Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2011, **9**, 3428

www.rsc.org/obc

PAPER

An efficient synthesis of dihydro- and tetrahydropyrans *via* oxonium–ene cyclization reaction†

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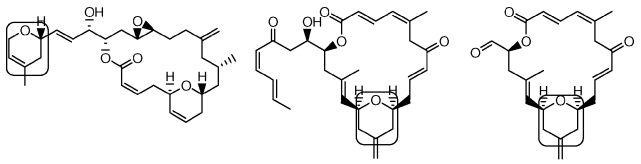
Received 6th January 2011, Accepted 16th February 2011
DOI: 10.1039/c1ob00033k

An efficient method has been developed for the synthesis of 2,3-dihydropyrans and 4-methylenetetrahydropyrans from aldehydes and substituted homoallyl alcohols in benzene mediated by boron trifluoride etherate in good yields. The reaction proceeds *via* oxonium–ene reaction.

Introduction

Oxonium–ene reactions are powerful tools for the construction of various cyclic ethers.[1] Mikami and coworkers have made an extensive study on oxonium–ene cyclization reactions.[2] Recently, several oxygen containing heterocyclic compounds have been synthesized using this protocol.[1,2] Among these, the tetrahydropyran unit is considered to be interesting as they are found in many biologically active natural products and pharmaceuticals.[3] The synthesis of dihydropyrans and 4-methylene tetrahydropyrans are synthetically attractive since the olefin function can be further functionalized to obtain polysubstituted tetrahydropyrans.[4] These units are also present in macrolide natural products such as laulimalide **1**, (–)-zampanolide **2**, and (–)-dactylolide **3** as shown in Fig. 1.[1d,5] The 2-alkyl-4-aryldihydropyrans are used as a flavoring or aroma material for food and other products.[6] On the other hand, the 4-amido-tetrahydropyran unit is found in many biologically active molecules and natural products such as ambruticins VS, glycamino acid, sialic acid, and others.[7] The 4-amidotetrahydropyran **4** exhibits anti diabetic properties (Fig. 1).[8] 4-Aminotetrahydropyrans are also used as a photosensitive materials in photographic films,[9] and have been found to be melanocortin receptor agonists.[10] There are a few methods in the literature for the synthesis of 4-substituted dihydropyrans.[11] In most of the cases Lewis acids are used and the products are 4-halogenated dihydropyrans. The synthesis of 4-aryl or alkyl substituted dihydropyrans is limited.[12] These methods suffer from disadvantages such as low yield and multistep synthesis. Loh and coworkers have reported the synthesis of 4-methylene tetrahydropyrans from 1,1-disubstituted homoallylic alcohols and aldehydes *via* oxonium–ene cyclization reaction using indium triflate as catalyst.[1d] The reaction is not diastereoselective and provides *cis* and *anti* isomers with different



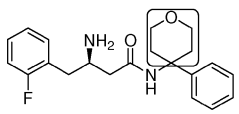


Fig. 1

ratios. We now report a diastereoselective methodology for the synthesis of dihydro- and tetrahydropyrans from 1,1-disubstituted homolallylic alcohols and aldehydes *via* oxonium–ene cyclization reaction mediated by boron trifluoride etherate. The synthesis of 4-amidotetrahydropyrans is also accomplished using the same protocol.

Results and discussion

In continuation of our interest in oxygen heterocyclic compounds,[13] we were in search of an efficient method for the synthesis of 4-alkyl/aryl substituted-dihydropyrans and 4-methylene tetrahydropyrans. It is known in the literature that the reaction of carbonyl compounds with simple homoallylic and monosubstituted homoallylic alcohols gives tetrahydropyrans under Prins cyclization conditions.[13,14] In our previous work we demonstrated that simple homoallylic alcohol[13c] and homopropargyl alcohol[15] reacts with aldehyde in arene to give 4-aryltetrahydropyran and 4-aryldihydropyran, respectively under Prins–Friedel–Crafts conditions. The limitation of these methods is that they provide only 4-aryl tetrahydropyran or 4-aryldihydropyran. This limitation can be overcome by using 1,1-disubstituted homoallylic alcohol, under oxonium–ene cyclization reaction conditions.[2b] It is important that the disubstitution at the double bond is essential for this oxonium–ene type cyclization.[1b] Thus, the reaction of

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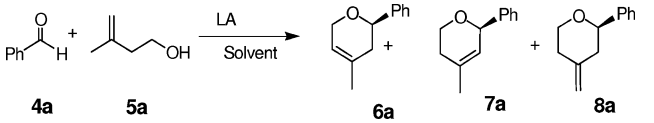
† Electronic supplementary information (ESI) available: General experimental methods, copies of ^{1}H and ^{13}C NMR spectra of all compounds. CCDC reference numbers 765896, 765895 and 801332. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob00033k

Table 1 Synthesis of dihydro- and tetrahydropyrans with different Lewis acids and solvents



4a 5a 6a 7a 8a

Entry	Lewis acid (equiv)	Solvent	Product[a] **6a** : **7a** : **8a**	Yield[b]
1	$InCl_3$ (0.2)	CH_2Cl_2	3.5 : 1 : 2.5	64
2	$In(OTf)_3$ (0.1)	CH_3CN	—	—
3	$In(OTf)_3$(0.1)	CH_2Cl_2	2 : 0 : 1	72
4	$Bi(OTf)_3$(0.1)	CH_2Cl_2	1.8 : 1 : 1	56
5	$BF_3{\cdot}Et_2O$ (1)	CH_2Cl_2	3 : 0 : 1	68
6	$BF_3{\cdot}Et_2O$ (1)	toluene	4.5 : 0 : 1	70
7	$BF_3{\cdot}Et_2O$ (1)	benzene	8 : 0 : 1	78

[a] Ratios are on the basis of ^{1}H NMR. [b] Yields are isolated yield.

3-methyl-but-3-en-1-ol with benzaldehyde in benzene mediated by boron trifluoride etherate at room temperature gave 4-methyl-2-phenyl-3,6-dihydro-2*H*-pyran **6a** as the major product and also its exocyclic isomer 4-methylene-2-phenyl tetrahydropyran **8a** with a ratio of 8 : 1 in 78% overall yield. These products cannot be separated by using conventional TLC and column chromatography methods. So the major isomer was isolated in 62% yield using TLC impregnated with $AgNO_3$. A similar type of condensation reaction between ketones and homoallylic alcohols catalyzed by $Hg(OTf)_2$ or BF_3 in acetone at –20 °C was reported by Nishizawa and coworkers, but the reaction ends up with a mixture of 6-membered ether alcohol, bis ether and olefins.[16] In our conditions we have not isolated any alcohol or bis ether products.

The reaction was also performed with other Lewis acids such as $InCl_3$, $In(OTf)_3$ and $Bi(OTf)_3$ and in different solvents. Reaction of $InCl_3$ in CH_2Cl_2 gave three isomeric products **6a**, **7a** and **8a** with a ratio of 3.5 : 1 : 2.5 and 64% overall yield, but the reaction failed in CH_3CN. On the other hand reaction with $In(OTf)_3$ in CH_2Cl_2 gave only two isomers **6a** and **8a** with a ratio of 2 : 1 and 72% overall yield, but no reaction in CH_3CN. Similarly reaction with $Bi(OTf)_3$ in CH_2Cl_2 produced **6a**, **7a** and **8a** with a ratio of 1.8 : 1 : 1 and overall 56% yield. Boron trifluoride etherate worked in CH_2Cl_2, toluene and benzene, but benzene is the best solvent among these in terms of selectivity and yield (Table 1).

The scope of the reaction was investigated by using different types of aldehydes and alcohols and it was observed that the reaction of aromatic aldehydes (entries **4a–g**) with methyl substituted alcohols (entries **5a–g**) gave *endo* cyclic compounds **6a–g** as the major product with a minor exocyclic product **8a–g**, whereas the aliphatic aldehydes (entries **4h,i**) gave two isomeric endocyclic products with a ratio of 3 : 1. Conjugated aromatic aldehyde **4j** gave as a major endocyclic isomer **6j** with a minor exocyclic isomer **8j**. On the other hand, nitro-substituted conjugated aromatic aldehyde **4k** gave only endocyclic isomer **6k**. Reaction of phenyl substituted alcohols (**5l–m**, **5o**) with aromatic and conjugated aromatic aldehydes (entries **4l,m**, **4o**) gave single endocyclic isomers **6l,m** and **6o**. But reaction with aliphatic aldehyde **4n** gave two endocyclic isomers **6n** and **7n** with a ratio of 3 : 1. The structure of the compounds was determined by NMR and X-ray analysis† and comparison with authentic samples.[13] In contrast to the above, the reaction of alcohols (**5p–u**) with a substitution at the C-1 position gave only exocyclic *cis*-products **8p–u** in good yields and excellent diastereoselectivity. But reaction of alcohol **5v** with aliphatic aldehyde **4v** gave exocyclic **6v** and endocyclic **8v** with a ratio 3.5 : 6.5 (Table 2). All the major isomers were separated by using $AgNO_3$ impregnated thin layer chromatography. The *cis*-configuration was confirmed from the coupling constants of the two peaks at C-2 (J = 11.6 and 2.4 Hz) and C-6 (J = 11.2 and 2.3 Hz) as shown in Fig. 2. The formation of two isomeric endocyclic compounds is further confirmed by hydrogenation with hydrogen on palladium charcoal. The formation of mainly endocyclic compounds instead of the exocyclic compounds is due to the higher stability of the endocyclic compounds to the exocyclic one as demonstrated by Gil-Av and Shabtai[17] as well as by Turner and Garner.[18] The formation of major 2,6-disubstituted exocyclic products in the case of alcohols **5p–v** may be attributed to the presence of two substituents at 2 and 6 positions which makes them more stable.

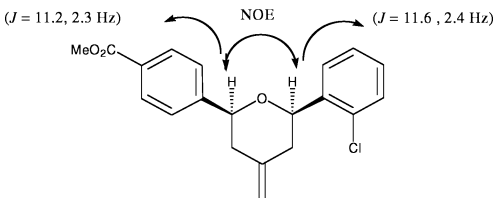
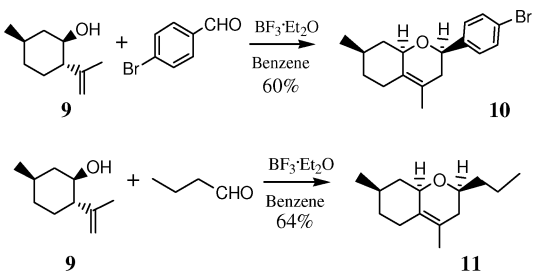


Fig. 2 Coupling constants and NOE of compound **8p**.

