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Direct synthesis of tetrahydropyrans via one-pot Babier–Prins cyclization of allylbromide with carbonyl compounds promoted by RTILs BPyX/SnX′$_2$ or BBIMBr/SnBr$_2$

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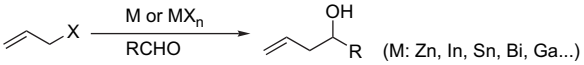
Abstract—Tetrahydropyran compounds can be directly synthesized from allylbromide and carbonyl compounds by means of one-pot Babier–Prins cyclization promoted by BPyX/SnX′$_2$ or BBIMBr/SnBr$_2$ complex (functionalized RTILs) under solvent-free conditions. 2,6-Homo-bissubstituted- and 2,6,6-trisubstituted, especially 6-(spirocycloalkyl)-, tetrahydropyran compounds can be prepared in good yields.

1. Introduction

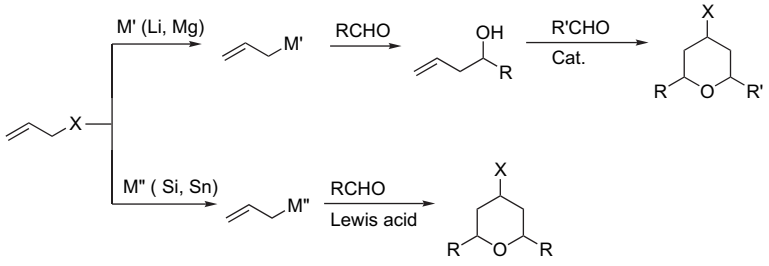
Tetrahydropyrans are common subunits in a variety of biologically important natural products such as polyether antibiotics, marine toxins, pheromones, and pharmaceutical agents.[1] The Prins cyclization[2] is one of the most effective reaction for construction of the tetrahydropyran unit. In most cases, the Prins cyclization involves the condensation of homoallylic alcohol with carbonyl compounds (Eq. 2) in the presence of protic acid[3] or Lewis acid, such as $TiBr_4$,[4] $ZrCl_4$,[5] $AlCl_3$,[6] $InCl_3$,[7] $Sc(OTf)_3$,[8] $Ce(OTf)_3 \cdot H_2O$ in ionic liquid,[9] as well as TMSCl/NaI.[10] The homoallylic alcohols can be prepared by means of Babier reaction[11] (Eq. 1), Grignard reaction (Eq. 2) or reaction of organolithium reagents with aldehydes (Eq. 2). Alternatively, allyl silyl[12] and allyltin[13] reagents can also react with aldehydes in the presence of Lewis acid to give tetrahydropyran compounds (Eq. 3). However, there are few examples of direct formation of tetrahydropyran compounds via one-pot reaction of allylhalide with carbonyl compounds. As reported by Li,[7a] during investigation of indium-mediated reaction of allylbromide with aldehyde under neat conditions, the formation of a mixture of tetrahydropyran-4-ol and 4-bromotetrahydropyran compounds was accidentally observed. It is interesting to combine Babier reaction with Prins cyclization into an one-pot tandem reaction system for direct formation of tetrahydropyran (Eq. 4). Recently, noticeable progress in the transformation under solvent-free condition has attracted considerable attention.[14] Herein, we report on the direct synthesis of tetrahydropyran compounds through one-pot Babier–Prins cyclization of allylbromide with carbonyl compounds promoted by BPyX/SnX$_2$ or BBIMBr/SnBr$_2$ complex (functionalized RTILs) without the use of organic solvent.

Babier Reaction



(1)

Prins Cyclization



(2)

(3)

Keywords: Babier–Prins cyclization; Allylbromide; Carbonyl compound; BBIMBr/SnBr$_2$; Tetrahydropyran; Direct synthesis.
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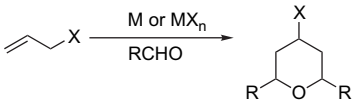
Babier-Prins Cyclization (one pot, tandem reaction)

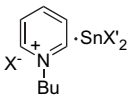


(4)

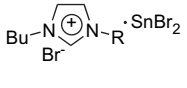
2. Results and discussion

2.1. Direct synthesis of 4-halo-2,6-homo-bissubstituted-tetrahydropyrans

$SnCl_2$-mediated Babier-type reaction of allylhalides with carbonyl compounds yield homoallylic alcohol, though requiring additional catalyst in most cases.[15] Among the catalysts suitable to this type of reaction, quaternary ammonium salts are more convenient.[16] It is also noteworthy that the combination of quaternary ammonium salts with stannous halides can generate a room temperature liquid state complex (so-called room temperature ionic liquid: RTILs).[17] Thus, it is expected that a complex of a quaternary ammonium salt with $SnCl_2$ can serve as both functionalized reagent with Lewis acidity and reaction media.



