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ARTICLE TYPE

Synthesis of 4-trifluoromethanesulfonate substituted 3,6-dihydropyrans and their application in various C-C coupling reactions

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Triflic acid mediated Prins cyclization of homopropargylic alcohols with aldehydes afforded 3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonates efficiently and highly regioselectively. The dihydropyran thus formed is transformed into different 4-alkyl and aryl substituted products using Suzuki, Heck, Stille and Sonogashira coupling reactions.

Introduction

Substituted pyran motifs constitute the core structural unit in numerous biologically active natural products such as calixyn L,[1] ambruticin,[2] kendomycin[3] (Figure 1) and have diverse applications in cosmetics and agro chemicals as well.[4] The dihydropyran skeleton of this family is distinctly important since functionalized dihydropyrans are versatile building blocks widely used in the synthesis of biologically active molecules[5] and this structural moiety exists in many natural products such as laulimalide[6] and aspergillide C (Figure 1).[7] The presence of double bond in cyclic system is not only responsible for their biological properties but also serve as a functional group for further manipulations in organic synthesis.[8] They can also be used as building blocks in organic synthesis.[9] Triflates, present at vinylic position, in general are valuable substrates for a number of organic reactions such as electrophilic aromatic substitution reaction[10] and various metal catalyzed cross-coupling reactions such as Suzuki,[11] Heck,[12] Stille,[13] and Sonogashira coupling.[14] Therefore, the synthesis of such valuable units in an easier and economical method is of value to organic chemists. There are different methods towards the construction of dihydropyrans including hetero-Diels-Alder reactions,[15] olefin metathesis,[16] base promoted cyclizations of sulfenyl dienols,[17] oxonium-ene reactions,[18] [4+2] annulations,[19] intramolecular C-C bond formation of alkyne-epoxide,[20] and Prins cyclization reactions.[21] Among various methods available, Prins cyclization is considered to be the most convenient tool as it provides the desired product in a single step with high diastereoselectivity. On the other hand, one pot, multi component and selective reactions are considered as green synthetic routes.[22] Considering these and in continuation of our research on Prins cyclization reaction,[23] herein, we report a one pot, three component and highly selective Prins cyclization reaction for efficient synthesis of 3,6-dihydro-2*H*-pyran-4-yl trifluoromethane-sulfonates from homopropargylic alcohols and aldehydes mediated by triflic acid in which triflic acid acts as Brønsted acid as well as a nucleophile. Although there are several reports which illustrate the preparation of 4-halotetrahydropyran derivatives, there are only a couple of reports which demonstrated the preparation of 4-halo-3,6-dihydro-2*H*-pyrans mediated by Lewis acids. Use of Fe(III) salts by Martin and co-workers have resulted in 2-alkyl-4-halo-3,6-dihydro-2*H*-pyrans.[9g,21h,i] The presence of the triflate group at the vinylic position of dihydropyran ring, which can be used in many coupling reactions, has not been reported so far.

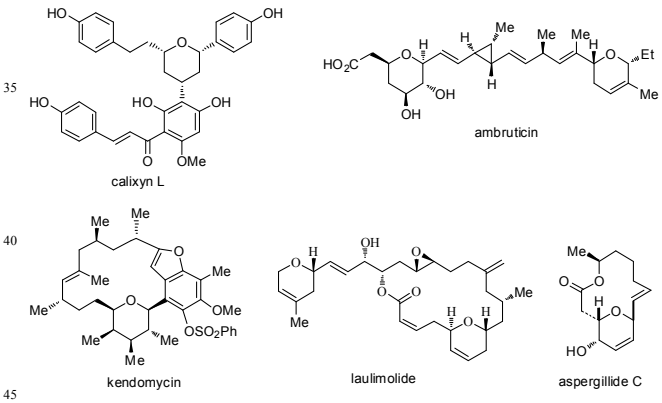

Figure 1. Structures of natural products containing pyran ring

Results and discussion

To start with homopropargyl alcohol **1** (1.5 equiv) and benzaldehyde **2a** (1.0 equiv) were treated with 1.2 equivalents of triflic acid in dry dichloromethane at room temperature for 12 h and 3,6-dihydro-2-phenyl-2*H*-pyran-4-yl trifluoromethane-sulfonate **3a** was obtained in 92% yield. The reaction is regioselective and only 3,6-dihydropyrans was formed in the reaction. The stereochemistry of the compounds was determined by ^{1}H, ^{13}C, DEPT and HMQC analysis. Finally the structure is confirmed by X-ray crystallographic analysis (Figure 2).[24] The scope of the reaction was examined with variety of aliphatic and aromatic aldehydes (Table 1). It was observed from the Table 1 that both aromatic and aliphatic aldehydes gave the good yields. Aromatic aldehydes are better substrates than the aliphatic substrates. There is no major role of electron withdrawing and donating groups on the aromatic rings, both groups are providing comparable yields. To study the steric effect, *ortho*-, *meta*- and

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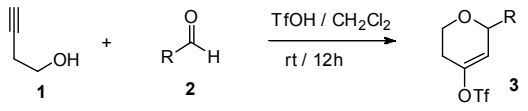
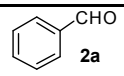
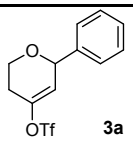
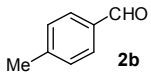
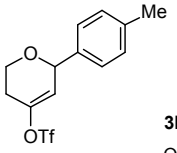
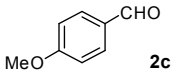
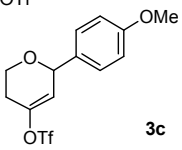
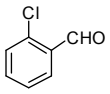
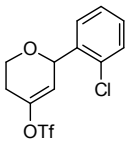
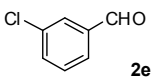
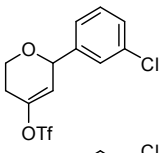
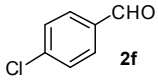
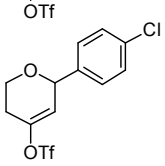
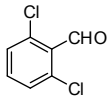
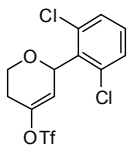
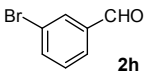
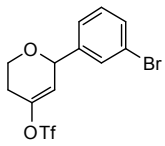
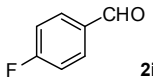
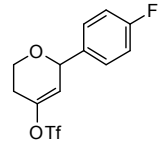
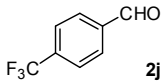
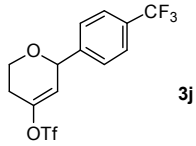
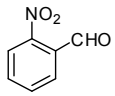
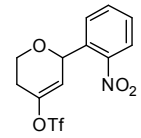
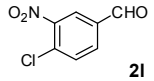
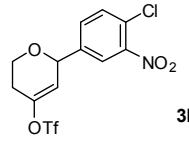
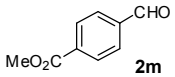
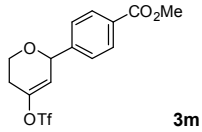
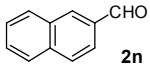
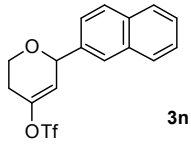
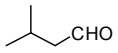
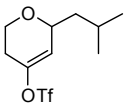
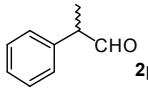
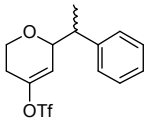
para-chlorobenazaldehydes (entries 4-6) were reacted with alcohol **1**, but the effect is not noticeable. On the other hand, highly sterically hindered 2,6-dichlorobenzaldehyde (entry 7) and 4-chloro-3-nitrobenzaldehyde (entry 12) gave low yields. 4-Methoxybenzaldehyde was found to be decomposed under these reaction conditions. Reaction of **2p** gave two inseparable diastereomers with a ratio of 2:1, which was determined by ^{1}H NMR.