The scope of the reaction was extended to chiral cyclic alcohols. Thus the reaction of 2-isopropenyl-5-methylcyclo-hexanol **9** with bromobenzaldehyde gave bicyclic2-(4-bromophenyl)-4,7-dimethyl-3,5,6,7,8,8a-hexa-hydro-2*H*-chromene **10** in 60% yield (Scheme 1). Similarly, butyraldehyde gave dihydropyran **11** in 64% yield (Scheme 1). The structure of the compounds was determined by NOE and X-ray analysis.†[19]

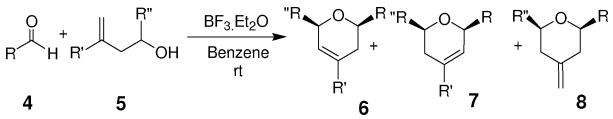


Scheme 1 Synthesis of chromene.

The mechanism of the reaction can be explained considering the oxonium–ene cyclization.[12] The aldehyde is activated by Lewis acid for nucleophilic attack by homoallylic alcohol to form acetal **12**, which after decomposition gives oxocarbenium ion **13**. Oxocarbenium ion **13** after cyclization gives carbocation **14**, which after subsequent proton elimination forms three different products (Scheme 2). The cationic oxonium–ene reaction was confirmed by the formation of the 4-amidotetrahydropyrans **17** and **18** (Table 3).[2b]

The diastereoselectivity of compounds **8p–v** was determined from the crude ^{1}H NMR and it was found that only *cis* diastereomer is formed. This can be explained on the basis of the more favoured six membered chair transition state being formed during the reaction (Scheme 3). As both the groups R and R″

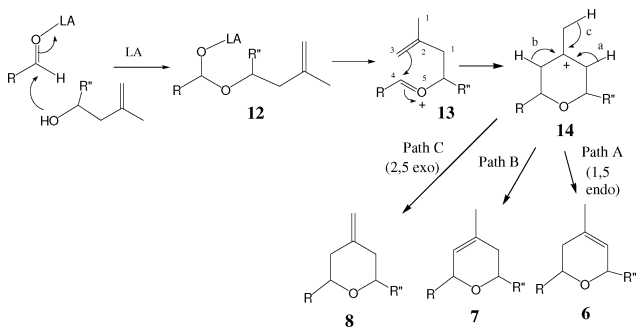
Table 2 Synthesis of 4-alkyl/aryl dihydropyrans and 4-methylene tetrahydropyrans



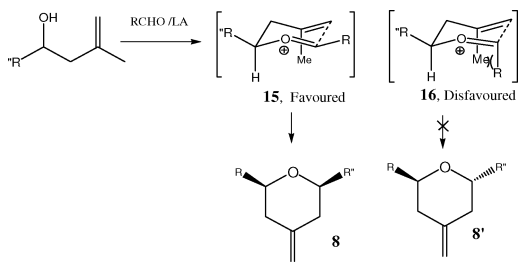
4 5 6 7 8

Sl. No.	Aldehyde **4**	Alcohol **5** R′	Alcohol **5** R″	Time/h	Product ratio[a] **6**	**7**	**8**	% Yield[b]
a	C_6H_5	Me	H	0.5	8	—	1	78
b	*p*-ClC_6H_4	Me	H	0.5	11	—	1	90
c	*m*-$NO_2C_6H_4$	Me	H	0.5	6	—	1	92
d	*p*-$MeO_2CC_6H_4$	Me	H	0.5	6	—	1	87
e	*p*-$TsOC_6H_4$	Me	H	0.5	9	—	1	85
f	*p*-MeC_6H_4	Me	H	0.5	10	—	1	84
g	*p*-$MeOC_6H_4$	Me	H	0.5	5	—	1	76
h	C_6H_{13}	Me	H	0.5	3	1	—	64
i	C_6H_5-CH_2	Me	H	0.5	4	1	—	78
j	C_6H_5-CH=CH	Me	H	0.5	6	—	1	90
k	*p*-$NO_2C_6H_4$-CH=CH	Me	H	0.5	1	—	—	95
l	*p*-BrC_6H_4	Ph	H	0.5	1	—	—	78
m	$MeOC_6H_4$	Ph	H	0.5	1	—	—	69
n	C_6H_{13}	Ph	H	0.5	3	1	—	80
o	C_6H_4-CH=CH	Ph	H	0.5	1	—	—	72
p	*o*-ClC_6H_4	Me	*p*-$MeO_2CC_6H_4$	3	—	—	1	75[c]
q	*p*-$MeOC_6H_4$	Me	*p*-$MeO_2CC_6H_4$	3	—	—	1	70[c]
r	C_6H_5	Me	*p*-$MeO_2CC_6H_4$	3	—	—	1	72[c]
s	*p*-BrC_6H_4	Me	*p*-$MeO_2CC_6H_4$	3	—	—	1	76[c]
t	*p*-MeC_6H_4	Me	*p*-ClC_6H_4	3	—	—	1	75[c]
u	*m*-$NO_2C_6H_4$	Me	*p*-ClC_6H_4	3	—	—	1	80[c]
v	C_6H_{13}	Me	*p*-$MeO_2CC_6H_4$	3	3.5	—	6.5	81[c]

[a] Ratios are on the basis of crude ^{1}H NMR. [b] Yield refers to isolated yield. The compounds are characterized by ^{1}H, ^{13}C NMR, Mass and X-ray analysis. [c] The de is 100% on the basis of crude ^{1}H NMR.



Scheme 2 Mechanism of the reaction.



Scheme 3 *cis*-Diastereoselectivity of tetrahydropyran synthesis.

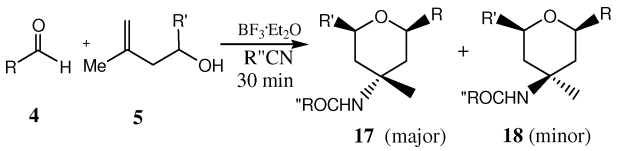
are bulky, they will be in equatorial positions to minimize the 1,3-diaxial interactions. This is in contrast to the $In(OTf)_3$-catalyzed oxonium–ene reaction where small amounts of *trans* isomer are formed.[1d]

The 4-amidotetrahydropyrans can be synthesized by trapping the carbocation **14** (Scheme 2) with nitrile nucleophiles to give the corresponding 4-amidotetrahydropyrans. The reaction is generalised by employing different aldehydes and nucleophiles and the results are summarized in Table 3. It was observed that all the aldehydes yielded two inseparable diastereomers with different ratios except *m*-nitrobenzaldehyde (**4j**), which produced only the major isomer. The aromatic aldehyde having electron-donating groups in the ring is not a good substrate (**4d**) for this reaction. The diastereomeric ratio was determined from crude ^{1}H NMR spectra. The structure and stereochemistry of the major isomer was determined from single crystal X-ray analysis,† which is also evident from the mechanism of the reaction (Scheme 4). The methyl group occupies a pseudo equatorial position to form the more favored intermediate **19**. The cation **19** is then attacked by the nitrile nucleophile from axial site to give species **21**, which after hydrolysis gives the major product **17**, whereas the less favoured species **20** gives the minor product **18**.

Conclusions

In conclusion, an efficient and diastereoselective method for the synthesis of 4-alkyl/aryl dihydro- and 4-methylene tetrahydropyrans in good yields has been developed. The method is also suitable for chromene synthesis. The scope and applications of this reaction are under investigation in our laboratory.

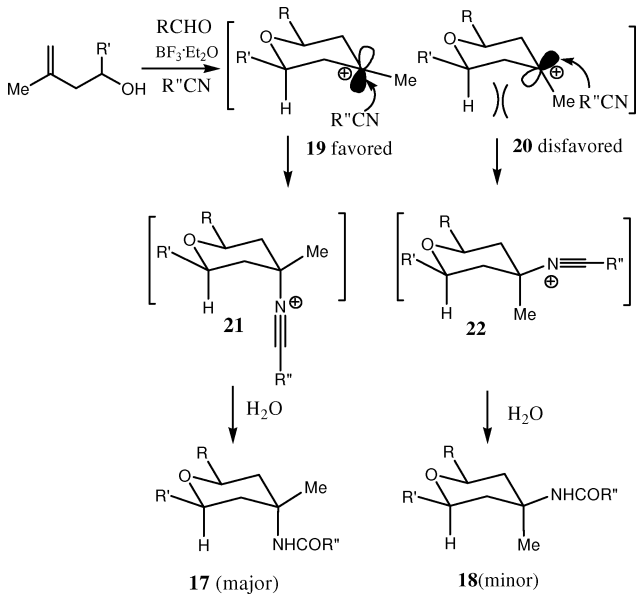
Table 3 Synthesis of 4-alkyl/aryl dihydropyrans and 4-methylene tetrahydropyrans



4 **5** **17** (major) **18** (minor)

Sl. No.	Aldehyde R =	Alcohol, R′ =	Nitrile R″ =	Ratio, (**17** : **18**)[b]	% Yield[a](**17** + **18**)
a	*m*-NO_2-C_6H_4	H	Me	2.2 : 1	82
b	C_6H_5	H	Me	2 : 1	91
c	*p*-Br-C_6H_4	H	Me	3 : 2	95
d	*p*-Me-C_6H_4	H	Me	2 : 1	67
e	*n*-C_2H_5	H	Me	4 : 1	89
f	$(CH_3)_2CHCH_2$	H	Me	3.5 : 1	92
g	C_6H_5-CH_2	H	Me	3.7 : 1	80
h	C_6H_5-CH=CH	H	Me	2.5 : 1	74
i	C_6H_5	H	Ph	3 : 1	70
j	*m*-NO_2-C_6H_4	H	Ph	1 : 0	72
k	*n*-C_3H_7	H	Ph	3 : 1	65
l	*o*-Cl-C_6H_4	H	Ph	3 : 2	78
m	*n*-C_3H_7	H	$CHCl_2$	3 : 1	60
n	*m*-NO_2-C_6H_4	H	$CHCl_2$	3.6 : 1	73
o	*m*-NO_2-C_6H_4	H	CH_2=$CHCH_2$	2 : 1	92
p	C_6H_5	$MeO_2CC_6H_4$	Me	3 : 2	84
q	*p*-Me-C_6H_4	$MeO_2CC_6H_4$	Me	1 : 1	78
r	*n*-C_3H_7	$MeO_2CC_6H_4$	Me	3 : 2	90

[a] Yield refers to isolated yield. The compounds are characterized by ^{1}H, ^{13}C NMR, Mass and X-ray analysis. [b] Ratios are on the basis of criude ^{1}H NMR.



