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Graphical Abstract

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$AlCl_3$ Catalyzed Oxa-Diels-Alder Reaction of Aromatic Aldehydes with Simple Dienes

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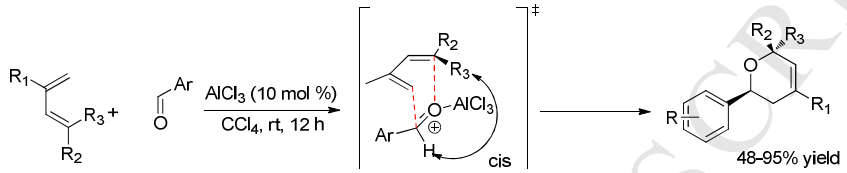

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$AlCl_3$ catalyzed oxa-diels-alder reaction of aromatic aldehydes with simple dienes

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ABSTRACT

Highly regioselective and diastereoselective oxa-Diels-Alder reaction catalyzed by $AlCl_3$ has been developed. This reaction is efficient and characterized by good functional group compatibility, F, Cl, CN, NO_2, OMe and thiophenyl group are tolerated. A Lewis acid catalyzed concerted cycloaddition mechanism is proposed based on the results.

1. Introduction

The oxa-Diels-Alder reaction between aldehydes and 1,3-dienes is a powerful synthetic method to construct dihydropyran scaffold and is widely applied in the synthesis of natural products.[1] However, previous reported oxa-Diels-Alder reaction has been limited either to the reaction of electron rich dienes such as Danishefsky's,[2] Brassard's[3] or Rawal's diene[4] with a broad range of aldehydes or the reaction of activated aldehydes containing electron-withdrawing groups (e.g., glyoxylates) with a broad range of dienes. The reaction between aldehydes and simple dienes mostly is guided by the interaction between the HOMO of diene and the LUMO of the dienophile (aldehydes).[5] As compare to the activated aldehydes, unactivated aldehydes have higher LUMO level of the π_{C-O} bond. On the other hand, in comparison to the electron rich dienes, the simple dienes have lower level of HOMO. The energy gaps between HOMO of simple dienes and LUMO of aldehydes are relatively higher than the energy gaps in other two types of Diels-Alder reactions mentioned above. This is the reason why the oxa-Diels-Alder reaction of aldehydes and simple dienes is much more challenging as compared to other Diels-Alder reactions and only a limited number of oxa-Diels-Alder reactions of unactivated aldehydes and simple dienes have been achieved. In the early time, Pd^{2+} catalysts,[6] $Sc(OPf)_3$,[7] $TiCl_4$,[8] HOTf[9] or a mixture of $AlCl_3$ and nitroalkane or $SnCl_4$ with nitroalkane were applied in the oxa-Diels-Alder reactions.[10] Later on, Matsubara and co-workers reported a big breakthrough of oxa-Diels–Alder reaction between unactivated dienes with unactivated aldehydes under mild reaction conditions catalyzed by iron(III) porphyrin[1b] or iron(IV) corrole complexes.[11] Lu and co-workers recently reported $AgBF_4$ catalyzed oxa-Diels-Alder reaction of electrically neutral 1,3-dienes and various aldehydes.[12] Heteroatoms at the β-position of the aryl aldehydes can greatly promote the reactivity of the substrates. Franzén and co-workers reported carbocation catalyzed oxa-Diels-Alder reaction.[13] Despite all developments in this field, there are still many issues that need to be solved in this reaction, for example, the efficiency of this reaction, the substrate scope and the readily availability of the catalysts. Due to the innate low reactivity of the substrates, much more equivalents of dienes or aldehydes were applied in most catalytic systems. Furthermore, some substrates like 4-methoxy-bezaldehyde tend to afford no product or product with low yield. Thus, the development of more efficient catalytic systems with readily available catalysts is necessary. Herein, we report the $AlCl_3$ catalyzed oxa-Diels-Alder reaction of unactivated aldehydes with simple dienes under mild conditions.