Table 1. Synthesis of dihydropyrans[a]



Entry	Aldehyde **2**	Product **3**	Yield (%)[b]
1	 **2a**	 **3a**	92
2	 **2b**	 **3b**	80
3	 **2c**	 **3c**	d
4	 **2d**	 **3d**	72
5	 **2e**	 **3e**	74
6	 **2f**	 **3f**	75
7	 **2g**	 **3g**	60
8	 **2h**	 **3h**	78
9	 **2i**	 **3i**	70
10	 **2j**	 **3j**	65
11	 **2k**	 **3k**	70
12	 **2l**	 **3l**	61
13	 **2m**	 **3m**	72
14	 **2n**	 **3n**	73
15	 **2o**	 **3o**	67
16	 **2p**	 **3p**	64[b]

[a]Yields refer to isolated yield. Compounds are characterized by IR, NMR and mass spectrometry. d = decomposed. [b]Two inseparable diastereomeric mixture with a ratio of 2:1 determined by ^{1}H NMR.

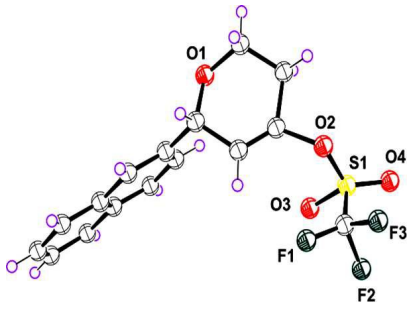


Figure 2. X-ray crystallographic structure of **3n**

The mechanism of the reaction can be explained as follows. The acidic proton activates the aldehyde for nucleophilic attack by homopropargylic alcohols to form oxocarbenium ion **5**, which

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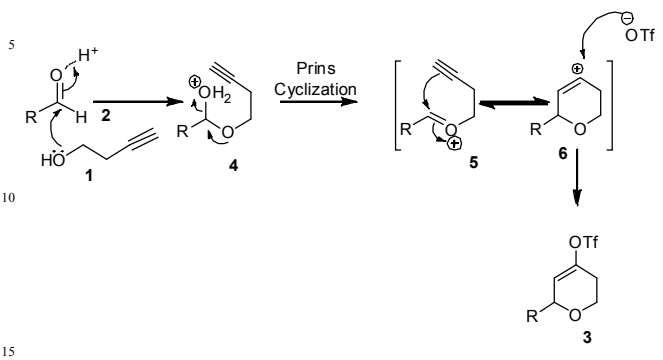
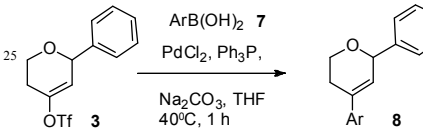
after Prins cyclization generates carbocation 6. The carbocation 6 is then attacked by triflate ion to give dihydropyran 3 (Scheme 1).

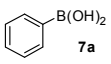
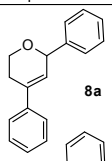
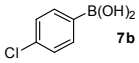
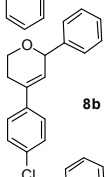
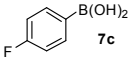
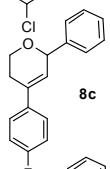
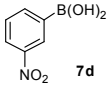
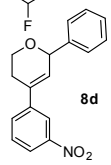
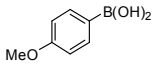
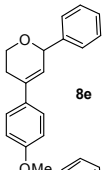
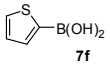
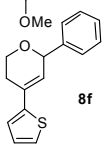


Scheme 1. Mechanism of the reaction

The reaction is further utilized for the synthesis of 4-arylated dihydropyrans. It may be noted that 4-arylated tetrahydropyrans are found in many biologically active natural products.[1] Generally 4-aryl tetrahydropyrans are prepared by Prins-Friedel-Crafts reactions.[23b,c,25] The major drawback of the existing methods is that the electron deficient aromatic rings cannot participate in this reaction. Therefore, use of triflates **3** as an arylating unit *via* Suzuki coupling would be a better alternative for introduction of various aryl groups including both electron donating and electron withdrawing groups. Thus the reaction of **3a** with different aryl and heteroaryl boronic acids **7a-f** under Suzuki coupling conditions afforded 4-aryl- dihydropyrans **8a-f** in good yields (Table 2). Similarly, Heck, Stille and Sonogashira coupling of **3a** produce corresponding coupling products **9**, **10** and **11**, respectively, in excellent yields (Schemes 2-4).

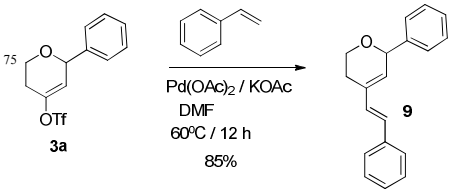
Table 2. Suzuki coupling reaction



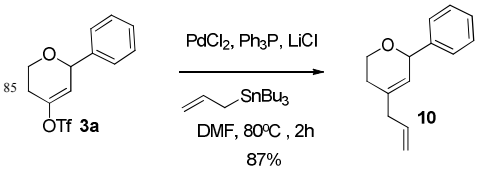
Sl. No.	boronic acid **7**	product **8**	yield (%)[a]
1	 **7a**	 **8a**	95
2	 **7b**	 **8b**	93
3	 **7c**	 **8c**	94
4	 **7d**	 **8d**	91
5	 **7e**	 **8e**	90
6	 **7f**	 **8f**	92

[a]Yields refer to isolated yield. Compounds are caharacterized by IR, NMR spectroscopy and mass spectrometry.

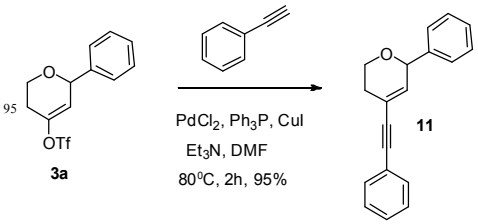
Scheme 2. Heck coupling reaction



Scheme 3. Stille coupling reaction



Scheme 4. Sonogashira coupling reaction



Conclusions

In conclusion, we have developed one pot, three component, mild and efficient method for the synthesis of 4-trifluoromethanesulfonate substituted dihydropyrans *via* Prins cyclization reaction in good yields. The reaction is compatible with a wide range of functional groups such as ester, ether, nitro, and bromo. The aspect of this reaction is that it introduces trifluoromethanesulfonate group at 4-position of the dihydropyrans, which can be used for subsequent coupling reactions such as Suzuki, Heck, Stille and Sonogashira coupling reactions.

