred for 12 h. Work up as described for 91a afforded 92a as a liquid, which was used as such for next step.

To a solution of 92a (0.60 g, 1.73 mmol) in dry benzene (25 mL) and n-Bu₃SnH (0.93 mL, 3.47 mmol) at reflux, catalytic amount of AIBN was added and heated at reflux for 12 h. Work up as described for 68a and purification of the residue by column chromatography (60-120 Silica gel, ethyl acetate: pet. ether, 0.9:9.1) gave 69a (0.33 g, 72%) as a colorless liquid; [α]D = -153.2 (c 0.2, CHCl₃); IR (neat): 3231, 2892, 1755, 1176, 1051, 786 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.88 (t, 3H, J = 6.3 Hz, CH₃), 1.25 (m, 14H, 7xCH₂), 3.23 (t, 1H, J = 6.8 Hz, H-3a), 3.51 (s, 3H, OCH₃), 3.78 (m, 1H, H-4), 4.28 (m, 2H, OCH₂), 4.58 (m, 1H, H-6a), 4.65 (d, 1H, J = 4.1 Hz, H-6), 4.90 (s, 1H, olefinic), 5.07 (s, 1H, olefinic).

(3aR,4S,6R,6aS)-Hexahydro-6-methoxy-3-methylene-4-octylfuro[3,4-b]furan (69b): To a solution of 90b (0.80 g, 2.19 mmol) and pyridine (0.35 mL, 4.38 mmol) in CH₂Cl₂ (10 mL) at -20 °C, TfO (0.40 g, 2.63 mmol) was added and stirred for 30 min. Work up as described for 72a gave 73b (1.01 g, 93%) as a yellow syrup, which was used as such for the next reaction.

To a stirred solution of 73b (0.80 g, 1.60 mmol) in DMSO (5 mL), DBU (0.49 mL, 3.21 mmol) was added at 0 °C and stirred for 12 h. Work up as described for 91a afforded 92b as a liquid, which was used as such for next reaction.

A solution of 92b (0.60 g, 1.73 mmol) in dry benzene (25 mL), n-Bu₃SnH (0.93 mL, 3.47 mmol) at reflux was treated with catalytic amount of AIBN and heated at reflux for 12 h. Workup as described for 68a and purification of the residue by column chromatography (60-120 Silica gel, ethyl acetate: pet. ether, 0.9:9.1) gave 69b (0.30 g, 65%) as a colourless liquid; [α]D = -192.8 (c 0.14, CHCl₃); IR (neat): 3412, 2891, 2797, 1764, 1176, 1083, 804 cm⁻¹; ¹H NMR (300
Chapter II, Section-A, Experimental Section

107 MHz, CDCl₃): δ 0.88 (t, 3H, J = 6.1 Hz, CH₃), 1.27 (m, 14H, 7xCH₂), 3.17 (t, 1H, J = 6.8 Hz, H-3a), 3.29 (s, 3H, OCH₃), 4.02 (m, 1H, H-4), 4.17 (s, 2H, OCH₂), 4.50 (d, 1H, J = 6.4 Hz, H-6a), 4.81 (s, 1H, H-6), 4.92 (s, 1H, olefinic), 5.06 (s, 1H, olefinic); ¹³C NMR (CDCl₃, 75 MHz): δ 145.3, 111.7, 105.1, 82.5, 79.9, 71.6, 61.0, 55.2, 31.9, 29.7, 26.8, 26.3, 22.6, 14.1; HRMS (ESI): m/z calculated for C₁₆H₂₉O₃ (M⁺+H) 269.2038, found 269.2072.
References:


Spectrum 1: $^1$H NMR Spectrum of compound 77 in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 77 in CDCl$_3$ (75 MHz)
Spectrum 2: $^1$H NMR Spectrum of compound 81 in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 81 in CDCl$_3$ (75 MHz)
Spectrum 3: $^1$H NMR Spectrum of compound 82a in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 82a in CDCl$_3$ (125 MHz)
Spectrum 4: $^1$H NMR Spectrum of compound 82b in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 82b in CDCl$_3$ (125 MHz)
Spectrum 5: $^1$H NMR Spectrum of compound 83a in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 83a in CDCl$_3$ (125 MHz)
Spectrum 6: $^1$H NMR Spectrum of compound 83b in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 83b in CDCl$_3$ (75 MHz)
Spectrum 7: $^1$H NMR Spectrum of compound 87b in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 87b in CDCl$_3$ (75 MHz)
Spectrum 8: $^1$H NMR Spectrum of compound 88b in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 88b in CDCl$_3$ (75 MHz)
Spectrum 9: $^1$H NMR Spectrum of compound 68b in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 68b in CDCl$_3$ (75 MHz)
Spectrum 10: $^1$H NMR Spectrum of compound 69b in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 69b in CDCl$_3$ (75 MHz)
CHAPTER-II

SECTION-B

Radical mediated synthesis of cis-fused bicyclic systems from L-arabinose and D-xylose
SECTION-B: Radical mediated synthesis of cis-fused bicyclic systems from L-arabinose and D-xylose

Section B deals with radical mediated synthesis of cis-fused bicyclic systems from L-arabinose and D-xylose

The nature has its creation by diversity oriented synthesis (DOS), whereby nature designs molecules of skeletal, structural, stereochemical and functional diversity. For eg: macrosphelides, a macrotriolide class of natural products, which differ in the stereochemistry and arrangement of the functional groups. Yet another example of nature’s DOS is reflected by the presence of a variety of α-methylene bis-butyrolactones. This class of natural products differs in the length of their side chains and the arrangement of the bicyclic systems to result in diversely fused furo-furan systems.

Earlier, we have extensively worked on the synthesis of this class of natural products such as xylobovide 17, canadensolide 18, sporothriolide 19, epi-ethisolide 20, avenaciolide 21, discocoiolide 22 (Figure 2) and others by the adoption of 5-exo-dig radical route to introduce both cis-fused bicyclic systems besides the simultaneous introduction of efficient introduction of exo-methylene group.

Further studies revealed that all types of bis-butyro-lactones could not be prepared by radical cyclization approach. It was found from our studies that the side chain in a specific stereochemistry has an impact on the cyclization by radical route. However, to encounter such situations, yet another protocol was adopted, where, the inversion of centre takes place during radical cyclization. Hence, to encounter such situations and to create diversity of side chains and functionalized side chains, it was proposed to first build different types of cis-fused bicyclic systems, which on further transformations could create further diversity.

As was discussed in the Chapter I, the side chain effect was amply evident in furanoside systems with L-Ara configuration, rather than in systems with D-Xylo configuration. The synthesis of iso-avenaciolide 4 by 5-exo-dig mode was not possible in our hands probably due to side chain effect. In addition, nature has a diversity of bis-butyro-lactone containing natural products such as, ethisolide 3 and iso-avenaciolide 4 along with non-natural products such as, iso-canadensolide 1 and iso-sporothriolide 2 (Figure 1). Hence, in this study it was proposed to undertake the synthesis of cis-fused bicyclic systems by 5-exo-dig radical cyclization from the precursors with L-Ara and D-Xylo configurations, so that requisite side chain or other diversity
can be introduced accordingly on these bicyclic systems. Since, the problems were encountered with L-Ara configuration, the work was initiated on the synthesis of bicyclic systems 5 and 6 from L-Ara.

According to the retrosynthetic strategy, the bicyclic systems 5 and 6 could be made from the radical precursors 7 and 8, while, the xanthate derivatives 7 and 8 inturn could be realized from the known L-arabinose derivative 9 (Scheme 1).