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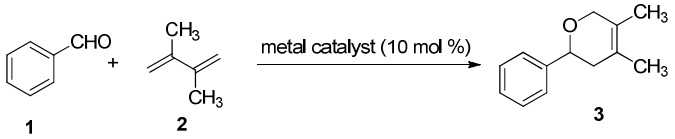
2. Results and discussion

We initiated our study with benzaldehyde (**1**) and 2,3-dimethyl-1,3-butadiene (**2**, DMB) as the model substrates. A range of potential catalysts were screened and $AlCl_3$ was found promote the reaction most (Table 1). Dihydropyran product **3** was obtained in benzene at 80 °C with 70% ^{1}H NMR yield when 10 mol % $AlCl_3$ was applied (Table 1, entry 5). Further reaction conditions screening showed CCl_4 is the best solvent and this reaction takes place at room temperature. To our delight, reducing the usage of diene's slightly increased the yield of the product. Product with 90% ^{1}H NMR yield (84% isolated yield) was obtained when 1:1 aldehyde to dienes was applied (Table 1, entry 12).

Table 1

Reaction conditions optimization.[a]



1 2 3

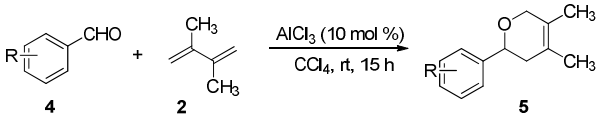
Entry	Catalyst	Solvent	Temp (°C)	Ratio of **2**:**1**	Yield (%)[b]
1	$Y(OAc)_3 \cdot 4H_2O$	benzene	80	4	0
2	$Sc(OAc)_3 \cdot 6H_2O$	benzene	80	4	0
3	$NiCl_2 \cdot 6H_2O$	benzene	80	4	0
4	$RuCl_3 \cdot 3H_2O$	benzene	80	4	49
5	$AlCl_3$	benzene	80	4	70
6	$AlCl_3$	toluene	rt	4	8
7	$AlCl_3$	xylene	rt	4	19
8	$AlCl_3$	n-hexane	rt	4	57
9	$AlCl_3$	CCl_4	rt	4	71
10	$AlCl_3$	CCl_4	rt	3	72
11	$AlCl_3$	CCl_4	rt	2	85
12	$AlCl_3$	CCl_4	rt	1	90 (84)[c]
13	$AlCl_3$	CCl_4	40	1	86
14	$AlCl_3$	CCl_4	60	1	86
15	$AlCl_3$	CCl_4	80	1	88

[a] Reactions were carried out using the catalyst (10 mol %), aldehyde **1** (1 mmol), and diene **2** (X mmol) in 2 mL of solvent for 15 h.
[b] Yields are determined by ^{1}H NMR.
[c] Yield of isolated product.

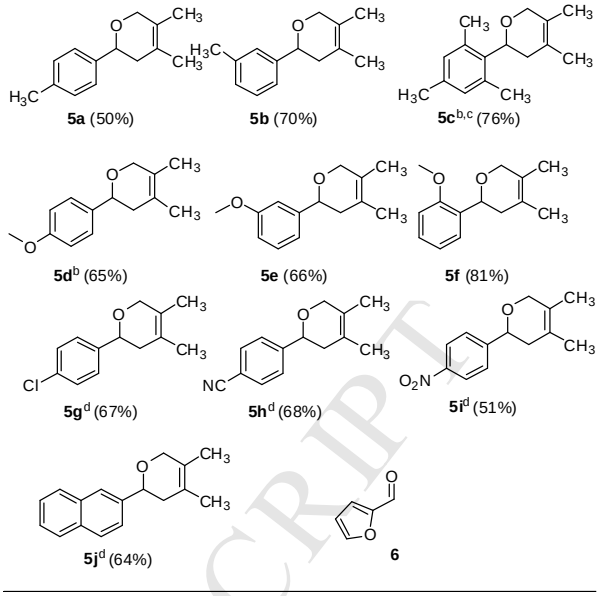
With the best conditions in hands, other aryl aldehydes were examined. In general, *para*-electron donating group substituted benzaldehydes afforded the products in relative lower yields (**5a** and **5d**). Four equivalents of *p*-methoxy-benzaldehyde were necessary to deliver the corresponding product in moderate yield (**5d**, 65%). Aldehydes with *para*-electron withdrawing groups, like 4-chloro, 4-nitrile and 4-nitro benzaldehyde failed to deliver corresponding products at room temperature. Increasing the reaction temperature to 70 °C lead to better reactivities (**5g**, **5h** and **5i**). *Meta*-substituted benzaldehydes had showed better reactivity (**5e**). *Ortho*-substituents, especially coordinating substituent benefit this reaction (**5f**, 81%). The effect of *ortho*-substituent was investigated comprehensively in Lu's work.[12] 2-Naphthaldehyde reacted with DMB (**2**) at 70 °C and afforded product in 64% yield. Furfural (**6**) was proved not reactive at all.