Scheme 4 Mechanism of formation of major isomer.

Experimental section

General procedure for the synthesis of 2,3-dihydropyrans and 4-methylene tetrahydropyrans

To a stirring solution of aldehyde (1.0 equiv) and boron trifluoride etherate (1.0 equiv) in benzene (2 mL) at room temperature was added homoallyl alcohol (1.1 equiv) in benzene (2 mL) drop by drop over 5 min. The reaction mixture was stirred at the same temperature for 45 min. The progress of the reaction was monitored by TLC. After completion of the reaction the reaction mixture was quenched with saturated sodium bicarbonate solution, extracted with ethyl acetate, and then washed with brine and water. The organic layer was dried over Na_2SO_4 and evaporated to leave the crude product. This was purified by preparative TLC impregnated with silver nitrate to furnish the title compounds.

Synthesis of 4-methyl-2-phenyl-2,3-dihydro-2*H* pyrans

To a stirring solution of benzaldehyde (106 mg, 1.0 mmol) and boron trifluoride etherate (141 mg, 1.0 mmol) in benzene (2 mL) at room temperature was added 3-methyl-3-butene-1-ol (95 mg, 1.1 mmol) in benzene (2 mL) drop by drop over 5 min. The reaction mixture was stirred at the same temperature for 45 min. The progress of the reaction was monitored by TLC. After completion of the reaction the reaction mixture was quenched with saturated sodium bicarbonate solution. The product was extracted with ethyl acetate, and then washed with brine and water. The organic layer was dried (Na_2SO_4) and evaporated to leave the crude product. This was purified by preparative TLC impregnated with silver nitrate to furnish the 4-methyl-2-phenyl-2,3-dihydro-2*H* pyran (136 mg, 78%) as an oily liquid.

Separation of alkene regio-isomeric mixture by using preparative TLC impregnated with $AgNO_3$

A slurry was prepared from 60 g of TLC silica gel (SRL) containing 13% $CaSO_4 \cdot 1/2H_2O$ as binder with 5% methanol in ethyl acetate (120 mL). Four thin glass plates of 21 × 11 cm were coated uniformly with the slurry. The chromatoplates were allowed to dry for an hour at room temperature and then the plates were dipped into a silver nitrate solution (5 gm in 75 mL of water) chamber

for 60–70 min. The plates were allowed to dry in a hot oven at 100 °C for an hour, the lower portion of the plates changed to gray color, indicating the impregnation of silver nitrate. The regio-isomeric mixture dissolved in an adequate amount of ethyl acetate was applied to the plate, which was then developed in hexane–ethyl acetate solvent system. The plates were taken out from the solvent chamber and dried at room temperature for 15 min and then kept in the iodine chamber. A yellow colored band appeared after a few minutes. The bands were eluted with ethyl acetate and the solvent was evaporated in rotary vapor to give:

4-Methyl-2-phenyl-2,3-dihydro-2*H*-pyran (6a)

(108 mg, 62% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.76 (s, 3 H, -CH_3), 2.06–2.14 (m, 1 H), 2.26–2.37 (m, 1 H), 4.33 (bs, 2 H), 4.54 (dd, J = 10.4 and 3.2 Hz, 1 H), 5.51 (t, J = 1.2 Hz, 1 H), 7.26–7.31 (m, 2 H, ArH), 7.34–7.41 (m, 3 H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.1, 37.9, 66.6, 76.0, 120.0, 126.0, 127.6, 128.6, 132.2, 142.8; IR: 2924, 1604, 1496, 1451, 1383, 1245, 1123, 1092, 1040, 864, 756, 699 cm^{-1}. Found: C 82.84, H 8.02. Calc. For $C_{12}H_{14}O$: C 82.72, H 8.10.

2-(4-Chlorophenyl)-4-methyl-2,3-dihydro-2*H*-pyran (6b)

(144 mg, 69% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.74 (s, 3 H, -CH_3), 2.04–2.10 (m, 1 H), 2.18–2.26 (m, 1 H), 4.28–4.33 (m, 2 H), 4.48 (dd, J = 10.4 and 3.6 Hz, 1 H), 5.48 (t, J = 1.6 Hz, 1 H), 7.26–7.34 (m, 4 H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.1, 37.8, 66.6, 75.2, 120.0, 127.4, 128.6, 131.9, 133.2, 141.4; IR: 2925, 1598, 1493, 1436, 1123, 1089, 1043, 948, 824 cm^{-1}. HRMS (APCI) m/z calcd for $C_{12}H_{13}ClO$: $(M+H)^+$ 209.0733, found 209.0729.

4-Methyl-2-(3-nitrophenyl)-2,3-dihydro-2*H*-pyran (6c)

(158 mg, 72% yield) yellow color oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.77 (s, 3 H, -CH_3), 2.14–2.23 (m, 1 H), 2.24–2.30 (m, 1 H), 4.30–4.35 (m, 2 H), 4.63 (dd, J = 10.0 and 4.4 Hz, 1 H), 5.52 (t, J = 1.6 Hz, 1 H), 7.53 (t, J = 8.0 Hz, 1 H, ArH), 7.72 (d, J = 7.6 Hz, 1 H, ArH), 8.13 (dd, J = 8.4 and 1.2 Hz, 1 H, ArH), 8.27 (s, 1 H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.0, 37.6, 66.6, 74.6, 120.0, 121.0, 122.5, 122.6, 129.5, 131.6, 132.1, 145.0; IR: 2929, 2853, 1530, 1445, 1348, 1122, 1098, 1042, 812, 737, 686 cm^{-1}. Found: C 65.65, H 6.10, 6.32. Calc. for $C_{12}H_{13}NO_3$: C 65.74, H 5.98, N 6.39.

2-(4-Methyl-2,3-dihydro-2*H*-pyran-2yl)-benzoic acid methyl ester (6d)

(148 mg, 64% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.75 (s, 3 H, -CH_3), 2.08–2.15 (m, 1 H), 2.19–2.23 (m, 1 H), 3.90 (s, 3 H, CH_3), 4.30–4.34 (m, 2 H), 4.58 (dd, J = 10.0 and 3.6 Hz, 1 H), 5.50 (t, J = 1.6 Hz, 1 H), 7.45 (d, J = 8.4, 2 H, ArH), 8.02 (d, J = 8.0, 2 H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.1, 37.8, 52.2, 66.6, 75.4, 120.0, 125.8, 129.3, 129.9, 131.9, 148.0, 167.2; IR: 2952, 2857, 1614, 1436, 1280, 1112, 1043, 1018, 854, 768, 705 cm^{-1}. HRMS (APCI) m/z calcd for $C_{14}H_{16}O_3$: $(M+H)^+$ 233.1178, found 233.1187.

Toluene 4-sulfonic acid 4-(4-methyl-2,3-dihydro-2*H*-pyran-2-yl) phenyl ester (6e)

(220 mg, 64% yield) yellowish solid; MP: 80–82 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.73 (s, 3 H, -CH_3), 2.02–2.10 (m, 1 H), 2.16–2.24 (m, 1 H), 2.43 (s, 3 H, -CH_3), 4.24–4.31 (m, 2 H), 4.48 (dd, J = 10.0 and 2.8 Hz, 1 H), 5.48 (t, J = 1.6 Hz, 1 H), 6.95 (d, J = 8.4 Hz, 2 H, ArH), 7.29 (d, J = 7.6 Hz, 4 H, ArH), 7.68 (d, J = 6.8 Hz, 2 H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9, 23.0, 37.8, 66.6, 75.1, 119.9, 122.4, 127.2, 128.7, 129.9, 131.9, 132.4, 141.8, 145.5, 148.9; IR: 2929, 2911, 2824, 1597, 1503, 1372, 1197, 1154, 1119, 1093, 865, 744, 659 cm^{-1}. HRMS (APCI) m/z calcd for $C_{19}H_{20}O_4S$: $(M+H)^+$ 345.1161, found 345.1169.

4-Methyl-2-*p*-tolyl-2,3-dihydro-2*H*-pyran (6f)

(127 mg, 68% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.73 (s, 3 H, -CH_3), 2.02–2.11 (m, 1 H), 2.22–2.30 (m, 1 H), 2.33 (s, 3 H, -CH_3), 4.28–4.32 (m, 2 H), 4.48 (dd, J = 10.4 and 3.2 Hz, 1 H), 5.48 (t, J = 1.6 Hz, 1 H), 7.15 (d, J = 7.6, 2 H, ArH), 7.26 (d, J = 8.0 Hz, 2 H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3, 23.1, 37.8, 66.6, 75.8, 120.0, 126.0, 129.2, 132.3, 137.2, 139.8; IR: 3016, 2922, 1610, 1493, 1444, 1382, 1167, 1122, 1091, 1042, 1020, 946, 813 cm^{-1}. Found: C 83.15, H, 8.49. Calc. for $C_{13}H_{16}O$: C 82.94, H 8.57.

2-(4-Methoxyphenyl)-4-methyl-2,3-dihydro-2*H*-pyran (6g)

(120 mg, 59% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.74 (s, 3 H, -CH_3), 2.03–2.09 (m, 1 H), 2.27–2.35 (m, 1 H), 3.80 (s, 3 H, CH_3), 4.27–4.30 (m, 2 H), 4.47 (dd, J = 10.4 and 3.6 Hz, 1 H), 5.48 (t, J = 1.6 Hz, 1 H), 6.88 (d, J = 8.8 Hz, 2 H, ArH), 7.30 (d, J = 8.8 Hz, 2 H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.1, 37.7, 55.5, 66.6, 75.6, 113.9, 120.0, 127.4, 132.3, 134.9, 159.2; IR: 2929, 2836, 1614, 1248, 1175, 1109, 1035, 828, 779 cm^{-1}. HRMS (APCI) m/z calcd for $C_{13}H_{16}O_2$: $(M+H)^+$ 205.1229, found 205.1235.

2-Hexyl-4-methyl-2,3-dihydro-2*H*-pyran and 2-hexyl-4-methyl-5,6-dihydro-2*H*-pyran (6h and 7h; 3 : 1).