Experimental

General Information: All the reagents were of reagent grade (AR grade) and were used as purchased without further

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purification. Silica gel (60-120 mesh size) was used for column chromatography. Reactions were monitored by TLC on silica gel GF_{254} (0.25 mm). Melting points were recorded in an open capillary tube and are uncorrected. Fourier transform-infra red (FT-IR) spectra were recorded as neat liquid or KBr pellets. NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard for ^1H (600 MHz, 400 MHz) or ^{13}C (150 MHz, 100 MHz) NMR. Chemical shifts (δ) are reported in ppm and spin-spin coupling constants (J) are given in Hz. HRMS spectra were recorded using Q-TOF mass spectrometer.

General Procedure for the formation of 4-trifluoromethanesulfonate 3,6-dihydropyan:

To a stirring solution of aldehyde (1.0 equiv) and 3-butyn-1-ol (1.5 equiv) in dry dichloromethane (5.0 mL) was added triflic acid (1.2 equiv) dropwise at 0 ^{0}C. The reaction mixture was brought to room temperature and stirred for a specific time. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluents. After completion of the reaction, the reaction mixture was treated with saturated sodium bicarbonate solution (5.0 mL). The product was extracted with CH_2Cl_2 (2 x 10.0 mL) and washed with brine. Organic layer was separated and dried over anhydrous Na_2SO_4 and evaporated using rotary evaporator to obtain the crude product. The crude product was purified by silica gel column chromatography using ethyl acetate and hexane as eluents to afford the cyclic compounds.

Synthesis of 6-phenyl-3,6-dihydro-2H-pyran-4-yl trifluoromethanesulfonate (3a). To a stirring solution of benzaldehyde (0.1 mL, 1 mmol) and 3-butyn-1-ol (0.11 mL, 1.5 mmol) in CH_2Cl_2 (5 mL) was added TfOH (0.1 mL, 1.2 mmol) dropwise at 0^{0}C. The reaction mixture was brought to room temperature and stirred for 12 h. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluents. After completion of the reaction, CH_2Cl_2 (10 mL) was added and the reaction mixture was washed with saturated sodium bicarbonatesolution and brine solution. The organic layer was separated and dried over anhydrous Na_2SO_4 and evaporated using rotary evaporator to leave the crude product which was purified by column chromatography over silica gel using ethyl acetate and hexane as eluents to give 6-phenyl-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate **3a**; colourless oil; R_f (hexane/ EtOAc 50:1) 0.20; yield 292 mg, 92%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.05 (dd, *J* = 16.0 and 6.0 Hz, 1 H), 2.68-2.73 (m, 1 H), 3.86 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 4.11 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 5.26 (d, *J* = 4.0 Hz, 1 H), 5.93 (s, 1 H), 7.34-7.38 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.5, 63.1, 75.8, 118.7 (q, *J* = 318.0 Hz), 120.2, 127.8, 128.9, 128.9, 139.0, 146.9; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 2.03 (s, -F); IR (KBr, neat) 2929, 2869, 1690, 1455, 1422, 1351, 1246, 1141, 1029, 894, 762 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{12}F_3O_4S$ $(M + H)^+$ 309.0403, found 309.0408.

6-(*p*-Tolyl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3b). Colourless oil; R_f (hexane/ EtOAc 50:1) 0.21; yield 257mg, 80%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3 H), 2.40 (dd, *J* = 12.0 and 4.0 Hz, 1 H), 2.65-2.70 (m, 1 H), 3.83 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 4.11 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 5.22 (d, *J* = 4.0 Hz, 1 H), 5.91 (s, 1 H), 7.18 (d, *J* = 7.2 Hz, 2 H), 7.23 (d, *J* = 7.2 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.3, 28.5, 62.9, 75.5, 118.7 (q, *J* = 318.0 Hz), 120.3, 127.7, 129.6, 136.0, 138.8, 146.8; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 1.99 (s, -F); IR (KBr, neat) 2926, 2866, 1689, 1420, 1349, 1212, 1142, 1071, 899, 816 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{14}F_3O_4S$ $(M + H)^+$ 323.0559, found 323.0565.

6-(2-Chlorophenyl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3d). Colourless oil; R_f (hexane/ EtOAc 50:1) 0.2; yield 246 mg, 72%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.38 (dd, *J* = 12.0 and 4.0 Hz, 1 H), 2.70-2.76 (m, 1 H), 3.88 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 4.16 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 5.70 (d, *J* = 4.0 Hz, 1 H), 5.90 (s, 1 H), 7.24-7.29 (m, 2 H), 7.39 (dd, *J* = 7.2 and 4.0 Hz, 1 H), 7.45 (d, *J* = 7.2 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.4, 63.4, 72.4, 117.4 (q, *J* = 319.5 Hz), 119.7, 127.3, 128.9, 129.9, 130.0, 133.1, 136.4, 147.1; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 2.01 (s, -F); IR (KBr, neat) 2928, 2872, 1690, 1420, 1219, 1142, 1065, 764 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{11}ClF_3O_4S$ (M + H)+ 343.0013, found 343.0010.

6-(3-Chlorophenyl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3e). Colourless oil; R_f (hexane/ EtOAc 50:1) 0.2; yield 253 mg, 74%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.41 (dd, *J* = 12.0 and 4.0 Hz, 1 H), 2.66-2.73 (m, 1 H), 3.86 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 4.11 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 5.24 (d, *J* = 4.0 Hz, 1 H), 5.90 (s, 1 H), 7.21-7.23 (m, 1 H), 7.31-7.32 (m, 2 H), 7.35 (d, *J* = 7.2 Hz, 1 H); ^{13}C NMR (150 MHz, CDCl3) δ 28.4, 63.1, 75.0, 118.7 (q, *J* = 318.0 Hz), 119.7, 125.7, 127.9, 129.0, 130.2, 134.8, 141.1, 147.2; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 2.08 (s, -F); IR (KBr, neat) 2928, 2870, 1689, 1421, 1214, 1142, 1073, 875 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{11}ClF_3O_4S$ (M + H)+ 343.0013, found 343.0035.

6-(4-Chlorophenyl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3f). Colourless oil; R_f (hexane/ EtOAc 50:1) 0.2; yield 256 mg, 75%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.42 (dd, *J* = 12.0 and 6.0 Hz, 1 H), 2.67-2.74 (m, 1 H), 3.86 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 4.16 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 5.25 (d, *J* = 6.0 Hz, 1 H), 5.89 (s, 1 H), 7.28 (d, *J* = 7.2 Hz, 2 H), 7.36 (d, *J* = 7.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 63.0, 74.9, 115.4 (q, *J* = 318.0 Hz), 120.2, 129.0 (2C), 134.6, 137.6, 147.1; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 1.97 (s, -F); IR (KBr, neat) 2929, 2869, 1692, 1421, 1213, 1148, 1091, 1066, 900, 765, 613 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{11}ClF_3O_4S$ $(M + H)^+$ 343.0013, found 343.0017.