Table 2

$AlCl_3$ catalyzed oxa-Diels-Alder reaction of **2** and aldehydes **4**.[a]



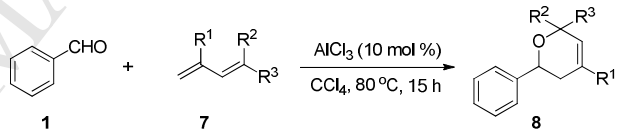
4 2 5



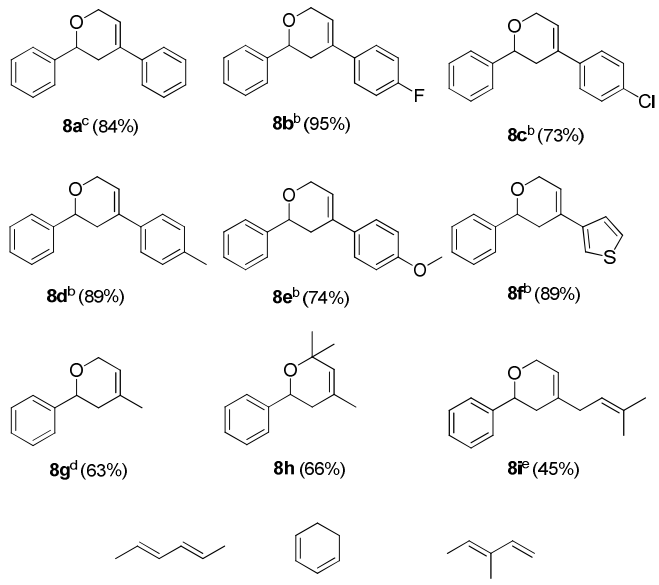
[a] Reactions were carried out using the catalyst (10 mol %), aldehyde **4** (1 mmol), and diene **2** (1 mmol) in 2 mL of solvent at room temperature for 15 h. Isolated yields based on aldehyde **4**.
[b] At 80 °C, the ratio of **4**:**2** is 1:4.
[c] Benzene as solvent.
[d] At 70 °C.

Table 3

$AlCl_3$ catalyzed oxa-Diels-Alder reaction of benzaldehyde and substituted dienes **7.**[a]



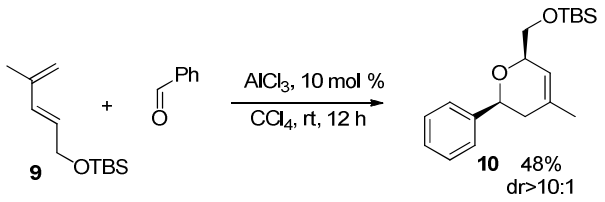
1 7 8



[a] Reactions were carried out using the catalyst (10 mol %), aldehyde **1** (1 mmol), and diene **7** (1 mmol) in 2 mL of solvent at 80 °C for 15 h. Isolated yields based on aldehyde **1**.
[b] At room temperature.
[c] **7a** (1.5 mmol, 1.5 equiv).
[d] **7g** (3 mmol, 3 equiv).
[e] **7i** (2 mmol, 2 equiv).

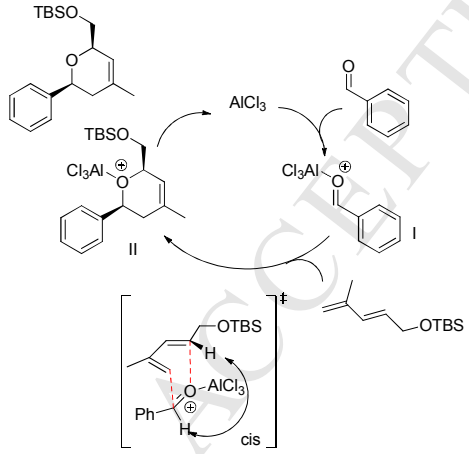
Next, substituted 1,3-dienes have been examined. The results are summarized in Table 3. The reaction of 2-phenyl-1,3-butadiene with benzaldehyde proceeded smoothly and delivered corresponding product in 84% yield (**8a**). Substituents on the phenyl ring of the dienes affect the reaction slightly and afforded products from good to excellent yields (**8b**, **8c**, **8d** and **8e**). 2-Thiophenyl-1,3-diene has the similar reactivity as 2-phenyl-1,3-diene does (**8f**). 2-Methyl-1,3-diene is less reactive (**8g**). Higher reaction temperature (70 ^{o}C) and more usage of dienes are necessary to afford the corresponding product for 2-methyl-1,3-butadiene (**8g**). Reaction of myrcene with benzaldehyde needed 2 equivalents of myrcene and still yielded product in poor yield (**8i**, 45%). Trisubstituted 1,3-diene, 2,4-dimethyl-1,3-pentadiene reacted with benzaldehyde smoothly at room temperature at 1:1 ratio of the two reactants (**8h**). Cyclobutadiene, 2-methyl-1,3-pentadiene and 2,4-hexadiene failed to give any product. These experimental results indicate that the diene must possess a substituent at the C-2 position and no substituent at the C-1 position for the smooth reaction.

