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Reactivity Switch in Glycal Dienes toward Different Nucleophiles: Mechanistic Insight and Applications toward the Synthesis of Naphthalene-Fused Pyran Derivatives

Ram Pratap Pandey, Bindu Tiwari, Navneet Sharma, Kousik Giri, and Nazar Hussain*

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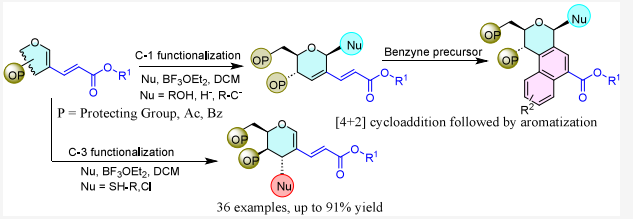
ABSTRACT: The stereo- and regioselective formation of chiral molecules is an interesting and important topic in organic synthesis due to its wide applicability and intricacy during synthesis. Herein, we disclose a method for the selective functionalization of glycal dienes for synthesizing different glycosides and branched sugars stereo- and regioselectively. The methodology is broad regarding the substrate scope in which various nucleophiles and glycals were explored. Furthermore, we delve into converting the synthesized products into naphthalene-fused pyran derivatives, achieved through a 4 + 2 cycloaddition followed by aromatization. Additionally, we conducted density functional theory studies to gain insight into the formation of regioselective products when different nucleophiles were employed.



INTRODUCTION

Glycals, the enol-ethers of sugars, are crucial in constructing intricate organic molecules and serve as valuable chiral pool starting materials.[1−5] A common Ferrier rearrangement is often employed to explore the synthetic potential of these sugars, leading to the stereoselective formation of various glycosides.[6−8] Recent advancements have introduced strategies to functionalize the C2 position of glycals, enabling the synthesis of branched sugars through either metal-catalyzed C−H functionalization or cross-coupling reactions.[9−15] The distinctive reactivity of glycals arises from an enol-ether that imparts altered reactivity to both carbons. The selection of an external reactant becomes crucial, determining whether the attack occurs at the C1 or C2 position. Achieving selectivity at a specific position poses a significant challenge in these reactions, which is attributed to the anomeric effect and the presence of various protecting groups. Despite considerable efforts to control selectivity at the anomeric carbon, further research is needed to enhance our understanding and control both regio- and stereoselectivity for synthesizing diverse glycosides and branched sugars.

Glycal-derived dienes can be readily synthesized through C−H activation or cross-coupling reactions,[12,16,17] serving as versatile synthons for assembling diverse annulated sugars and chiral aromatic building blocks. In our ongoing investigation into the reactivity of glycals and their derivatives, we hypothesized that glycal dienes exhibit a conjugated system and could be effective substrates for the regio- and stereoselective incorporation of external nucleophiles.[18,19] The presence of an electron-withdrawing group at the C2 position enhances the reactivity of the C3 position after the formation of oxocarbonium in the presence of a Lewis acid, making it as susceptible to nucleophilic attack as the C1 position. Various documented methods have achieved site-selective functionalization using activators and organometallic catalysis. Galan and co-workers employed a thiourea/cinchona-based bifunctional catalyst for the stereoselective α-glycosylation of 2-nitrogalactal (Scheme 1A).[20] Although effective across a broad substrate scope, this approach required bulky catalysts and exhibited α-selectivity exclusively. More recently, Yao et al. accomplished the site-selective functionalization of 3,4-*O*-carbonate glycals using organometallic catalysts such as Pd and Co to control the regioselectivity (Scheme 1B).[21] However, this method is limited to 3,4-*O*-carbonate-protected glycals and requires organometallic catalysts with thiols as aglycon sources. In our recent work, we explored site-selective functionalization by employing a Lewis acid in the presence of azide as an external nucleophile (Scheme 1C).[18] This strategy specifically focused on C3 functionalization with azides, expanding the repertoire of regioselective transformations for glycals and offering an alternative pathway in the realm of glycal chemistry. Driven by our enduring fascination with probing the reactivity of glycals and fuelled by the insights gained from our latest research, we aimed to investigate the potential of glycal-derived dienes for precise and selective functionalization with a range of

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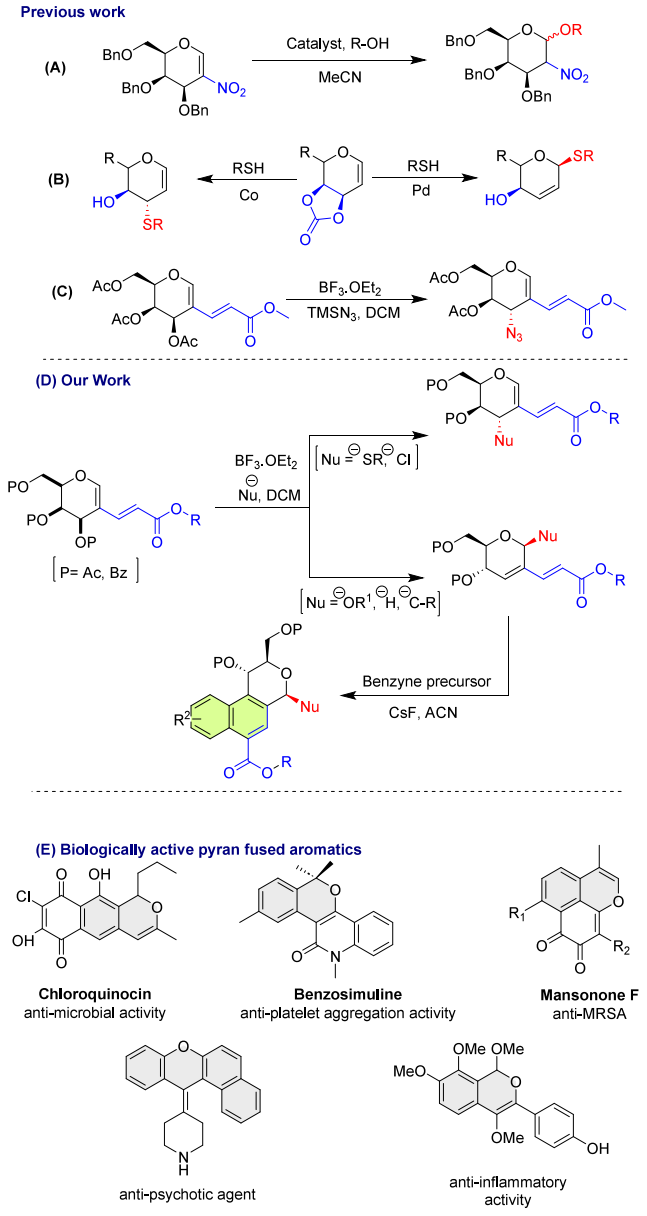
Scheme 1. Previous Work and Our Approach

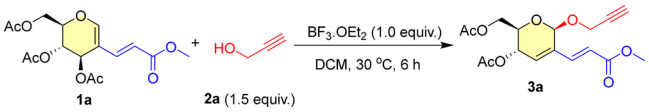


nucleophiles, including those based on thiols, alcohols, C, and Cl. The choice of dienes as substrates was motivated by their versatility in subsequent cycloaddition and aromatization reactions. During our exploration, we noted the selective attack of thiols and Cl-nucleophiles at the C3 position. At the same time, C- and O-nucleophiles exhibited a distinct preference for the C-1 position, demonstrating complete β-selectivity. The preference of nucleophiles at C1/C3 can be explained using the hard and soft acids and bases (HSAB) principle. When an oxacarbonium ion forms after the reaction of glycal dienes in the presence of a Lewis acid, the anomeric position (C1) becomes hard due to the ring oxygen, favoring hard nucleophiles such as those based on oxygen and carbon. Conversely, the C3 position becomes softer and prefers soft nucleophiles. Moreover, these derivatives emerged as promising substrates for 4 + 2 cycloaddition, leading to the synthesis of pyran-fused naphthalene derivatives. Pyran-fused aromatic compounds are a privileged class of organic compounds and possess a wide range of biological activities, such as antimicrobial activity, antiviral activity, antitumor activity, etc. (Scheme 1E).[22−24] Naphthalene derivatives showed potency against various biological targets and have intriguing electrochemical and optical properties, making them valuable in materials chemistry.[25−27] Considering these important features, we planned to cyclize the synthesized products via Diels−Alder cycloaddition followed by aromatization to achieve pyran-fused naphthalene derivatives.

RESULTS AND DISCUSSION

We commenced our investigation by subjecting tri-*O*-acetyl-D-glucal diene **1a** and propargyl alcohol **2a**, chosen as model substrates, to $BF_3{\cdot}OEt_2$ (1.0 equiv) in DCM as the solvent for 6 h at 30 °C. To our satisfaction, *O*-glycoside **3a** was successfully synthesized, yielding an impressive 91% yield (Table 1). The structure and stereochemistry were subsequently confirmed through 2D NMR analysis (additional details can be found in the Supporting Information). Altering the standard reaction conditions—replacing $BF_3{\cdot}OEt_2$ with TMSOTf—resulted in the formation of the desired product, although with a diminished yield (refer to Table 1, entry 2). Conversely, the use of $Sc(OTf)_3$ proved entirely ineffective, leading to the recovery of the starting material without any discernible transformation (Table 1, entry 3). Employing a basic reaction medium with TEA did not initiate the reaction, and the starting material was recovered. Exploring temperature variations, a deviation from 30 to 60 °C did not yield improved results; instead, a lower yield was observed (entry 5). Further investigation into solvent variability revealed that DCE provided the desired product in a commendable yield of 78%, while in water only a meager 28% yield of the isolated yield was achieved (Table 1, entries 6 and 7, respectively).

Table 1. Optimization of Reaction Conditions[a]



entry	deviation from the standard conditions[a]	yield[b] [%]
01	none	91
02	TMSOTf instead of $BF_3{\cdot}OEt_2$	72
03	$Sc(OTf)_3$ instead of $BF_3{\cdot}OEt_2$	n.r.
04	NEt_3 instead of $BF_3{\cdot}OEt_2$	n.r.
05	60 °C instead of 30 °C	47
06	DCE instead of DCM	78
07	H_2O instead of DCM	28

[a]Reactions were performed using **1a** (1 equiv), **2a** (1.5 equiv), and $BF_3{\cdot}OEt_2$ (1.0 equiv) in 2 mL of DCM at 30 °C for 6 h. [b]Yield was calculated after column chromatography. n.r. = no reaction.