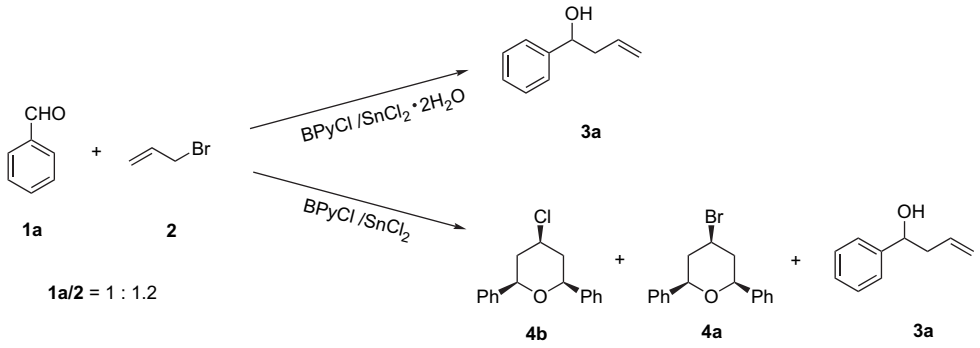
IA, X:Cl, X':Cl
IB, X:Cl, X':Br
IC, X:Br, X':Cl
ID, X:Br, X':Br
IE, X: I, X': Cl



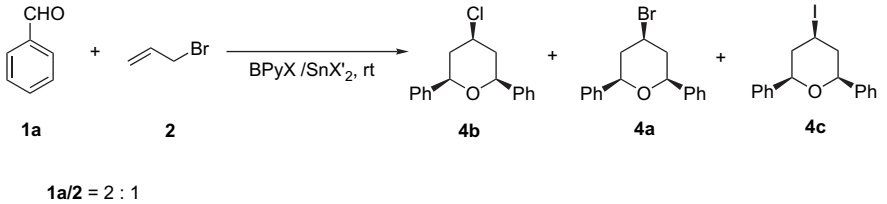
IIA, R:CH_3
IIB, R: Bu

According to the authors,[18] the complexes (**IA**–**E**) of *N*-benzylpyridine halides (BPyX) with SnX'_2 (1:2) were easily synthesized. At first, the complex **IA**·$2H_2O$ (BPyCl/$SnCl_2$·$2H_2O$) was employed in the reaction of allylbromide **2** with benzaldehyde **1a** (**IA**·$2H_2O$:**2**:**1a**=2:1.2:1) without the use of any organic solvent at room temperature for 24 h (Scheme 1). The homoallylic alcohol **3a** was obtained in 93% yield, which is consistent with the observation of Li.[19] However, it is interesting to note that if complex **IA** derived from anhydrous $SnCl_2$ and BPyCl was used under the same reaction conditions, a mixture of **3a** (22%), 4-chloro-(**4b**), and 4-bromo-2,6-diphenyltetrahydropyran (**4a**) (67%, **4a**+**4b**) produced (Scheme 1). When the ratio of **2** to **1a** was changed to 1:2, only tetrahydropyran compounds (**4a** and **4b**) were obtained in 78% yield, but no homoallylic alcohol **3a** was detected (Scheme 2, Table 1, entry 1). A series of RTILs (**IA**–**IE**) containing various tin halides were synthesized and employed in the reaction of **1a** with **2**. The results in Table 1 showed that the halide atom in the 4-position of the formed tetrahydropyran unit originates from substrate **2** and complex BPyX/SnX'_2. The use of **ID** (X and X′=Br) provided a single product **4a** in 80% yield (entry 4). However, in most cases, the reaction system became too sticky to be stirred during the course of the reaction promoted by **ID** without using organic solvent. For improving the fluidity of the complex as a reaction medium, two complexes of imidazole salts with $SnBr_2$ (1:1.5, **IIA** and **IIB**)[18] were synthesized and also employed in the reaction of **2** with **1a**. As shown in Table 1 BBIMBr/$SnBr_2$ (**IIB**) is a better reaction system than **ID** and **IIA** (entry 4 vs 7 and 6 vs 7). Moreover, for most substrates used, the reaction systems employed **IIB** were in a liquid state during the course of the reaction. If $SnBr_2$ was used alone (without quaternary ammonium salt), the reaction of **1a** with **2** did not proceed and starting materials were recovered, even after 24 h (entry 8).