6-(2,6-Dichlorophenyl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3g). Colourless oil; R_f (hexane/ EtOAc 50:1) 0.19; yield 225mg, 60%; ^1H NMR (400 MHz, $CDCl_3$) δ 2.38 (dd, *J* = 12.0 and 4.0 Hz, 1 H), 2.81-2.91 (m, 1 H), 3.88 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 4.24 (dd, *J* = 12.0 and 4.0 Hz, 1 H), 5.78 (s, 1 H), 5.97 (s, 1 H), 7.17 (t, *J* = 7.2 Hz, 1 H), 7.31 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.1, 65.2, 72.7, 118.6 (q, *J* = 318.0 Hz), 119.7, 129.6, 130.5, 133.1, 136.1, 146.9; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 1.91 (s, -F); IR (KBr, neat) 2923, 2857, 1659, 1437, 1219, 1119, 1052, 775 cm^{-1}; HRMS

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(ESI) calcd. for $C_{12}H_{10}Cl_2F_3O_4S$ $(M + H)^+$ 376.9623, found 376.9627.

6-(3-Bromophenyl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3h). Colourless oil; R_f (hexane/ EtOAc 50:1) 0.18; yield 301mg, 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (dd, *J* = 12.0 and 4.0 Hz, 1 H), 2.66-2.74 (m, 1 H), 3.87 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 4.11 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 5.24 (d, *J* = 4.0 Hz, 1 H), 5.90 (s, 1 H), 7.25 (d, *J* = 8.0 Hz, 2 H), 7.46-7.51 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.4, 63.1, 74.9, 118.6 (q, *J* = 319.5 Hz), 119.7, 122.9, 126.2, 130.5, 130.8, 131.9, 141.4, 147.2; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 2.04 (s, -F); IR (KBr, neat) 2871, 1690, 1420, 1213, 1141, 1072, 784 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{11}BrF_3O_4S$ $(M + H)^+$ 386.9508, found 386.9520.

6-(4-Fluorophenyl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3i). Colourless oil; R_f (hexane/ EtOAc 50:1) 0.19; yield 228mg, 70%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.41 (dd, *J* = 12.0 and 6.0 Hz, 1 H), 2.67-2.74 (m, 1 H), 3.86 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 4.11 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 5.25 (d, *J* = 6.0 Hz, 1 H), 5.90 (s, 1 H), 7.07 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.4, 63.0, 75.0, 115.7, 118.7 (q, *J* = 318.0 Hz), 119.9, 129.4, 134.9, 147.0, 163.0 (q, *J* = 246.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 2.06 (s, -F); IR (KBr, neat) 2925, 2869, 1690, 1421, 1219, 1141, 1071, 897, 775 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{11}F_4O_4S$ $(M + H)^+$ 327.0309, found 327.0313.

6-(4-(Trifluoromethyl)phenyl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3j). Pale yellow oil; R_f (hexane/ EtOAc 50:1) 0.20; yield 244mg, 65%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.42 (dd, *J* = 18.0 and 6.0 Hz, 1 H), 2.69-2.76 (m, 1 H), 3.90 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 4.14 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 5.33 (d, *J* = 6.0 Hz, 1 H), 5.92 (s, 1 H), 7.48 (d, *J* = 8.0 Hz, 2 H), 7.66 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.4, 63.3, 75.1, 118.7 (q, *J* = 319.5 Hz), 119.5, 121.9, 124.1 (q, *J* = 270.0 Hz), 126.0, 128.0, 130.3, 143.0, 147.3; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 2.20 (s, -F), 13.27 (s, -F); IR (KBr, neat) 2928, 2872, 1622, 1421, 1327, 1216, 1130, 1069, 858, 792 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{11}F_6O_4S$ $(M + H)^+$ 377.0277, found 377.0249.

6-(2-Nitrophenyl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3k). Yellow oil; R_f (hexane/ EtOAc 50:1) 0.25; yield 247mg, 70%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.39 (dd, *J* = 18.0 and 6.0 Hz, 1 H), 2.79-2.85 (m, 1 H), 3.91 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 4.22 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 5.86 (d, *J* = 6.0 Hz, 1 H), 6.02 (s, 1 H), 7.50 (t, *J* = 7.2 Hz, 1 H), 7.66 (d, *J* = 7.2 Hz, 1 H), 7.73 (d, *J* = 7.2 Hz, 1 H), 7.98 (d, *J* = 7.2 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.3, 63.9, 71.4, 118.6 (q, *J* = 318.0 Hz), 119.9, 124.8, 129.3, 129.4, 133.9, 134.6, 147.1, 148.2; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 1.97 (s, -F); IR (KBr, neat) 2929, 2873, 1689, 1531, 1419, 1353, 1211, 1141, 1073, 901, 789, 751 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{11}F_3NO_6S$ $(M + H)^+$ 354.0259, found 354.0259.

6-(4-Chloro-3-nitrophenyl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3l). Yellow oil; R_f (hexane/ EtOAc 50:1) 0.25; yield 236mg, 61%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.44 (dd, *J* = 18.0 and 6.0 Hz, 1 H), 2.70-2.76 (m, 1 H), 3.90 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 4.13 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 5.33 (d, *J* = 4.0 Hz, 1 H), 5.90 (s, 1 H), 7.51 (d, *J* = 7.2 Hz, 1 H), 7.57 (d, *J* = 7.2 Hz, 1 H), 7.89 (d, *J* = 7.2 Hz, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.3, 63.3, 74.0, 118.6, 118.7 (q, *J* = 318.0 Hz), 124.6, 127.3, 131.9, 132.5, 139.8, 147.8, 148.2; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 2.1 (s, -F); IR (KBr, neat) 2927, 2873, 1690, 1539, 1421, 1353, 1214, 1141, 1073, 888, 792 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_9F_3NO_6SNa$ $(M + Na)^+$ 409.9689, found 409.9691.

Methyl 4-(4-(((trifluoromethyl)sulfonyl)oxy)-3,6-dihydro-2*H*-pyran-2-yl)benzoate (3m). Colourless oil; R_f (hexane/ EtOAc 50:1) 0.23; yield 263 mg, 72%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.41 (dd, *J* = 16.0 and 6.0 Hz, 1 H), 2.68-2.74 (m, 1 H), 3.88 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 3.91 (s, 3 H), 4.12 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 5.31 (s, 1 H), 5.91 (s, 1 H), 7.42 (d, *J* = 7.2 Hz, 2 H), 8.04 (d, *J* = 7.2 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.4, 52.4, 63.2, 75.2, 118.6 (q, *J* = 319.5 Hz), 119.7, 127.5, 130.2, 130.6, 144.0, 147.1, 166.8; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 2.07 (s, -F); IR (KBr, neat) 2925, 2850, 1725, 1690, 1418, 1282, 1213, 1142, 1113, 1072, 860, 771 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{14}F_3O_6S$ $(M + H)^+$ 367.0458, found 367.0465.

6-(Naphthalen-2-yl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3n). Colourless solid; mp 71-73 °C R_f (hexane/ EtOAc 50:1) 0.20; yield 261mg, 73%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.42 (dd, *J* = 12.0 and 4.0 Hz, 1 H), 2.67-2.83 (m, 1 H), 3.86 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 4.10 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 5.39 (d, *J* = 4.0 Hz, 1 H), 5.99 (s, 1 H), 7.43 (d, *J* = 8.0 Hz, 1 H), 7.47-7.50 (m, 2 H), 7.77 (s, 1 H), 7.81-7.85 (m, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.5, 62.9, 75.7, 118.7 (q, *J* = 318.0 Hz), 120.1, 125.2, 126.5, 126.6, 127.0, 127.9, 128.3, 128.9, 133.3, 133.5, 136.4, 147.0; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 2.04 (s, -F); IR (KBr, neat) 2976, 2868, 1689, 1464, 1422, 1244, 1114, 1058, 886, 757 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{14}F_3O_4S$ $(M + H)^+$ 359.0559, found 359.0564.