Armed with the finely tuned reaction conditions, we turned our attention to exploring the compatibility of various nucleophiles as part of a site-selective functionalization strategy aimed at generating a diverse compound library (Scheme 2). By employing glycal dienes **1a** and **1b** with propargyl alcohol under the optimized reaction conditions, we successfully obtained products **3a** and **3b** in exceptional yields (Scheme 2). Expanding our investigation, we subjected other primary alcohols, including benzyl alcohol and *n*-butyl alcohol, to the glycal diene, resulting in the respective products **3c** and **3d** with outstanding yields and complete regioselectivity. Aromatic alcohols, such as 3,5-dimethyl phenol and simple

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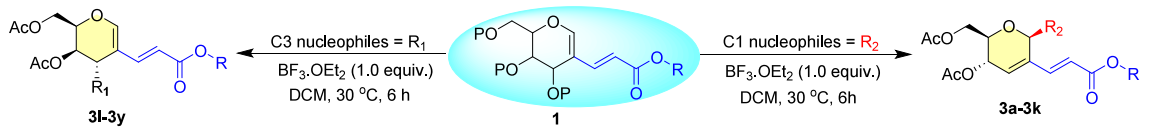
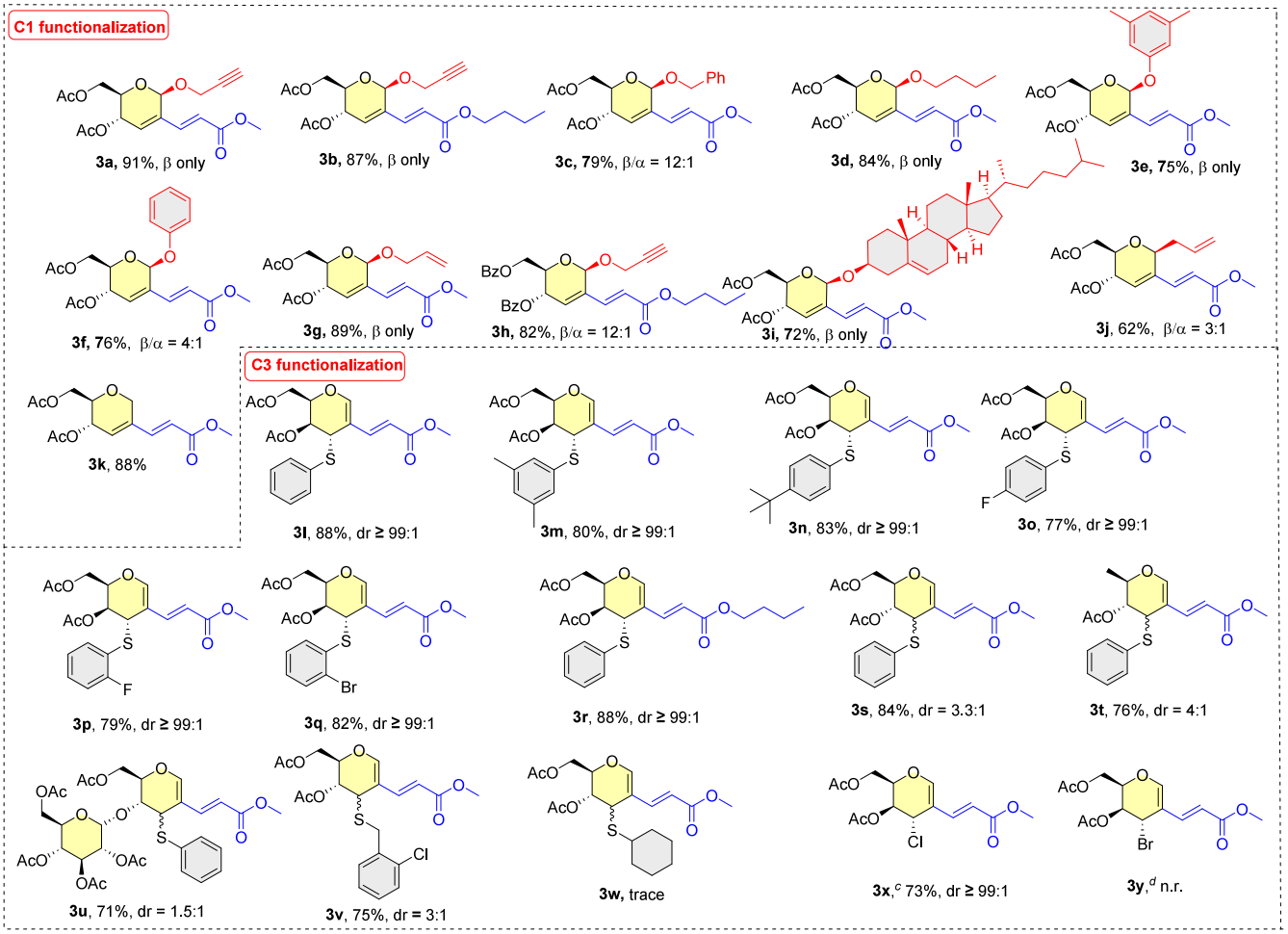
Scheme 2. Substrate Scope: Variation in Glycal Dienes and Nucleophiles[a,b,c,d]





[a]Reaction conditions: **1** (1 equiv), nucleophiles (1.5 equiv), and $BF_3{\cdot}OEt_2$ (1.0 equiv) in DCM for 6 h at 30 °C. [b]Yields are of the purified products after column chromatography. [c]TMSCl was used as the nucleophile. [d]TMSBr was used as the nucleophile, n.r. = no reaction.

phenol, reacted with the diene under standard conditions, yielding the desired products **3e**−**3f** in good yields. Allylic alcohol exhibited remarkable efficiency in the glycosylation reaction, yielding the respective product **3g** with an outstanding 89% yield. Our exploration extended to examining the compatibility of various protecting groups, revealing that benzoyl-protected glycal diene successfully underwent the reaction with propargyl alcohol to yield product **3h** with an 82% yield. Under standard reaction conditions, the *β*-selective cholesterol glycoside **3i** was also formed in 72% yield. Shifting our focus, we investigated the compatibility of alternative nucleophiles, such as allyl trimethylsilane and triethyl silane. As anticipated, both nucleophiles selectively attacked at the C1 position, yielding the desired glycosides **3j** and **3k** in good to excellent yields. Subsequently, we explored the substrate scope for the C3 functionalization of glycal dienes with thiophenols, as outlined in Scheme 2. Initiating the examination with simple thiophenol resulted in the formation of product **3l**, which exhibited an inversion in configuration at the C3 position. Similarly, 3,5-dimethyl thiophenol smoothly attacked at the C3 position, producing the respective product **3m** in an 80% yield. *p-tert*-Butyl thiophenol emerged as a suitable substrate under the standard conditions, delivering product **3n** with an 83% yield. Thiophenols with halogen substituents, such as 2-fluoro, 4-fluoro, and 2-bromo thiophenols, proved to be compatible substrates, leading to the successful synthesis of desired products **3o**−**3q**, respectively, in good yields. The synthesis of galactal diene, achieved through the coupling of tri-*O*-acetyl-D-galactal and butyl acrylate, was investigated with simple thiophenol, resulting in the formation of product **3r** with a yield comparable to that obtained with diene derived from methyl acrylate. Expanding the versatility of the substrate scope, we probed the reactivity of other glycal dienes derived from D-glucal, L-rhamnal, and D-maltal. In each case, the expected C3-selective functionalized products **3s**−**3u** were obtained in good yields, albeit with poor stereoselectivity at the C3 position. The observed constraints in selectivity were attributed to the stereochemistry of the C4 group, which was

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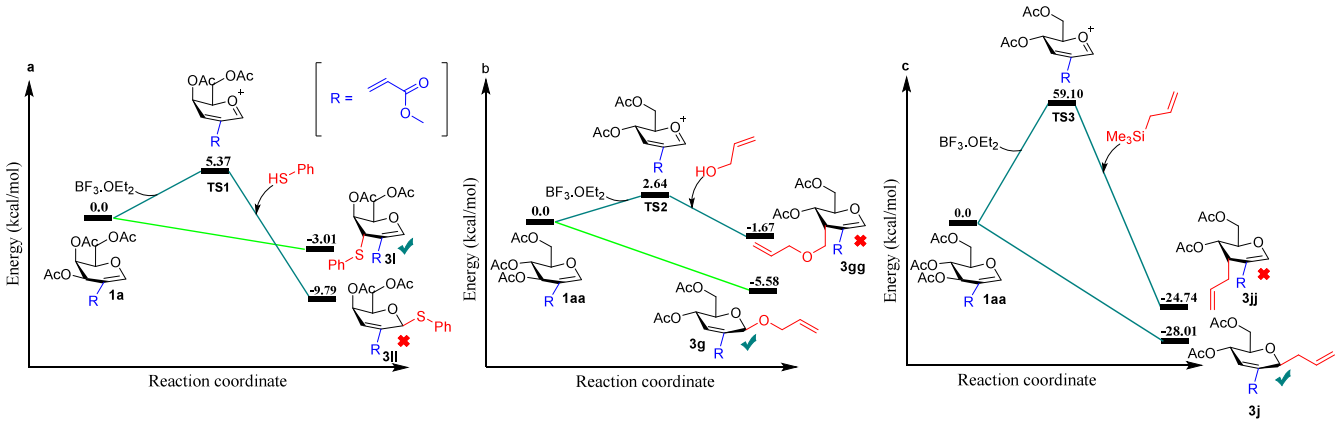
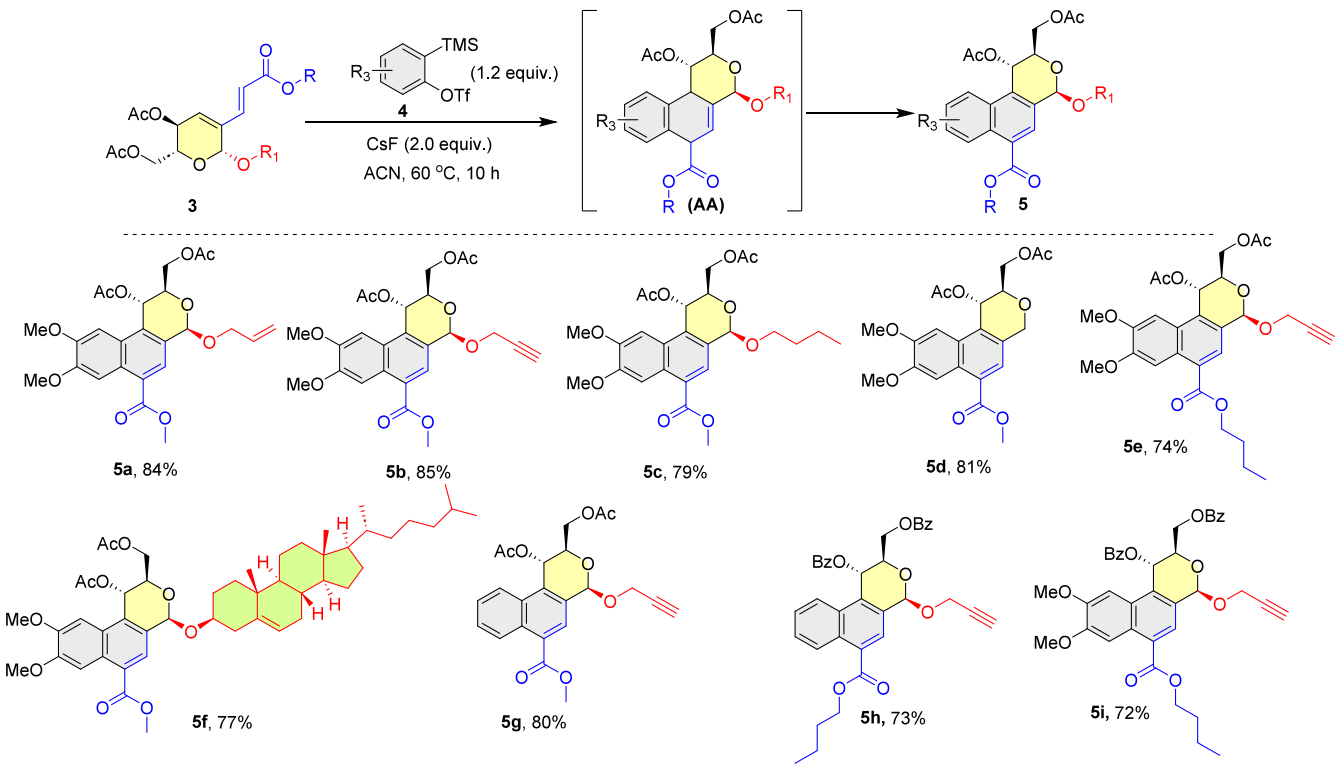
Scheme 3. Free Energy Profiles for the Formation of Different Products in the Presence of Different Nucleophiles