Meanwhile, in order to examine solvent effects, various solvents were used as reaction media in the reaction of **1a** with **2** promoted by **IIB** (Scheme 3, Table 2). It was found that in organic solvents the reactions gave homoallylic alcohol **3a**



Scheme 1.



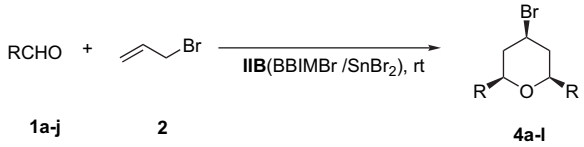
Scheme 2.

Table 1. The reaction of **1a** with **2** promoted by complex **I** or **II**[a]

Entry	Complexes (**I** and **II**)[b]	Yield[c] (%) (**4b**:**4a**:**4c**)[d]
1	**IA**	78 (5.3:1:0)
2	**IB**	90 (1:1:0)
3	**IC**	77 (3.2:1:0)
4	**ID**	80 (0:1:0)
5	**IE**	89 (1.6:1:2.5)
6	**IIA**	81 (0:1:0)
7	**IIB**	86 (0:1:0)
8	$SnBr_2$	—[e]

[a] Reaction time: 24 h at rt.
[b] BPyX/SnX'_2=1:2.
[c] Isolated yield.
[d] Determined by ^1H NMR.
[e] Starting materials were recovered.

solely or a mixture of **3a** and tetrahydropyran compound **4a**. Only under solvent-free conditions the single product, tetrahydropyran compound **4a** was obtained in 86% yield (Table 2, entry 5).



Scheme 3.

Table 2. The reaction of **1a** with **2**[a]

Entry	Solvent[b]	Yield[c] (%) (**3a**:**4a**)
1	THF	44 (44:0)
2	DMF	72 (72:0)
3	CH_3CN	67 (13:54)
4	CH_2Cl_2	73 (8:65)
5	None	86 (0:86)

[a] **1a**:**2**:**IIB**=2:1:2, 24 h at rt.
[b] All solvents are anhydrate.
[c] Isolated yield.

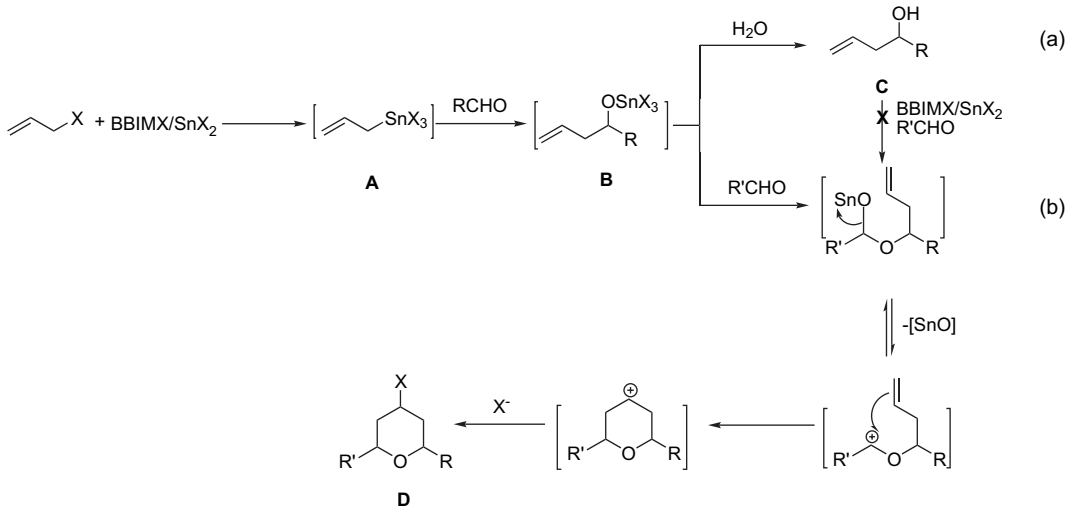
On the basis of the above experimental results, a variety of aldehydes were employed in the reactions with allylbromide **2** promoted by **IIB** without the use of organic solvent, affording the products of 4-bromo-2,6-homo-bissubstituted-tetrahydropyrans (Scheme 3, Table 3). As shown in Table 3 both aromatic and aliphatic aldehydes are able to react with **2** to directly generate tetrahydropyran compounds **4a–l** in moderate to good yields (52–86%). The stereochemistry of 2,4,6-trisubstituents of the tetrahydropyran ring was found to be all-cis in all cases. The assignment was based on the coupling constants of the protons at the C-2, C-4, and C-6 positions. The coupling constants of 11.0–12.7 Hz were observed for all such protons, indicating the presence of axial–axial coupling. The three substituents are therefore all in equatorial positions, in agreement with an all-cis stereochemistry.[12b]