Accordingly, known alcohol 9 (Scheme 2) was subjected to alkylation with propargyl bromide in the presence of NaH in THF at room temperature for 4 h to furnish the required 2-O-propargyl ether 10 in 91% yield. In the $^1$H NMR spectrum of 10, propargylic protons resonated at $\delta$ 2.42 as a broad singlet corresponding to acetylenic proton, whereas rest of the protons resonated at the appropriate chemical shifts. HRMS showed $m/z$ 489.20490 for $C_{27}H_{34}O_3NaSi (M+Na)^+$ confirming the structure of 10.

![Figure 1](image-url)
Methanolsysis of 10 with methanol containing conc. HCl (cat.) at 0 °C to room temperature for 6 h gave the diastereomeric mixture of α- and β-methyl glycosides 11 with concomitant hydrolysis of TBDPS group.

Hence, the anomeric mixture 11 was subjected to reaction with TBDPSCl and imidazole in dry CH₂Cl₂ at 0 °C to room temperature for 2 h to give the mixture of 12 and 12a (Scheme 3). Purification of the mixture by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.2:8.8) gave the α-anomer 12 (33%) and β-anomer 12a (49%).

In the ¹H NMR spectrum of α-anomer 12, H-2 resonated at δ 4.82 (J = 4.7 Hz) as a doublet and -OMe appears at δ 3.37 as a singlet, while in β-anomer 12a H-2 appeared at δ 4.94 as a singlet and -OMe appears at δ 3.41 as a singlet, while rest of the protons resonated at the appropriate chemical shifts. HRMS showed m/z 463.19078 and 463.19095 for C₂₅H₃₂O₅NaSi (M+Na)⁺ confirming the structures of 12 and 12a.

The β-anomer 12a on reaction with NaH, CS₂ and MeI in THF at 0 °C to room temperature for 2 h furnished the xanthate ester 7 in 90% yield (Scheme 4). In ¹H NMR spectrum of 7 the methylthio group resonated at δ 2.54 as a singlet, while the H-3 proton shifted to downfield and appeared at δ 5.85 as a singlet. HRMS showed m/z 531.16895 for C₂₇H₃₅O₅S₂Si (M+Na)⁺ confirming the structure of 7.
Radical cyclization of 7 under standard reaction conditions using n-Bu₃SnH and AIBN (cat.) in dry benzene at reflux for 12 h afforded 5 in 69% yield (Scheme 5). In ¹H NMR spectrum of 5, it showed the disappearance of the methylthio ester signals at δ 2.54. The H-4 proton resonated at δ 5.12 (J = 6.0 Hz) as a doublet, while the exo-cyclic double bond protons resonated at δ 5.05 as a broad singlet. HRMS showed m/z 447.19692 for C₂₅H₃₂O₄NaSi (M+Na)⁺ confirming the structure of 5. The optical rotation value for 5 in chloroform was [α]D = -45.7 (c 0.1).

Having successfully synthesized the cis-fused bicyclic furo-furan system 5, the study was then extended to the synthesis of the other furo-furan namely 6 by the use of radical generated at C-3. Accordingly, known PMB ether 13 on methanolysis in MeOH with conc. HCl at room temperature for 6 h gave the glycoside mixture 14, which on reaction with TBDPSCl and imidazole in CH₂Cl₂ at 0 °C to room temperature for 2 h gave the silyl ethers 14a (Scheme 6).

Alkylation reaction of 14a with propargyl bromide in the presence of NaH in THF at room temperature for 4 h afforded the ethers 15 (34%) and 15a (50%) (Scheme 7) after column
chromatography purification. In the $^1$H NMR spectrum of $\alpha$-anomer 15, H-5 resonated at $\delta$ 4.53 ($J = 4.4$ Hz) as a doublet, while H-3 and H-4 at $\delta$ 3.93 ($J = 5.9, 11.4$ Hz) as a quintet and $\delta$ 4.27 as a multiplet. The PMB signals at $\delta$ 6.81 and $\delta$ 7.12 ($J = 8.4$ Hz) as two doublets, while propargylic proton resonated at $\delta$ 2.19 as a broad singlet. In the $^1$H NMR spectrum of $\beta$-anomer 15a, H-5 appeared at $\delta$ 4.74 as a singlet, while H-3 and H-4 at $\delta$ 3.94 ($J = 3.4$ Hz) as a doublet and $\delta$ 4.27 as a singlet. The PMB signals at $\delta$ 6.76 and $\delta$ 7.03 ($J = 8.4$ Hz) as two doublets, while propargylic proton resonated at $\delta$ 2.20 as a broad singlet, while rest of the protons at the appropriate chemical shifts.

**Scheme 7**

![Scheme 7](image)

To create the radical precursor, 15a was subjected to oxidative deprotection of PMB group with DDQ in aq. CH$_2$Cl$_2$ at room temperature for 2 h to give the alcohol 16 in 75% yield (Scheme 8). In $^1$H NMR spectrum of 16, the aromatic protons disappeared, while rest of the protons resonated at the expected chemical shifts.

**Scheme 8**

![Scheme 8](image)

Thus, the derived alcohol 16 on reaction with NaH and CS$_2$ followed by MeI was converted into the xanthate ester 8 in 85% yield (Scheme 8). In $^1$H NMR spectrum of 8 the methylthio group resonated at $\delta$ 2.44 as a singlet, while the H-3 proton shifted to downfield and appeared at $\delta$ 6.04 ($J = 1.32, 3.39$ Hz) as a doublet of doublet. Rest of the protons resonated at the appropriate chemical shifts. HRMS showed $m/z$ 531.16889 for C$_{27}$H$_{35}$O$_7$S$_2$Si (M+Na)$^+$ confirming the structure of 8. The optical rotation value for 8 in chloroform are $[\alpha]_D = -87.5$ (c 0.32).
The xanthate ester 8 was subjected to radical cyclization reaction with n-Bu3SnH and AIBN (cat.) in dry benzene at reflux for 12 h. However, the reaction met with failure to give the expected cyclic system 6 (Scheme 9), unlike in the case of 7 giving 5. These findings become now very interesting, since, the resistance of the C-3 radical to undergo radical cyclization is attributable to the L-Ara configuration or to the bulkiness of the protecting group (-CH2OTBDPS).

Scheme 9

To understand the above discussed results and develop the other cis-fused bicyclic systems with different stereocentres, the study was extended to the synthesis of bicyclic systems having D-Xylo configuration. This study further acquires importance, since several natural products, as shown in Figure 2 have two different kinds of furo-furan moieties1-6 (17-22) with D-Xylo configuration.

Figure 2

The similar retrosynthetic strategy that was used for the synthesis of bicyclic systems from L-Ara was adopted for the synthesis of bicyclic systems 23 and 24. Thus, 23 and 24 could be made from the xanthates 25 and 26, which inturn could be realized from D-xylose derivative 27 (Scheme 10).
Accordingly, the known diol 27 was treated with TBDPSCI in presence of imidazole in CH$_2$Cl$_2$ at 0 °C to room temperature for 2 h to afford silyl ether 28 in 70% yield (Scheme 11). In the $^1$H NMR spectrum of 28, H-3a and H-6a protons resonated at $\delta$ 6.0 and 4.54 ($J$ = 3.5 Hz) as two doublets, while acetonide protons showed at $\delta$ 1.33 and 1.46 as two singlets. The TBDPS protons at $\delta$ 1.05 as singlet corresponding to tert. butyl proton and aromatic protons resonated at $\delta$ 7.41 and 7.69 as two multiplets. HRMS showed m/z 451.1895 for C$_{24}$H$_{32}$O$_5$NaSi (M+Na)$^+$ confirming the structure of 28.