Scheme 4. Applications Towards the Synthesis of Naphthalene-Fused Pyran Derivatives[a,b]



[a]Reaction conditions: **3** (1 equiv), **4** (1.2 equiv), and CsF (2 equiv) in ACN at 60 °C for 10 h [b]Yields are of the purified products after column chromatography

positioned below the plane in all cases. Intriguingly, D-galactal-derived dienes demonstrated complete stereocontrol. When glucal-derived diene was reacted with 2-chlorobenzyl thiol, the C3-selective product **3v** was obtained in a good yield with a diastereomeric ratio (dr) of 3:1. In contrast, the reaction with cyclohexyl thiol did not produce the desired product **3w**, yielding only trace amounts observable by TLC. Notably, when the reaction of galactal diene was conducted in the presence of TMS-Cl, the selective attack of Cl occurred at the C3 position, yielding product **3x** with a 73% yield. A similar attempt was made with TMSBr to obtain the C3-selective bromo sugar **3y**, but it proved ineffective, resulting in the recovery of only the starting material.

The density functional theory (DFT) approach included in ORCA 5.0.3 has been used for all of the computations.[28,29] The PBE0 functional[30] was employed, together with dispersion corrections derived from tight binding partial charges (D4), and the polarized double-ζ basis set (def2-svp) by Ahlrichs and colleagues was used.[31,32] Transition states were calculated using V. Asgeirsson and colleagues' nudged-elastic-band method. For improved outcomes, the same function was used in a higher-valence polarized triple-ζ basis set (def2-tzvp) for single-point energy calculations of optimized geometries and transition states. Additionally, the confirmatory analysis of vibrational frequencies verified the reactants, products, and transition states. For solvent effects, the implicit solvent model SMD was utilized.[33]

In Scheme 3a, upon reacting with thiophenol in the presence of $BF_3.OEt_2$, glycal diene **1a** converted into the desired C3-substituted product **3l** without any barrier, and the other

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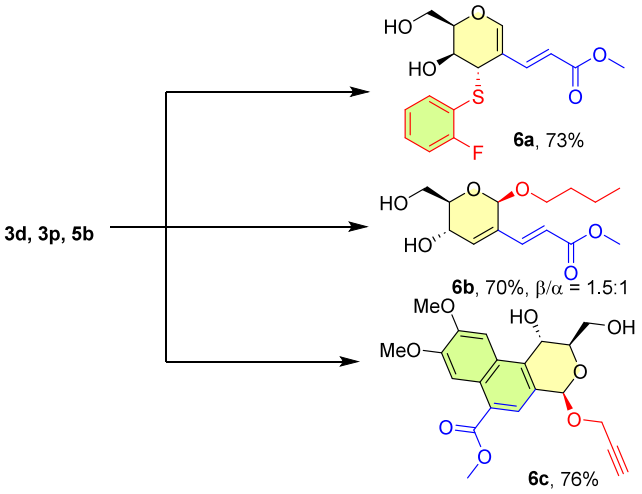
product **3ll** could be possible via transition state **TS1** (5.37 kcal/mol). Although the product energy of **3ll** (−9.79 kcal/mol) is lower than that of **3l** (−3.01 kcal/mol), product **3l** is favorable due to the barrier-less transformation. In Scheme 3b, upon reacting with allyl alcohol, glycal diene **1aa** leads to products **3g** and **3gg**. In the computational studies, it is found that product **3g** is a much more favorable product having a free energy of −5.58 kcal/mol, as it comes from a barrierless path, and there is a transition state (**TS2**, 2.64 kcal/mol) found in the pathway for product **3gg**, which also has a higher product energy (−1.67 kcal/mol). In Scheme 3c, upon reacting with allysilane in the presence of $BF_3{\cdot}OEt_2$, glycal diene **1aa** generates product **3jj** via high-energy transition state **TS3** (59.1 kcal/mol), while no transition state is found in the path of product **3j**. It is concluded from the DFT calculations that products, i.e., **3l**, **3g**, and **3j**, were formed due to the barrierless transformations. Additionally, the free energies of products **3g** and **3j** are lower compared to those of **3gg** and **3jj**, respectively.

The synthetic utility of the synthesized glycosides was then explored, as depicted in Scheme 4. The different *O*-glycosides synthesized in Scheme 2 contain a diene subunit and can easily undergo the cycloaddition reaction with an aryne precursor such as 2-(trimethylsilyl)phenyl trifluoromethanesulfonate. Toward this direction, when substrate **3g** was subjected to 4,5-dimethoxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate in the presence of CsF and acetonitrile as the solvent at 60 °C for 10 h, the product **5a** was observed with 84% isolated yield. In this transformation, the Diels−Alder adduct **AA** formed initially through the cycloaddition of diene with aryne, which further undergoes oxidative aromatization to yield the more stable naphthalene derivatives. To enhance the scope, other glycosides such as *O*-propargyl **3b** and *O*-butyl **3d** smoothly underwent the cycloaddition followed by aromatization and delivered the products **5b** and **5c**, respectively, in excellent yields. To determine if the functional group of anomeric carbon has any role, substrate **2k** was chosen and under a similar set of reaction conditions afforded the product **5d** without any shift in yield. The cholesterol glycosides **3i** similarly produced the naphthalene derivatives in good to excellent yield. The butyl group on the diene subunit rather than methyl has some effect on the transformation, and the respective product **5f** was obtained in a slightly lower yield. Simple 2-(trimethylsilyl) phenyl trifluoromethanesulfonate without any functional group on the aromatic group was also found to be compatible and led to the formation of products **5g** and **5h** in good yields. The benzoyl-protected glycosides also survived under the transformation and delivered the naphthalene-fused pyran derivatives **5i** and **5j.** Finally, the Zemplen deacetylation of the synthesized products was carried out to obtain unprotected products **6a−6c**, as shown in Scheme 5.

CONCLUSIONS

In conclusion, we have developed a general strategy for the site-selective functionalization of glycal dienes for the construction of different glycosides and branched sugar derivatives under a Lewis acid-mediated transformation. The results of DFT calculations indicate that the selective functionalization at C1/C3 occurs through a barrierless transformation, making it particularly favorable compared to pathways of other possible products relying on high-energy transition states. The method exhibits broad applicability,

Scheme 5. Deacetylation of Products[a]



[a]Reaction conditions: **3d, 3p, 5b** (1 equiv), NaOMe (50 mol %), and MeOH (3 mL) at 30 °C for 6h.

successfully accommodating a range of nucleophiles, including those based on thiols, alcohols, allyl silanes, and Cl, yielding their corresponding products smoothly. Furthermore, we explored the synthetic potential of this methodology in the production of chiral pyran-fused naphthalene derivatives via Diels−Alder cycloaddition with arynes, followed by concomitant aromatization.

EXPERIMENTAL SECTION

General Information. Unless otherwise specified, all reactions were carried out in dry solvents under anhydrous conditions in oven-dried round-bottom flasks, and the heating reactions were performed in an oil bath. All commercially available reagents were purchased from commercial sources and were used without further purification. All reactions were monitored using thin-layer chromatography over silica gel-coated TLC plates. The products were purified by column chromatography on silica gel (100−200 mesh) using hexane/ethyl acetate as the eluent to obtain the pure products. ^{1}H and ^{13}C NMR spectra were recorded using 400−600 MHz spectrometers with TMS as the internal standard. Chemical shifts are expressed in parts per million (δ ppm). The exact masses of all products were derived using a SCIEX X500R QTOF mass spectrometer. Coupling constants are given in hertz. Structural assignments were made with additional information from COSY, HMBC, HSQC, and NOESY experiments. Commercially available grades of organic solvents of adequate purity are used in all reactions.

General Procedure 1 for the Products (3a−3x). In an oven-dried round-bottom flask, substituted glycal **1a** (0.14 mmol, 1 equiv) was dissolved in 2 mL of DCM at rt, and the respective nucleophiles (0.21 mmol, 1.5 equiv) were added. To the mixture was slowly added $BF_3{\cdot}OEt_2$ (0.14 mmol, 1 equiv) at room temperature. Finally, the reaction mixture was stirred at the same temperature for 6 h. After the starting material was converted as confirmed through TLC, the mixture was quenched with a saturated sodium bicarbonate solution (10 mL), and the organic layer was extracted with DCM (10 × 2 mL). The organic layer was dried over sodium sulfate, and the residue left was purified by column chromatography over silica gel (100−200 mesh) using hexane/ethyl acetate as the eluent.