(116 mg, 64% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89–0.96 (m, 3 H, -CH_3), 1.33–1.65 (m, 8 H, -CH_2-), 1.69 (s, 3 H, -CH_3), 1.72–1.78 (m, 2 H, -CH_2-), 1.79–1.87 (m, 1 H), 1.88–1.99 (m, 1 H), 3.42–3.50 (m, 0.75 H), 3.62 (ddd, J = 10.0 and 4.0 Hz, 0.25 H), 3.95–4.00 (m, 0.50 H), 4.04–4.18 (m, 1.50 H), 5.32 (d, J = 3.2 Hz, 0.25 H), 5.40 (dd, J = 1.6 and 1.2 Hz, 0.75 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 22.8, 23.2, 25.5, 25.7, 29.6, 30.3, 32.0, 35.9, 36.1, 36.2, 66.1, 74.0, 74.3, 120.0, 124.4, 132.1; IR: 2956, 2928, 2856, 1654, 1458, 1380, 1166, 1139, 1020, 886, 831, 779 cm^{-1}. Found: C 80.12, H 12.22. Calc. for C_{12} $H_{22}O$: C 79.06, H 12.16.

2-Benzyl-4-methyl-2,3-dihydro-2*H*-pyran and 2-benzyl-4-methyl-5,6-dihydro-2*H*-pyran (6i and 7i; 3 : 1).

(146 mg, 78% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.65 (s, 2.25 H), 1.68 (s, 0.75 H), 1.73–1.80 (m, 1 H), 1.95–2.05 (m, 0.75 H), 2.10–2.23 (m, 0.75 H), 2.68 (dd, J = 9.6 and 6.4 Hz, 0.25 H), 2.72 (dd, J = 13.6 and 6.4 Hz, 0.75 H), 2.89 (dd, J = 12.8 and 7.2 Hz, 0.25 H), 2.96 (dd, J = 13.6 and 6.8 Hz, 1 H), 3.58–3.64 (m, 0.25 H), 3.68–3.75 (m, 0.75 H), 3.96–4.00 (m, 0.50 H), 4.05–4.25 (m, 1.50 H), 5.33 (brs, 0.25 H), 5.38 (br s, 0.75 H), 7.19–7.25 (m,

3 H), 7.27–7.31 (m, 2 H); ^{13}C NMR for **6i** (100 MHz, $CDCl_3$): δ 23.2, 35.7, 42.6, 66.2, 74.8, 119.9, 126.4, 126.5, 129.5, 131.8, 138.7 (major **6i**); IR: 3027, 2926, 2853, 1629, 1495, 1382, 1153, 1120, 1085, 1030, 858, 779 cm^{-1}. Found: C 83.15, H, 8.68. Calc. for $C_{13}H_{16}0$: C 82.94, H 8.57. To support these isomeric mixture, the mixture **6i** and **7i** was hydrogenated in the presence of H_2 and Pd on Charcoal (20% W/W) in MeOH at 28 °C for 24 h to afford the corresponding hydrogenated product as a mixture of two diastereomers at C-4 (4 : 1 ratio; identity of isomers not determined). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (d, J = 6.4 Hz, 2.40 H), 1.01 (d, J = 6.8 Hz, 0.60 H), 1.15–1.27 (m, 1.60 H), 1.31–1.38 (m, 0.40 H), 1.48–1.68 (m, 2.40 H), 1.75–1.83 (m, 0.60 H), 2.63 (dd, J = 13.6 and 6.4 Hz, 0.80 H), 2.72 (dd, J = 14.0 and 6.0 Hz, 0.20 H), 2.89 (dd, J = 13.6 and 6.4 Hz, 0.80 H), 2.96 (dd, J = 14.0 and 7.2 Hz, 1 H), 3.35–3.50 (m, 1.60 H), 3.58–3.86 (m, 0.40 H), 3.95–4.00 (m, 0.80 H), 4.08–4.15 (m, 0.20 H), 7.18–7.23 (m, 3 H), 7.26–7.30 (m, 2 H); ^{13}C NMR for major only (100 MHz, $CDCl_3$): δ 22.5, 30.5, 34.8, 40.2, 43.3, 68.4, 78.7, 126.3, 128.4, 129.6, 138.9. IR: 2950, 2925, 2840, 1604, 1494, 1454, 1377, 1174, 1090, 1030, 749, 699 cm^{-1}. Found: C 82.18, H 9.48. Calc. for $C_{13}H_{18}O$: C 82.06, H 9.53.

4-Methyl-2-styryl-2,3-dihydro-2*H*-pyran (6j)

(132 mg, 66% yield) yellow color oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.73 (s, 3 H, -CH_3), 1.95–2.03 (m, 1 H), 2.12–2.40 (m, 1 H), 4.14–4.21 (m, 1 H), 4.22–4.25 (m, 2 H), 5.46 (bs, 1 H), 6.28 (dd, J = 16.0, and 6.0 Hz, 1 H), 6.64 (d, J = 16.0 Hz, 1 H), 7.20–7.26 (m, 1 H), 7.28–7.31 (m, 2 H), 7.36–7.42 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2, 36.0, 65.9, 74.2, 119.9, 126.7, 127.8, 128.7, 130.1, 130.7, 131.7, 137.1; IR: 2929, 2852, 1599, 1449, 1382, 1132, 1028, 996, 747, 693 cm^{-1}. Found: C 84.19, H 7.96. Calc. for $C_{14}H_{16}O$: C 83.96, H 8.05.

4-Methyl-2-[2-(4-nitrophenyl)-vinyl]-2,3-dihydro-2*H*-pyran (6k)

(233 mg, 95% yield) yellow color oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.75 (s, 3 H, -CH_3), 1.90–2.10 (m, 1 H), 2.13–2.21 (m, 1 H), 4.20–4.27 (m, 2 H), 5.44–5.50 (m, 1 H), 6.47 (dd, J = 16.0, and 5.2 Hz, 1 H), 6.72 (d, J = 16.0 Hz, 1 H), 7.51 (d, J = 8.8 Hz, 2 H), 8.17 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.1, 35.8, 66.0, 73.6, 119.9, 124.1, 127.1, 128.0, 131.4, 135.1, 143.6, 147.0; IR: 2961, 2931, 2826, 1596, 1516, 1342, 1133, 1110, 1071, 1012, 970, 855, 746, 690 cm^{-1}. HRMS (APCI) m/z calcd for $C_{14}H_{15}NO_3$: $(M+H)^+$ 246.1142, found 246.1133.

2-(4-Bromophenyl)-4-phenyl-2,3-dihydro-2*H*-pyran (6l)

(244 mg, 78% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.62–2.67 (m, 2 H), 4.52–4.56 (m, 2 H), 4.64 (t, J = 6.8 Hz, 1 H), 6.28 (t, J = 2.0 Hz, 1 H), 7.26–7.41 (m, 7 H), 7.50 (d, J = 8.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.0, 66.9, 75.4, 121.6, 122.4, 124.9, 127.7, 127.9, 128.7, 131.8, 134.4, 140.1, 141.6; IR: 3060, 2926, 2851, 1650, 1489, 1447, 1375, 1267, 1127, 1071, 1010, 820, 753, 697 cm^{-1}. Found: C 64.85, H 4.70. Calc. for $C_{17}H_{15}BrO$: C 64.78, H 4.80.

2-(4-Methoxyphenyl)-4-phenyl-2,3-dihydro-2*H*-pyran (6m)

(183 mg, 69% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.60–2.65 (m, 1 H), 2.67–2.76 (m, 1 H), 3.78 (s, 3 H), 4.50–4.54 (m, 2 H), 4.62 (dd, J = 10.0 and 3.6 Hz, 1 H), 6.20 (d, J = 2.4 Hz, 1 H), 6.91 (d, J = 8.8 Hz, 2 H), 7.26 (t, J = 7.2 Hz, 1 H), 7.31–7.42 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 34.9, 55.5, 67.0, 75.8, 114.1, 122.4, 124.5, 124.9, 127.5, 128.7, 134.6, 134.7, 140.2, 159.3; IR: 2929, 2836, 1613, 1514, 1446, 1249, 1176, 1124, 1033, 830, 751, 697 cm^{-1}. Found: C 81.29, H 6.87. Calc. for $C_{18}H_{18}O_2$: C 81.17, H 6.81.

2-Hexyl-4-phenyl-2,3-dihydro-2*H*-pyran (6n) and 2-hexyl-4-phenyl-5,6-dihydro-2*H*-pyran (7n) (6n : 7n = 3 : 1).

(195 mg, 80% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86–0.98 (m, 3 H), 1.24–1.40 (m, 7 H), 1.41–1.72 (m, 3 H), 2.20–2.24 (m, 0.25 H), 2.29–2.42 (m, 0.75 H), 2.60–2.66 (m, 0.25 H), 3.55–3.62 (m, 0.75 H), 3.75 (ddd, J = 10.8, and 3.6 Hz, 0.25 H), 4.10–4.25 (m, 1 H), 4.29–4.43 (m, 2 H), 6.04 (s, 0.25 H), 6.12 (s, 0.75 H), 7.20–7.60 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 14.3, 22.7, 22.8, 22.9, 24.2, 25.7, 28.7, 28.9, 29.1, 29.3, 29.6, 31.1, 31.8, 32.0, 33.2, 36.2, 66.5, 74.2, 122.6, 125.0, 127.4, 128.6, 134.4, 140.6, 144.1, 155.6; IR: 3027, 2955, 2857, 1643, 1458, 1376, 1267, 1171, 1092, 1031, 749, 696 cm^{-1}. Found: C 83.67, H 9.82. Calc. for $C_{17}H_{24}O$: C 83.55, H 9.90.

4-Phenyl-2-styryl-2,3-dihydro-2*H*-pyran (6o)

(189 mg, 72% yield) pale yellow color oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.51–2.62 (m, 2 H), 4.30–4.36 (m, 1 H), 4.41–4.52 (m, 2 H), 6.15–6.17 (m, 1 H), 6.36 (dd, J = 16.0 and 6.0 Hz, 1 H), 6.70 (d, J = 16.0 Hz, 1 H), 7.22–7.36 (m, 6 H), 7.40–7.43 (m, 4 H), ^{13}C NMR (100 MHz, $CDCl_3$): δ 33.2, 66.3, 74.3, 122.4, 124.9, 126.7, 127.6, 127.9, 128.7, 128.8, 129.8, 131.0, 134.0, 136.9, 140.2; IR: 3027, 2926, 2851, 1599, 1495, 1448, 1374, 1269, 1132, 1073, 1027, 967, 750, 694 cm^{-1}. Found: C 87.18, H 6.87. Calc. for $C_{19}H_{18}O$: C 86.99, H 6.92.