Alcohol 28 was subjected to alkylation with propargyl bromide in the presence of NaH in THF at room temperature for 4 h to furnish 29 in 80% yield (Scheme 12). In the $^1$H NMR spectrum of 29, propargylic protons resonated at $\delta$ 2.42 ($J$ = 2.3 Hz) as a triplet corresponding to acetylenic proton, while, rest of the protons resonated at the appropriate chemical shifts. HRMS showed m/z 489.20490 for C$_{27}$H$_{34}$O$_5$NaSi (M+Na)$^+$ confirming the structure of 29.
Hydrolysis of acetonide 29 on reaction with methanol containing conc. HCl (cat.) at 0 °C to room temperature for 6 h gave the α- and β-methyl glycoside mixture 30 with concomitant hydrolysis of TBDPS group (Scheme 13).

The anomeric mixture 30 on reaction with TBDPSCl and imidazole in CH2Cl2 at 0 °C to room temperature for 2 h furnished β-anomer as a major anomer 31 (44%) after column chromatography purification (Scheme 14). In the 1H NMR spectrum of β-anomer 31 H-2 proton appeared at δ 4.69 as a singlet and H-3 appeared at δ 4.57 as a multiplet, while anomeric OCH3 showed at δ 3.19 as a singlet. Rest of the protons resonated at the appropriate chemical shifts. HRMS showed m/z 463.19078 for C25H32O5NaSi (M+Na)+ confirming the structure of 31.

The β-anomer 31 on reaction with NaH, CS2 and MeI in THF at 0 °C to room temperature for 2 h furnished the xanthate ester 25 in 70% yield (Scheme 15). In 1H NMR spectrum of 25 the methylthio group resonated at δ 2.46 as a singlet, while the H-2 proton resonated at δ 4.69 as a singlet and the H-3 proton at δ 5.99 (J = 5.0 Hz) as a doublet. HRMS showed m/z 531.16949 for C27H35O5S2Si (M+Na)+ confirming the structure of 25. The optical rotation value for 25 in chloroform was [α]D = -20.46 (c 0.17).
Radical cyclization of 25 on reaction with n-Bu₃SnH in the presence AIBN (cat.) in dry benzene at reflux for 12 h afforded 23 in 71% yield (Scheme 16). In ¹H NMR spectrum of 23, the exo-cyclic double bond protons resonated at δ 5.02 as broad singlet, while H-4, H-6a and H-3a at δ 4.96 (J = 6.0 Hz) as a doublet and δ 4.65 as a multiplet. The rest of the protons resonated at the appropriate chemical shifts. HRMS showed m/z 447.19538 for C₂₅H₃₂O₄NaSi (M+Na)⁺ confirming the structure of 23. The optical rotation value for 23 in chloroform was [α]D = -32.7 (c 0.31).

Having successfully synthesized the bicyclic systems using C-2 radical, the study was then extended to the C-3 radical mediated formation of bicyclic system. Accordingly, the known silyl ether 28 on reaction with PMBBr in the presence of NaH in dry THF at 0 °C to room temperature for 4 h furnished 32 in 83% yield (Scheme 17). In ¹H NMR spectrum of 32, the newly introduced PMB protons resonated at δ 3.79 as a singlet for Ar-OCH₃ and at δ 6.82 and δ 7.22 (J = 8.6 Hz) as two doublets for aromatic group, while rest of the protons at the expected chemical shifts. HRMS showed m/z 571.2512 for C₃₂H₄₀O₆NaSi (M+Na)⁺ confirming the structure of 32.
The PMB ether 32 on methanolysis (MeOH, conc. HCl) gave the glycosidic mixture 33, which on further reaction with TBDPSCl and imidazole in CH₂Cl₂ at 0 °C to room temperature for 2 h gave 33a (Scheme 18).

Scheme 18

\[
\begin{align*}
32 & \xrightarrow{\text{MeOH, H}^+} 0^\circ\text{C-rt, 6 h} \quad \text{HO-PMBO} \quad \text{TBDPSCl, imidazole} \quad \text{dry CH}_2\text{Cl}_2, 0^\circ\text{C-rt, 2 h} \quad \text{33a} \\
32 & \xrightarrow{\text{MeOH, H}^+} 0^\circ\text{C-rt, 6 h} \quad \text{HO} \quad \text{33} \quad \text{TBDPSCl, imidazole} \quad \text{dry CH}_2\text{Cl}_2, 0^\circ\text{C-rt, 2 h} \quad \text{33a} \\
\end{align*}
\]

Alkylation of 33a with propargyl bromide in the presence of NaH in THF at room temperature for 4 h afforded the β-anomer as a major anomer 34a (53%) after chromatography purification (Scheme 19). In ¹H NMR spectrum of 34a, the H-5 proton resonated at δ 4.81 as a singlet, while H-4 and H-3 at δ 4.44 (J = 5.9, 10.9 Hz) as a quintet and δ 4.07 (J = 11.4 Hz) as a doublet. The PMB protons appeared at δ 6.70 and δ 6.90 (J = 7.9 Hz) as two doublets, while rest of the protons resonated at the expected chemical shifts.

Scheme 19

\[
\begin{align*}
\text{TBDPSO} & \quad \text{O} \quad \text{OMe} \quad \text{PMBO} \quad \text{OH} \quad \text{NaH, Br} \quad \text{THF, rt, 4 h} \quad \text{TBDPSO} \quad \text{O} \quad \text{OMe} \quad \text{PMBO} \quad \text{OH} \\
\text{33a} & \xrightarrow{\text{NaH, Br}} \text{34a (53%)} \\
\end{align*}
\]

Oxidative deprotection of PMB group in 34a with DDQ in aq. CH₂Cl₂ at room temperature for 2 h to give the alcohol 35 in 76% yield (Scheme 20). In ¹H NMR spectrum of 35 showed the disappearance of PMB protons, while rest of the protons resonated at the expected chemical shifts. HRMS showed m/z 463.19086 for C₂₅H₅₂O₅NaSi (M+Na)⁺ confirming the structure of 35.

Scheme 20

\[
\begin{align*}
\text{TBDPSO} & \quad \text{O} \quad \text{OMe} \quad \text{PMBO} \quad \text{OH} \quad \text{DDQ} \quad \text{CH}_2\text{Cl}_2:H_2\text{O (19:1)} \quad \text{TBDPSO} \quad \text{O} \quad \text{OMe} \quad \text{PMBO} \quad \text{OH} \\
\text{34a} & \xrightarrow{\text{DDQ}} \text{35} \\
\end{align*}
\]

Reaction of alcohol 35 with NaH and CS₂ followed by alkylation with MeI, it was converted into the xanthate ester 26 in 81% yield (Scheme 21). In ¹H NMR spectrum of 26 the
methylthio group resonated at $\delta$ 2.33 as a singlet and H-3 proton at $\delta$ 6.06 ($J = 1.5, 4.5$ Hz) as doublet of doublet. The rest of the protons resonated at the appropriate chemical shifts.

**Scheme 21**

Finally, radical cyclization of 26 was carried out with $n$-Bu$_3$SnH and AIBN (cat.) in dry benzene at reflux for 12 h which however met with failure to give the expected cyclic system 24 (Scheme 22), unlike in the case of 25 giving 23. These findings become now very interesting, since, the resistance of the C-3 radical to undergo radical cyclization may be attributed to the bulkyness of the protecting group (-CH$_2$OTBDPS).