*Methyl (E)-3-((2R,5S,6R)-5-Acetoxy-6-(acetoxymethyl)-2-(prop-2-yn-1-yloxy)-5,6-dihydro-2H-pyran-3-yl)acrylate (**3a**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a pale-yellow sticky solid (45.0 mg, 91% yield). R_f (hexane/EtOAc = 60:40): 0.42. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.08 (d, J = 16.2 Hz, 1H), 6.09 (dd, J = 8.9, 7.2 Hz, 2H), 5.42−5.38 (m, 2H), 4.36 (dd, J = 15.9, 2.2 Hz, 1H), 4.29 (dd, J

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= 15.9, 2.3 Hz, 1H), 4.16 (dd, J = 5.5, 4.1 Hz, 2H), 4.09−4.06 (m, 1H), 3.68 (s, 3H), 2.53 (t, J = 2.3 Hz, 1H), 2.03 (s, 6H). **$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$)** δ 170.6, 170.0, 166.9, 140.5, 135.3, 134.5, 120.4, 92.1, 78.5, 75.8, 67.1, 65.4, 62.5, 54.6, 51.7, 20.8, 20.7. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{17}H_{20}O_8Na$ 375.1056, found 375.1042.

*Butyl (E)-3-((2R,5S,6R)-5-Acetoxy-6-(acetoxymethyl)-2-(prop-2-yn-1-yloxy)-5,6-dihydro-2H-pyran-3-yl)acrylate (**3b**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a light-yellow gummy solid (43.1 mg, 87% yield). R_f (hexane/EtOAc = 70:30): 0.49. **^1H NMR (600 MHz, $CDCl_3$)** δ 7.07 (d, J = 16.1 Hz, 1H), 6.07 (d, J = 16.1 Hz, 2H), 5.42−5.37 (m, 2H), 4.36 (dd, J = 15.9, 2.3 Hz, 1H), 4.29 (dd, J = 15.9, 2.4 Hz, 1H), 4.19−4.15 (m, 2H), 4.10−4.07 (m, 3H), 2.51 (t, J = 2.3 Hz, 1H), 2.03 (d, J = 2.0 Hz, 6H), 1.60−1.55 (m, 2H), 1.33 (dd, J = 15.0, 7.5 Hz, 2H), 0.87 (t, J = 7.4 Hz, 3H). **$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$)** δ 170.6, 170.0, 166.5, 140.2, 135.3, 134.2, 120.9, 92.2, 78.5, 75.8, 67.1, 65.4, 64.4, 62.6, 54.7, 30.7, 20.8, 20.7, 19.1, 13.7. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{20}H_{26}O_8Na$ 417.1525, found 417.1542.

*Methyl (E)-3-((2R,5S,6R)-5-Acetoxy-6-(acetoxymethyl)-2-(benzyloxy)-5,6-dihydro-2H-pyran-3-yl)acrylate (**3c**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a white liquid (44.8 mg, 79% yield). R_f (hexane/EtOAc = 70:30): 0.43. **^1H NMR (600 MHz, $CDCl_3$)** δ 7.32−7.27 (m, 5H), 7.06 (d, J = 16.1 Hz, 1H), 6.06 (s, 1H), 5.76 (d, J = 16.1 Hz, 1H), 5.38 (d, J = 8.7 Hz, 1H), 5.19 (s, 1H), 4.78 (d, J = 11.5 Hz, 1H), 4.62 (d, J = 11.5 Hz, 1H), 4.20−4.14 (m, 2H), 4.07 (d, J = 10.1 Hz, 1H), 3.67 (s, 3H), 2.03 (s, 6H). **$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$)** δ 170.7, 170.2, 166.9, 140.9, 140.9, 136.8, 135.9, 134.1, 134.1, 128.6, 128.5, 128.3, 120.0, 93.5, 70.4, 67.0, 65.6, 62.7, 51.8, 20.9, 20.8. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{21}H_{24}O_8Na$ 427.1369, found 427.1365.

*Methyl (E)-3-((2R,5S,6R)-5-Acetoxy-6-(acetoxymethyl)-2-butoxy-5,6-dihydro-2H-pyran-3-yl)acrylate (**3d**).* The compound was synthesized according to the general procedure and purified by column chromatography to give a pale yellow sticky solid (43.7 mg, 84% yield). R_f (hexane/EtOAc = 60:40): 0.46. **^1H NMR (600 MHz, $CDCl_3$)** δ 7.09 (d, J = 16.1 Hz, 1H), 6.05 (d, J = 2.0 Hz, 1H), 5.86 (d, J = 16.1 Hz, 1H), 5.37 (d, J = 9.6 Hz, 1H), 5.10 (s, 1H), 4.20−4.09 (m, 3H), 3.79 (dt, J = 9.4, 6.6 Hz, 1H), 3.69 (s, 3H), 3.53 (dt, J = 9.4, 6.5 Hz, 1H), 2.03 (d, J = 1.5 Hz, 6H), 1.58−1.55 (m, 2H), 1.37−1.31 (m, 2H), 0.88 (t, J = 7.4 Hz, 3H). **$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$)** δ 170.7, 170.2, 166.9, 141.1, 136.1, 133.9, 119.9, 94.6, 68.8, 66.8, 65.6, 62.8, 51.8, 31.7, 20.9, 20.8, 19.5, 13.8. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{18}H_{26}O_8Na$ 393.1525, found 393.1523.

*Methyl (E)-3-((2S,5S,6R)-5-Acetoxy-6-(acetoxymethyl)-2-(3,5-dimethylphenoxy)-5,6-dihydro-2H-pyran-3-yl)acrylate (**3e**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a pale-yellow sticky solid (44.0 mg, 75% yield). R_f (hexane/EtOAc = 70:30): 0.50. **^1H NMR (600 MHz, $CDCl_3$)** δ 7.16 (d, J = 8.8 Hz, 1H), 7.07−6.67 (m, 3H), 6.24 (s, 1H), 5.86−5.79 (m, 2H), 5.51 (d, J = 9.0 Hz, 1H), 4.31−4.24 (m, 2H), 4.14 (d, J = 10.3 Hz, 1H), 3.72 (s, 3H), 2.27 (s, 3H), 2.14 (s, 3H), 2.12 (s, 3H), 1.98 (s, 3H). **$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$)** δ 170.8, 170.3, 166.9, 153.0, 140.9, 135.6, 134.7, 131.8, 131.8, 127.4, 127.2, 120.1, 114.1, 93.1, 67.7, 65.4, 62.5, 51.9, 21.0, 20.7, 20.6, 16.2. **HRMS (ESI)** m/z: $[M + H]^+$ calcd for $C_{22}H_{27}O_8$ 419.1706, found 419.1702.

*Methyl (E)-3-((2S,5S,6R)-5-Acetoxy-6-(acetoxymethyl)-2-phenoxy-5,6-dihydro-2H-pyran-3-yl)acrylate (**3f**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a spring green sticky solid (44.0 mg, 76% yield). R_f (hexane/EtOAc = 70:30): 0.49. **^1H NMR (600 MHz, $CDCl_3$)** δ 7.26 (t, J = 7.9 Hz, 2H), 7.19 (s, 1H), 7.08 (d, J = 8.1 Hz, 2H), 7.00 (d, J = 7.3 Hz, 1H), 6.19 (d, J = 1.6 Hz, 1H), 5.83 (d, J = 16.2 Hz, 1H), 5.77 (s, 1H), 5.44 (d, J = 9.2 Hz, 1H), 4.24−4.20 (m, 2H), 4.10 (d, J = 10.8 Hz, 1H), 3.67 (s, 3H), 2.05 (s, 3H), 1.89 (s, 3H). **$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$)** δ 169.7, 169.2, 165.8, 155.7, 139.6, 134.3, 133.8, 128.7, 128.7, 121.9, 119.2, 115.9, 115.9, 91.9, 66.7, 64.3, 61.4, 50.8, 19.9, 19.6. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{20}H_{22}O_8Na$ 413.1212, found 413.1205.

*Methyl (E)-3-((2R,5S,6R)-5-Acetoxy-6-(acetoxymethyl)-2-(allyloxy)-5,6-dihydro-2H-pyran-3-yl)acrylate (**3g**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a colorless sticky solid (44.3 mg, 89% yield). R_f (hexane/EtOAc = 70:30): 0.46. **^1H NMR (600 MHz, $CDCl_3$)** δ 7.13 (d, J = 16.0 Hz, 1H), 6.10 (d, J = 1.8 Hz, 1H), 6.01−5.89 (m, 2H), 5.42 (d, J = 9.3 Hz, 1H), 5.32 (d, J = 17.5 Hz, 1H), 5.24 (d, J = 10.2 Hz, 1H), 5.21 (s, 1H), 4.29 (dd, J = 12.8, 5.4 Hz, 1H), 4.24−4.19 (m, 2H), 4.18−4.11 (m, 2H), 3.73 (s, 3H), 2.07 (d, J = 3.8 Hz, 6H). **$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$)** δ 170.7, 170.2, 166.9, 141.0, 136.0, 134.2, 133.5, 120.0, 118.7, 93.7, 69.4, 67.0, 65.6, 62.8, 51.8, 20.9, 20.8. **HRMS (ESI)** m/z: $[M + H]^+$ calcd for $C_{17}H_{23}O_8$ 355.1393, found 355.1389.

*(E)-(3-(Benzoyloxy)-5-(3-butoxy-3-oxoprop-1-en-1-yl)-6-(prop-2-yn-1-yloxy)-3,6-dihydro-2H-pyran-2-yl)methyl Benzoate (**3h**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a light greenish sticky solid (36.4 mg, 82% yield). R_f (hexane/EtOAc = 80:20): 0.50. **^1H NMR (600 MHz, $CDCl_3$)** δ 7.92 (dd, J = 8.3, 1.2 Hz, 4H), 7.48−7.42 (m, 2H), 7.34−7.28 (m, 4H), 7.10 (d, J = 16.1 Hz, 1H), 6.22 (d, J = 2.1 Hz, 1H), 6.10 (d, J = 16.1 Hz, 1H), 5.75 (dd, J = 9.4, 1.6 Hz, 1H), 5.45 (s, 1H), 4.52 (dt, J = 5.0, 2.3 Hz, 1H), 4.39−4.42 (m, 2H), 4.06 (m, 2H), 2.48 (t, J = 2.4 Hz, 1H), 1.57−1.53 (m, 2H), 1.30 (dd, J = 15.0, 7.5 Hz, 2H), 0.83 (t, J = 7.4 Hz, 3H). **$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$)** δ 166.6, 166.2, 165.7, 140.3, 135.6, 134.4, 133.6, 133.6, 133.2, 129.9, 129.9, 129.7, 129.7, 128.5, 128.5, 128.4, 128.4, 121.0, 92.3, 78.6, 75.9, 67.4, 66.5, 64.5, 63.5, 54.8, 30.7, 19.2, 13.7. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{30}H_{30}O_8Na$ 541.1838, found 541.1834.