We next examined the diastereoselectivity of this reaction. 2,4-Disubstituted diene **9** was applied and dihydropyran **10** was obtained in 48% yield with a diastereomeric ratio more than 10:1 (Scheme 1).



Scheme 1. $AlCl_3$ catalyzed oxa-Diels-Alder reaction.

Considering the regioselectivities and diastereoselectivities of this reaction, a Lewis acid catalyzed concerted mechanism is proposed (Scheme 2). We cannot rule out the stepwise addition mechanism since it is possible that the ring closing step is much faster than the isomerization of the allylic cation.



Scheme 2. Proposed catalytic cycle for oxa-Diels-Alder reaction.

3. Conclusion

In summary, we have developed $AlCl_3$ catalyzed oxa-Diels-Alder reaction between unactivated 1,3-dienes and aryl-aldehydes. This reaction is characterized by good functional group compatibility, for instance, F, Cl, CN, NO_2, OMe and thiophenyl groups are tolerated. This reaction is efficient, one equivalent of dienes is enough to deliver product in good yield for most of the substrates. This regioselective and diastereoselective reaction has expanded the substrate scope to more dienes and arylaldehydes with readily available catalyst.

4. Experimental section

4.1. General

All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring unless otherwise indicated. Commercially obtained reagents were used as received. Solvents were dried by distillation from sodium or CaH2. Liquids and solutions were transferred via syringe. All reactions were monitored by thin-layer chromatography. 1H and 13C NMR spectra were recorded on Bruker-BioSpin AVANCE III HD. Data for 1H NMR spectra are reported relative to chloroform as an internal standard (7.26 ppm) and are reported as follows: chemical shift (ppm), multiplicity, coupling constant (Hz), and integration. Data for 13C NMR spectra are reported relative to chloroform as an internal standard (77.23 ppm) and are reported in terms of chemical shift (ppm). IR data were obtained from Bruker VERTEX 70. HRMS data were recorded on Agilent Technologies 6224 TOF LC/MS.

4.2. General Procedure the $AlCl_3$ Catalyzed Oxa-Diels-Alder Reaction

Aldehyde (1 mmol), diene (1 mmol), $AlCl_3$ (13.4 mg, 10 mol%) and dry CCl_4 (2 mL) were added to a flame dried schlenk tube with a rubber septum under the argon atmosphere. The reaction mixture was stirred at room temperature for 15 hours. Then, the mixture was purified by column chromatography on silica gel(petroleum ether/ethyl acetate = 100/0~50/1) to yield product.

4.3. Characterization data of compounds

3,4-Dimethyl-6-phenyl-5,6-dihydro-2H-pyran (**3**). Clear oil, 157.2 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.37-7.31 (m, 4H), 7.25-7.23 (m, 1H), 4.53 (dd, J_1 = 4.0 Hz, J_2 = 8.0 Hz, 1H), 4.21-4.07 (m, 2H), 2.32 (t, J = 12.0 Hz, 1H), 2.08 (d, J = 16.0 Hz, 1H), 1.67 (s, 3H), 1.57 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 141.61, 127.29, 126.32, 124.77, 123.49, 122.79, 75.28, 69.27, 37.54, 17.31, 12.81. IR (thin film): 2959, 2929, 2871, 1509, 1454, 1374, 1233, 1096 cm^{-1}.