**Scheme 22**

Thus, the present study resulted in the formation of two cis-fused furo-furan bicyclic systems by the successful utilization of C-2 radical. These bicyclic systems, which look similar to canadensolide (18) class of natural products. Hence, synthesis of natural products and non-natural products structurally relevent to canadensolide (18) and others can be undertaken from these new bicyclic systems. Further studies on the utilization of C-3 radical cyclization of D-Xylo/L-Ara derived xanthates are in progress.
Experimental Section:

(3aR,5S,6S,6aR)-Tetrahydro-2,2-dimethyl-6-(prop-2-ynyloxy)furo[2,3-d][1,3]dioxol-5-yl methoxy)(tert.-butyl)diphenylsilane (10): A stirred suspension of NaH (0.36 g, 14.95 mmol) in THF (6 mL) under N₂ atmosphere at 0 °C, was treated with a solution of alcohol 9 (3.20 g, 7.47 mmol) in THF (5 mL) and stirred for 15 min. Propargyl bromide (0.83 mL, 7.47 mmol) was added to the reaction mixture at 0 °C and stirred at room temperature for 4 h. Reaction mixture was quenched with aq. NH₄Cl solution (5 mL) and extracted with EtOAc (2 x 20 mL). Organic layer was washed with water (10 mL), brine (10 mL) and dried (Na₂SO₄). Solvent was evaporated and purified the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.2:8.8) afforded 10 (3.20 g, 91%) as a liquid; [α]D = -52.5 (c 4.1, CHCl₃); IR (neat): 3451, 3282, 2924, 1720, 1611, 1513, 1248, 1065, 1050, 943, 771 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): 1.06 (s, 9H, C(CH₃)₃), 1.23-1.34 (m, 6H, 2xCH₃), 2.42 (s, 1H, acetylenic-H), 3.78-3.85 (m, 2H, OCH₂), 4.11-4.35 (m, 4H, H-5, H-6 and OCH₂), 4.62 (d, 1H, J = 3.2 Hz, H-6a), 5.85 (d, 1H, J = 3.2 Hz, H-3a), 7.35-7.44 (m, 6H, Ar-H), 7.66-7.71 (m, 4H, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 135.5 (2C), 133.0 (2C), 129.6 (2C), 127.6 (4C), 112.3, 105.6, 84.9, 84.6, 82.1, 74.9, 63.1, 56.8, 26.7 (3C), 25.9 (2C), 19.1; HRMS (ESI): m/z calculated for C₂₇H₃₅O₃NaSi (M⁺+Na) 489.20677, found 489.20490.

(2S,3R,4R,5R)-5-((tert.-Butyldiphenylsilyl)methyl)-tetrahydro-2-methoxy-4-(prop-2-ynyloxy)furan-3-ol (12) and (2R,3R,4R,5R)-5-((tert.-Butyldiphenylsilyl)methyl)-tetrahydro-2-methoxy-4-(prop-2-ynyloxy)furan-3-ol (12a): To a solution of 10 (1.50 g, 6.57 mmol) in dry MeOH (20 mL) under N₂ atmosphere, 3 drops of conc. HCl was added at 0 °C and stirred for 6 h. The reaction mixture was cooled to 0 °C and neutralized with solid NaHCO₃ (0.5 g) at 0 °C. It was filtered, evaporated the solvent and purified the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.8:8.2) to afford anomeric mixture 11 (1.0 g, 75%) as a liquid, which was used as such for the next reaction.

To a stirred solution of anomeric mixture 11 (0.70 g, 3.46 mmol) in CH₂Cl₂ (10 mL), imidazole (0.47 g, 6.93 mmol) was added and the reaction mixture was stirred at 0 °C. After 10 min, TBDPSCI (0.95 g, 3.46 mmol) and DMAP (0.01 g) were added and stirred at room temperature for 2 h. The reaction mixture was diluted with CH₂Cl₂ (20 mL), washed with water (10 mL), brine (10 mL) and dried (Na₂SO₄). Solvent was evaporated and purified the residue by
column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.9:8.1) to afford α- and β-
anomers in 1:1.5 ratio. First eluted was α-anomer 12 (0.50 g, 33%) as a syrup; [α]D = -1.07 (c 0.9, CHCl3); IR (neat): 3590, 3500, 2237, 1724, 1256, 867, 793 cm⁻¹; ¹H NMR (300 MHz, CDCl3): δ 1.07 (s, 9H, C(CH3)3), 2.40 (t, 1H, J = 2.4 Hz, acetylenic-H), 3.37 (s, 3H, OCH3), 3.70-3.81 (m, 2H, OCH2), 3.98 (q, 1H, J = 5.1, 10.5 Hz, H-5), 4.09 (t, 1H, J = 6.0 Hz, H-4), 4.17-4.22 (m, 1H, H-3), 4.32 (m, 2H, OCH2), 4.82 (d, 1H, J = 4.7 Hz, H-2), 7.35-7.44 (m, 6H, Ar-H), 7.68-7.71 (m, 4H, Ar-H); ¹³C NMR (CDCl3, 75 MHz): δ 135.6 (2C), 129.6 (4C), 127.6 (2C), 102.2, 83.5, 81.8, 77.7, 74.5, 64.8, 57.3, 55.4, 26.7 (3C), 19.1; HRMS (ESI): m/z calculated for C25H32NaO5Si (M⁺+Na) 463.19112, found 463.19078.

Second eluted was β-anomer 12a (0.75 g, 49%) as a syrup; [α]D = -41.9 (c 1.6, CHCl3); IR (neat): 3590, 3500, 2237, 1724, 1256, 867, 793 cm⁻¹; ¹H NMR (500 MHz, CDCl3): δ 1.07 (s, 9H, C(CH3)3), 2.41 (t, 1H, J = 2.4 Hz, acetylenic-H), 3.41 (s, 3H, OCH3), 3.77-3.89 (m, 3H, H-5 and OCH2), 4.15-4.31 (m, 4H, H-3, H-4 and OCH2), 4.94 (s, 1H, H-2), 7.35-7.44 (m, 6H, Ar-H), 7.68-7.71 (m, 4H, Ar-H); ¹³C NMR (CDCl3, 75 MHz): δ 135.6 (2C), 132.4 (2C), 129.9 (2C), 127.8 (4C), 109.8, 84.5, 84.0, 77.6, 74.9, 57.6, 55.1, 26.7 (3C), 19.1; HRMS (ESI): m/z calculated for C25H32NaO5Si (M⁺+Na) 463.19112, found 463.19095.