2.2. A plausible reaction mechanism

In the mechanism for the present reaction, it is assumed that at the first is a Babier-type reaction of allylbromide with $SnBr_2$ in the presence of quaternary ammonium salt to produce allyltin compound **A**,[15d] which subsequently undergoes reaction with aldehyde to generate the reactive intermediate **B**. This intermediate exhibits high reactivity to give two different products (**C** and **D**) by two pathways (Scheme 4, path a and b). In pathway (a), **B** could be hydrolyzed by the water in the reaction system or during work-up procedure, giving homoallylic alcohol **C** as product. However, under strict anhydrous conditions the intermediate **B** was sufficiently activated to react with another aldehyde molecule via pathway (b) affording a Prins cyclization product, tetrahydropyran compound **D**.[8] It is interesting to note that when homoallylic alcohol **C** was mixed with aldehyde in the presence of **IIB**, no reaction product **D** was detected.

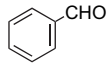
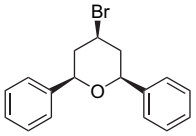
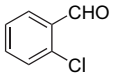
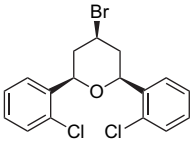
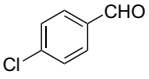
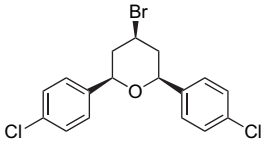
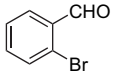
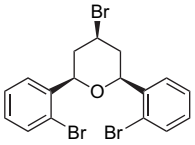
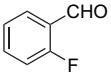
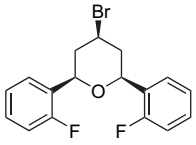
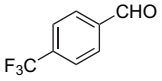
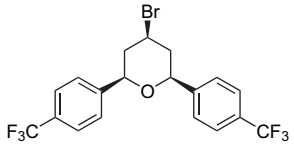
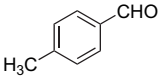
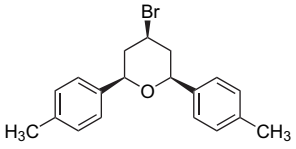
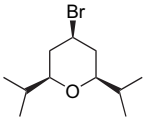
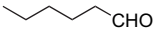
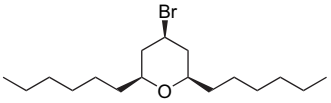
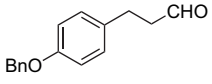
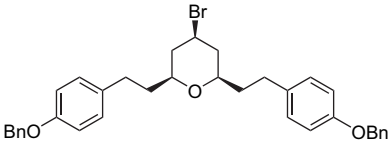
2.3. Direct synthesis of 4-bromo-2,6,6-trisubstituted-tetrahydropyran

For preparing 2,6-cross-substituted-tetrahydropyran, two different aromatic aldehydes were used in the reaction; a mixture of the products containing 2,6-homo- and 2,6-cross-bissubstituted-tetrahydropyrans was obtained. In view



Scheme 4.