3,4-Dimethyl-6-(4-methylphenyl)-5,6-dihydro-2H-pyran (**5a**). Clear oil, 101.8 mg, 50%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 4.52 (dd, J_1 = 4.0 Hz, J_2 = 8.0 Hz, 1H), 4.21-4.07 (m, 2H), 2.33 (s, 3H), 2.31-2.26 (m, 1H), 2.06 (d, J = 16.0 Hz, 1H), 1.68 (s, 3H), 1.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.63, 135.95, 127.97, 124.76, 123.49, 122.86, 75.17, 69.29, 37.50, 20.10, 17.33, 12.83. HRMS (ESI) calcd for $[C_{14}H_{22}NO]^+$($[M+NH_4]^+$): 220.1696, found: 220.1701.

3,4-Dimethyl-6-(3-methylphenyl)-5,6-dihydro-2H-pyran (**5b**). Clear oil, 140.4 mg, 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.20 (m, 2H), 7.16 (d, J = 8.0 Hz, 1H), 7.09 (d, J = 8.0 Hz, 1H), 4.52 (dd, J_1 = 4.00 Hz, J_2 = 8.0 Hz, 1H), 4.22-4.09 (m, 2H), 2.35 (s, 3H), 2.32-2.27 (m, 1H), 2.09 (d, J = 16.0 Hz, 1H), 1.69 (s, 3H), 1.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.56, 138.00, 128.23, 128.13, 126.49, 124.50, 123.90, 122.91, 76.42, 70.36, 38.58, 21.47, 18.36, 13.86. IR (thin film): 3025, 2918, 2859, 1611, 1448, 1374, 1233, 1096 cm^{-1}. HRMS (ESI) calcd for $[C_{14}H_{22}NO]^+$($[M+NH_4]^+$): 220.1696, found: 220.1700.

3,4-Dimethyl-6-mesityl-5,6-dihydro-2H-pyran (**5c**). Clear oil, 176.9 mg, 77%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (s, 2H), 4.90 (dd, J_1= 4.0 Hz, J_2= 8.0 Hz, 1H), 4.13-4.03 (m, 2H), 2.53 (t, J = 12.0 Hz,1H), 2.37 (s, 6H), 2.21 (s, 3H), 1.85 (d, J = 16.0 Hz, 1H), 1.66 (s, 3H), 1.57 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.44, 136.07, 135.05, 130.07, 125.09, 124.08, 74.36, 70.41,

35.18, 31.82, 22.87, 20.90, 18.47, 14.31, 14.11. IR (thin film): 2953, 2924, 2856, 1458, 1376, 1099 cm^{-1}. HRMS (ESI) calcd for $[C_{16}H_{26}NO]^+$([M+NH_4]$^+$): 248.2009, found: 248.2016.

3,4-Dimethyl-6-(4-methoxyphenyl)-5,6-dihydro-2H-pyran (**5d**). Clear oil, 142.6 mg, 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.0 Hz, 2H), 4.43 (dd, J_1= 4.0 Hz, J_2= 8.0 Hz, 1H), 4.14-3.99 (m, 2H), 3.72 (s, 3H), 2.27 (t, *J* = 16.0 Hz, 1H), 2.00 (d, *J* = 20.0 Hz, 1H), 1.61 (s, 3H), 1.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ157.91, 133.81, 126.14, 123.48, 122.85, 112.71, 74.93, 69.31, 54.25, 37.41, 17.33, 12.82. IR (thin film): 2916, 2857, 1613, 1515, 1248, 1097, 1035, 828 cm^{-1}. HRMS (ESI) calcd for $[C_{14}H_{18}Na]^+$([M+Na]$^+$): 241.1204, found: 241.1193.

3,4-Dimethyl-6-(3-methoxyphenyl)-5,6-dihydro-2H-pyran (**5e**). Clear oil,144.7 mg, 66%. as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (t, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 8.0, 1H), 4.54 (dd, J_1 = 4.0 Hz, J_2 = 12.0 Hz, 1H), 4.22-4.09 (m, 2H), 3.81 (s, 3H), 2.33 (t, *J* = 16.0 Hz, 1H), 2.10 (d, *J* = 16.0 Hz, 1H), 1.69 (s, 3H),1.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.72, 144.33, 129.33, 124.53, 123.84, 118.16, 113.17, 111.05, 76.26, 70.31, 55.23, 38.60, 18.35, 13.86. IR (thin film): 2918, 2857, 1604, 1454, 1261, 1105, 1048 cm^{-1}. HRMS (ESI) calcd for $[C_{14}H_{22}NO_2]^+$([M+NH_4]$^+$): 236.1645, found: 236.1653.