4-[6-(2-Chlorophenyl)-4-methylenetetrahydropyran-2-yl]-benzoic acid methyl ester (8p)

(256 mg, 75% yield) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.15 (t, J = 12.0 Hz, 1 H), 2.33 (t, J = 12.0 Hz, 1 H), 2.58 (d, J = 13.6 Hz, 1 H), 2.76 (d, J = 13.2 Hz, 1 H), 3.92 (s, 3 H), 4.64 (dd, J = 11.6 and 1.6 Hz, 1 H), 4.86 (dd, J = 11.2 and 2.4 Hz, 1 H), 4.94 (d, J = 1.6 Hz, 1 H), 4.97 (d, J = 1.6 Hz, 1 H), 7.15 (dt, J = 8.0 and 1.6 Hz, 1 H), 7.39 (t, J = 7.2 Hz, 1 H), 7.53 (dd, J = 8.4 and 2.0 Hz, 3 H), 7.72 (dd, J = 8.0 and 1.6 Hz, 1 H), 8.04 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 41.4, 42.9, 52.3, 79.9, 80.4, 110.3, 121.7, 125.9, 127.7, 128.1, 129.1, 130.0, 132.8, 141.7, 143.4, 147.6, 167.2; IR: 2926, 2851, 1724, 1610, 1436, 1277, 1110, 1081, 1020, 895, 753, 703 cm^{-1}. Found: C 70.25, H 5.50. Calc. for $C_{19}H_{17}ClO_3$: C 70.07, H 5.59.

4-[6-(4-Methoxyphenyl)-4-methylenetetrahydropyran-2-yl]-benzoic acid methyl ester (8q)

(236 mg, 70% yield) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.29 (t, J = 12.4 Hz, 1 H), 2.37 (t, J = 12.0 Hz, 1 H), 2.50–2.57 (m, 2 H), 3.81 (s, 3 H), 3.91 (s, 3 H), 4.48 (dd, J = 11.2 and 2.4 Hz, 1 H), 4.57 (dd, J = 11.6 and 2.4 Hz, 1 H), 4.90 (s, 2 H), 6.90 (d, J = 8.8 Hz, 2 H), 7.38 (d, J = 8.8 Hz, 2 H), 7.51 (d, J = 8.4 Hz, 2 H), 8.02 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 42.9,

43.1, 52.3, 55.5, 80.3, 80.6, 109.8, 114.0, 125.9, 127.4, 129.4, 129.9, 134.7, 144.2, 147.8, 159.3, 167.2; IR: 3026, 2853, 1723, 1614, 1434, 1278, 1249, 1110, 1079, 1034, 827, 771, 703 cm^{-1}. Found: C 74.65, H 6.48 Calc. for $C_{21}H_{22}O_4$: C 74.54, H 6.55.

Methyl-4-(tetrahydro-4-methylene-6-phenyl-2*H*-pyran-2-yl)benzoate (8r)

(222 mg, 72% yield) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.27–2.40 (m, 2 H), 2.53–2.59 (m, 2 H), 3.91 (s, 3 H), 4.52–4.61 (m, 2 H), 4.92 (s, 2 H), 7.30 (d, J = 7.6 Hz, 1 H), 7.38 (t, J = 7.2 Hz, 2 H), 7.46 (d, J = 7.6 Hz, 2 H), 7.53 (d, J = 8.4 Hz, 2 H), 8.03 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.9, 43.1, 52.3, 80.3, 80.9, 110.0, 125.9, 126.0, 127.8, 128.6, 129.4, 129.9, 142.4, 144.0, 147.8, 167.2; IR: 2925, 2851, 1722, 1610, 1434, 1277, 1110, 1072, 755, 699 cm^{-1}. Found: C 78.05, H 6.42 Calc. for $C_{20}H_{20}O_3$: C 77.90, H 6.54.

Methyl-4-(6-(4-bromophenyl)-tetrahydro-4-methylene-2*H*-pyran-2-yl)benzoate (8s)

(294 mg, 76% yield) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26–2.34 (m, 2 H), 2.50–2.59 (m, 2 H), 3.92 (s, 3 H), 4.50 (d, J = 11.2 Hz, 1 H), 4.98 (d, J = 12.0 Hz, 1 H), 4.92 (s, 2 H), 7.33 (d, J = 8.4 Hz, 2 H), 7.48–7.53 (m, 4 H), 8.03 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 42.9 (2C), 52.3, 80.1, 80.3, 110.3, 121.6, 125.9, 127.8, 129.5, 130.0, 131.7, 141.4, 143.5, 147.5, 167.1; IR: 2925, 2852, 1722, 1612, 1434, 1278, 1110, 1071, 767, 704 cm^{-1}. Found: C 62.15, H 4.86 Calc. for $C_{20}H_{19}BrO_3$: C 62.03, H 4.95.

2-(4-Chlorophenyl)-tetrahydro-4-methylene-6-*p*-tolyl-2*H*-pyran (8t)

(224 mg, 75% yield) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.24–2.37 (m, 2 H), 2.34 (s, 3 H), 2.48–2.53 (m, 2 H), 4.45–4.50 (m, 2 H), 4.88 (s, 2 H), 7.16 (d, J = 7.6 Hz, 2 H), 7.29–7.34 (m, 4 H), 7.37 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.4, 43.0, 43.1, 80.0, 80.7, 109.7, 126.0, 127.4, 128.6, 129.2, 133.2, 137.4, 139.5, 141.3, 144.3; IR: 3027, 2922, 2852, 1647, 1490, 1085, 1059, 809, 758 cm^{-1}. Found: C 76.55, H 6.32 Calc. for $C_{19}H_{19}ClO$: C 76.37, H 6.41.

2-(4-Chlorophenyl)-tetrahydro-4-methylene-6-(3-nitrophenyl)-2*H*-pyran (8u)

(263 mg, 80% yield) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.27–2.38 (m, 2 H), 2.52–2.63 (m, 2 H), 4.53 (d, J = 10.0 Hz, 1 H), 4.63 (d, J = 10.0 Hz, 1 H), 4.96 (s, 2 H), 7.34–7.40 (m, 4 H), 7.54(t, J = 8.0 Hz, 1 H), 7.78 (d, J = 8.0 Hz, 1 H), 8.16 (d, J = 8.0 Hz, 1 H), 8.31 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 42.7 (2C), 79.6, 80.3, 110.7, 121.1, 122.8, 127.4, 128.8, 129.6, 132.2, 133.6, 140.5, 142.9, 144.5, 148.5; IR: 3076, 2925, 2853, 1651, 1529, 1492, 1349, 1089, 1072, 806, 772, 737 cm^{-1}. Found: C 65.48, H 4.75, N 4.34 Calc. for $C_{18}H_{16}ClNO_3$: C 65.56, H 4.89, N 4.25.

4-[6-Hexyl-4-methyl-4,6-2*H*-pyran-2yl)-benzoic acid methyl ester (6v)

(88 mg, 28% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 7.4 Hz, 3 H), 1.27–1.37 (m, 6 H), 1.40–1.51 (m, 2 H), 1.55–1.63 (m, 2 H), 1.74 (s, 3 H), 2.00–2.20 (m, 2 H), 3.91 (s, 3 H), 4.20–4.28 (m, 1 H), 4.63 (dd, J = 10.0 and 4.4 Hz, 1 H), 5.42 (brs, 1 H), 7.46 (d, J = 8.4 Hz, 2 H), 8.01 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 22.9, 23.1, 25.3, 29.7, 32.1, 36.1, 38.2, 52.2, 75.4, 75.6, 124.5, 125.8, 129.2, 129.9, 132.1, 148.6, 167.3; IR: 2950, 2928, 2828, 1726, 1684, 1614, 1435, 1377, 1277, 1175, 1109, 1019, 851, 767, 704 cm^{-1}. Found: C 76.12, H 8.85. Calc. for $C_{20}H_{28}O_3$: C 75.91, H 8.92.

4-[6-Hexyl-4-methylene-tetrahydropyran-2-yl)-benzoic acid methyl ester (8v)

(168 mg, 53% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 6.8 Hz, 3 H), 1.25–1.35 (m, 6 H), 1.38–1.72 (m, 4 H), 2.02 (t, J = 12.8, 1 H), 2.17 (t, J = 8.8, 1 H), 2.30 (d, J = 13.2, 1 H), 2.47 (d, J = 12.8, 1 H), 3.40–3.48 (m, 1 H), 3.91 (s, 3 H), 4.37 (dd, J = 11.6 and 2.0 Hz, 1 H), 4.81 (brs, 2 H), 7.45 (d, J = 8.4, 1 H), 8.01 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 22.8, 25.6, 29.6, 32.0, 36.5, 40.7, 43.0, 52.3, 79.1, 79.7, 109.2, 125.9, 129.3, 129.9, 144.7, 148.1, 167.3; IR: 2929, 2856, 2365, 1725, 1643, 1434, 1277, 1110, 1080, 1017, 891, 705, cm^{-1}. Found: C 76.08, H 8.83. Calc. for $C_{20}H_{28}O_3$: C 75.91, H 8.92.

2-(4-Bromophenyl)-4,7-dimethyl-3,5,6,7,8,8a-hexahydro-2,4-chromene (10)

(192 mg, 60% yield) colorless solid; MP: 73–75 °C (MeOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84–0.97 (m, 1 H), 0.95 (d, J = 6.4 Hz, 3 H), 1.07 (q, J = 11.6 Hz, 1 H), 1.58–1.80 (m, 3 H), 1.68 (3 H), 1.98–2.05 (m, 1 H), 2.08–2.14 (m, 1 H), 2.22–2.28 (m, 1 H), 2.71–2.75 (m, 1 H), 4.11–4.15 (m, 1 H), 4.49 (dd, J = 10.8 and 2.8 Hz, 1 H), 7.25 (d, J = 8.4 Hz, 2 H), 7.45 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.4, 22.3, 26.7, 31.2, 35.2, 39.6, 43.0, 74.7, 76.5, 121.2, 122.0, 127.9, 131.6, 131.7, 142.3; IR: 2951, 2882, 1401, 1265, 1114, 1087, 1010, 823, 738 cm^{-1}. HRMS (APCI) m/z calcd for $C_{17}H_{21}BrO$: $(M+H)^+$ 321.0854, found 321.0863. Specific rotation $[\alpha]_D^{25}$ = +121° (C = 0.4, $CHCl_3$).

4,7-Dimethyl-2-propyl-3,5,6,7,8,8a-hexahydro-2*H*-chromene (11)

(134 mg, 64% yield) colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84–0.97 (m, 6 H), 1.32–1.49 (m, 4 H), 1.50–1.60 (m, 3 H), 1.64 (s, 3 H), 1.65–1.70 (m, 1 H), 1.74 (q, J = 2.4 Hz, 1 H), 1.78 (q, J = 2.4 Hz, 1 H), 1.94–2.06 (m, 3 H), 2.66–2.72 (m, 1 H), 3.40–3.48 (m, 1 H), 3.91–3.95 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3, 18.4, 19.0, 22.2, 26.7, 31.2, 35.3, 37.8, 38.3, 43.1, 73.1, 75.9, 122.2, 131.5; IR: 2926, 2871, 1457, 1379, 1126, 1103, 1080, 1020, 872 cm^{-1}. Found: C 80.86, H 11.51. Calc. for $C_{14}H_{24}O$: C 80.71, H 11.61. Specific rotation $[\alpha]_D^{25}$: +52°(C = 0.2, $CHCl_3$).