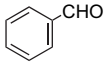
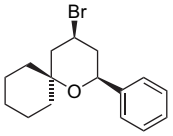
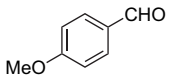
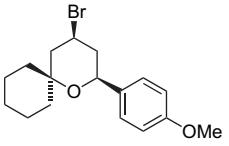
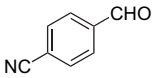
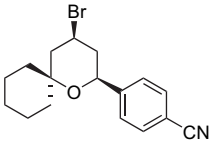
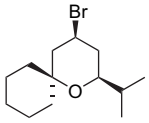
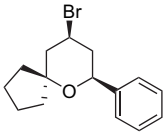
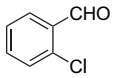
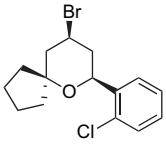
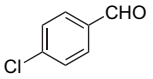
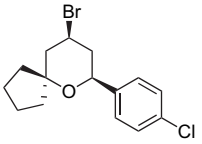
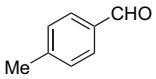
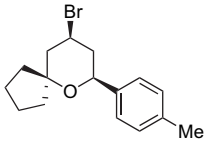
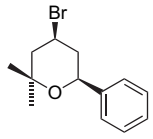
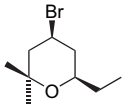
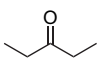
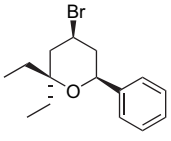
Table 3. Direct synthesis of **4** via reaction of **2** with **1** promoted by **IIB**[a]

Entry	Aldehyde	Product	Yield (%)[b]
1	**1a** 	**4a** 	86
2	**1b** 	**4d** 	78
3	**1c** 	**4e** 	78
4	**1d** 	**4f** 	82
5	**1e** 	**4g** 	75
6	**1f** 	**4h** 	54
7	**1g** 	**4i** 	60
8	**1h** 	**4j** 	82
9	**1i** 	**4k** 	72
10	**1j** 	**4l** 	79

[a] Reaction time: 24 h at rt, **1**:**2**=2:1.
[b] Isolated yield.

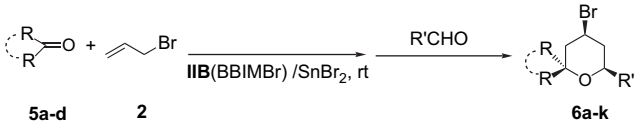
of the plausible reaction mechanism discussed above, formation of 2,6-homo-bissubstituted product may be retarded by use of a relatively less reactive carbonyl compound in the first step. Thus, the reaction could stop at intermediate **B** and not go on to generate homo-bissubstituted-tetrahydropyran compound. Then, more active aldehyde may be added to continue the reaction with **B** to give 2,6-cross-bissubstituted-tetrahydropyran. Interestingly, when cyclic ketones with less reactivity were used, 6-(spirocycloalkyl)-2-substituted-tetrahydropyran compounds were obtained

Table 4. Direct synthesis of cross-bissubstituted tetrahydropyrans **6** via reaction of **2** with carbonyl compounds

Entry	Ketone	Time[a] (h)	Aldehyde	Time[b] (h)	Product	Yield[c] (%)
1	**5a** 	6	**1a** 	10	**6a** 	85
2		6	**1k** 	10	**6b** 	76
3		6	**1l** 	10	**6c** 	78
4		6	**1h** 	10	**6d** 	72
5	**5b** 	5	**1a**	10	**6e** 	74
6		5	**1b** 	10	**6f** 	68
7		5	**1c** 	10	**6g** 	70
8		5	**1g** 	10	**6h** 	64
9	**5c** 	8	**1a**	10	**6i** 	67
10		8	**1i** 	10	**6j** 	54
11	**5d** 	8	**1a**	10	**6k** 	64

[a] Reaction time with ketone in the first step.
[b] Reaction time with aldehyde in the second step.
[c] Isolated yield.

(Scheme 5). For example, cyclohexanone **5a** was allowed to react with allylbromide **2** in the presence of **IIB** for 6 h. Then, benzaldehyde **1a** was added, followed by stirring for 10 h to give the product, 4-bromo-2-phenyl-6-(spirocyclohexyl)tetrahydropyran **6a** in 85% yield (Table 4, entry 1). No 2,6-diphenyltetrahydropyran **4a** and 2,6-bis(spirocyclohexyl)tetrahydropyran were observed in the reaction mixture. It is indicated in Table 4 that either cyclic or acyclic ketones, and aromatic or aliphatic aldehydes can be employed in the one-pot Babier–Prins cyclization, affording the products of 4-bromo-2,6,6-trisubstituted-tetrahydropyrans **6a–i** in good yields of 64–85%. The stereochemistry of the substituents at C-4 and C-2 positions was deduced as cis in consideration of the coupling constants for the protons (J∼11 Hz). The method of one-pot Babier–Prins cyclization provided a direct and convenient synthesis of 2,6,6-trisubstituted-tetrahydropyran compounds, especially for constructing a structural unit of 6-(spirocycloalkyl)-2-substituted-tetrahydropyran, which is of importance in organic synthesis and not easily prepared by conventional methods.[20]



Scheme 5.

