2.1 Introduction

One of the common difficulties with natural product and other multi-step syntheses is the need to render one functional group inert to a particular reagent while keeping another group open for further chemical elaboration. Despite the great advances made in the involved syntheses of multifunctional products, selectivity in functional group transformations remains a critical issue in organic synthesis. Unfortunately for the synthetic chemist, there is no perfect protecting group applicable to any functional group in any situation. Thus, the need exists for the synthetic chemist to have a handy toolbox of selective and efficient protecting groups that can be applied and easily removed under a variety of conditions.

For a protecting group to find wide application in organic synthesis, it must fulfill several criteria. In particular it must be introduced into the molecule to be protected under mild conditions in a selective manner and in high yield; functional groups other than that to be protected must not be attacked. Be stable under all the conditions used during the synthesis, including those of the purification steps, up to the step in which the protecting group is removed, it should, as Par as possible, have a stabilizing effect on the molecule and should suppress racemization or epimerization. Be cleavable under very mild conditions in a highly selective manner and in high yield; other protecting groups present in the molecule and unprotected functionalities should not be affected by the cleavage condition. In addition to these minimum requirements, the protecting group should also be introduced and removed with the help of readily available reagents. Such that both transformations the products can be easily purified. Introduce no additional stereo centers. Lend the protected intermediates advantageous physical properties; for example the compounds should be easily crystallized and/or readily soluble.

Only a few protecting groups meet all of these demands, and in most cases a compromise must be found, in which the most important criteria are addressed. In most cases guaranteeing that the protecting group is very stable and, at the same time, readily liberated (an apparent contradiction) is the crucial problem and overshadows the
requirements for efficient and the provision of desirable physical and chemical properties. The most commonly used protecting groups for alcohols and phenols are THP, MOM, MEM, BOM and MTM.

The tetrahydropyranyl ether is a useful protecting group for the protection of alcohols and phenols, offering stability towards strongly basic reaction conditions, organometallics, hydrides, acylating reagents and alkylation reagents. A drawback is the formation of an additional stereo center that may lead to diastereomeric mixtures if the alcohol already possesses a stereogenic center. THP ethers are formed under acidic conditions from alcohols and dihydropyran. The OTHP protecting group is stable to many reagents that would normally consume an alcohol. These include

i) Bases such as NaH, KOrBu, LDA, LiTMP
ii) Nucleophiles such as NaOCH₃, X⁻, lithium enolates, RLi (organolithiums), RMeBr (Grignards), Ph₃P=CH₂ (Wittig reagents)
iii) Reductants such as H₂ and Ni or Pd, Na/NH₃, NaBH₄, LiAlH₄, DIBAL-H (iBu₂AlH)
iv) Oxidants such as OsO₄, PCC/PDC, Swern, H₂O₂
When it is desired to recover the alcohol, normally this is done via some combination of H^+ and H_2O, taking advantage of the acid sensitivity of acetals. Numerous methods have been reported for tetrahydropyranlylation and detetrahydropyranlylation. Protection is normally achieved with a mild acidic reagent in an aprotic solvent such as CH_2Cl_2, THF, acetone etc.; and deprotection also with an acidic reagent but in a polar or protic solvent such as methanol, ethanol, isopropanol, acetonitrile, etc. The chemistry involved in both the introduction and deprotection stages is the reversible acid-catalyzed formation and hydrolysis of an acetal.

The THP group is introduced by an acid-catalyzed addition of the alcohol to the vinyl ether moiety in dihydropyran. A wide variety of catalysts have already been applied to the tetrahydropyranlylation of alcohols and phenols, and their detetrahydropyranlylation including the use of protic acids, Lewis acids, ion exchange resins, heteropolyacids, p-toluene sulfonic acid and or its pyridinium salt are frequently used as the catalyst. Various Lewis acids also promote hydrolysis of THP groups. A disadvantage of the THP group is that a new stereogenic center is produced at C(2) of the tetrahydropyran ring. This presents no difficulty if the alcohol is achiral, since a racemic mixture results.