*Methyl (E)-3-((2R,5S,6R)-5-Acetoxy-6-(acetoxymethyl)-2-(((3S,10R,13R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)-5,6-dihydro-2H-pyran-3-yl)acrylate (**3i**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a light greenish solid (69.0 mg, 72% yield). R_f (hexane/EtOAc = 60:40): 0.50. **^1H NMR (600 MHz, $CDCl_3$)** δ 7.13 (d, J = 16.1 Hz, 1H), 6.10 (s, 1H), 5.97 (d, J = 16.1 Hz, 1H), 5.40 (d, J = 9.7 Hz, 1H), 5.35 (d, J = 4.1 Hz, 1H), 5.32 (s, 1H), 4.23 (dd, J = 13.1, 4.8 Hz, 3H), 3.74 (s, 3H), 3.69−3.63 (m, 1H), 2.41−2.34 (m, 2H), 2.08 (s, 6H), 2.02−1.94 (m, 4H), 1.91 (s, 1H), 1.84−1.79 (m, 1H), 1.60−1.44 (m, 9H), 1.34−1.30 (m, 3H), 1.16−1.07 (m, 7H), 0.90 (m, 4H), 0.85 (m, 9H), 0.66 (s, 3H). **$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$)** δ 170.8, 170.2, 166.9, 141.2, 140.6, 136.3, 134.0, 122.1, 119.8, 92.9, 78.5, 66.7, 65.7, 63.0, 56.7, 56.2, 51.8, 50.2, 42.4, 40.4, 39.8, 39.5, 37.1, 36.7, 36.2, 35.8, 31.9, 31.9, 29.7, 28.3, 28.2, 28.0, 24.3, 23.8, 22.8, 22.6, 21.1, 20.9, 20.8, 19.4, 18.7, 11.9. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{41}H_{62}O_8Na$ 705.4342, found 705.4370.

*Methyl (E)-3-((5R,6R)-5-Acetoxy-6-(acetoxymethyl)-2-allyl-5,6-dihydro-2H-pyran-3-yl)acrylate (**3j**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a white liquid (29.4 mg, 62% yield). R_f (hexane/EtOAc = 60:40): 0.46. **^1H NMR (600 MHz, $CDCl_3$)** δ 7.14 (d, J = 16.2 Hz, 1H), 6.05 (d, J = 2.0 Hz, 1H), 5.94−5.80 (m, 2H), 5.33 (d, J = 8.4 Hz, 1H), 5.18−5.04 (m, 2H), 4.50 (d, J = 10.3 Hz, 1H), 4.21−4.11 (m, 2H), 4.01−3.88 (m, 1H), 3.75 (s, 3H), 2.54 (m, 1H), 2.45−2.34 (m, 1H), 2.09 (s, 3H), 2.07 (s, 3H). **$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$)** δ 170.9, 170.3, 166.8, 141.9, 140.0, 134.1, 131.0, 119.3, 117.6, 72.4, 67.6, 65.7, 63.4, 51.9, 35.9, 21.0, 20.9. **HRMS (ESI)** m/z: $[M+NH_4]^+$ calcd for $C_{17}H_{26}O_7N$ 356.1709, found 356.1719.

*Methyl (E)-3-((5R,6R)-5-Acetoxy-6-(acetoxymethyl)-5,6-dihydro-2H-pyran-3-yl)acrylate (**3k**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a yellowish liquid (36.8 mg, 88% yield). R_f (hexane/EtOAc = 70:30): 0.46. **^1H NMR (600 MHz, $CDCl_3$)** δ 7.12 (d, J = 16.3 Hz, 1H), 6.02 (s, 1H), 5.68 (d, J = 16.3 Hz, 1H), 5.34−5.31 (m, 1H), 4.37 (d, J = 15.8 Hz, 1H), 4.28 (d, J = 15.8 Hz, 1H),

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4.19 (dd, J = 12.2, 2.5 Hz, 1H), 4.12 (dd, J = 12.2, 5.9 Hz, 1H), 3.69 (s, 3H), 3.64 (ddd, J = 8.5, 5.8, 2.5 Hz, 1H), 2.03 (d, J = 2.1 Hz, 6H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 170.8, 170.2, 166.7, 141.3, 136.3, 131.4, 118.4, 74.0, 65.4, 64.7, 63.0, 51.8, 20.9, 20.8. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{14}H_{19}O_7Na$ 321.0950, found 321.0930.

*Methyl (E)-3-((2R,3S,4S)-3-Acetoxy-2-(acetoxymethyl)-4-(phenylthio)-3,4-dihydro-2H-pyran-5-yl)acrylate (**3l**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a yellowish liquid (50.2 mg, 88% yield). R_f (hexane/EtOAc = 70:30): 0.54. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.47 (d, J = 7.4 Hz, 2H), 7.31 (t, J = 7.5 Hz, 2H), 7.25 (t, J = 7.4 Hz, 1H), 7.18 (d, J = 15.7 Hz, 1H), 6.90 (s, 1H), 5.92 (d, J = 15.7 Hz, 1H), 5.06 (s, 1H), 4.78 (t, J = 6.3 Hz, 1H), 4.23−4.14 (m, 2H), 3.88 (d, J = 1.9 Hz, 1H), 3.67 (s, 3H), 2.02 (s, 3H), 1.95 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 169.4, 169.0, 166.7, 151.4, 140.9, 132.0, 130.5, 130.5, 128.4, 128.4, 127.1, 112.8, 107.7, 70.0, 66.4, 61.6, 50.5, 40.5, 19.8, 19.7. **HRMS (ESI)** m/z: $[M + H]^+$ calcd for $C_{20}H_{23}O_7S$ 407.1164, found 407.1160.

*Methyl (E)-3-((2R,3S,4S)-3-Acetoxy-2-(acetoxymethyl)-4-((3,5-dimethylphenyl)thio)-3,4-dihydro-2H-pyran-5-yl)acrylate (**3m**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a green sticky solid (48.8 mg, 80% yield). R_f (hexane/EtOAc = 70:30): 0.50. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.17 (d, J = 15.7 Hz, 1H), 7.07 (s, 2H), 6.88 (d, J = 21.4 Hz, 2H), 5.91 (d, J = 15.7 Hz, 1H), 5.09 (s, 1H), 4.78 (t, J = 6.2 Hz, 1H), 4.18 (dd, J = 12.9, 7.0 Hz, 2H), 3.89 (d, J = 1.9 Hz, 1H), 3.67 (s, 3H), 2.26 (s, 6H), 2.02 (s, 3H), 1.97 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 170.5, 169.9, 167.7, 152.3, 142.0, 139.1, 139.1, 132.6, 129.6, 129.6, 128.4, 113.8, 108.8, 71.1, 67.4, 62.7, 51.8, 41.1, 21.2, 21.2, 20.8, 20.7. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{22}H_{26}O_7SNa$ 457.1297, found 457.1318.

*Methyl (E)-3-((2R,3S,4S)-3-Acetoxy-2-(acetoxymethyl)-4-((4-(tert-butyl)phenyl)thio)-3,4-dihydro-2H-pyran-5-yl)acrylate (**3n**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a pale yellow gummy solid (53.9 mg, 83% yield). R_f (hexane/EtOAc = 70:30): 0.53. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.39 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 15.7 Hz, 1H), 6.89 (s, 1H), 5.90 (d, J = 15.7 Hz, 1H), 5.12 (s, 1H), 4.77 (t, J = 6.2 Hz, 1H), 4.19 (d, J = 6.3 Hz, 2H), 3.85 (d, J = 2.0 Hz, 1H), 3.67 (s, 3H), 2.02 (s, 3H), 1.96 (s, 3H), 1.25 (s, 9H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 169.5, 169.0, 166.7, 151.2, 150.3, 141.0, 130.0, 130.0, 128.6, 125.5, 125.5, 112.8, 107.9, 70.1, 66.6, 61.7, 50.5, 40.5, 33.6, 30.2, 30.2, 30.2, 19.8, 19.7. **HRMS (ESI)** m/z: $[M + H]^+$ calcd for $C_{24}H_{31}O_7S$ 463.1790, found 463.1814.

*Methyl (E)-3-((2R,3S,4S)-3-Acetoxy-2-(acetoxymethyl)-4-((4-fluorophenyl)thio)-3,4-dihydro-2H-pyran-5-yl)acrylate (**3o**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a green sticky solid (45.9 mg, 77% yield). R_f (hexane/EtOAc = 70:30): 0.50. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.48−7.45 (m, 2H), 7.17 (d, J = 15.7 Hz, 1H), 7.03−6.99 (m, 2H), 6.90 (s, 1H), 5.91 (d, J = 15.7 Hz, 1H), 5.03 (s, 1H), 4.74 (t, J = 6.3 Hz, 1H), 4.19 (d, J = 6.3 Hz, 2H), 3.78 (d, J = 2.0 Hz, 1H), 3.67 (s, 3H), 2.02 (s, 3H), 1.94 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 169.4, 169.0, 166.6, 162.7, 161.1, 151.5, 140.9, 133.6, 133.6, 126.9, 115.6, 112.9, 107.6, 69.9, 66.3, 61.6, 50.5, 41.4, 19.7, 19.7. **HRMS (ESI)** m/z: $[M + H]^+$ calcd for $C_{20}H_{22}FO_7S$ 425.1070, found 425.1077.

*Methyl (E)-3-((2R,3S,4S)-3-Acetoxy-2-(acetoxymethyl)-4-((2-fluorophenyl)thio)-3,4-dihydro-2H-pyran-5-yl)acrylate (**3p**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a light green sticky solid (47.0 mg, 79% yield). R_f (hexane/EtOAc = 70:30): 0.47. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.52 (t, J = 7.4 Hz, 1H), 7.33 (dd, J = 13.3, 7.3 Hz, 1H), 7.19 (s, 1H), 7.12 (dd, J = 12.2, 6.0 Hz, 2H), 6.93 (s, 1H), 6.12 (d, J = 15.7 Hz, 1H), 4.92 (s, 1H), 4.87 (t, J = 6.2 Hz, 1H), 4.23−4.14 (m, 2H), 3.92 (s, 1H), 3.69 (s, 3H), 2.03 (s, 3H), 1.92 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 170.5, 170.0, 167.9, 152.7, 141.8, 135.7, 131.3, 131.2, 124.9, 116.4, 116.3, 114.3, 108.6, 70.8, 66.9, 62.5, 51.5, 41.2, 20.7, 20.7. **HRMS (ESI)** m/z: $[M + H]^+$ calcd for $C_{20}H_{22}FO_7S$ 425.1070, found 425.1077.