3. Conclusion

Babier and Prins reactions can be combined into an one-pot tandem reaction system promoted by functionalized RTILs derived from quaternary ammonium salt and Sn(II) halides. By utilizing this method, either 2,6-homo-bissubstituted or 2,6,6-trisubstituted-tetrahydropyran, especially 6-(spirocycloalkyl)-2-substituted-tetrahydropyran compounds can be directly synthesized from allylbromide and carbonyl compounds. The study on scope of the reaction and application in the synthesis of natural compounds is in process.

4. Experimental

4.1. General

IR spectra were recorded on a Bruker Tensor 27 infra-red spectrometer. ^{1}H and ^{13}C NMR spectra were measured by Bruker AV-300 spectrometers in $CDCl_3$ with tetramethylsilane as an internal standard. Mass spectra were recorded on a GCT–MS Micromass spectrometer. Elemental analyses were performed on a Carlo Flash 1112 Element Analysis instrument. Melting points were measured by a Beijing-Tike X-4 apparatus and were uncorrected. Common reagents and materials were purchased from commercial sources and purified before used. Complexes **IA–IE** and **IIA–IIB** were synthesized according to literature procedures.[18]

4.2. Typical experimental procedure for the synthesis of 4-bromo-2,6-homo-bissubstituted-tetrahydropyrans

A mixture of benzaldehyde (**1a**, 212 mg, 2.0 mmol), allylbromide (**2**, 120 mg, 1.0 mmol) and complex **IIB** derived from BBIMBr (522 mg, 2.0 mmol), and $SnCl_2$ (1100 mg, 4.0 mmol) was stirred at ambient temperature for 24 h. The reaction mixture was extracted with diethyl ether. The combined ether phases were washed by 2 mL aqueous HCl, and dried over Na_2SO_4. The solvent was removed in vacuum and the crude product was purified by flash chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:40) to afford a white solid **4a** (273 mg, 86%).

4.3. Typical experimental procedure for the synthesis of 4-bromo-2,6,6-trisubstituted-tetrahydropyrans

A mixture of cyclohexanone (294 mg, 3.0 mmol), allylbromide (120 mg, 1.0 mmol) and complex **IIB** derived from BBIMBr (522 mg, 2.0 mmol), and $SnBr_2$ (840 mg, 3.0 mmol) was stirred at ambient temperature for 6 h. Then benzaldehyde **1a** (106 mg, 1.0 mmol) was added, followed by stirring for 10 h. The reaction mixture was extracted with diethyl ether. The combined ether phases were washed by 2 M aqueous HCl, and dried over Na_2SO_4. The solvent was removed in vacuum and the crude product was purified by flash chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:40) to afford a pale-yellow oil **6a** (260 mg, 85%).

4.3.1. 2-Phenyl-4-bromo-1-oxaspiro[5.5]undecane 6a. ^{1}H NMR ($CDCl_3$) δ 7.28–7.58 (m, 5H), 4.65 (d, J=10.1 Hz, 1H), 4.45–4.58 (m, 1H), 2.49–2.58 (dm, J=10.7 Hz, 1H), 2.26–2.36 (dm, J=11.8 Hz, 1H), 1.73–2.10 (m, 5H), 1.37–1.57 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 142.2, 128.4, 127.5, 125.8, 75.2, 71.6, 47.1, 45.6, 45.5, 40.0, 30.3, 26.0, 21.7, 21.3. FTIR (film): 2931, 1494, 1447, 1331, 1172, 1060 cm^{-1}. HRMS (EI): m/z calcd for $C_{16}H_{21}OBr$: 308.0775, found: 308.0776.