**Figure 1: Introduction and removal of tetrahydropyran group.**
However, if the alcohol is chiral, the reaction gives a mixture of diastereomers, which may complicate purification and/or characterization.

2.2 Literature survey

Hajipour et al.,\(^4\) described the deprotection method for tetrahydropyranyl ethers with silica sulfuric acid in methanol at room temperature.

\[
\text{Silica sulfuric acid} \quad \text{Methanol, RT, 30 min} \quad \rightarrow \quad \text{R-OH}
\]

Sunggak Kim et al.,\(^5\) reported a method for selective removal of tetrahydropyranyl ethers in the presence of tert-butyldimethylsilyl ethers with magnesium bromide in ether.

\[
\text{MgBr}_2 \quad \text{Ether, RT} \quad \rightarrow \quad \text{HO} \quad \text{OSi}
\]

Tong-Shuang Li et al.,\(^6\) reported that, a variety of tetrahydropyranyl ethers of alcohols and phenols are easily removed in the presence of catalytic amount of montmorillonite clays in methanol at 40-50 °C in excellent yield.

\[
\text{montmorillonite clay} \quad \text{Methanol, 40-50°C} \quad \rightarrow \quad \text{R-OH}
\]

Jianbo wang et al.,\(^7\) described that tetrahydropyranyl ethers (THP groups) and 1-ethoxyethyl ethers (EE groups) are removed upon refluxing in 95\% EtOH or Me\(_2\)CO–H\(_2\)O (95:5) in the presence of a catalytic amount of copper(II) chloride dihydrate (2–5 mol%).

Gupta et al.,\(^8\) reported that, a variety of tert-butyldimethylsilyl (TBDMS) and tetrahydropyranyl (THP) ethers were cleaved with ceric ammonium nitrate in methanol at 0 °C in short time. It has been shown that the reaction is chemoselective in a few
cases. The primary TBDMS ethers have been cleaved selectively in the presence of THP ether and ketal.

Iraj Mohammadpoor-Baltork et al.,\textsuperscript{9} described that primary and secondary trimethylsilyl and tetrahydropyranyl (THP) ethers are oxidative deprotection efficiently by using 3-carboxypyridinium chlorochromate under non-aqueous conditions.

Jung et al.,\textsuperscript{10} described that tetrahydropyranyl ethers are efficiently deprotected by using catalytic amount of decaborane at room temperature in methanol.

Zhengong Li et al.,\textsuperscript{11} described that poly(4-vinylpyridinium) $p$-toluenesulfonate is used as an immobilized catalyst for the hydrolysis of tetrahydropyranyl ethers. This method is mild, efficient and convenient, giving the corresponding products in good to excellent yields and purity.

Sudhakar reddy et al.,\textsuperscript{12} described that treatment of tetrahydropyranyl ethers with cerium(III) chloride heptahydrate in methanol provides a simple, convenient and selective method for detetrahydropyranylation, and the parent alcohols are obtained in high yields.

Salahi et al.,\textsuperscript{13} reported an efficient method for protection of alcohols and Phenols with dihydropyran(DHP) in the presence of catalytic amounts of zirconium tetrachloride in dichloromethane. Deprotection of THP-ethers is also afforded in a methanolic solution at room temperature.
Sarma et al.,\textsuperscript{14} described a method for protection of alcohols as their 2-tetrahydropyranyl ethers and their subsequent hydrolysis can be easily achieved through a microwave irradiated reaction catalyzed by iodine.

Yadav et al.,\textsuperscript{15} described the tetrahydropyranylation of alcohols and phenols are obtained in high yields in the presence of resublimed iodine in DCM at room temperature. Depyranylation is affected readily by refluxing with iodine in methanol for few hours.

Hon et al.,\textsuperscript{16} reported that both acetonyltriphenylphosphonium bromide (ATPB) and poly-p-styryldiphenylacetonylphosphonium bromide were effective catalysts in the protection of alcohols as THP, THF, and EE ethers as well as the cleavage of THP, THF, and EE ethers to the corresponding alcohols.