*Methyl (E)-3-((2R,3S,4S)-3-Acetoxy-2-(acetoxymethyl)-4-((2-bromophenyl)thio)-3,4-dihydro-2H-pyran-5-yl)acrylate (**3q**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a light brownish gummy solid (55.8 mg, 82% yield). R_f (hexane/EtOAc = 70:30): 0.50. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.66 (dd, J = 7.8, 1.3 Hz, 1H), 7.57 (dd, J = 8.0, 1.1 Hz, 1H), 7.30 (td, J = 7.7, 1.2 Hz, 1H), 7.18 (d, J = 15.7 Hz, 1H), 7.11 (td, J = 7.8, 1.4 Hz, 1H), 6.96 (s, 1H), 6.00 (d, J = 15.7 Hz, 1H), 4.97 (d, J = 11.4 Hz, 1H), 4.91 (t, J = 6.3 Hz, 1H), 4.23−4.16 (m, 2H), 4.05 (d, J = 2.0 Hz, 1H), 3.66 (s, 3H), 2.01 (s, 3H), 1.96 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 169.4, 169.1, 166.6, 151.9, 140.8, 133.0, 132.6, 131.2, 128.1, 127.3, 125.0, 112.9, 106.9, 70.1, 65.5, 61.4, 50.5, 39.9, 19.8, 19.7. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{20}H_{21}BrO_7SNa$ 507.0089, found 507.0102.

*Butyl (E)-3-((2R,3S,4S)-3-Acetoxy-2-(acetoxymethyl)-4-(phenylthio)-3,4-dihydro-2H-pyran-5-yl)acrylate (**3r**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a light yellow gummy solid (49.5 mg, 88% yield). R_f (hexane/EtOAc = 70:30): 0.50. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.49−7.46 (m, 2H), 7.31 (dd, J = 10.3, 4.7 Hz, 2H), 7.27−7.24 (m, 1H), 7.16 (d, J = 15.7 Hz, 1H), 6.90 (s, 1H), 5.91 (d, J = 15.7 Hz, 1H), 5.06 (s, 1H), 4.78 (t, J = 6.3 Hz, 1H), 4.19 (dd, J = 12.1, 5.0 Hz, 2H), 4.10−4.06 (m, 2H), 3.90 (d, J = 2.1 Hz, 1H), 2.02 (s, 3H), 1.95 (s, 3H), 1.58 (dd, J = 9.8, 5.2 Hz, 2H), 1.36−1.32 (m, 2H), 0.87 (t, J = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 170.5, 170.0, 167.4, 152.3, 141.6, 133.0, 131.5, 131.5, 129.4, 129.4, 128.1, 114.3, 108.7, 70.9, 67.4, 64.2, 62.7, 41.5, 30.8, 20.8, 20.7, 19.2, 13.8. **HRMS (ESI)** m/z: $[M + H]^+$ calcd for $C_{23}H_{29}O_7S$ 449.1634, found 449.1631.

*Methyl (E)-3-((2R,3R)-3-Acetoxy-2-(acetoxymethyl)-4-(phenylthio)-3,4-dihydro-2H-pyran-5-yl)acrylate (**3s**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a light gray sticky solid (49.5 mg, 84% yield). R_f (hexane/EtOAc = 70:30): 0.50. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.39 (d, J = 7.3 Hz, 2H), 7.25 (t, J = 7.6 Hz, 2H), 7.19−7.15 (m, 2H), 6.80 (s, 1H), 6.01 (d, J = 15.7 Hz, 1H), 5.12 (dd, J = 10.6, 4.2 Hz, 1H), 4.70−4.66 (m, 1H), 4.48 (d, J = 4.2 Hz, 1H), 4.31 (dd, J = 6.1, 3.1 Hz, 2H), 3.68 (s, 3H), 1.99 (s, 3H), 1.34 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 170.6, 169.8, 167.6, 152.3, 140.9, 132.4, 131.3, 131.3, 129.2, 129.2, 127.4, 113.9, 109.7, 71.9, 67.6, 61.7, 51.5, 42.6, 20.7, 19.7. **HRMS (ESI)** m/z: $[M + H]^+$ calcd for $C_{20}H_{23}O_7S$ 407.1164, found 407.1160.

*Methyl (E)-3-((3R)-3-Acetoxy-2-methyl-4-(phenylthio)-3,4-dihydro-2H-pyran-5-yl)acrylate (**3t**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a light yellow sticky solid (44.4 mg, 76% yield). R_f (hexane/EtOAc = 80:20): 0.50. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.04 (d, J = 7.9 Hz, 2H), 7.89 (t, J = 7.9 Hz, 2H), 7.85−7.80 (m, 2H), 7.44 (s, 1H), 6.64 (d, J = 15.8 Hz, 1H), 5.50 (dd, J = 10.1, 4.3 Hz, 1H), 5.23−5.15 (m, 1H), 5.09 (d, J = 4.0 Hz, 1H), 4.32 (s, 3H), 2.02 (s, 3H), 1.92 (d, J = 6.2 Hz, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 169.5, 167.1, 152.5, 141.0, 135.3, 130.6, 130.6, 128.6, 128.6, 126.6, 112.64, 109.0, 72.1, 69.8, 50.8, 42.3, 19.3, 16.5. **HRMS (ESI)** m/z: $[M + H]^+$ calcd for $C_{18}H_{21}O_5S$ 349.1110, found 349.1114.

*(2R,3R,4S,5R,6R)-2-(Acetoxymethyl)-6-(((2R,3R)-2-(acetoxymethyl)-5-((E)-3-methoxy-3-oxoprop-1-en-1-yl)-4-(phenylthio)-3,4-dihydro-2H-pyran-3-yl)oxy)tetrahydro-2H-pyran-3,4,5-triyl Triacetate (**3u**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a white sticky solid (38.3 mg, 71% yield). R_f (hexane/EtOAc = 60:40): 0.45. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.44 (d, J = 7.9 Hz, 1H), 7.40 (d, J = 7.8 Hz, 2H), 7.37 (d, J = 7.2 Hz, 2H), 7.33−7.29 (m, 1H), 7.29 (s, 1H), 6.94 (s, 1H), 6.07 (d, J = 15.8 Hz, 1H), 5.49−5.45 (m, 1H), 5.34−5.28 (m, 1H), 5.05 (d, J = 3.8 Hz, 1H), 4.94 (t, J = 9.9 Hz, 1H), 4.68−4.63 (m, 2H), 4.35 (dd, J = 8.7, 3.2 Hz, 2H), 4.23−4.20 (m, 1H), 4.03 (d, J = 2.1 Hz, 1H), 3.96 (s, 1H), 3.74 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H), 1.99 (s, 3H), 1.91 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz,**

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$CDCl_3$) δ 170.6, 170.5, 170.2, 170.1, 169.7, 167.6, 151.4, 142.3, 136.9, 131.6, 131.6, 129.8, 129.8, 129.2, 128.4, 114.2, 108.2, 95.8, 73.6, 70.8, 69.9, 68.4, 68.1, 63.4, 61.9, 51.6, 41.5, 21.2, 20.9, 20.7, 20.7, 14.2. **HRMS (ESI)** m/z: $[M + H]^+$ calcd for $C_{32}H_{39}O_{15}S$ 695.2010, found 695.2039.

*Methyl (E)-3-((2R,3R)-3-Acetoxy-2-(acetoxymethyl)-4-((2-chlorobenzyl)thio)-3,4-dihydro-2H-pyran-5-yl)acrylate (**3v**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a yellowish liquid (47.8 mg, 75% yield). R_f (hexane/EtOAc = 70:30): 0.45. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.39−7.36 (m, 2H), 7.21 (dd, J = 8.8, 4.1 Hz, 3H), 7.01 (s, 1H), 6.73 (s, 1H), 5.32 (t, J = 4.6 Hz, 1H), 5.26−5.21 (m, 1H), 4.47−4.45 (m, 1H), 3.91 (s, 1H), 3.85 (d, J = 4.0 Hz, 1H), 3.65 (s, 3H), 2.17 (s, 2H), 2.06 (m, 6H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 170.6, 169.7, 167.5, 151.4, 141.6, 140.5, 135.0, 131.0, 130.2, 129.1, 127.3, 113.8, 110.5, 72.5, 67.9, 61.7, 51.3, 39.9, 36.1, 21.0, 20.7. HRMS (ESI) m/z: [M + H]+ calcd for $C_{21}H_{24}ClO_7S$ 455.0931, found 455.1268

*Methyl (E)-3-((2R,3S)-3-Acetoxy-2-(acetoxymethyl)-4-chloro-3,4-dihydro-2H-pyran-5-yl)acrylate (**3x**).* The compound was synthesized according to general procedure 1 and purified by column chromatography to give a yellowish liquid (34.0 mg, 73% yield). R_f (hexane/EtOAc = 70:30): 0.40. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 7.16 (d, J = 15.9 Hz, 1H), 6.83 (s, 1H), 5.89 (d, J = 15.3 Hz, 1H), 5.14 (dd, J = 11.3, 3.8 Hz, 1H), 5.03 (d, J = 3.9 Hz, 1H), 4.60−4.56 (m, 1H), 4.40 (d, J = 2.2 Hz, 2H), 3.74 (s, 3H), 2.16 (s, 3H), 2.07 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 170.5, 169.6, 167.4, 152.0, 139.6, 114.8, 112.3, 71.4, 66.4, 61.4, 51.7, 50.5, 20.7, 20.7. **HRMS (ESI)** m/z: $[M + H]^+$ calcd for $C_{14}H_{18}ClO_7$ 333.0741, found 333.0737.

Gram-Scale Synthesis of the Product 3a. In an oven-dried round-bottom flask, substituted glycal **1a** (1 g, 2.8 mmol, 1 equiv) was dissolved in 10 mL of DCM at rt, and to the solution was added propargyl alcohol (4.2 mmol, 1.5 equiv). To the mixture was slowly added $BF_3{\cdot}OEt_2$ (2.8 mmol, 1 equiv) at room temperature. Finally, the reaction mixture was stirred at the same temperature for 6 h. After the starting material was converted as confirmed through TLC, the mixture was quenched with a saturated sodium bicarbonate solution (70 mL), and the organic layer was extracted with DCM (50 × 2 mL). The organic layer was dried over sodium sulfate, and the residue left was purified by column chromatography over silica gel (100−200 mesh) using hexane/ethyl acetate as the eluent to afford resultant product **3a** (0.831 g, 84%).