O-(2R,3R,4R,5R)-5-(((tert-Butyldiphenylsilyl)methyl)-tetrahydro-2-methoxy-4-(prop-2-
ynyloxy)furan-3-yl S-methyl carbonodithioate (7): A stirred suspension of NaH (0.08 g, 3.63 mmol) in dry THF (10 mL) under N₂ atmosphere was treated with a solution of 12a (0.80 g, 1.81 mmol) in THF (5 mL) at 0 °C and stirred at room temperature for 10 min. CS₂ (0.21 mL, 2.72 mmol) was added at 0 °C and stirred at room temperature for 10 min. MeI (0.17 mL, 2.72 mmol) was added at 0 °C and stirred at room temperature for 2 h. The reaction mixture was quenched with aq. NH₄Cl solution (5 mL) and extracted with EtOAc (3 x 10 mL). Organic layer was washed with water (10 mL), brine (10 mL) and dried (Na₂SO₄). Solvent was evaporated and purified the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1:9) to afford 7 (0.90 g, 90%) as light yellow liquid; [α]D = -35.6 (c 1.8, CHCl₃); IR (neat): 3453, 2867, 1742, 1489, 1224, 1057, 786 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): 1.10 (s, 9H, C(CH₃)₃), 2.39 (bs, 1H, acetylenic-H), 2.54 (s, 3H, S(CH₃)), 3.41 (s, 3H, OCH₃), 3.90 (t, 2H, J = 4.2 Hz, OCH₂), 4.18 (q, 1H, J = 4.6, 8.9 Hz, H-5), 4.28 (s, 2H, OCH₂), 4.38 (d, 1H, J = 4.6 Hz, H-4), 5.04 (s, 1H, H-2), 5.85 (s, 1H, H-3), 7.35-7.44 (m, 6H, Ar-H), 7.66-7.71 (m, 4H, Ar-H); ¹³C
NMR (CDCl₃, 75 MHz): δ 214.6, 135.6 (2C), 133.3 (2C), 129.7 (2C), 127.6 (4C), 106.4, 89.1, 83.4, 82.2, 75.2, 62.9, 58.1, 54.8, 26.8 (3C), 19.3; HRMS (ESI): m/z calculated for C₂₇H₃₅O₅S₂Si (M+H)⁺ 531.16897, found 531.16895.

(((3aS,4R,6S,6aR)-Hexahydro-4-methoxy-3-methylenefuro[3,4-b]furan-6-yl)methoxy)(tert-butyl)diphenylsilane (5): A solution of 7 (0.80 g, 1.45 mmol) in dry benzene (25 mL) under N₂ atmosphere was treated with n-Bu₂SnH (0.78 mL, 2.91 mmol) at room temperature and heated at reflux for 30 min. After 30 min, catalytic amount of AIBN was added at reflux and stirred for 12 h. The reaction mixture was cooled to room temperature, evaporated under reduced pressure and purified the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.2:8.8) to afford 5 (0.43 g, 69%) as a colorless liquid; [α]D = -45.7 (c 0.1, CHCl₃); IR (neat): 2948, 1756, 1612, 1387, 1234, 1113, 768 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.05 (s, 9H, C(CH₃)₃), 3.40 (s, 4H, H-3a and OCH₂), 3.77 (d, 2H, J = 3.3 Hz, OCH₂), 4.25-4.38 (m, 2H, OCH₂), 4.49-4.54 (m, 1H, H-6), 4.68 (dd, 1H, J = 2.2, 6.7, 9.0 Hz, H-6a), 5.05 (bs, 2H, olefinic), 5.12 (d, 1H, J = 6.0 Hz, H-4), 7.34-7.42 (m, 6H, Ar-H), 7.64-7.70 (m, 4H, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 146.2, 135.5 (4C), 129.67 (2C), 127.6 (4C), 106.7, 105.9, 85.9, 84.1, 73.4, 64.5, 55.6, 54.9, 26.7, 19.2; HRMS (ESI): m/z calculated for C₂₅H₃₂O₄NaSi (M+Na)+ 447.19621, found 447.19692.

(((2S,3S,4R,5S)-3-(4-Methoxybenzylxloxy)-tetrahydro-5-methoxy-4-(prop-2-ynyloxy)furan-2-yl)methoxy)(tert-butyl)diphenylsilane (15) and (((2S,3S,4R,5R)-3-(4-methoxybenzylxloxy)-tetrahydro-5-methoxy-4-(prop-2-ynyloxy)furan-2-yl)methoxy)(tert-butyl)diphenylsilane (15a): To a solution of 13 (1.10 g, 3.54 mmol) in dry MeOH (15 mL) under N₂ atmosphere 2-3 drops of conc. HCl was added at 0 °C and stirred for 6 h. Work up as described for 11 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.8:8.2) afforded anomeric mixture 14 (0.36 g, 66%) as a liquid, which was used as such for the next reaction.

To a stirred solution of 14 (0.56 g, 1.97 mmol) in CH₂Cl₂ (5 mL), imidazole (0.26 g, 3.94 mmol) was added and the reaction mixture was stirred at 0 °C. After 10 min, TBDPSCl (0.51 mL, 1.97 mmol) and DMAP (0.01 g) were added and stirred at room temperature for 2 h. Work
up described for 12 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.2:8.8) afforded anomeric mixture 14a (0.74 g, 72% ) as syrups.

A stirred suspension of NaH (0.08 g, 3.44 mmol) in dry THF (4 mL) under N₂ atmosphere was treated with a solution of anomeric mixture 14a (0.90 g, 1.72 mmol) in THF (4 mL) at 0 °C and stirred for 15 min. Propargyl bromide (0.25 mL, 1.72 mmol) was added to the reaction mixture at 0 °C and stirred for 4 h. Work up as described for 12 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 8.8:1.2) gave the α- and β-anomers. First eluted was α-anomer 15 (0.33 g, 34%) as a syrup; [α]D = -28.1 (c 0.81, CHCl₃); IR (neat): 3323, 3295, 2941, 1753, 1631, 1578, 1234, 1103, 1061, 955, 769 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 1.06 (s, 9H, (CH₃)₃), 2.19 (bs, 1H, H-7), 3.06 (s, 3H, OCH₃), 3.66-3.74 (m, 2H, OCH₂), 3.78 (m, 4H, H-2 and Ar-OCH₃), 3.93 (q, 1H, J = 5.9, 11.4 Hz, H-3), 4.02 (d, 2H, J = 3.9 Hz, OCH₂), 4.12 (t, 2H, J = 6.9 Hz, OCH₂), 4.27 (m, 1H, H-4), 4.53 (d, 1H, J = 4.4 Hz, H-5), 6.81 (d, 2H, J = 8.4 Hz, Ar-H), 7.12 (d, 2H, J = 8.4 Hz, Ar-H), 7.29-7.41 (m, 6H, Ar-H), 7.66-7.72 (m, 4H, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 159.0, 135.9 (2C), 135.8 (2C), 135.5 (2C), 130.3 (2C), 129.7, 129.6, 129.2, 127.6, 127.5, 113.6 (2C), 102.2, 84.3, 81.4, 78.8, 72.4, 66.3, 54.6, 26.9 (3C), 19.2.

Second eluted was β-anomer 15a (0.48 g, 50%) as a syrup; [α]D = -56.4 (c 0.7, CHCl₃); IR (neat): 3423, 3361, 2848, 1741, 1629, 1582, 1187, 1109, 1072, 955, 742 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 1.07 (s, 9H, (CH₃)₃), 2.20 (s, 1H, H-7), 3.14 (s, 3H, OCH₃), 3.76-3.85 (m, 6H, H-2, OCH₂ and Ar-OCH₃), 3.94 (d, 1H, J = 3.4 Hz, H-3), 4.07-4.17 (m, 4H, 2xOCH₂), 4.27 (s, 1H, H-4), 4.74 (s, 1H, H-5), 6.76 (d, 2H, J = 8.4 Hz, Ar-H), 7.03 (d, 2H, J = 8.4 Hz, Ar-H), 7.32-7.42 (m, 6H, Ar-H), 7.62-7.72 (m, 4H, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 159.0, 135.8 (2C), 135.6 (2C), 135.2 (2C), 134.7 (2C), 129.8, 129.6, 129.0, 127.6, 113.6 (2C), 109.6, 85.8, 84.1, 81.6, 77.2, 71.3, 64.6, 55.2, 26.8 (3C), 19.3.