6-Isobutyl-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (3o). Colourless oil; R_f (hexane/ EtOAc 50:1) 0.20; yield 193mg, 67%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.93 (s, 3 H), 0.94 (s, 3 H), 1.27-1.32 (m, 1 H), 1.55-1.60 (m, 1 H), 1.79-1.87 (m, 1 H), 2.26 (dd, *J* = 12.0 and 4.0 Hz, 1 H), 2.58-2.64 (m, 1 H), 3.71 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 4.09 (ddd, *J* = 12.0, 6.0 and 6.0 Hz, 1 H), 4.27 (d, *J* = 6.0 Hz, 1 H), 5.72 (s, 1 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 22.1, 23.3, 24.5, 28.6, 43.8, 63.2, 71.9, 117.6 (q, *J* = 318.0 Hz), 121.2, 146.4; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 2.05 (s, -F); IR (KBr, neat) 2960, 2872, 1690, 1442, 1211, 1143, 1072, 884, 614 cm^{-1}; HRMS (ESI) calcd. for $C_{10}H_{16}F_3O_4S$ $(M + H)^+$ 289.0721, found 289.0715.

6-(1-Phenylethyl)-3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonate (diastereomeric mixture, 2:1, 3p). Colourless oil; R_f (hexane/ EtOAc 50:1) 0.20; yield 215mg, 64%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (d, *J* = 4.0 Hz, 3 H, minor), 1.35 (d, *J* = 8.0 Hz, 3 H, major), 2.07-2.12 (m, 1 H, minor), 2.16-

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2.24 (m, 1 H, major), 2.56-2.64 (m, 1 H), 2.82-2.89 (m, 1 H, major), 3.08-3.15 (m, 1 H, minor), 3.62-3.71 (m, 1 H), 4.09-4.13 (m, 1 H), 4.24-4.26 (m, 1 H, major), 4.36-4.37 (m, 1 H, minor), 5.54 (s, 1 H, major), 5.68 (s, 1 H, minor), 7.20-7.26 (m, 3 H), 7.29-7.35 (m, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 15.0, 17.0, 28.4, 43.6, 44.7, 63.4, 63.8, 78.1, 78.2, 118.6 (q, J = 319.5 Hz), 119.7, 126.9, 127.0, 128.0, 128.1, 128.6, 128.7, 142.1, 142.9, 147.0, 147.3; ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ 1.9 (s, -F); IR (KBr, neat) 2972, 2873, 1690, 1420, 1213, 1143, 1073, 891, 763 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{16}F_3O_4S$ $(M + H)^+$ 337.0716, found 337.0722.

General procedure of Suzuki coupling reaction.

To a solution of **3** (1.0 mmol) in THF (4.0 mL) were added PPh_3 (5 mol %), $PdCl_2$ (5 mol %), boronic acid **7** (1.56 mmol) and 2M aqueous solution of Na_2CO_3 (2.0 mL) under inert atmosphere. The reaction mixture was stirred at 40 ^{0}C for 1hr. Then water was added to reaction mixture and extracted with EtOAc (3×10 mL). Combined organic layer was dried and concentrated under reduced pressure. Residue obtained was purified by silica gel column chromatography using EtOAc/hexane as eluent to furnish the compound **8**.

Synthesis of 4,6-Diphenyl-3,6-dihydro-2*H*-pyran (8a). To a solution of 3,6-dihydro-2-phenyl-2H-pyran-4-yl trifluoromethanesulfonate **3a** (308 mg, 1 mmol) in THF (4.0 mL) were added PPh_3(14 mg, 5 mol %), $PdCl_2$ (9 mg, 5 mol%), phenyl boronic acid **7a** (183 mg, 1.56 mmol) and 2M aqueous solution of Na_2CO_3 (2.0 mL) under inert atmosphere. The reaction mixture was stirred at 40 ^{o}C for 1h. Then water was added to reaction mixture and extracted with EtOAc (3×10 mL). Combined organic layer was dried and concentrated under reduced pressure. Residue obtained was purified by silica gel column chromatography using EtOAc/hexane as eluent to furnish the 2,4-diphenyl-3,6-dihydro-2*H*-pyran as a yellow oil; R_f (hexane/ EtOAc 50:1) 0.3; yield 224 mg, 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49 (dd, J = 12.0 and 4.0 Hz, 1 H), 2.71-2.80 (m, 1 H), 2.92 (ddd, J = 12.0, 8.0 and 4.0 Hz, 1 H), 4.19 (ddd, J = 12.0, 8.0 and 4.0 Hz, 1 H), 5.31 (d, J = 4.0 Hz, 1 H), 6.22 (s, 1 H), 7.27-7.39 (m, 6 H), 7.41-7.45 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2, 63.6, 76.9, 125.1, 125.5, 127.7, 127.8, 128.2, 128.6, 128.7, 135.0. 140.2, 141.5; IR (KBr, neat) 2924, 2853, 1600, 1493, 1263, 1120, 1029, 771 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{17}O$ $(M + H)^+$ 237.1274, found 237.1277.

4-(4-Chlorophenyl)-6-phenyl-3,6-dihydro-2*H*-pyran (8b). Pale yellow oil; R_f (hexane/ EtOAc 50:1) 0.28; yield 251 mg, 93%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (dd, J = 12.0 and 4.0 Hz, 1 H), 2.67-2.76 (m, 1 H), 3.91 (ddd, J = 12.0, 8.0 and 4.0 Hz, 1 H), 4.19 (ddd, J = 12.0, 8.0 and 4.0 Hz, 1 H), 5.29 (d, J = 4.0 Hz, 1 H), 6.20 (s, 1 H), 7.29-7.42 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2, 63.5, 76.8, 126.1, 126.4, 127.7, 128.2, 128.8 (2C), 133.5, 134.0, 138.6. 141.2; IR (KBr, neat) 2924, 2853, 1598, 1493, 1368, 1177, 1074, 762 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{16}ClO$ $(M + H)^+$ 271.0884, found 271.0886.

4-(4-Fluorophenyl)-6-phenyl-3,6-dihydro-2*H*-pyran (8c). Pale yellow oil; R_f (hexane/ EtOAc 50:1) 0.25; yield 238 mg, 94%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.45 (dd, J = 16.0 and 4.0 Hz, 1 H), 2.68-2.77 (m, 1 H), 3.92 (ddd, J = 12.0, 8.0 and 4.0 Hz, 1 H), 4.19 (ddd, J = 12.0, 8.0 and 4.0 Hz, 1 H), 5.30 (d, J = 4.0 Hz, 1 H), 6.16 (s, 1 H), 7.03 (t, J = 8.0 Hz, 2 H), 7.29-7.43 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.3, 63.6, 76.9, 115.5 (d, J = 21.0 Hz), 125.4, 126.3 (d, J = 8.0 Hz), 127.8, 128.2, 128.7, 134.1, 136.3 (d, J = 3.3 Hz), 141.3, 162.5 (d, J = 245.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$/TFA) δ -39.2 (s, -F); IR (KBr, neat) 2925, 2854, 1601, 1451, 1275, 1231, 1160, 1071, 836, 700 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{16}FO$ $(M + H)^+$ 255.1180, found 255.1185.