3,4-Dimethyl-6-(2-methoxyphenyl)-5,6-dihydro-2H-pyran (**5f**). Clear oil, 178.6 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.0 Hz, 1H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.00 (t, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 4.92 (dd, J_1 = 4.0 Hz, J_2 = 8.0 Hz, 1H), 4.23-4.09 (m, 2H), 3.82 (s, 3H), 2.21-2.10 (m, 2H), 1.67 (s, 3H), 1.59 (s, 3H). ^{13}C NMR (100 MHz, CDCl3) δ 155.80, 131.29, 128.01, 126.05, 124.36, 124.22, 120.88, 110.15, 70.77, 70.43, 55.33, 37.41, 18.35, 13.88. IR (thin film): 2918, 2884, 1589, 1493, 1463, 1243, 1099, 1050, 1032, 753 cm^{-1}. HRMS (ESI) calcd for $[C_{14}H_{22}NO_2]^+$([M+NH_4]$^+$): 219.1380, found: 219.1387.

3,4-Dimethyl-6-(4-chlorophenyl)-5,6-dihydro-2H-pyran (**5g**). Clear oil, 150.5 mg, 67%. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.33-7.27 (m, 4H), 4.53 (dd, J_1 = 4.0 Hz, J_2 = 8.0 Hz, 1H), 4.21-4.07 (m, 2H), 2.27 (t, *J* = 12.0 Hz, 1H), 2.08 (d, *J* = 16.0 Hz, 1H), 1.68 (s, 3H), 1.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ141.23, 132.98, 128.45, 127.19, 124.58, 123.61, 75.54, 70.23, 38.50, 18.34, 13.85. IR (thin film): 2919, 2886, 2858, 1491, 1090, 1014, 821 cm^{-1}.

3,4-Dimethyl-6-(4-benzonitrile)-5,6-dihydro-2H-pyran (**5h**). Clear oil, 145.7 mg, 68% as. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.65 (d, *J* = 12.0 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H),4.61 (dd, J_1 = 4.0 Hz, J_2 = 12.0 Hz, 1H), 4.22-4.10 (m, 2H), 2.24-2.16 (m, 1H), 2.12 (d, *J* = 16.0 Hz, 1H), 1.69 (s, 3H), 1.60 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 148.10, 132.19, 126.34, 124.67, 123.33, 118.94, 111.02, 75.35, 70.12, 38.35, 18.32, 13.84. IR (thin film): 2919, 2887, 2858, 2227, 1506, 1101 cm^{-1}. HRMS (ESI) calcd for $[C_{14}H_{19}N_2O]^+$([M+NH_4]$^+$): 231.1492, found: 231.1484.

3,4-Dimethyl-6-(4-nitrophenyl)-5,6-dihydro-2H-pyran (**5i**). Clear oil, 120.5 mg, 52%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 2H),4.66 (dd, J_1 = 4.0 Hz, J_2 = 8.0 Hz, 1H), 4.24-4.11 (m, 2H), 2.25-2.11 (m, 2H), 1.70 (s, 3H), 1.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ150.15, 147.13, 126.37, 124.70, 123.59, 123.28, 75.17, 70.12, 38.41, 18.31, 13.84. IR (thin film): 2919, 2887, 2858, 1605, 1520, 1346, 1104, 852 cm^{-1}. HRMS (ESI) calcd for $[C_{13}H_{19}N_2O_3]^+$([M+NH_4]$^+$): 251.1390, found: 251.1390.

3,4-Dimethyl-6-(naphthalen-2-yl)-5,6-dihydro-2H-pyran (**5j**). White solid, 153.0 mg, 64%. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.82 (d, *J* = 4.0 Hz, 4H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 4.0 Hz, 2H), 4.72 (dd, J_1 = 4.0 Hz, J_2 = 12.0 Hz, 1H), 4.27-4.14 (m, 2H), 2.41 (t, *J* = 12.0 Hz, 1H), 2.18 (d, *J* = 16.0 Hz, 1H), 1.70 (s, 3H), 1.61 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 140.15, 133.39, 132.91, 128.08, 128.03, 127.67, 125.99, 125.68, 124.61, 124.36, 124.20, 123.87, 138.9, 76.37, 70.37, 38.61, 18.42,13.94. IR (thin film): 3055, 2916, 2884, 2856, 1508, 1447, 1383, 1102 cm^{-1}. HRMS (ESI) calcd for $[C_{17}H_{22}NO]^+$([M+NH_4]$^+$): 256.1696, found: 256.1694.