(((2S,3S,4R,5R)-Tetrahydro-5-methoxy-4-(prop-2-ynyloxy)furan-2-yl)methoxy)(tert.-butyl)diphenylsilane-ol (16): To a stirred solution of 15a (0.10 g, 0.18 mmol) in aq. CH₂Cl₂ (1:19, H₂O:CH₂Cl₂, 10 mL) at 0 °C, DDQ (0.08 g, 0.36 mmol) was added and stirred at room temperature for 2 h. The reaction mixture was quenched with aq. NaHCO₃ solution (3 mL) and extracted with CH₂Cl₂ (2 × 10 mL). Organic layer was washed with aq. NaHCO₃ solution (5 mL), water (5 mL) and brine (5 mL). It was dried (Na₂SO₄), evaporated the solvent and purified
the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 4:1) to give 16 (0.06 g, 75%) as a syrup; [α]_D = -32.4 (c 0.94, CHCl₃); IR (neat): 3372, 2856, 1767, 1395, 1031, 792 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.07 (s, 9H, -(CH₃)₃), 2.18 (d, 1H, J = 9.0 Hz, H-7), 3.17 (s, 3H, OCH₃), 3.80-3.90 (m, 3H, H-2 and OCH₂), 4.04-4.14 (m, 4H, OCH₂, H-3 and H-4), 4.70 (s, 1H, H-5), 7.35-7.44 (m, 6H, Ar-H), 7.60-7.72 (m, 4H, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 135.5 (4C), 134.7 (2C), 129.6 (2C), 127.6 (2C), 109.0, 86.6, 82.0, 78.6, 64.6, 54.7, 26.8 (3C), 19.2; ESI-MS: m/z 440.

O-(2S,3S,4R,5R)-Tetrahydro-2-(tert.-butyl-diphenylsilyloxy)methyl)-5-methoxy-4-(prop-2-ynyloxy)furan-3-yl S-methyl carbonodithioate (8): A stirred suspension of NaH (0.08 g, 3.63 mmol) in dry THF (4 mL) under N₂ atmosphere was treated with a solution of 16 (0.80 g, 1.81 mmol) in THF (4 mL) at 0 °C, CS₂ (0.21 mL, 2.72 mmol), MeI (0.17 mL, 2.72 mmol) was added at 0 °C and stirred for 2 h. Work up as described for 7 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 9:1) afforded 8 (0.85 g, 85%) as yellow syrup; [α]_D = -87.5 (c 0.32, CHCl₃); IR (neat): 3465, 2953, 2816, 1737, 1512, 1293, 1165, 761 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.07 (s, 9H, (CH₃)₃), 2.44 (s, 4H, SCH₂ and acetylenic-H), 3.11 (s, 3H, OCH₃), 3.93-4.05 (m, 3H, OCH₂ and H-2), 4.20-4.32 (m, 3H, OCH₂ and H-4), 4.71 (s, 1H, H-5), 6.04 (dd, 1H, J = 1.5, 3.3, 4.7 Hz, H-3), 7.31-7.42 (m, 6H, Ar-H), 7.61-7.72 (m, 4H, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 214.1, 135.6 (4C), 133.3 (2C), 129.6 (2C), 127.7 (2C), 109.0, 87.4, 83.2, 80.8, 77.2, 74.2, 64.5, 54.8, 31.9, 29.7, 26.8, 22.7, 14.1; HRMS (ESI): m/z calculated for C₂₇H₃₅O₅S₂Si(M+H)+ 531.16897, found 531.16889.

5-(tert.-Butyl-diphenylsilyloxy)methyl)-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-6-ol (28): To a stirred solution of diol 27 (2.4 g, 12.63 mmol) in CH₂Cl₂ (20 mL), imidazole (1.71 g, 25.26 mmol) was added and the reaction mixture was stirred at 0 °C. After 10 min, TBDPSCI (3.28 g, 12.63 mmol) and DMAP (0.01 g) were added and stirred for 2 h. Work up as described for 12 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1:2:8:8) afforded 28 (3.8 g, 70%) as syrup; [α]_D = -4.2 (c 0.86, CHCl₃); IR (neat): 3554, 3312, 2878, 1720, 1643, 1231, 1071, 1026, 967, 741 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): 0.85 (s, 9H, C(CH₃)₃), 3.33 (s, 3H, CH₃), 1.46 (s, 3H, CH₃), 3.96 (d, 1H, J = 2.5 Hz, H-5), 4.09-4.14 (m, 2H, OCH₂), 4.36 (s, 1H, H-6), 4.54 (d, 1H, J = 3.5 Hz, H-6a), 6.0 (d,
Chapter II, Section-B, Experimental section

1H, J = 3.5 Hz, H-3a), 7.38-7.44 (m, 6H, Ar-H), 7.66-7.71 (m, 4H, Ar-H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \(\delta\) 135.3 (2C), 135.2 (2C), 132.4 (2C), 129.8 (2C), 127.7 (2C), 111.2, 104.7, 85.2, 78.6, 76.1, 62.3, 26.3 (3C), 26.0 (2C), 18.9; HRMS (ESI): m/z calculated for C\(_{24}\)H\(_{32}\)NaO\(_3\)Si (M\(^{+}\)+Na) 451.1916, found 451.1895.

(3aR,5R,6S,6aR)-Tetrahydro-2,2-dimethyl-6-(prop-2-ynyloxy)furo[2,3-\(d\)][1,3]dioxol-5-yl) methoxy)(tert.-butyl)diphenylsilane (29): A stirred suspension of NaH (0.36 g, 14.95 mmol) in dry THF (20 mL) under N\(_2\) atmosphere was treated with a solution of 28 (3.20 g, 7.47 mmol) in THF (7 mL) at 0 °C and stirred for 15 min. Propargyl bromide (0.83 mL, 7.47 mmol) was added and stirred at room temperature for 4 h. Work up as described for 10 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate:pet. ether, 1.2:8.8) afforded 29 (2.80 g, 80%) as a liquid; \([\alpha]_D = -16.3\) (c 1.88, CHCl\(_3\); IR (neat): 3312, 2897, 1754, 1598, 1232, 1012, 956, 783 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): 1.05 (s, 9H, C(CH\(_3\))\(_3\)), 1.33-1.58 (m, 6H, 2xCH\(_3\)), 2.42 (t, 1H, J = 2.3 Hz, acetylenic-H), 3.69-3.94 (m, 2H, OCH\(_2\)), 4.13 (t, 1H, J = 2.3 Hz, H-5), 4.17-4.36 (m, 3H, OCH\(_2\) and H-6), 4.65 (d, 1H, J = 3.7 Hz, H-6a), 5.87 (d, 1H, J = 3.5 Hz, H-3a), 7.35-7.44 (m, 6H, Ar-H), 7.66-7.71 (m, 4H, Ar-H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \(\delta\) 135.6 (2C), 135.5 (2C), 130.0 (2C), 129.7 (2C), 127.7 (2C), 111.7, 104.9, 84.6, 82.3, 80.9, 75.0, 67.8, 60.3, 57.7, 26.8 (3C), 26.2 (2C), 19.1; HRMS (ESI): m/z calculated for C\(_{27}\)H\(_{34}\)NaO\(_5\)Si (M\(^{+}\)+Na) 489.20677, found 489.20490.