4.3.2. 2-(4′-Methoxyphenyl)-4-bromo-1-oxaspiro[5.5]undecane 6b. A yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.33 (d, J=8.7 Hz, 2H), 6.9 (d, J=8.8 Hz, 2H), 4.46–4.58 (m, 2H), 3.82 (s, 3H), 2.43–2.51 (dm, J=11.4 Hz, 1H), 2.23–2.32 (dm, 12.6 Hz, 1H), 1.99–2.10 (m, 1H), 1.60–1.90 (m, 3H), 1.31–1.59 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 158.9, 134.3, 127.1, 113.7, 75.2, 71.2, 55.3, 45.6, 45.3, 40.0, 30.3, 26.0, 21.7, 21.3. FTIR (film): 2932, 2856, 1613, 1513, 1446, 1246, 987, 829 cm^{-1}. HRMS (EI): m/z calcd for $C_{17}H_{23}O_2Br$: 338.0881, found: 338.0887.

4.3.3. 2-(4′-Nitrilphenyl)-4-bromo-1-oxaspiro[5.5]undecane 6c. A yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.60 (d, J=7.9 Hz, 2H), 7.52 (d, J=7.9 Hz, 2H), 4.63 (d, J=11.2 Hz, 1H), 4.39–4.54 (m, 1H), 2.45–2.55 (dm, J=11.9 Hz, 1H), 2.24–2.33 (dm, J=12.0 Hz, 1H), 1.99–2.10 (m, 1H), 1.67–1.84 (m, 4H), 1.36–1.52 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 147.4, 132.2, 126.4, 118.8, 111.1, 75.5, 70.9, 46.8, 45.1, 44.4, 39.8, 30.1, 25.8, 21.6, 21.2. FTIR (film): 2932, 2851, 2227, 1609, 1447, 1172, 1071, 986, 831 cm^{-1}. HRMS (EI): m/z calcd for $C_{17}H_{20}OBr$: 333.0728, found: 333.0726.

4.3.4. 2-(Isopropyl)-4-bromo-1-oxaspiro[5.5]undecane 6d. A light-yellow oil. ^{1}H NMR ($CDCl_3$) δ 4.31–4.42 (m, 1H), 3.17–3.08 (m, 1H), 2.34–2.25 (m, 1H), 2.17–2.10 (m, 1H), 1.99–2.07 (m, 1H), 1.58–1.76 (m, 7H); ^{13}C NMR

($CDCl_3$) δ 74.8, 74.1, 48.0, 46.7, 41.4, 39.9, 33.5, 33.1, 30.0, 26.0, 21.6, 20.9, 18.8, 18.5. FTIR (film): 2933, 2857, 1447, 1384, 1167, 1065 cm^{-1}. HRMS (EI): *m/z* calcd for $C_{13}H_{23}OBr$: 274.0932, found: 274.0929.

4.3.5. 2-Phenyl-4-bromo-1-oxaspiro[5.4]decane 6e. A yellow oil. ^1H NMR ($CDCl_3$) δ 7.25–7.45 (m, 5H), 4.5 (d, J=11.4 Hz, 1H), 4.33–4.45 (m, 1H), 2.43–2.52 (dm, J=12.7 Hz, 1H), 2.11–2.23 (m, 2H), 1.90–2.04 (m, 3H), 1.27–1.69 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 141.9, 128.4, 127.6, 125.9, 85.8, 73.9, 46.6, 46.1, 45.3, 41.5, 33.0, 24.6, 23.1. FTIR (film): 2958, 2868, 1448, 1335, 1059, 995, 753, 699 cm^{-1}. HRMS (EI): *m/z* calcd for $C_{15}H_{19}OBr$: 294.0619, found: 294.0615.

4.3.6. 2-(2′-Chlorophenyl)-4-bromo-1-oxaspiro[5.4]-decane 6f. A yellow oil. ^1H NMR ($CDCl_3$) δ 7.69 (d, J=7.2 Hz, 1H), 7.35–7.21 (m, 3H), 4.90 (d, J=11.2 Hz, 1H), 4.45–4.34 (m, 1H), 2.63–2.55 (dm, J=12.6 Hz, 1H), 2.24–2.10 (m, 2H), 1.94–1.83 (m, 2H), 1.60–1.26 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 139.3, 131.6, 129.2, 128.5, 127.4, 127.2, 86.0, 70.7, 46.7, 45.7, 43.5, 41.6, 32.9, 24.7, 23.1. FTIR (film): 2956, 2870, 1474, 1438, 1067, 994 cm^{-1}. HRMS (EI): *m/z* calcd for $C_{15}H_{18}OClBr$: 328.0230, found: 328.0234.