4-(3-Nitrophenyl)-6-phenyl-3,6-dihydro-2*H*-pyran (8d). Yellow oil; R_f (hexane/ EtOAc 50:1) 0.30; yield 255 mg, 91%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (dd, J = 16.0 and 4.0 Hz, 1 H), 2.76-2.85 (m, 1 H), 3.96 (ddd, J = 12.0, 8.0 and 4.0 Hz, 1 H), 4.25 (ddd, J = 12.0, 8.0 and 4.0 Hz, 1 H), 5.34 (d, J = 4.0 Hz, 1 H), 6.38 (s, 1 H), 7.31-7.43 (m, 5 H), 7.52 (t, J = 8.0 Hz, 1 H), 7.76 (t, J = 8.0 Hz, 1 H), 8.13 (d, J = 8.0 Hz, 1 H), 8.28 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.0, 63.4, 76.8, 119.9, 122.4, 127.6, 128.4, 128.8, 129.6, 130.9, 133.1, 140.8, 141.8, 148.7; IR (KBr, neat) 2924, 2855, 1528, 1453, 1349, 1269, 1121, 1063, 892, 737 cm^{-1}; HRMS (ESI) calcd. for $C_{17}H_{16}NO_3$ $(M + H)^+$ 282.1125, found 282.1130.

Synthesis of 4-(4-methoxyphenyl)-6-phenyl-3,6-dihydro-2*H*-pyran (8e). A mixture of **3a** (308 mg, 1.0 mmol), aqueous sodium carbonate (1.4 mL, 2.80 mmol), lithium chloride (125 mg, 2.98 mmol), $Pd(Ph_3P)_4$ (23 mg, 0.02 mmol), 4-methoxyphenylboronic acid (166 mg, 1.09 mmol), and THF (5 mL) was refluxed for 3 h. After completion of the reaction the solvent was removed by evaporation; water was added and the mixture was extracted with ethyl acetate (2x10 mL). Combined organic layer was dried and concentrated under reduced pressure. The product was purified by column chromatography on silica gel (ethyl acetate/hexane, 1/4) to give **8e** as a pale yellow oil; R_f (hexane/ EtOAc 50:1) 0.40; yield 239 mg, 90%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.51 (dd, J = 16.0 and 6.0 Hz, 1 H), 2.68-2.74 (m, 1 H), 3.80 (s, 3 H), 3.91 (ddd, J = 12.0, 8.0 and 4.0 Hz, 1 H), 4.17 (ddd, J = 12.0, 8.0 and 4.0 Hz, 1 H), 5.29 (d, J = 4.0 Hz, 1 H), 6.12 (s, 1 H), 6.88 (d, J = 8.0 Hz, 2 H), 7.30 (t, J = 8.0 Hz, 1 H), 7.34-7.38 (m, 4 H), 7.42 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 27.3, 55.5, 63.7, 76.9, 114.0, 123.8, 126.2, 127.8, 128.1, 128.7, 132.8, 134.4, 141.7, 159.4; IR (KBr, neat) 2957, 2836, 1607, 1456, 1309, 1248, 1180, 1062, 1034, 832, 761, 700 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{19}O_2$ $(M + H)^+$ 267.1385, found 267.1385.

6-Phenyl-4-(thiophen-2-yl)-3,6-dihydro-2*H*-pyran (8f). Yellow oil; R_f (hexane/ EtOAc 50:1) 0.30; yield 222 mg, 92%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49 (dd, J = 16.0 and 4.0 Hz, 1 H), 2.71-2.78 (m, 1 H), 3.90 (ddd, J = 16.0, 8.0 and 4.0 Hz, 1 H), 4.15 (ddd, J = 12.0, 8.0 and 4.0 Hz, 1 H), 5.28 (d, J = 4.0 Hz, 1 H), 6.20 (s, 1 H), 6.99 (t, J = 8.0 Hz, 1 H), 7.03 (d, J = 8.0 Hz, 1 H), 7.17 (d, J = 8.0 Hz, 1 H), 7.30 (d, J = 8.0 Hz, 1 H), 7.32-7.42 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.6, 63.3, 76.6, 122.5, 124.1, 127.5, 127.8, 128.2, 128.7, 129.7, 141.1, 144.8; IR (KBr, neat) 2924, 2854, 1639, 1453, 1361, 1263, 1116, 1062, 879, 698 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{15}OS$ $(M + H)^+$ 243.0844, found 243.0851.

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(*E*)-6-Phenyl-4-styryl-3,6-dihydro-2*H*-pyran (9). To a solution of **3** (308 mg, 1.0 mmol) in DMF (10 mL) were added $Pd(OAc)_2$ (11 mg, 5 mol%) and AcOK (196 mg, 2 mmol) under inert atmosphere. The reaction mixture was stirred at 60 ^{0}C for overnight. Then water was added to reaction mixture and extracted with EtOAc (3×10 mL). Combined organic layer was dried and concentrated under reduced pressure. Residue obtained was purified by silica gel column chromatography using EtOAc/Pet. ether as eluent to furnish the compound **9** as yellow oil; R_f (hexane/ EtOAc 50:1) 0.35; yield 222 mg, 85%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (dd, *J* = 12.0 and 4.0 Hz, 1 H), 2.53-2.62 (m, 1 H), 3.87 (ddd, *J* = 16.0, 8.0 and 4.0 Hz, 1 H), 4.15 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 5.27 (d, *J* = 4.0 Hz, 1 H), 5.92 (s, 1 H), 6.57 (d, *J* = 16.0 Hz, 1 H), 6.81 (d, *J* = 16.0 Hz, 1 H), 7.20-7.25 (m, 1 H), 7.30-7.43 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.0, 63.4, 76.9, 126.5, 127.3, 127.6, 127.7, 128.2, 128.7, 128.8, 130.2, 130.5, 134.2, 137.4, 141.3; IR (KBr, neat) 2924, 2853, 1593, 1492, 1274, 1118, 1092, 1012, 830, 699 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{19}O$ $(M + H)^+$ 263.1430, found 263.1436.

Synthesis of 4-allyl-6-phenyl-3,6-dihydro-2*H*-pyran (10). A dried reaction tube was charged with triflate **3** (308 mg, 1mmol). To this PPh_3 (14 mg, 5 mol%), $PdCl_2$ (9 mg, 5 mol %) was added and reaction tube was evacuated. Then LiCl (126 mg, 3 mmol), dry DMF (10 mL) and allyltributylstannane (397 mg, 1.21mmol) were added under nitrogen atmosphere. Reaction mixture was heated at 80 ^{0}C for 2 h. Reaction was quenched with saturated NH_4Cl solution and extracted with EtOAc (4×5 mL). Combined organic layer was dried and concentrated under reduced pressure. Residue obtained was purified by silica gel column chromatography using EtOAc/hexane as eluent to furnish 4-allyl-3,6-dihydro-2-phenyl-2*H*-pyran **10** (174 mg, 87%) as yellow oil; R_f (hexane/ EtOAc 50:1) 0.35; yield 174 mg, 87%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98 (dd, *J* = 16.0 and 4.0 Hz, 1 H), 2.25-2.33 (m, 1 H), 2.80 (d, *J* = 8.0 Hz, 2 H), 3.78 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 4.02 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 5.05-5.12 (m, 3 H), 5.56 (s, 1 H), 5.76-5.87 (m, 1 H), 7.27-7.37 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.4, 41.7, 63.5, 76.4, 116.8, 124.0, 127.6, 127.9, 128.6, 135.3, 135.7, 141.9; IR (KBr, neat) 2924, 2854, 1689, 1450, 1364, 1220, 1075, 771 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{17}O$ $(M + H)^+$ 201.1274, found 201.1277.