(2R,3R,4R,5S)-5-((tert.-Butyldiphenylsilyl)methyl)-tetrahydro-2-methoxy-4-(prop-2-ynyloxy)furan-3-ol (31): To a solution of 29 (1.0 g, 4.38 mmol) in dry MeOH (15 mL) under N\(_2\) atmosphere 3 drops of conc. HCl was added at 0 °C and stirred for 6 h. Work up as described for 11 and purification of residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.8:8.2) afforded anomic mixture 30 (0.71 g, 80%) as a liquid, which was used as such for the next reaction.

To a stirred solution of 30 (1.50 g, 7.42 mmol) in CH\(_2\)Cl\(_2\) (25 mL), imidazole (1.0 g, 14.8 mmol) was added and stirred at 0 °C. After 10 min, TBDPSCl (1.93 g, 7.42 mmol) and DMAP (0.01 g) were added stirred at room temperature for 2 h. Work up as described for 12 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.2:8.8) afforded \(\beta\)-anomer as major anomer 31 (1.44 g, 44%) as syrup; \([\alpha]_D = -25.1\) (c 1.5,
Chapter II, Section-B, Experimental section

**O-(2R,3R,4R,5S)-5-((tert-Butyldiphenylsilyl)methyl)-tetrahydro-2-methoxy-4-(prop-2-ynyloxy)furan-3-yl S-methyl carbonodithioate (25):** A stirred suspension of NaH (0.08 g, 3.63 mmol) in dry THF (10 mL) under N₂ atmosphere at 0 °C, a solution of 31 (0.80 g, 1.81 mmol) in THF (5 mL) was added and stirred at room temperature for 10 min. CS₂ (0.21 mL, 2.72 mmol) followed by MeI (0.17 mL, 2.72 mmol) were added stirred at room temperature for 2 h. Work up as described for 7 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1:9) afforded 25 (0.70 g, 70%) as light yellow liquid; [α]D = -20.46 (c 0.17, CHCl₃); IR (neat): 3323, 2808, 1744, 1674, 1426, 1354, 1210, 1165, 767 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 1.06 (s, 9H, C(CH₃)₃), 2.41 (t, 1H, J = 2.4 Hz, acetylenic-H), 4.06 (t, 1H, J = 2.4 Hz, H-5), 4.19 (t, 2H, J = 2.4 Hz, OCH₂), 4.31 (m, 1H, H-4), 4.69 (s, 1H, H-2), 5.99 (d, 1H, J = 5.0 Hz, H-3), 7.35-7.44 (m, 6H, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 215.7, 135.8 (2C), 133.3 (2C), 129.9 (2C), 127.7 (4C), 109.2, 99.5, 85.2, 79.5, 74.6, 68.8, 58.5, 55.2, 26.8 (3C), 19.1; HRMS (ESI): m/z calculated for C₂₅H₃₂NaO₅Si (M⁺+Na) 463.19112, found 463.19078.

**(((3aS,4R,6R,6aR)-Hexahydro-4-methoxy-3-methylenefuro[3,4-b]furan-6-yl)methoxy)(tert-butyl)diphenylsilane (23):** A solution of 25 (0.12 g, 0.22 mmol) in dry benzene (25 mL) under N₂ atmosphere was treated with n-Bu₃SnH (0.17 mL, 0.43 mmol) at room temperature and heated at reflux for 30 min. After 30 min, catalytic amount of AIBN was added at reflux and stirred for 12 h. Work up as described for 5 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1:2:8.8) afforded 23 (0.07 g, 71%) as a colorless liquid; [α]D = -32.7 (c 0.31, CHCl₃); IR (neat): 2934, 2889, 1744, 1674, 1426, 1218, 1165, 767 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.05 (s, 9H, C(CH₃)₃), 3.32 (s, 1H, H-6), 127.
6-(4-Methoxybenzoyloxy)-2,2-dimethyl-(3aR,5R,6S,6aR)-perhydrofuro[2,3-d][1,3]dioxol-5-(tert.-butyldiphenylsilyl)-methylether (32): A stirred suspension of NaH (0.42 g, 17.52 mmol) in dry THF (10 mL) under N₂ atmosphere was treated with a solution of 28 (3.0 g, 7.01 mmol) in THF (10 mL) at 0 °C and stirred for 30 min. PMBBr (1.54 mL, 7.71 mmol) was added to the reaction mixture at 0 °C and stirred at room temperature for 4 h. Reaction mixture was quenched with aq. NH₄Cl solution (10 mL) and extracted with EtOAc (2 x 30 mL). Organic layer was washed with water (20 mL), brine (20 mL) and dried (Na₂SO₄). Solvent was evaporated and purified the residue by column chromatography (60-120 Silica gel, ethyl acetate: pet. ether, 0.5:9.5) to afford 32 (3.20 g, 83%) as a colorless syrup; [α]D = -21.25 (c 2.4, CHCl₃); IR (Neat): 3243, 2987, 2828, 1782, 1724, 1631, 1576, 1245, 1187, 1135, 1071, 873, 798, 671, 527 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.05 (s, 9H, (CH₃)₃), 1.25 (s, 3H, CH₃), 1.48 (s, 3H, CH₃), 3.79 (s, 3H, OCH₃), 3.86-3.98 (m, 2H, OCH₂), 4.03 (d, 1H, J = 2.6 Hz, H-6), 4.29 (m, 1H, H-5), 4.48-4.63 (m, 3H, H-6a and OCH₂), 5.88 (d, 1H, J = 3.4 Hz, H-3a), 6.82 and 7.22 (d, 2H each, J = 8.6 Hz, Ar-H), 7.30-7.42 (m, 6H, Ar-H), 7.60-7.70 (m, 4H, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 159.2, 135.5 (4C), 129.1 (2C), 127.6 (4C), 113.7, 111.6, 105.0, 82.5, 81.1, 80.5, 71.9, 60.8, 55.1, 26.8 (3C), 26.3, 19.1; HRMS (ESI): m/z calculated for C₃₂H₄₀NaO₆Si (M⁺+Na) 571.2491, found 571.2512.

(((2R,3S,4R,5R)-3-(4-Methoxybenzoyloxy)-tetrahydro-5-methoxy-4-(prop-2-ynyloxy)furan-2-yl)methoxy)(tert.-butyl) diphenylsilane (34a): To a solution of 32 (1.20 g, 3.87 mmol) in dry MeOH (15 mL) under N₂ atmosphere 3 drops of conc. HCl was added at 0 °C and stirred for 6 h. Work up as described for 11 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.8:8.2) afforded anomeric mixture 33 (0.75 g, 68%) as a liquid, which was used as such for the next reaction.
To a stirred solution of 33 (0.70 g, 2.46 mmol) in CH₂Cl₂ (5 mL), imidazole (0.33 g, 4.93 mmol) was added and stirred at 0 °C. After 10 min, TBDPSCl (0.64 mL, 2.46 mmol) and DMAP (0.01 g) were added and stirred at room temperature for 2 h. Work up as described for 12 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.2:8.8) afforded anomic mixture 33a (0.98 g, 76%) as syrup.