4.3.7. 2-(4′-Chlorophenyl)-4-bromo-1-oxaspiro[5.4]-decane 6g. A yellow oil. ^1H NMR ($CDCl_3$) δ 7.28–7.34 (m, 5H), 4.51 (d, J=11.4 Hz, 1H), 4.32–4.44 (m, 1H), 2.40–2.50 (dm, J=12.7 Hz, 1H), 2.15–2.21 (m, 2H), 1.90–1.98 (m, 3H), 1.57–1.77 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 140.4, 133.2, 128.5, 127.3, 85.9, 73.2, 46.5, 45.6, 45.3, 41.4, 32.9, 24.6, 23.0. FTIR (film): 2959, 2868, 1490, 1335, 1207, 1066, 822, 729 cm^{-1}. HRMS (EI): *m/z* calcd for $C_{15}H_{18}OClBr$: 328.0230, found: 328.0233.

4.3.8. 2-(4′-Methylphenyl)-4-bromo-1-oxaspiro[5.4]-decane 6h. A yellow oil. ^1H NMR ($CDCl_3$)n δ 7.23 (d, J=7.1 Hz, 2H), 7.13 (d, J=7.7 Hz, 2H), 4.48 (d, J=11.4 Hz, 1H), 4.31–4.43 (m, 1H), 2.39–2.48 (dm, J=12.6 Hz, 1H), 2.17 (s, 3H), 1.98–2.04 (m, 2H), 1.75–1.87 (m, 3H), 1.39–1.52 (m, 6H). FTIR (film): 2957, 2867, 1514, 1445, 1288, 1063, 996, 812 cm^{-1}. HRMS (EI): *m/z* calcd for $C_{16}H_{21}OBr$: 308.0776, found: 308.0777.

4.3.9. 2-Phenyl-6,6-dimethyl-tetrahydropyran 6i. A yellow oil. ^1H NMR ($CDCl_3$) δ 7.21–7.55 (m, 5H), 4.59 (d, J=11.2 Hz, 1H), 4.39–4.55 (m, 1H), 2.40–2.50 (dm, J=12.7 Hz, 1H), 2.18–2.28 (dm, J=12.7 Hz, 1H), 1.87–2.02 (m, 2H), 1.30 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 141.9, 128.5, 127.8, 126.0, 79.7, 74.4, 73.3, 47.8, 45.4, 31.6, 22.4. FTIR (film): 2975, 2924, 2876, 1450, 1190, 1061, 973, 754 cm^{-1}. HRMS (EI): *m/z* calcd for $C_{13}H_{17}OBr$: 268.0464, found: 268.0463.

4.3.10. 2-Ethyl-6,6-dimethyl-tetrahydropyran 6j. A light-yellow oil. ^1H NMR ($CDCl_3$) δ 4.28–4.38 (m, 1H), 3.42–3.46 (m, 1H), 2.16–2.22 (dm, J=10.6 Hz, 1H), 1.82 (t, J=12.5 Hz, 1H), 1.46–1.65 (m, 4H), 1.24 (s, 3H), 1.18 (s, 3H), 0.94 (t, J=7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 73.6, 72.2, 48.0, 46.0, 43.5, 31.4, 29.1, 22.3, 9.7. FTIR (film): 2974, 2877, 1464, 1381, 1195, 1084 cm^{-1}. HRMS (EI): *m/z* calcd for $C_9H_{17}BrO$: 220.0460, found: 220.0463.

4.3.11. 2-Phenyl-6,6-diethyl-tetrahydropyran 6k. A yellow oil. ^1H NMR ($CDCl_3$) δ 7.28–7.41 (m, 5H), 4.50–4.60 (m, 2H), 2.42–2.50 (dm, J=12.6 Hz, 1H), 2.17–2.26 (dm, J=12.9 Hz, 1H), 1.87–2.02 (m, 3H), 1.55–1.64 (m, 3H), 0.92 (t, J=7.5 Hz, 6H); ^{13}C NMR ($CDCl_3$) δ 142.1, 128.4, 127.6, 125.9, 78.5, 72.4, 45.9, 45.5, 43.5, 31.8, 24.0, 7.5, 7.1. FTIR (film): 2968, 2936, 2878, 1452, 1335, 1058, 987, 757, 699 cm^{-1}. HRMS: *m/z* calcd for $C_{15}H_{21}OBr$: 296.0776, found: 296.0772.

Acknowledgements

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