***N*-[4-methyl-2-(3-nitrophenyl)-tetrahydropyran-4-yl]-acetamide (17a/18a, two isomeric mixture with a ratio 3.5 : 1.6)**

To a stirring solution of 3-nitrobenzaldehyde (151 mg, 1.0 mmol) with acetonitile (82 mg, 2 mmol) and boron trifluoride etherate (141 mg, 1.0 mmol) in benzene (2 mL) at room temperature was added 3-methyl-3-butene-1-ol (95 mg, 1.1 mmol) in benzene (2 mL) drop by drop over 5 min. The reaction mixture was stirred at the same temperature for half an hour. The progress of the reaction was monitored by TLC. After completion of the reaction the reaction mixture was quenched with saturated sodium bicarbonate

solution. The product was extracted with ethyl acetate, and then washed with brine and water. The organic layer was dried (Na_2SO_4) and evaporated to leave the crude product. This was further purified by column chromatography to furnish *N*-[4-methyl-2-(3-nitrophenyl)-tetrahydropyran-4-yl]-acetamide (228 mg, 82%) as a semisolid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 2.1 H), 1.65 (s, 0.9 H), 1.66–1.74 (m, 1 H), 1.79–1.90 (m, 1 H), 1.93 (s, 0.9 H), 1.96–2.10 (m, 1 H), 2.06 (s, 2.1 H), 2.33–2.36 (m, 0.3 H), 2.66–2.72 (m, 0.7 H), 3.74–3.85 (m, 1 H), 4.03–4.13 (m, 1 H), 4.56 (d, J = 11.6 Hz, 0.3 H), 4.61 (d,, J = 11.6 Hz, 0.7 H), 5.52 (s, 0.3 H), 5.60 (s, 0.7 H), 7.49 (t, J = 8.0 Hz, 1 H), 7.66 (d, J = 7.6 Hz, 1 H), 8.11 (d, J = 8.0 Hz, 1 H), 8.23 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 24.3, 24.4, 27.7, 36.0, 36.5, 43.5, 44.5, 52.0, 63.9, 64.4, 73.8, 74.7, 120.7, 122.2, 122.4, 129.3, 132.1, 144.5, 144.8, 148.1, 170.1, 170.9; IR: 3298, 3079, 2966, 2928, 2865, 1651, 1531, 1439, 1350, 1259, 1158, 1097, 1052, 967, 908, 848, 737, 697, 684 cm^{-1}. Found: C 60.56, H 6.61, N 10.15. Calc. for $C_{14}H_{18}N_2O_4$: C 60.42, H 6.52, N 10.07.

_N_-[4-Methyl-2-phenyltetrahydropyran-4-yl]-acetamide (17b/18b; 2 : 1)

(212 mg, 91%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 2 H), 1.51 (dd, J = 14.0 and 11.6 Hz, 0.67 H), 1.63 (s, 1 H), 1.67 (dd, J = 13.6 and 4.8 Hz, 0.33 H), 1.82 (t, J = 12.4 Hz, 0.33 H), 1.90 (s, 1 H), 1.94–1.98 (m, 0.67 H), 2.03 (s, 2 H), 2.13–2.21 (m, 1 H), 2.45 (dt, J = 14.0 and 1.6 Hz, 1 H), 3.70–3.75 (m, 0.33 H), 3.77 (dt, J = 14.4 and 2.0 Hz, 0.67 H), 4.99 (dd, J = 12.4 and 4.8 Hz, 0.67 H), 4.03–4.10 (m, 0.33 H), 4.46 (dd, dt, J = 11.6 and 2.0 Hz, 0.33 H), 4.48 (dd, J = 12.0 and 2.0 Hz, 0.67 H), 5.47 (brs, 0.33 H), 5.51 (brs, 0.67 H), 7.24–7.38 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7, 24.2, 27.7, 29.4, 29.6, 35.8, 36.7, 43.6, 44.8, 51.9, 63.8, 64.4, 74.9, 75.9, 125.8, 127.4, 128.2, 142.1, 142.2, 169.8, 170.5; IR: 3444, 3060, 2967, 2930, 2857, 1650, 1540, 1448, 1286, 1156, 1093, 1050, 963, 861, 751, 699 cm^{-1}. Found: C 72.25, H 8.15, N 6.12. Calc. for $C_{14}H_{19}NO_2$: C 72.07, H 8.21, N 6.00.

_N_-[2-(4-Bromophenyl)-tetrahydro4-methyl-2*H*-pyran-4-yl]-acetamide (17c/18c; 3 : 2)

(296 mg, 95%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.42 (s, 1.80 H), 1.62 (s, 1.20 H), 1.64–1.69 (m, 0.60 H), 1.70–1.80 (m, 0.40 H), 1.92 (s, 1.20 H), 1.96–2.08 (m, 1 H), 2.04 (s, 1.80 H), 2.17–2.23 (m, 1 H), 2.53 (d, J = 14.4 1 H), 3,77 (t, J = 12.4 Hz, 0.60 H), 3.90 (t, J = 5.6 Hz, 0.40 H), 4.01 (dd, J = 12.4 and 4.8 Hz, 0.60 H), 4.04–4.13 (m, 0.40 H), 4.44 (d, J = 11.6 Hz, 1 H), 5.24 (brs, 0.60 H), 5.31 (brs, 0.40 H), 7.21 (d, J = 8.0 Hz, 2 H), 7.44 (J = 8.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.7, 24.5, 27.8, 29.6, 36.3, 36.8, 43.6, 44.8, 52.1, 59.9, 63.9, 64.5, 74.4, 75.3, 121.1, 127.6, 131.4, 141.3, 141.5, 169.9, 170.6; IR: 3307, 2966, 2859, 1651, 1553, 1402, 1373, 1094, 1010, 820, 733 cm^{-1}. Found: C 54.02, H 5.72, N 4.65. Calc. for $C_{14}H_{18}BrNO_2$: C 53.86, H 5.81, N 4.49.

_N_-[4-Methyl-2-*p*-tolyl-tetrahydropyran-4-yl]-acetamide (17d/18d; 2 : 1)

(165 mg, 67%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.40 (s, 2 H), 1.49 (dd, J = 14.0 and 12.0 Hz, 0.67 H), 1.61 (s, 1 H), 1.64 (dd, J = 13.2 and 4.8 Hz, 0.33 H), 1.81 (t, J = 12.0 Hz, 0.33 H), 1.90 (s, 1 H), 1.92–1.98 (m, 0.67 H), 2.02 (s, 2 H), 2.12–2.20 (m, 1 H), 2.32 (s, 0.67 H), 2.36–2.42 (m, 1 H), 3.68–3.79 (m, 1 H), 3.97 (dd, 3.99 (dd, J = 12.0 and 4.4 Hz, 0.67 H), 4.02–4.11 (m, 0.33 H), 4.42–4.47 (m, 1 H), 5.54 (brs, 0.33 H), 5.62 (brs, 0.67 H), 7.12 (d, J = 7.6 Hz, 2 H), 7.21 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 21.9, 24.5, 24.6, 27.9, 36.1, 37.1, 44.0, 45.1, 52.2, 64.0, 64.6, 75.0, 75.9, 125.9, 129.1, 137.2, 139.3, 170.3; IR: 3446, 2961, 2859, 1650, 1550, 1373, 1094, 1053, 1023, 812, 768 cm^{-1}. Found: C 72.71, H 8.48, N 5.72. Calc. for $C_{15}H_{21}NO_2$: C 72.84, H 8.56, N 5.66.

_N_-[2-Ethyl-4-methyltetrahydropyran-4-yl]-acetamide (17e/18e; 4 : 1)

(164 mg, 89%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (t, J = 7.6 Hz, 3 H), 1.20 (dd, J = 14.8 and 14.0 Hz, 1 H), 1.39 (s, 2.4 H), 1.42–1.56 (m, 2.40 H), 1.51 (s, 0.60 H), 1.78–1.91 (m, 0.60 H), 1.93 (s, 0.60 H), 1.98 (s, 2.4 H), 2.00–2.05 (m, 0.40 H), 2.09–2.16 (m, 1.60 H), 3.29–3.36 (m, 1 H), 3.51–3.60 (m, 1 H), 3.83 (ddd, J = 12.0, 4.8 and 1.2 Hz, 0.80 H), 3.90 (ddd, J = 12.4, 5.2 and 1.6 Hz, 0.20 H), 5.37 (brs, 0.80 H), 5.47 (brs, 0.20 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.9, 21.9, 24.4, 27.9, 28.9, 29.2, 29.7, 36.2, 37.4, 41.8, 42.8, 51.8, 63.5, 64.1, 74.1, 75.1, 170.2; IR: 3308, 2961, 2930, 2856, 1651, 1549, 1372, 1289, 1146, 1073, 1037, 964, 758 cm^{-1}. Found: C 64.92, H 10.39, N 7.45. Calc. for $C_{10}H_{19}NO_2$: C 64.83, H 10.34, N 7.56.

_N_-[2-Isobutyl-4-methyltetrahydropyran-4-yl]-acetamide (17f/18f; 3.5 : 1)

(195 mg, 92%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (d, J = 6.4 Hz, 6 H), 1.10–1.26 (m, 2 H), 1.38 (s, 3 H), 1.41–1.56 (m, 2 H), 1.78 (quint., J = 6.8, 1 H), 1.98 (s, 3 H), 2.06–2.16 (m, 2 H), 3.42–3.49 (m, 1 H), 3.55 (dt, J = 12.0, 4.8 and 2.0 Hz, 1 H), 3.82 (dd, J = 11.6 and 4.4 Hz, 1 H), 5.33 (brs, 0.78 H), 5.53 (brs, 0.22 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.3, 23.3, 24.3, 24.4, 27.9, 36.3, 42.4, 45.2, 51.8, 63.5, 71.0, 170.2 (major); IR: 3307, 2958, 2928, 2870, 1652, 1549, 1372, 1288, 1115, 1088, 1043, 964, 758, 604; cm^{-1}. Found: C 67.66, H 10.75, N 6.49. Calc. for $C_{12}H_{23}NO_2$: C 67.57, H 10.87, N 6.57.