2-Phenyl-4-phenyl-3,6-dihydro-2H-pyrane (**8a**). White solid, 198.3 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.28 (m, 7H), 7.24-7.15 (m, 3H), 6.13 (s, 1H), 4.61 (dd, J_1 = 4.0 Hz, J_2 = 12.0 Hz, 1H), 4.53-4.41 (m, 2H), 2.69-2.55 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 142.42, 140.06, 134.43, 128.51, 128.49, 127.67, 127.40, 125.99, 124.80, 122.26, 76.00, 66.86, 34.96. IR (thin film): 3060, 3031, 2926, 17174, 1448, 1266, 1131, 1027 cm^{-1}.

2-Phenyl-4-(4-fluorophenyl)-3,6-dihydro-2H-pyrane (**8b**). White solid, 241.4 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.31 (m, 7H), 7.03 (t, *J* = 8.0 Hz, 2H), 6.14 (s, 1H), 4.66 (d, *J* = 8.0 Hz, 1H), 4.58-4.48 (m, 2H), 2.71-2.59 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 163.45, 161.00, 142.29, 136.20, 136.17, 133.50, 128.53, 127.72, 126.40, 126.32, 125.95, 122.13, 122.11, 115.40, 115.19, 75.95, 66.79, 35.09. ^{19}F (376 MHz, $CDCl_3$) δ115.12. IR (thin film): 3061, 3032, 2926, 2819, 1602, 1509, 1372, 1229, 1160, 1126, 805 cm^{-1}. HRMS (ESI) calcd for $[C_{17}H_{15}FNa]^+$([M+Na]$^+$): 277.1005, found: 277.1017.

2-Phenyl-4-(4-chlorophenyl)-3,6-dihydro-2H-pyrane (**8c**). White solid, 197.4 mg, 73%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.28 (m, 9H), 6.21-6.20 (m, 1H), 4.67 (dd, J_1 = 4.0 Hz, J_2 = 8.0 Hz, 1H), 4.60-4.48 (m, 2H), 2.73-2.57 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 142.20, 138.45, 133.42, 133.11, 128.60, 128.53, 127.74, 126.05, 125.94, 122.80, 75.91, 66.78, 34.86. IR (thin film): 3062, 3032, 2925, 2820, 1492, 1372, 1262, 1126, 1095, 1012, 751 cm^{-1}.

2-Phenyl-4-(p-tolyl)-3,6-dihydro-2H-pyran (**8d**). White solid, 224.4 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.0 Hz, 2H), 7.39 (t, *J* = 4.0 Hz,2H), 7.31 (d, *J* = 4.0 Hz,3H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.16 (s, 1H), 4.67-4.64 (m, 1H), 4.58-4.49 (m, 2H), 2.73-2.62 (m, 2H), 2.34 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 142.49, 137.21, 137.14, 134.21, 129.17, 128.50, 127.65, 125.99, 124.65, 121.35, 76.03, 66.88, 34.97, 21.12. IR (thin film): 3056, 3028, 2923, 2817, 1514, 1452, 1371, 1126, 1022, 699 cm^{-1}. HRMS (ESI) calcd for $[C_{18}H_{18}Na]^+$([M+Na]$^+$): 273.1255, found: 273.1271.

2-Phenyl-4-(4-methoxyphenyl)- 3,6-dihydro-2H-pyran (**8e**). White solid, 196.1 mg, 74%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.0 Hz, 2H), 7.40-7.30 (m, 5H), 6.88 (d, *J* = 8.00 Hz, 2H), 6.11 (s, 1H), 4.68 (dd, J_1 = 8.0 Hz, J_2 = 12.0 Hz, 1H), 4.58-4.48 (m, 2H), 3.80 (s, 3H), 2.71-2.65 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 159.03, 142.49, 133.75, 132.67, 128.48, 127.63, 125.98, 125.84, 120.46, 113.82, 76.03, 66.87, 55.31, 35.02. IR (thin film): 3060, 3033, 2927, 2833, 1607, 1513, 1272, 1250, 1186, 1126, 1035, 700 cm^{-1}.HRMS (ESI) calcd for $[C_{18}H_{19}O_2]^+$([M+H]$^+$): 267.1385, found: 267.1398.