Synthesis of 6-phenyl-4-(phenylethynyl)-3,6-dihydro-2*H*-pyran (11). A dried reaction flask was charged with triflate **3** (308 mg, 1.0 mmol). To this PPh_3 (14 mg, 5 mol %), $PdCl_2$ (9 mg, 5 mol %), CuI (19 mg, 1 mol %) were added and the reaction flask was evacuated. Then Et_3N (2.5 mL, 18 mmol), dry DMF (10 mL) and phenyl acetylene (0.17 ml, 1.58 mmol) were added under nitrogen atmosphere. Reaction mixture was heated at 80 ^{0}C for 2 h. Reaction was quenched with saturated NH_4Cl solution and extracted with EtOAc (4×5 mL). Combined organic layer was dried and concentrated under reduced pressure. Residue obtained was purified by silica gel column chromatography using EtOAc/hexane as eluent to furnish the *6-phenyl-4-(phenylethynyl)-3,6-dihydro-2H-pyran* **11** (247 mg, 95 %) as yellow oil; R_f (hexane/ EtOAc 50:1) 0.35; yield 247mg, 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (dd, *J* = 12.0 and 4.0 Hz, 1 H), 2.53-2.62 (m, 1 H), 3.83 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 4.06 (ddd, *J* = 12.0, 8.0 and 4.0 Hz, 1 H), 5.23 (d, *J* = 4.0 Hz, 1 H), 6.25 (s, 1 H), 7.28-7.32 (m, 4 H), 7.33-7.40 (m, 4 H), 7.42-7.45 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.2, 63.2, 76.6, 89.1, 89.2, 119.6, 123.3, 127.7, 128.3, 128.4, 128.5, 128.8, 131.7, 135.2, 140.6; IR (KBr, neat) 2919, 2850, 1597, 1490, 1450, 1253, 1120, 1062, 756, 699 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{17}O$ $(M + H)^+$ 261.1274, found 261.1279.

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Notes and references

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1 (a) X. Tian and S. D. Rychnovsky, *Org. Lett*., 2007, **9**, 4955-4958; (b) T. Washio, H. Nambu, M. Anada and S. Hashimoto, *Tetrahedron: Asymmetry*, 2007, **18**, 2606-2612.

2 S. M. Ringel, R. C. Greenough, S. Roemer, D. Connor, A. L. Gutt, B. Blair, G. Kanter and M. von Strandtmann, *J. Antibiot*., 1977, **30**, 371-375.

3 (a) Y. Funahashi, N. Kawamura and T. Ishimaru, JP Patent 08231551 [A296090], 1996; (b) M. H. Su, M. I. Hosken, B. J. Hotovec and T. L. Johnston, US Patent 5728727 [A980317], 1998; (c) H. B.; Bode and A. Zeeck, *J. Chem. Soc., Perkin Trans. 1,* 2000, 2665-2670.

4 (a) T. Yasumoto and M. Murata, *Chem. Rev.*, 1993, **93**, 1897-1909; (b) D. J. Faulkner, *Nat. Prod. Rep*., 1984, **1**, 251 and 551; (c) R. E. Moore, In *Marine Natural Products*; Scheuer, P. J., Ed.; Academic Press: New York, 1978; Vol. 1, pp 43-121.

5 (a) M. R. Lambu, S. Kumar, S. K. Yousuf, D. K. Sharma, A. Hussain, A. Kumar, F. Malik and D. Mukherfee, *J. Med. Chem*., 2013, **56**, 6122-6135; (b) D. S. Reddy, B. Padhi and D. K. Mohapatra, *J. Org. Chem*., 2015, **80**, 1365-1374; (c) S. Sultana, K. Indukuri, M. J. Deka and A. K. Saikia, *J. Org. Chem*., 2013, **78**, 12182-12188.

6 (a) P. A. Wender, S. G. Hegde, R. D. Hubbard and L. Zhang, *J. Am. Chem. Soc*., 2002, **124**, 4956-4957.

7 T. Nagasawa and S. Kuwahara, *Org. Lett*., 2009, **11**, 761-764.

8 (a) L. Yet, *Chem. Rev*., 2000, **100**, 2963–3007; (b) T. L. B. Boivin, *Tetrahedron*, 1987, **43**, 3309–3362; (c) L. Coppi, A. Ricci and M. Taddei, *J. Org. Chem*., 1988, **53**, 911–913; (d) C.-J. Li and W.-C. Zhang, *Tetrahedron*, 2000, **56**, 2403–2411; (e) B. Schmidt and M. Westhus, *Tetrahedron*, 2000, **56**, 2421–2421; (f)

View Article Online
DOI: 10.1039/C6RA02343F

M. Pham, A. Allatabakhsh and T. G. Minehan, *J. Org. Chem*., 2008, **73**, 741–744; (g) P. O. Miranda, D. V. Diaz, J. I. Padrón, J. Bermejo and V. S. Martin, *Org. Lett*. 2003, **5**, 1979-1982.

9 (a) B. S. Donslund, A. Monleón, L. Ibsen and K. A. Jørgensen, *Chem. Commun*., 2015, **51**, 13666-13669; (b) D. J. Mack, B. Guo and J. T. Njardarson, *Chem. Commun*., 2012, **48**, 7844-7846; (c) P. V. Chouthaiwale and F. Tanaka, *Chem. Commun*., 2014, **50**, 14881-14884; (d) L. M. Mori-Quiroz and R. E. Jr. Maleczka, *J. Org. Chem*., 2015, **80**, 1163-1191; (e) S. Sun, C. Cheng, J. Yang, A. Tahery, D. Jiang, B. Zhang and Y. Gu, *Org. Lett*., 2014, **16**, 4520-4523; (f) G. R. Peh and P. E. Floreancig, *Org. Lett*., 2015, **17**, 3750-3753; (g) M. Isobe, W.C. Chang, P.-K. Tsou, C. Ploysuk and C.-H. J. Yu, *Org. Lett*., 2015, **80**, 6222-6237; (h) C. F. Weise, V. H. Lauridsen, R. S. Rambo, E. H. Iversen, M.-L. Olsen and K. A. Jørgensen, *J. Org. Chem*., 2014, **79**, 3537-3546.

10 P. J. Stang and A. G. Anderson, *J. Am. Chem. Soc*., 1978, **100**, 1520-1525.

11 (a) N. Miyaura and A. Suzuki, *Chem. Rev*., 1995, **95**, 2457-2483; (b) N. Marion, O. Navarro, J. Mei, E. D. Stevens, N. M. Scott and S. P. Nolan, *J. Am. Chem. Soc.*, 2006, **128**, 4101–4111; (c) K. Umei, Y. Nishigaya, M. Kamiya, Y. Kohno and S. Seto, *Synthesis*, 2015, **47**, 3221-3230.