_N_-[2-Benzyl-4-methyltetrahydropyran-4-yl]-acetamide (17g/18g; 3.7 : 1)

(197 mg, 80%) colorless solid; M.P. 86–88 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (s, 2.37 H), 1.44 (s, 0.63 H), 1.49 (dd, J = 14.0 and 4.8 Hz, 2 H), 1.87 (d, J = 1.6 Hz, 0.63 H), 1.91 (d, J = 1.2 Hz, 2.37 H), 1.93–2.03 (m, 0.42 H), 2.08–2.18 (m, 1.58 H), 2.65 (dd, J = 13.6, and 4.8 Hz, 1 H), 2.81 (dd, J = 14.0, and 7.2 Hz, 1 H), 3.52 (dt, J = 12.0 and 1.6 Hz, 1 H), 3.61–3.67 (m, 1 H), 3.80 (dd, J = 12.0, and 4.8 Hz, 0.79 H), 3.85–3.99 (m, 0.21 H), 5.45 (s, 0.79 H), 5.57 (s, 0.21 H), 7.13–7.40 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.4, 27.8, 35.8, 42.0, 42.5, 51.7, 63.6, 73.6, 126.3, 128.3, 129.4, 138.5, 170.2 (major); IR: 3310, 2926, 2856, 1650, 1551, 1439, 1371, 1101, 1031, 700 cm^{-1}. Found: C 72.75, H 8.42, N 5.81. Calc. for $C_{15}H_{21}NO_2$: C 72.84, H 8.56, N 5.66.

_N_-(Tetrahydro-4-methyl-2-styryl-2*H*-pyran-4-yl)acetamide (17h/18h; 2.5 : 1)

(191 mg, 74%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38 (dd, J = 11.6 and 2.4 Hz, 0.70 H), 1.42 (s, 2.10 H), 1.55 (s, 0.90 H),

1.60 (dd, J = 12.8, and 4.8 Hz, 0.30 H), 1.72–1.97 (m, 1 H), 1.94 (s, 0.90 H), 2.02 (s, 2.10 H), 2.08–2.14 (m, 1 H), 2.32–2.38 (m, 1 H), 3.63–3.74 (m, 1 H), 3.93 (dd, J = 12.0 and 4.0 Hz, 0.70 H), 3.98 (dd, J = 12.0 and 5.2 Hz, 0.30 H), 4.08–4.17 (m, 1 H), 5.47 (s, 0.70 H), 5.53 (s, 0.30 H), 6.15 (dd, J = 16.0, and 5.6 Hz, 1 H), 6.60 (d, J = 15.6 Hz, 0.30 H), 6.62 (d, J = 16.0 Hz, 0.70 H), 7.20–7.40 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0, 24.5, 27.7, 29.5, 35.8, 36.5, 41.8, 42.5, 51.8 (2C), 63.4, 63.9, 73.1, 74.1, 126.4 (2C), 127.6, 128.0, 128.5, 128.9, 129.5, 129.6, 130.4, 130.5, 136.5, 136.7 170.2, 170.8; IR: 3318, 2963, 2856, 1651, 1547, 1447, 1372, 1107, 1085, 966, 746, 694 cm^{-1}. Found: C 74.28, H 8.25, N 5.24. Calc. for $C_{16}H_{21}NO_2$: C 74.10, H 8.16, N 5.40.

N-[4-Methyl-2-phenyltetrahydropyran-4-yl]-benzamide (17i/18i; 3 : 1)

(206 mg, 70%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (s, 2.25 H), 1.62 (dd, J = 14.0 and 12.4 Hz, 1 H), 1.75 (s, 0.75 H), 1.76–1.82 (m, 0.75 H), 1.94 (t, J = 11.6 Hz, 0.25 H), 2.09 (dd, J = 7.6 and 3.2 Hz, 0.75 H), 2.25–2.35 (m, 0.50 H), 2.64 (dt, J = 14.4 and 2.0 Hz, 0.75 H), 3.76–3.97 (m, 1 H), 3.97–4.14 (m, 1 H), 4.56 (dd, J = 11.6 and 1.6 Hz, 0.75 H), 4.70 dd, J = 11.2 and 2.0 Hz, 0.25 H), 6.00 (brs, 1 H), 7.23–7.53 (m, 8 H), 7.66 (d, J = 7.2 Hz, 1 H), 7.77 (d, J = 7.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.3, 24.4, 27.7, 36.0, 36.5, 43.5, 44.5, 52.0, 63.9, 64.4, 73.8, 74.7, 120.7, 122.2, 122.4, 129.3, 132.1, 144.5, 144.8, 148.1, 170.1, 170.9; IR: 3298, 3079, 2966, 2928, 2865, 1651, 1531, 1439, 1350, 1259, 1158, 1097, 1052, 967, 908, 848, 737, 697, 684 cm^{-1}. Found: C 77.45, H 7.12, N 4.66. Calc. for $C_{19}H_{21}NO_2$: C 77.26, H 7.17, N 4.74.

N-[4-Methyl-2-(3-nitrophenyl)-tetrahydropyran-4-yl]-benzamide (17j)

(244 mg, 72%) solid; M.P. 153–155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.51–1.60 (m, 1 H), 1.56 (s, 3 H), 1.84 (ddd, J = 13.2 and 5.2 Hz, 1 H), 2.15–2.20 (m, 1 H), 2.91 (dt, J = 14.0 and 2.0 Hz, 1 H), 3.92 (dt, J = 12.4 and 1.6 Hz, 1 H), 4.12 (dd, J = 12.0 and 4.0 Hz, 1 H), 4.67 (d, J = 9.2 Hz, 1 H), 6.00 (brs, 1 H), 7.40–7.55 (m, 4 H), 7.67 (d, J = 7.6 Hz, 1 H), 7.79 (d, J = 8.4 Hz, 2 H), 8.11 (d, J = 8.0 Hz, 1 H), 8.26 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.9, 37.0, 43.4, 52.6, 64.0, 74.2, 120.9, 122.5, 126.9, 128.8, 129.4, 131.7, 132.2, 135.7, 144.6, 148.4, 167.9; IR: 3326, 2927, 2858, 1644, 1530, 1350, 1097, 1051, 736, 715, 695 cm^{-1}. Found: C 66.87, H 5.81, N 8.37. Calc. for $C_{19}H_{20}N_2O_4$: C 67.05, H 5.92, N 8.23.

N-[4-methyl-2-propyltetrahydropyran-4-yl]-benzamide (17k/18k; 3 : 1)

(169 mg, 65%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, J = 6.8 Hz, 2.25 H), 0.95 (t, J = 6.8 Hz, 0.75 H), 1.20–1.38 (m, 2 H), 1.45–1.52 (m, 1 H), 1.48 (s, 2.25 H), 1.54–1.65 (m, 1 H), 1.61 (s, 0.75 H), 1.83–1.92 (m, 1 H), 1.98–2.03 (m, 1 H), 2.06–2.15 (m, 1 H), 2.19–2.30 (m, 2 H), 3.43–3.50 (m, 1 H), 3.54–3.65 (m, 1 H), 3.70–3.81 (m, 0.75 H), 3.85 (dd, J = 16.4 and 4.4 Hz, 0.75 H), 3.91 (dd, J = 12.0 and 4.4 Hz, 0.25 H), 4.07 (dd, J = 13.2 and 7.2 Hz, 0.25 H), 5.92 (brs, 0.75 H), 6.00 (brs, 0.25 H), 7.35–7.48 (m, 3 H), 7.67–7.71 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 18.7, 27.9, 36.5, 37.5, 38.3, 38.4, 38.5, 38.7, 42.3, 43.3, 44.7, 52.2, 63.7, 64.1, 72.7, 72.9, 73.5, 126.8, 128.5, 128.6, 131.3, 135.8, 167.5; IR: 3322, 2957, 2930, 2870, 1645, 1539, 1314, 1286, 1110, 1075, 1048, 714, 693 cm^{-1}. Found: C 73.38, H 9.06, N 5.29. Calc. for $C_{16}H_{23}NO_2$: C 73.53, H 8.87, N 5.36.

N-[2-(2-Chlorophenyl)-4-methyltetrahydropyran-4-yl]-benzamide (17l/18l; 3 : 2)

(256 mg, 78%) colorless solid; M.P. 105–107 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.46 (dd, J = 14.4 and 11.6 Hz, 1 H), 1.54 (s, 1.80 H), 1.76 (ddd, J = 13.2 and 4.8 Hz, 1 H), 1.77 (s, 1.20 H), 2.15–2.20 (m, 1 H), 2.37–2.44 (m, 1 H), 2.65 (d, J = 14.4 Hz, 1 H), 3.80–3.89 (m, 1 H), 3.99–4.18 (m, 1 H), 4.93 (d, J = 11.6 Hz, 0.4 H), 5.00 (d, J = 11.2 Hz, 0.60 H), 5.98 (brs, 0.40 H), 6.07 (brs, 0.60 H), 7.19–7.34 (m, 3 H), 7.39–7.59 (m, 4 H), 7.67–7.71 (m, 1 H), 7.78–7.81 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.9, 27.8, 29.8, 31.7, 35.1, 37.1, 38.5, 43.8, 44.4, 45.4, 52.7, 52.8, 64.4, 64.8, 65.0, 68.1, 72.3, 73.1, 126.8, 127.1, 127.3, 127.3, 127.5, 128.4, 128.7, 128.9, 129.3, 131.2, 131.4, 131.6, 135.6, 135.8, 139.7, 139.9, 167.0, 167.4; IR: 3333, 2963, 2859, 1645, 1531, 1441, 1374, 1094, 1048, 753, 709 cm^{-1}. Found: C 69.30, H 6.17, N 4.15. Calc. for $C_{19}H_{20}ClNO_2$: C 69.19, H 6.11, N 4.25.