Gram-Scale Synthesis of the Product 3l. In an oven-dried round-bottom flask, substituted glycal **1b** (1 g, 2.8 mmol, 1 equiv) was dissolved in 10 mL of DCM at rt, and to the solution was added thiophenol (4.2 mmol, 1.5 equiv). To the mixture was slowly added $BF_3{\cdot}OEt_2$ (2.8 mmol, 1 equiv) at room temperature. Finally, the reaction mixture was stirred at the same temperature for 6 h. After the starting material was converted as confirmed through TLC, the mixture was quenched with a saturated sodium bicarbonate solution (70 mL), and the organic layer was extracted with DCM (50 × 2 mL). The organic layer was dried over sodium sulfate, and the residue left was purified by column chromatography over silica gel (100−200 mesh) using hexane/ethyl acetate as the eluent to afford resultant product **3l** (0.872 g, 80%).

General Procedure 2 for the Products (5a−5i). In an oven-dried round-bottom flask, product **3a** (0.14 mmol, 1 equiv) was dissolved in 2 mL of ACN at rt. To this mixture were added CsF (0.28 mmol, 2 equiv) and 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (0.21 mmol, 1.5 equiv) subsequently. Then the reaction mixture was stirred for 10 h at 60 °C. After the starting material was converted as confirmed through TLC, the organic layer was extracted with EtOAc (10 × 2 mL). The organic layer was dried over sodium sulfate, and the residue left was purified by column chromatography over silica gel (100−200 mesh) using hexane/ethyl acetate as the eluent.

*Methyl (1S,2R)-1-Acetoxy-2-(acetoxymethyl)-4-(allyloxy)-8,9-dimethoxy-1,4-dihydro-2H-benzo[f]isochromene-6-carboxylate (**5a**).* The compound was synthesized according to general procedure 2 and purified by column chromatography to give a green liquid (57.9 mg, 84% yield). R_f (hexane/EtOAc = 60:40): 0.50. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.44 (s, 1H), 7.89 (s, 1H), 6.96 (d, J = 8.4 Hz, 1H), 6.59 (d, J = 8.1 Hz, 1H), 6.00 (ddd, J = 22.5, 11.1, 5.9 Hz, 1H), 5.70 (s, 1H), 5.33 (dt, J = 11.0, 5.5 Hz, 1H), 5.22 (d, J = 10.3 Hz, 1H), 4.44 (ddd, J = 8.2, 5.9, 2.7 Hz, 1H), 4.36−4.31 (m, 2H), 4.28−4.22 (m, 2H), 3.98 (d, J = 5.0 Hz, 3H), 3.92 (s, 3H), 3.84 (s, 3H), 2.07 (s, 3H), 2.04 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 170.3, 169.7, 166.5, 149.8, 148.9, 132.9, 130.3, 129.9, 127.2, 126.8, 125.7, 124.8, 117.1, 104.5, 101.7, 95.4, 68.3, 67.9, 63.6, 62.5, 54.8, 54.8, 51.2, 20.0, 19.8. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{25}H_{28}O_{10}Na$ 511.1580, found 511.1584.

*Methyl (1S,2R)-1-Acetoxy-2-(acetoxymethyl)-8,9-dimethoxy-4-(prop-2-yn-1-yloxy)-1,4-dihydro-2H-benzo[f]isochromene-6-carboxylate (**5b**).* The compound was synthesized according to general procedure 2 and purified by column chromatography to give a light green sticky solid (58.7 mg, 85% yield). R_f (hexane/EtOAc = 60:40): 0.52. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.42 (s, 1H), 7.88 (s, 1H), 6.93 (s, 1H), 6.58 (d, J = 8.2 Hz, 1H), 5.86 (s, 1H), 4.42−4.33 (m, 4H), 4.26 (dd, J = 12.1, 5.5 Hz, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.83 (s, 3H), 2.51 (s, 1H), 2.07 (s, 3H), 2.04 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 170.2, 169.7, 166.4, 149.8, 148.9, 130.4, 129.1, 127.3, 126.6, 125.6, 124.9, 104.5, 101.7, 94.6, 78.0 74.4, 68.1, 63.5, 62.4, 54.8, 54.8, 54.2, 51.2, 19.9, 19.8. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{25}H_{26}O_{10}Na$ 509.1424, found 509.1436.

*Methyl (1S,2R)-1-Acetoxy-2-(acetoxymethyl)-4-butoxy-8,9-dimethoxy-1,4-dihydro-2H-benzo[f]isochromene-6-carboxylate (**5c**).* The compound was synthesized according to general procedure 2 and purified by column chromatography to give a light greenish sticky solid (53.8 mg, 79% yield). R_f (hexane/EtOAc = 60:40): 0.45. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.50 (s, 1H), 7.94 (s, 1H), 7.02 (s, 1H), 6.63 (d, J = 8.3 Hz, 1H), 5.70 (s, 1H), 4.48−4.45 (m, 1H), 4.40 (t, J = 6.0 Hz, 1H), 4.32 (dd, J = 12.1, 5.5 Hz, 1H), 4.03 (s, 3H), 3.98 (s, 3H), 3.90 (s, 3H), 3.52−3.39 (m, 2H), 2.12 (s, 3H), 2.10 (s, 3H), 1.71−1.68 (m, 2H), 1.46 (dd, J = 11.5, 3.9 Hz, 2H), 0.97 (d, J = 6.8 Hz, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 171.4, 170.8, 167.6, 150.8, 150.0, 131.3, 131.3, 128.3, 127.9, 126.9, 125.9, 105.6, 102.8, 97.4, 68.9, 68.9, 64.7, 63.7, 55.9, 52.3, 52.3, 31.8, 21.1, 20.9, 19.6, 14.0. HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{26}H_{32}O_{10}Na$ 527.1893, found 527.1896.

*Methyl 1-Acetoxy-2-(acetoxymethyl)-8,9-dimethoxy-1,4-dihydro-2H-benzo[f]isochromene-6-carboxylate (**5d**).* The compound was synthesized according to general procedure 2 and purified by column chromatography to give a light greenish sticky solid (58.7 mg, 81% yield). R_f (hexane/EtOAc = 60:40): 0.50. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.46 (s, 1H), 7.77 (s, 1H), 7.09 (s, 1H), 6.47 (d, J = 4.1 Hz, 1H), 4.95 (d, J = 8.6 Hz, 2H), 4.30 (dd, J = 8.6, 5.6 Hz, 2H), 4.24−4.22 (m, 1H), 4.02 (s, 3H), 3.96 (s, 3H), 3.92 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 171.0, 170.8, 167.6, 150.5, 150.3, 131.4, 128.6, 127.2, 126.0, 124.8, 124.8, 105.7, 102.0, 76.0, 65.4, 64.0, 62.6, 55.9, 55.9, 52.3, 21.1, 20.9. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{22}H_{24}O_9Na$ 455.1318, found 455.1322.

*Butyl (1S,2R,4R)-1-Acetoxy-2-(acetoxymethyl)-8,9-dimethoxy-4-(prop-2-yn-1-yloxy)-1,4-dihydro-2H-benzo[f]isochromene-6-carboxylate (**5e**).* The compound was synthesized according to general procedure 2 and purified by column chromatography to give a light yellow sticky solid (49.6 mg, 74% yield). R_f (hexane/EtOAc = 60:40): 0.55. **^{1}H NMR (600 MHz, $CDCl_3$)** δ 8.46 (s, 1H), 7.93 (s, 1H), 7.01 (s, 1H), 6.65 (d, J = 8.0 Hz, 1H), 5.93 (s, 1H), 4.46 (dt, J = 6.1, 2.8 Hz, 3H), 4.41−4.37 (m, 3H), 4.34−4.30 (m, 1H), 4.02 (s, 3H), 3.89 (s, 3H), 2.54 (d, J = 2.0 Hz, 1H), 2.12 (s, 3H), 2.09 (s, 3H), 1.82−1.78 (m, 2H), 1.52−1.48 (m, 2H), 1.01−0.97 (m, 3H). **^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$)** δ 171.3, 170.8, 167.3, 150.8, 150.0, 131.3, 130.2, 128.3, 127.7, 126.7, 126.6, 105.7, 102.9, 95.8, 79.2, 75.3, 69.3, 65.2, 64.6, 63.5, 55.9, 55.9, 55.4, 30.9, 21.1, 20.9, 19.4, 13.9. **HRMS (ESI)** m/z: $[M + Na]^+$ calcd for $C_{28}H_{32}O_{10}Na$ 551.1893, found 551.1895.

Methyl (1S,2R,4R)-1-Acetoxy-2-(acetoxymethyl)-4-(((3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl)oxy)-8,9-dimethoxy-1,4-dihydro-

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*2H-benzo[f]isochromene-6-carboxylate (**5f**).* The compound was synthesized according to general procedure 2 and purified by column chromatography to give a white gummy solid (46.1 mg, 77% yield). R_f (hexane/EtOAc = 70:30): 0.50. **^{1}H NMR (600 MHz, CDCl$_3$)** δ 8.43 (s, 1H), 7.83 (s, 1H), 6.96 (s, 1H), 6.57−6.56 (m, 1H), 5.79 (s, 1H), 5.33 (d, J = 4.7 Hz, 1H), 4.52−4.49 (m, 1H), 4.37 (dd, J = 12.2, 2.5 Hz, 1H), 4.26 (dd, J = 12.1, 6.1 Hz, 1H), 3.97 (s, 3H), 3.93 (s, 3H), 3.84 (s, 3H), 3.75 (s, 1H), 2.39 (d, J = 6.8 Hz, 2H), 2.06 (s, 3H), 2.05 (s, 3H), 2.00−1.88 (m, 6H), 1.54−1.47 (m, 9H), 1.28 (m, 3H), 1.09−1.03 (m, 7H), 0.86 (m, 4H), 0.81−0.79 (m, 9H), 0.62 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$)** δ 170.8, 168.2, 167.6, 150.7, 149.9, 140.7, 131.4, 131.4, 128.1, 127.8, 126.7, 125.9, 122.0, 105.6, 102.8, 100.6, 95.7, 78.3, 68.8, 64.7, 63.7, 56.8, 56.2, 55.9, 52.2, 50.2, 42.4, 40.3, 39.8, 39.5, 37.2, 36.8, 36.2, 35.8, 31.9, 28.3, 28.0, 24.3, 23.9, 22.8, 22.7, 22.6, 21.1, 21.0, 20.9, 19.4, 18.7, 14.1, 11.9. **HRMS (ESI)** m/z: [M + Na]$^+$ calcd for $C_{49}H_{68}O_{10}Na$ 839.4710, found 839.4754.