2-Phenyl-4-(thiophen-3-yl)-3,6-dihydro-2H-pyran (**8f**). White solid, 214.5 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.37 (m, 4H), 7.33-7.25 (m, 3H), 7.12 (s, 1H), 6.19 (s, 1H), 4.67-4.64 (m, 1H), 4.57-4.48 (m, 1H), 2.72-2.63 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ142.32, 141.92, 129.91, 128.52, 127.71, 125.99, 125.83, 124.44, 121.23, 118.97, 75.87, 66.53, 35.03. IR (thin film): 3061, 3028, 2924, 2852, 2818, 2360, 1453, 1365, 1217, 1123, 1021, 773 cm^{-1}. HRMS (ESI) calcd for $[C_{15}H_{15}OS]^+$([M+H]$^+$): 243.0844, found: 243.0861.

2-Phenyl-4-methyl-3,6-dihydro-2H-pyran (**8g**). Clear oil, 110.0 mg, 63%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.22 (m, 4H), 7.18-7.14 (m, 1H), 5.39 (s, 1H), 4.44 (dd, J_1 = 4.0 Hz, J_2 = 12.0 Hz, 1H), 4.21 (s, 2H), 2.23 (t, *J* = 12.0 Hz, 1H), 2.02 (d, *J* = 20.0 Hz, 1H), 1.64 (s, 3H).^{13}C NMR (100 MHz, CDCl3) δ

142.71, 132.05, 128.42, 127.48, 125.91, 119.91, 75.84, 66.52, 37.81, 23.01. IR (thin film): 2929, 2910, 2890, 2821, 1450, 1380, 1162, 1119, 1036, 699 cm^{-1}.HRMS (ESI) calcd for $[C_{12}H_{14}Na]^+$($[M+Na]^+$): 197.0942, found: 197.0926.

2-Phenyl-4,6,6-trimethyl-3,6-dihydro-2H-pyran (**8h**). Clear oil, 133.7 mg, 66%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.0 Hz, 2H), 7.56 (t, J = 8.0 Hz, 2H), 7.47 (t, J = 8.0 Hz, 1H), 5.62 (s, 1H), 4.94 (dd, J_1 = 4.0 Hz, J_2 = 12.0 Hz, 1H), 2.43-2.36 (m, 1H), 2.23-2.18 (m, 1H), 1.94 (s, 3H),1.57 (s, 3H), 1.55 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.46, 130.17, 129.13, 128.55, 128.51, 127.42, 126.31, 126.26, 73.59, 71.02, 37.90, 30.21, 26.30, 23.22. IR (thin film): 2971, 2928, 2911, 1705, 1451, 1379, 1201, 1069, 698 cm^{-1}.HRMS (ESI) calcd for $[C_{14}H_{19}O]^+$($[M+H]^+$): 203.1436, found: 203.1421.

4-(4-Methylpent-3-en-1-yl)-2-phenyl-3,6-dihydro-2H-pyran (**8i**). Clear oil, 101.8 mg, 45%. ^{1}H NMR (400 MHz, $CDCl_3$) δ7.39-7.24 (m, 5H), 5.50 (s, 1H), 5.12 (s, 1H), 4.53 (d, J = 12.0 Hz, 1H), 4.34 (s, 2H), 2.34-2.28 (m, 1H), 2.14-2.05 (m, 5H), 1.69 (s, 3H), 1.61 (s, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 142.71, 135.80, 131.83, 128.39, 127.46, 125.89, 123.89,119.44, 75.89, 66.55, 36.99, 36.34, 25.95, 25.73, 17.75. IR (thin film): 2964, 2930, 1717, 1452, 1378, 1267,1120, 1062, 1027, 700 cm^{-1}. HRMS (ESI) calcd for $[C_{17}H_{22}Na]^+$($[M+Na]^+$): 265.1568, found: 256.1576.

10. Clear oil, 77.4 mg, 48%, dr> 10:1, determined by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.17 (m, 5H), 5.50 (s, 1H), 4.52 (dd, J_1 = 4.0 Hz, J_2 = 12.0 Hz, 1H), 4.24 (m, 1H), 3.74 (m, 1H), 3.51 (m, 1H), 2.16 (m, 1H), 2.02 (d, J = 16.0 Hz, 1H), 1.68 (s, 3H),0.84 (s, 9H), 0.01 (d, J = 8.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.74, 132.12, 127.23, 126.25, 124.80, 120.37, 75.28, 74.88, 65.36, 37.19, 24.91, 21.93, 17.35, -6.19, -6.27. HRMS (ESI) calcd for $[C_{19}H_{34}NO_2Si]^+$ ($[M+NH_4]^+$): 336.2353, found: 336.2355.

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