A stirred suspension of NaH (0.08 g, 3.45 mmol) in dry THF (3 mL) under N₂ atmosphere was treated with a solution of 33a (0.90 g, 1.72 mmol) in THF (5 mL) at 0 °C and stirred for 15 min. Propargyl bromide (0.25 mL, 1.72 mmol) was added to the reaction mixture at 0 °C and stirred at room temperature for 4 h. Worked up as described for 10 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 1.2:8.8) afforded β-anomer as major anomer 34a (0.51 g, 53%) as a syrup; [α]₀ = -24.25 (c 2.7, CHCl₃); IR (neat): 3345, 3279, 2965, 1764, 1645, 1597, 1224, 1106, 1051, 986, 742 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 1.06 (s, 9H, (CH₃)₃), 2.27 (bs, 1H, H-7), 3.16 (s, 3H, OCH₃), 3.74 (s, 3H, Ar-OCH₃), 3.78 (bs, 1H, H-2), 3.82-3.93 (m, 4H, 2xOCH₂), 4.07 (d, 1H, J = 11.4 Hz, H-3), 4.23 (s, 2H, Ar-OCH₂), 4.44 (q, 1H, J = 5.9, 10.9 Hz, H-4), 4.81 (s, 1H, H-5), 6.70 (d, 2H, J = 7.9 Hz, Ar-H), 6.90 (d, 2H, J = 7.9 Hz, Ar-H), 7.27-7.44 (m, 6H, Ar-H), 7.64-7.71 (m, 4H, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 158.8, 135.8 (2C), 135.5 (2C), 135.2 (2C), 134.7 (2C), 129.9, 129.5, 129.4, 128.9, 127.6, 113.5, 110.3, 82.6, 82.5, 80.0, 77.2, 71.2, 63.0, 55.1, 26.9, 19.1.

(2R,3S,4R,5R)-Tetrahydro-2-(tert.-butyl-diphenylsilyloxy)methyl-5-methoxy-4-(prop-2-ynyloxy)furan-3-ol (35): A solution of 34a (0.20 g, 0.35 mmol) in aq. CH₂Cl₂ (1:19, H₂O:CH₂Cl₂, 10 mL) was treated with DDQ (0.16 g, 0.71 mmol) and stirred at 0 °C for 2 h. Work up as described for 16 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate: pet. ether, 4:1) gave 35 (0.12 g, 76%) as a syrup; [α]₀ = -46.96 (c 0.66, CHCl₃); IR (neat): 3387, 2984, 2812, 1765, 1321, 771 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.06 (s, 9H, (CH₃)₃), 2.23 (bs, 1H, H-7), 3.19 (s, 3H, OCH₃), 3.86-3.91 (m, 2H, H-2 and H-3), 4.00-4.07 (m, 2H, OCH₂), 4.17 (s, 2H, OCH₂), 4.48 (q, 1H, J = 5.2, 9.4 Hz, H-4), 4.70 (s, 1H, H-5), 7.35-7.44 (m, 6H, Ar-H), 7.62-7.73 (m, 4H, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 135.6 (4C), 134.7 (2C), 129.6 (2C), 127.6 (2C), 109.1, 83.0, 81.1, 76.8, 63.2, 55.3, 26.5 (3C), 19.1; HRMS (ESI): m/z calculated for C₂₅H₃₃NaO₅Si (M⁺+Na) 463.19112, found 463.19086.
O-(2R,3S,4R,5R)-Tetrahydro-2-(tert.-butyl-diphenylsilyloxymethyl)-5-methoxy-4-(prop-2-ynyloxy)furan-3-yl S-methyl carbonodithioate (26): A stirred suspension of NaH (0.08 g, 3.63 mmol) in dry THF (4 mL) under N₂ atmosphere was treated with a solution of 35 (0.80 g, 1.81 mmol) in THF (4 mL) at 0 °C and stirred at room temperature for 10 min, CS₂ (0.21 mL, 2.72 mmol) followed by MeI (0.17 mL, 2.72 mmol) were added at 0 °C and stirred at room temperature for 2 h. Work up as described for 7 and purification of the residue by column chromatography (60-120 Silica gel; ethyl acetate; pet. ether, 9:1) afforded 26 (0.81 g, 81%) as yellow syrup; [α]₀ = -36.71 (c 0.64, CHCl₃); IR (neat): 3387, 2892, 2851, 1743, 1478, 1234, 1056, 779 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 1.01 (s, 9H, (CH₃)₃), 2.33 (s, 3H, SCH₃), 2.44 (bs, 1H, H-7), 3.03 (s, 3H, OCH₃), 3.78 (m, 3H, OCH₂ and H-2), 4.15-4.23 (m, 1H, H-4), 4.33-4.44 (m, 2H, OCH₂), 4.64 (s, 1H, H-5), 6.06 (dd, 1H, J = 1.5, 4.5, 6.4 Hz, H-3), 7.31-7.43 (m, 6H, Ar-H), 7.61-7.77 (m, 4H, Ar-H); ¹³C NMR (CDCl₃, 75 MHz): δ 214.3, 135.8 (4C), 134.7 (2C), 129.8 (2C), 127.6 (2C), 109.2, 84.8, 80.8, 79.8, 77.2, 73.4, 62.2, 55.1, 31.9, 29.7, 26.8, 22.8, 19.1; HRMS (ESI): m/z calculated for C₂₇H₃₅O₅S₂Si (M⁺+H) 531.16897, found 531.16965.
References:

SPECTRA
Spectrum 1: $^1$H NMR Spectrum of compound 12a in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 12a in CDCl$_3$ (75 MHz)
Spectrum 2: $^1$H NMR Spectrum of compound 7 in CDCl$_3$ (500 MHz)
$^{13}$C NMR Spectrum of compound 7 in CDCl$_3$ (75 MHz)
Spectrum 3: $^1$H NMR Spectrum of compound 5 in CDCl$_3$ (300 MHz)
$^{13}$C NMR Spectrum of compound 5 in CDCl$_3$ (75 MHz)
Spectrum 4: $^1$H NMR Spectrum of compound 15 in CDCl$_3$ (500 MHz)
$^{13}$C NMR Spectrum of compound 15 in CDCl$_3$ (75 MHz)
Spectrum 5: $^1$H NMR Spectrum of compound 15a in CDCl$_3$ (500 MHz)

$^{13}$C NMR Spectrum of compound 15a in CDCl$_3$ (75 MHz)
Spectrum 6: $^1$H NMR Spectrum of compound 8 in CDCl$_3$ (300 MHz)
$^{13}$C NMR Spectrum of compound 8 in CDCl$_3$ (75 MHz)
TBDPSO

Spectrum 7: $^1$H NMR Spectrum of compound 29 in CDCl$_3$ (300 MHz)
$^{13}$C NMR Spectrum of compound 29 in CDCl$_3$ (75 MHz)
Spectrum 8: $^1$H NMR Spectrum of compound 31 in CDCl$_3$ (300 MHz)
$^{13}$C NMR Spectrum of compound 31 in CDCl$_3$ (75 MHz)
Spectrum 9: $^1$H NMR Spectrum of compound 25 in CDCl$_3$ (500 MHz)
$^{13}$C NMR Spectrum of compound 25 in CDCl$_3$ (75 MHz)
Spectrum 10: $^1$H NMR Spectrum of compound 23 in CDCl$_3$ (300 MHz)
$^{13}$C NMR Spectrum of compound 23 in CDCl$_3$ (150 MHz)
Spectrum 11: $^1$H NMR Spectrum of compound 34a in CDCl$_3$ (5300 MHz)
$^{13}$C NMR Spectrum of compound 34a in CDCl$_3$ (75 MHz)
Spectrum 12: $^1$H NMR Spectrum of compound 26 in CDCl$_3$ (300 MHz)

$^{13}$C NMR Spectrum of compound 26 in CDCl$_3$ (75 MHz)