*Methyl 1-Acetoxy-2-(acetoxymethyl)-4-(prop-2-yn-1-yloxy)-1,4-dihydro-2H-benzo[f]isochromene-6-carboxylate (**5g**).* The compound was synthesized according to general procedure 2 and purified by column chromatography to give a green sticky solid (48.4 mg, 80% yield). R_f (hexane/EtOAc = 60:40): 0.50. **^{1}H NMR (600 MHz, CDCl$_3$)** δ 8.82 (d, J = 8.6 Hz, 1H), 7.94 (s, 1H), 7.63 (d, J = 8.5 Hz, 1H), 7.58−7.55 (m, 1H), 7.49 (t, J = 7.6 Hz, 1H), 6.62 (d, J = 8.0 Hz, 1H), 5.89 (s, 1H), 4.45 (dd, J = 15.7, 2.3 Hz, 1H), 4.42−4.38 (m, 2H), 4.36 (dd, J = 12.2, 2.7 Hz, 1H), 4.29 (dd, J = 12.2, 5.6 Hz, 1H), 3.94 (s, 3H), 2.51 (t, J = 2.3 Hz, 1H), 2.06 (s, 3H), 2.02 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$)** δ 171.0, 170.8, 167.3, 132.9, 131.8, 131.5, 131.3, 128.8, 128.0, 127.9, 127.3, 126.8, 123.7, 95.3, 78.9, 75.5, 69.4, 64.3, 63.4, 55.3, 52.4, 20.9, 20.8. **HRMS (ESI)** m/z: [M + H]$^+$ calcd for $C_{23}H_{23}O_8$ 426.1315, found 426.1311.

*Butyl (1S,2R)-1-(Benzoyloxy)-2-((benzoyloxy)methyl)-4-(prop-2-yn-1-yloxy)-1,4-dihydro-2H-benzo[f]isochromene-6-carboxylate (**5h**).* The compound was synthesized according to general procedure 2 and purified by column chromatography to give a greenish solid (41.7 mg, 73% yield). R_f (hexane/EtOAc = 70:30): 0.50. **^{1}H NMR (600 MHz, CDCl$_3$)** δ 8.78 (d, J = 8.6 Hz, 1H), 7.97 (s, 1H), 7.92 (d, J = 7.4 Hz, 2H), 7.87 (d, J = 7.7 Hz, 2H), 7.75 (d, J = 8.6 Hz, 1H), 7.50 (d, J = 7.5 Hz, 1H), 7.45 (dd, J = 7.3, 3.6 Hz, 2H), 7.37 (d, J = 7.3 Hz, 1H), 7.30 (m, 4H), 6.98 (d, J = 7.6 Hz, 1H), 5.97 (s, 1H), 4.73−4.67 (m, 2H), 4.62−4.59 (m, 1H), 4.44 (td, J = 13.5, 3.1 Hz, 2H), 4.37 (t, J = 6.7 Hz, 2H), 2.47 (t, J = 2.3 Hz, 1H), 1.78−1.74 (m, 2H), 1.46 (m, 2H), 0.95 (d, J = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$)** δ 167.1, 166.6, 166.3, 133.6, 133.1, 132.8, 132.0, 131.5, 131.4, 130.1, 130.1, 129.7, 129.7, 129.5, 129.1, 128.5, 128.5, 128.4, 128.4, 128.4, 128.0, 127.6, 127.4, 126.6, 124.0, 95.5, 79.0, 75.3, 69.9, 65.4, 65.1, 64.2, 55.4, 30.8, 19.4, 13.8. **HRMS (ESI)** m/z: [M + Na]$^+$ calcd for $C_{36}H_{32}O_8Na$ 615.1995, found 615.1991.

*Butyl (1S,2R)-1-(Benzoyloxy)-2-((benzoyloxy)methyl)-8,9-dimethoxy-4-(prop-2-yn-1-yloxy)-1,4-dihydro-2H-benzo[f]isochromene-6-carboxylate (**5i**).* The compound was synthesized according to general procedure 2 and purified by column chromatography to give a light green sticky solid (46.0 mg, 72% yield). R_f (hexane/EtOAc = 70:30): 0.50. **^{1}H NMR (600 MHz, CDCl$_3$)** δ 8.39 (s, 1H), 7.96−7.92 (m, 3H), 7.88 (d, J = 7.7 Hz, 2H), 7.48−7.45 (m, 2H), 7.33−7.28 (m, 4H), 7.03 (s, 1H), 6.94 (d, J = 8.2 Hz, 1H), 5.95 (s, 1H), 4.73−4.70 (m, 1H), 4.67 (dd, J = 12.1, 2.7 Hz, 1H), 4.59 (dd, J = 12.1, 5.8 Hz, 1H), 4.49−4.43 (m, 2H), 4.35 (dd, J = 6.5, 5.1 Hz, 2H), 3.93 (s, 3H), 3.59 (s, 3H), 2.48 (s, 1H), 1.78−1.74 (m, 2H), 1.48−1.44 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$)** δ 167.3, 166.8, 166.3, 150.7, 149.8, 133.8, 133.1, 131.5, 130.2, 130.0, 130.0, 129.8, 129.8, 129.7, 129.7, 128.9, 128.6, 128.4, 128.4, 128.4, 127.8, 126.7, 126.6, 105.5, 103.1, 95.8, 79.1, 75.2, 69.4, 65.5, 65.2, 64.1, 55.8, 55.5, 55.4, 30.8, 19.4, 13.8. **HRMS (ESI)** m/z: [M + Na]$^+$ calcd for $C_{38}H_{36}O_{10}Na$ 675.2206, found 675.2203.

General Procedure 3 for the Products (6a−6c). In an oven-dried round-bottom flask, product **3p** (0.12 mmol, 1 equiv) was dissolved in 3 mL of methanol at rt. To this mixture was added NaOMe (0.06 mmol, 0.5 equiv). Then the reaction mixture was stirred for 6 h at 30 °C. After the starting material was converted as confirmed through TLC, the organic layer was extracted with EtOAc (10 × 2 mL). The organic layer was dried over sodium sulfate, and the residue left was purified by column chromatography over silica gel (100−200 mesh) using hexane/ethyl acetate as the eluent.

*methyl (E)-3-((2R,3S,4S)-4-((2-Fluorophenyl)thio)-3-hydroxy-2-(hydroxymethyl)-3,4-dihydro-2H-pyran-5-yl)acrylate (**6a**).* The compound was synthesized according to general procedure 3 and purified by column chromatography to give a white solid (29.3 mg, 73% yield). R_f (hexane/EtOAc = 50:50): 0.50. **^{1}H NMR (600 MHz, CDCl$_3$)** δ 7.39 (dd, J = 8.6, 5.2 Hz, 2H), 7.19 (d, J = 10.7 Hz, 1H), 6.99 (t, J = 8.6 Hz, 2H), 6.94 (s, 1H), 5.98 (d, J = 15.7 Hz, 1H), 4.40 (t, J = 3.7 Hz, 1H), 4.07−4.02 (m, 2H), 3.94 (dd, J = 12.3, 3.9 Hz, 1H), 3.69 (d, J = 1.7 Hz, 1H), 3.68 (s, 3H). **^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$)** δ 168.0, 163.6, 161.9, 153.4, 142.8, 134.5, 134.4, 116.7, 116.6, 113.4, 108.7, 73.0, 68.3, 63.7, 51.6, 45.4. **HRMS (ESI)** m/z: [M + Na]$^+$ calcd for $C_{16}H_{17}FO_5SNa$ 363.0678, found 363.0667.

*Methyl (E)-3-(2-Butoxy-5-hydroxy-6-(hydroxymethyl)-5,6-dihydro-2H-pyran-3-yl)acrylate (**6b**).* The compound was synthesized according to general procedure 3 and purified by column chromatography to give a white liquid (27.0 mg, 70% yield). R_f (hexane/EtOAc = 50:50): 0.55. **^{1}H NMR (600 MHz, CDCl$_3$)** δ 7.10 (d, J = 16.1 Hz, 1H), 6.14 (s, 1H), 5.82 (d, J = 16.1 Hz, 1H), 5.04 (s, 1H), 4.28 (d, J = 9.2 Hz, 1H), 3.78 (m, 4H), 3.69 (s, 3H), 3.49 (dd, J = 16.0, 6.7 Hz, 1H), 1.57−1.51 (m, 2H), 1.32 (m, 2H), 0.86 (t, J = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$)** δ 167.3, 141.9, 139.4, 134.5, 119.0, 94.5, 71.4, 68.7, 64.5, 62.3, 51.8, 31.7, 19.4, 13.8. **HRMS (ESI)** m/z: [M + Na]$^+$ calcd for $C_{14}H_{22}O_6Na$ 309.1314, found 309.1309.

*Methyl (1S,2R)-1-Hydroxy-2-(hydroxymethyl)-8,9-dimethoxy-4-(prop-2-yn-1-yloxy)-1,4-dihydro-2H-benzo[f]isochromene-6-carboxylate (**6c**).* The compound was synthesized according to general procedure 3 and purified by column chromatography to give a colorless liquid (31.4 mg, 76% yield). R_f (hexane/EtOAc = 50:50): 0.48. **^{1}H NMR (600 MHz, CDCl$_3$)** δ 8.41 (s, 1H), 7.85 (s, 1H), 7.76 (s, 1H), 5.81 (s, 1H), 5.21 (t, J = 8.1 Hz, 1H), 4.42 (dd, J = 17.7, 1.8 Hz, 2H), 4.16 (dd, J = 8.3, 4.0 Hz, 1H), 4.04 (d, J = 8.3 Hz, 1H), 3.96 (s, 6H), 3.92 (s, 3H), 3.86−3.77 (m, 1H), 2.50 (s, 1H). **^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$)** δ 167.7, 150.9, 149.5, 135.3, 128.8, 128.6, 128.0, 126.8, 125.4, 105.2, 105.0, 95.9, 79.2, 75.3, 73.1, 64.4, 63.1, 55.9, 55.8, 55.3, 52.2. **HRMS (ESI)** m/z: [M + Na]$^+$ calcd for $C_{21}H_{22}O_8Na$ 425.1212, found 425.1234.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its online Supporting Information

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.4c01210.

Computational details, copies of ^{1}H and ^{13}C{^{1}H} NMR spectra for all compounds, and 2D NMR spectra for **3d** and **4g** (PDF)

FAIR data, including the primary NMR FID files, for compounds **3a−3v**, **3x**, **4a−4i**, and **5a−5c** (ZIP)

■ AUTHOR INFORMATION

Corresponding Author

Nazar Hussain − *Department of Medicinal Chemistry, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh 221005, India;* orcid.org/0000-0003-4387-3971; Email: nazar.hussain10@gmail.com

Authors

Ram Pratap Pandey − *Department of Medicinal Chemistry, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh 221005, India*

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Bindu Tiwari − *Department of Medicinal Chemistry, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh 221005, India*

Navneet Sharma − *Department of Computational Sciences, Central University of Punjab, Bathinda, Punjab 151401, India*

Kousik Giri − *Department of Computational Sciences, Central University of Punjab, Bathinda, Punjab 151401, India*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.4c01210

Notes

The authors declare no competing financial interest.

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