2,2-Dichloro-N-(4-methyl-2-propyltetrahydropyran-4-yl)-acetamide (17m/18m; 2.5 : 1)

(160 mg, 60%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, J = 7.2 Hz, 3 H), 1.28 (dd, J = 14.0 and 12.0 Hz, 1 H), 1.35–1.52 (m, 4 H), 1.42 (s, 2.1 H), 1.55 (s, 0.90 H), 1.61 (ddd, J = 13.6, 8.8 and 4.8 Hz, 0.70 H), 1.78–1.91 (m, 0.30 H), 1.99 (dd, J = 14.4 and 12.4 Hz, 0.60 H), 2.13 (dd, J = 14.4 and 12.4 Hz, 1.40 H), 3.36–3.44 (m, 1 H), 3.56 (t, J = 12.4 Hz, 1 H), 3.87 (dd, J = 12.0 and 4.8 Hz, 0.70 H), 3.93 (dd, J = 12.0 and 4.0 Hz, 0.30 H), 5.82 (s, 0.30 H), 5.84 (s, 0.70 H), 6.22 (s, 0.70 H), 6.28 (s, 0.30 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 18.7, 21.5, 27.3, 36.1, 36.8, 38.2, 38.4, 41.8, 42.6, 52.9, 53.1, 63.4, 64.0, 67.1, 67.3, 72.7, 73.4, 163.5; IR: 3297, 2961, 2933, 2872, 1682, 1557, 1450, 1346, 1144, 1113, 1079, 1008, 814, 658 cm^{-1}. Found: C 49.43, H 7.02, N 5.16. Calc. for $C_{11}H_{19}Cl_2NO_2$: C 49.26, H 7.14, N 5.22.

2,2-Dichloro-N-[4-methyl-2-(3-nitrophenyl)-tetrahydropyran-4-yl]-acetamide (17n/18n; 3.6 : 1)

(252 mg, 73%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.33 (s, 0.60 H), 1.42–1.60 (m, 1 H), 1.47 (s, 2.4 H), 1.75–1.90 (m, 1 H), 2.07–2.14 (m, 1 H), 2.32–2.37 (m, 0.2 H), 2.72 (dd, J = 14.4 and 1.6 Hz, 0.8 H), 3.82 (dt, J = 12.4 and 2.0 Hz, 0.8 H), 3.97–4.04 (m, 0.2 H), 4.06–4.20 (m, 1 H), 4.57 (d, J = 11.6 Hz, 0.8 H), 4.83 (d, J = 11.6 Hz, 0.20 H), 5.82 (s, 0.2 H), 5.92 (s, 0.8 H), 6.37 (brs, 1 H), 7.48–7.53 (m, 1 H), 7.64–7.70 (m, 1 H), 8.10–8.15 (m, 1 H), 8.24 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 27.3, 29.8, 31.7, 36.5, 38.4, 42.9, 46.6, 53.1, 63.8, 64.2, 67.3, 68.0, 74.1, 74.8, 120.9, 121.0, 122.3, 122.6, 129.0, 129.5, 132.1, 144.3, 148.4, 163.9; IR: 3305, 2966, 2867, 1682, 1530, 1476, 1351, 1096, 1051, 811, 737, 716 cm^{-1}. Found: C 48.26, H 4.71, N 8.15. Calc. for $C_{14}H_{16}Cl_2N_2O_4$: C 48.43, H 4.64, N 8.07.

But-3-enoic acid [4-methyl-2-(3-nitrophenyl)-tetrahydropyran-4-yl]-amide (17o/18o; 2 : 1)

(265 mg, 92%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.38–1.50 (m, 1 H), 1.43 (s, 2 H), 1.65 (s, 1 H), 1.71 (ddd, J = 13.6, 8.4

and 5.2 Hz, 0.67 H), 1.80 (t, J = 12.4 Hz, 0.33 H), 1.89 (d, J = 12.4 Hz, 0.33 H), 2.04 (d, J = 14.0 Hz, 0.67 H), 2.33 (dd, J = 13.2 and 2.4 Hz, 0.33 H), 2.71(dt, J = 14.0 and 2.0 Hz, 0.67 H), 2.93 (dt, J = 7.2 and 1.2 Hz, 0.66 H), 3.06 (dt, J = 7.2 and 1.2 Hz, 1.34 H), 3.64 (t, J = 15.2 Hz, 0.33 H), 3.77 (tt, J = 12.4 and 3.2 Hz, 0.67 H), 4.05 (dd, J = 12.0 and 4.0 Hz, 0.67 H), 4.11 (dd, J = 11.6 and 4.8 Hz, 0.33 H), 4.45–4.59 (m, 1 H), 5.16–5.23 (m, 1 H), 5.25–5.32 (m, 1 H), 5.55 (s, 0.33 H), 5.60 (s, 0.67 H), 5.89 (ddd, J = 10.0, 7.2 and 2.8 Hz, 0.33 H), 6.00 (ddd, J = 9.6, 7.2 and 3.2 Hz, 0.67 H), 7.49 (t, J = 8.0 Hz, 1 H), 7.66 (d, J = 7.6 Hz, 1 H), 8.11 (d, J = 8.4 Hz, 1 H), 8.23 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.8, 27.7, 36.2, 36.5, 42.3, 42.5, 43.3, 44.5, 48.2, 52.0, 63.8, 64.4, 73.8, 74.7, 119.2, 120.7, 122.2, 122.3, 129.2, 129.3, 131.5, 131.8, 132.0, 144.5, 144.7, 148.1, 170.3, 171.0; IR: 3394, 3310, 2927, 2863, 1650, 1531, 1350, 1097, 1052, 735, 683 cm^{-1}. Found: C 63.32, H 6.50, N 9.32. Calc. for $C_{16}H_{20}N_2O_4$: C 63.14, H 6.62, N 9.20.

Methyl-4-(4-acetamido-tetrahydro-4-methyl-6-phenyl-2*H*-pyran-2-yl)benzoate (17p/18p; 3 : 2)

(308 mg, 84%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45 (s, 1.8 H), 1.77 (s, 1.2 H), 1.91 (s, 1.2 H), 2.11 (s, 1.8 H), 2.20 (dm, J = 13.6 Hz, 1 H), 2.35 (dm, J = 12.8 Hz, 1 H), 2.43 (dm, J = 14.4 Hz, 1 H), 2.68 (dm, J = 14.0 Hz, 1 H), 3.91 (s, 3 H), 4.72–4.83 (m, 2 H), 5.32 (s, 0.4 H), 5.39 (s, 0.6 H), 7.28–7.31 (m, 1 H), 7.34–7.39 (m, 2 H), 7.43 (d, J = 7.2 Hz, 2 H), 7.50 (d, J = 8.4 Hz, 2 H), 8.01 (d, J = 8.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.5, 24.5, 24.8, 27.8, 43.4, 43.9, 44.4, 44.6, 52.2, 53.0, 53.1, 74.8, 75.2, 75.5, 76.0, 125.8, 125.9, 127.6, 127.7, 128.4, 129.0, 129.1, 129.6, 129.7, 141.9, 142.1, 147.5, 147.8, 167.2, 167.3, 170.3, 171.1; IR: 3368, 3060, 2926, 1718, 1657, 1543, 1371, 1280, 1112, 1091, 754, 700 cm^{-1}. Found: C 72.05, H 6.94, N 3.72. Calc. for $C_{22}H_{25}NO_4$: C 71.91, H 6.86, N 3.81.

Methyl-4-(4-acetamido-tetrahydro-4-methyl-6-*p*-tolyl-2*H*-pyran-2yl)benzoate (17q/18q; 1 : 1)

(298 mg, 78%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 1.5 H), 1.48 (dd, J = 11.6 and 2.0 Hz, 1 H), 1.59 (dd, J = 12.0 and 2.4 Hz, 1 H), 1.75 (s, 1.5 H), 1.80–1.86 (m, 0.5 H), 1.90 (s, 1.5 H), 2.10 (s, 1.5 H), 2.20 (dm, J = 13.2 Hz, 0.5 H), 2.34 (s, 1.5 H), 2.34 (s, 1.5 H), 2.38 (dm, J = 12.0 Hz, 0.5 H), 2.70 (dm, J = 14.0 Hz, 0.5 H), 3.90 (s, 3 H), 4.67–4.82 (m, 2 H), 5.43 (s, 0.50 H), 5.59 (s, 0.50 H), 7.15–7.18 (m, 2 H), 7.30–7.33 (m, 2 H), 7.48–7.50 (m, 2 H), 7.99–8.00 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 22.4, 24.4, 24.6, 27.8, 43.3, 44.1, 44.6, 44.7, 52.1, 52.8, 52.9, 74.8, 75.1, 75.5, 75.9, 125.7, 125.8, 125.9, 129.1, 129.6, 129.7, 137.2, 137.3, 239.0, 139.2, 147.6, 147.9, 167.1, 169.8, 170.6; IR: 3305, 2951, 2924, 2861, 1721, 1656, 1547, 1436, 1280, 1111, 1089, 759 cm^{-1}. Found: C 72.31, H 7.29, N 3.61. Calc. for $C_{23}H_{27}NO_4$: C 72.42, H 7.13, N 3.67.

Methyl-4-(4-acetamido-tetrahydro-4-methyl-6-propyl-2*H*-pyran-2yl)benzoate (17r/18r; 3 : 2)

(300 mg, 90%) semisolid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90–0.99 (m, 3 H), 1.25 (s, 1.2 H), 127–1.38 (m, 1 H), 1.41 (s, 1.8 H), 1.43–1.52 (m, 1 H), 1.54–1.69 (m, 2 H), 1.93 (s, 1.2 H), 1.98 (dm, (dm, J = 12.8 Hz, 0.40 H), 2.04 (s, 1.80 H), 2.11 (dm, J = 14.0 Hz, 0.60 H), 2.24–2.33 (m, 2 H), 2.63 (dm, J = 14.0 Hz, 1 H), 3.61–3.72 (m, 1 H), 3.90 (s, 3 H), 4.54 (d, J = 12.0 Hz, 0.40 H), 4.59 (d, J = 11.2 Hz, 0.60 H), 5.58–5.75 (brm, 1 H), 7.42 (d, J = 8.0 Hz, 2 H), 7.98 (d, J = 8.4 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 14.2, 14.3, 18.4, 18.8, 22.6, 24.5, 24.7, 27.9, 29.8, 36.2, 38.2, 38.4, 42.3, 42.6, 43.2, 44.7, 52.2, 52.9, 53.0, 73.0, 73.7, 74.3, 75.0, 125.8, 125.8, 129.0, 129.1, 129.7, 147.9, 148.1, 167.3, 170.1, 170.7, 177.9; IR: 3368, 2960, 1718, 1657, 1543, 1436, 1280, 1112, 1091, 754, 700 cm^{-1}. Found: C 68.38, H 8.25, N 4.31 Calc. for $C_{19}H_{27}NO_4$: C 68.44, H 8.16, N 4.20.

Acknowledgements

A.K.S. and S. B. are grateful to Council and Industrial Research (CSIR), New Delhi for financial support (Grant No. 01(2332)/09/EMR-II) and a fellowship, respectively. The authors gratefully acknowledge the X-ray facility provided by the Department of Science and Technology (DST), under FIST programme.

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19 The crystallographic data for compounds **6e**, **10** and **17j** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication Nos. CCDC 765896, 765895 and 801332, respectively.