12 G. T. Crisp and P. T. Glink, *Tetrahedron*, 1992, **48**, 3541-3556.

13 S. P. H, Mee, V. Lee and J. E. Baldwin, *Angew. Chem. Int. Ed.,* 2004, 43, 1132-1136.

14 X.-F. Wu, B. Sundararaju, H. Neumann, P. H. Dixneuf and M. Beller, *Chem. Eur. J.*, 2011, **17**, 106-110.

15 (a) S. Sako, T. Kurahashi and S. Matsubara, *Chem. Commun*., 2011, **47**, 6150–6152; (b) Z. Li, H. Jung, M. Park, M. S. Lah, and S. Koo, *Adv. Synth. Catal*., 2011, **353**, 1913–1917; (c) K. Fujiwara, T. Kurahashi and S. Matsubara, *J. Am. Chem. Soc*., 2012, **134**, 5512–5515; (d) W. Chaladaj, R. Kowalczyk and J. Jurczak, *J. Org. Chem*., 2010, **75**, 1740–1743; (e) K. Mal, S. Das, N. C. Maiti, R. Natarajan and I. Das, *J. Org. Chem*., 2015, **80**, 2972–2988.

16 (a) B. Schmidt and H. Wildemann, *J. Org. Chem.*, 2000, **65**, 5817–5822; (b) H. Wildemann, P. Dünkelmann, M. Müller and B. Schmidt, *J. Org. Chem.*, 2003, **68**, 799–804; (c) M. Donnard, T. Tschamber, D. L. Nouën, S. Desrat, K. Hinsinger and J. Eustache, *Tetrahedron*, 2011, **67**, 339–357.

17 (a) R. F. de la Pradilla and M. Tortosa, *Org. Lett*., 2004, **6**, 2157–2160; (b) R. F. de la Pradilla, M. Tortosa, N. Lwoff, M. A. del Águila and A. Viso, *J. Org. Chem*., 2008, **73**, 6716–6727.

18 (a) S. Bonbdalapati, U. C. Reddy, P. Saha, and A. K. Saikia, *Org. Biomol. Chem*., 2011, **9**, 3428–3438; (b) P. Saha, P. Ghosh, S. Sultana, and A. K. Saikia, *Org. Biomol. Chem*., 2012, **10**, 8730–8738.

19 (a) H. Huang, and J. S. Panek, *J. Am. Chem. Soc*., 2000, **122**, 9836-9837; (b) W. Yao, X. Dou and Y. Lu, *J. Am. Chem. Soc*., 2015, **137**, 54-57.

20 P. Ghosh, P. Saha, S. Bondalapati, K. Indukuri, and A. K. Saikia, *J. Org. Chem*., 2014, **79**, 4119-4124.

21 (a) E. Arundale and L. A. Mikeska, *Chem. Rev*., 1952, **52**, 505-555; (b) D. R. Adams and S. P. Bhatnagar, *Synthesis*, 1977, 661-672; (c) B. B. Snider, In *The Prins Reaction and Carbonyl Ene Reactions*; Trost, B. M.; Fleming, I.; Heathcock, C. H.; Eds.; Pergamon Press: New York, 1991; Vol. 2, pp 527-561; (d) L. E. Overman and L. D. Pennington, *J. Org. Chem*., 2003, **68**, 7143-7157; (e) V. K. Yadav and N. V. Kumar, *J. Am. Chem. Soc*., 2004, **126**, 8652–8653; (f) J. S. Yadav, N. Thrimurtulu, K. A. Lakshmi, A. R. Prasad, and B. V. S. Reddy, *Tetrahedron Lett.*, 2010, **51**, 661–663; (g) S. R. Crosby, J. R. Harding, C. D. King, G. D. Parker and C. L. Willis, *Org. Lett*., 2002, **4**, 577–580; (h) P. O. Miranda, R. M. Carballo, V. S. Martin and J. I. Padrón, *Org. Lett*., 2009, **11**, 357-360; (i) P. O. Miranda, M. A. Ramírez, V. S. Martin and J. I. Padrón, *Org. Lett*., 2006, **8**, 1633-1636.

22 (a) J. C. Warner, A. S. Cannon and K. M. Dye, *Environment Impact Assesment Review*, 2004, **24**, 775-799; (b) P. A. Clarke, S. Santos and W. H. C. Martin, *Green Chem*., 2007, **9**, 438-440.

23 (a) U. C. Reddy, B. R. Raju, E. K. P. Kumar and A. K. Saikia, *J. Org. Chem*., 2008, **73**, 1628-1630; (b) U. C. Reddy, S. Bondalapati and A. K. Saikia, *Eur. J. Org. Chem*., 2009, 1625-1629; (c) U. C. Reddy, S. Bondalapati and A. K. Saikia, *J. Org. Chem*., 2009, **74**, 2605-2608; (d) M. Borah, P. Gogoi, K. Indukuri and A. K. Saikia, *J. Org. Chem*., 2015, **80**, 2641-2648; (e) A. K. Saikia, K. Indukuri and J. Das, *Org. Biomol. Chem*., 2014, **12**, 7026-7035; (f) K. Indukuri, R. Unnava, M. J. Deka, and A. K. Saikia, *J. Org. Chem*., 2013, **78**, 10629-10641; (g) P. Gogoi, V. K. Das and A. K. Saikia, *J. Org. Chem*., 2014, **79**, 8592-8598.

24 The crystallographic data for compound 3n has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1433323.

25 (a) X. Tian, J. James, J. J. Jaber and S. D. Rychnovsky, *J. Org. Chem.*, 2006, **71**, 3176–3183; (b) M. R. Dintzner, J. J. Maresh, C. R. Kinzie, A. F. Arena and T. Speltz, *J. Chem. Educ*., 2012, **89**, 265−267; (c) K. Indukuri, S. Bondalapati, T. Kotipalli, P. Gogoi, and A. K. Saikia, *Synlett*., 2012, **23**, 233-238; (d) U. C. Reddy, and A. K. Saikia, *Synlett.,* 2010, 1027-1032; (e) M. R. Dintzner, *Synlett.,* 2013, **24**, 1091-1092.

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Graphical Abstract

Synthesis of 4-trifluoromethanesulfonate substituted 3,6-dihydropyrans and their application in various C-C coupling reactions

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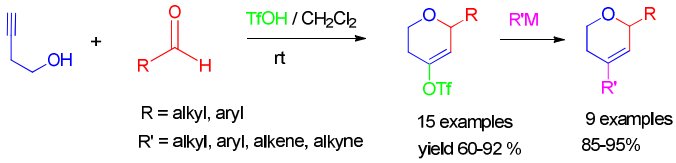

One-pot, three component reaction of homopropargylic alcohols with aldehydes and triflic acid afforded 3,6-dihydro-2*H*-pyran-4-yl trifluoromethanesulfonates via Prins cyclization reaction in good yields. The dihydropyran thus formed is transformed into different 4-alkyl and aryl substituted products using Suzuki, Heck, Stille and Sonogashira coupling reactions.