Patel et al.,\textsuperscript{17} reported for the synthesis of tetrahydropyranylated alcohols in high yields in the presence of catalytic amount of tetrabutylammonium tribromide (TBAB) in dichloromethane at room temperature. Depyranylation to their parent alcohol is achieved in quantitative yields by merely changing the solvent to methanol.

Moon Kim et al.,\textsuperscript{18} described a mild, chemoselective and convenient method for the formation and deprotection of tetrahydropranyl ethers with 1-5 mol\% of acetyl chloride and slightly excess dihydropyran in methylene chloride or in neat dihydropyran. Efficient cleavage of THP ethers was also accomplished with the same reagent by switching the solvent to methanol.
Kumar et al.,\textsuperscript{19} reported that tetrahydropyranyl (THP) ethers have been efficiently and simply deprotected by using silica supported sodium hydrogen sulphate (NaHSO$_4$-SiO$_2$) in methanol at room temperature to regenerate the parent alcohols in high yields.

\[
\begin{align*}
\text{O} & - \text{RO} + \text{NaHSO}_4 - \text{SiO}_2 \\
\text{MeOH} & \rightarrow \text{R-OH}
\end{align*}
\]

Varma et al.,\textsuperscript{20} reported that catalytic amount of aluminum chloride hexahydrate enables solvent-free tetrahydropyranylation (THP) of alcohols and phenols at moderate temperatures. A simple addition of methanol helps to regenerate the corresponding alcohols and phenols, thus rendering these protection and deprotection sequences as very efficient transformations at high substrate to catalyst ratios.

\[
\begin{align*}
\text{R-OH} + \text{AlCl}_3 \cdot 6\text{H}_2\text{O} & \rightarrow \text{RO} - \text{H}_3\text{CO} \\
\text{MeOH} & \rightarrow \text{Solvent-free}
\end{align*}
\]

These are the catalysts for using the de-tetrahydropyranylation transformation. Some more catalysts are also reported for this THP deprotection, like clay materials\textsuperscript{21-23} (montmorillonite K-10 and H-Y zeolites), alumina impregnated zinc chloride,\textsuperscript{24} polystyrene supported aluminum chloride,\textsuperscript{25} PdCl$_2$(CH$_3$CN)$_2$,\textsuperscript{26} 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ),\textsuperscript{27} molybdenyl(VI) acetylacetonate,\textsuperscript{28} AlPO$_4$ or AlPO$_4$-Al$_2$O$_3$,\textsuperscript{29} N-Bromosuccinimide (NBS),\textsuperscript{30} silica-supported perchloric acid (HClO$_4$-SiO$_2$),\textsuperscript{31} N,N'-bis[3,5-bis(trifluoromethyl)phenyl]thiourea,\textsuperscript{32} Zeolite H-beta.\textsuperscript{33} Although these methods are suitable for many synthetic conditions, many of these are associated with several drawbacks, which include long reaction time, reflux conditions, the use of catalysts which may affect other functionalities present, harsh and acidic conditions, poor selectivity, formation of polymeric byproducts of the dihydropyran, and isomerization. In
addition, some of these catalysts require a work-up of the reaction mixture. Thus, there is still a need for mild selective methods for this purpose.

Zinc (II) trifluoromethanesulphonate (zinc triflate) has recently been shown to be a versatile reagent for organic synthesis and it is used as a mild Lewis acid catalyst for wide range of organic transformations. \(^{34-36}\) Zinc triflate is commercially available or it may be prepared from reacting trifluoromethanesulphonic acid reacting with zinc carbonate in methanol.\(^{37}\)

**2.3 Main objective of the present work**

This chapter deals with the deprotection of tetrahydropyranyl ethers by using zinc (II) triflate (10 mol %) as a catalyst. This deprotection transformation is achieved with zinc triflate as a reagent in a protic solvent such as methanol at room temperature.

**2.4 Results and discussion**

Here an efficient method was described for deprotection of tetrahydropyranyl ethers by using zinc triflate as a catalyst. Several THP ethers were cleaved to produce the parent alcohols in excellent yields. The conversion occurred at room temperature. THP ethers were not deprotected with this zinc triflate in CH\(_2\)Cl\(_2\) at room temperature. In the present work, deprotection was carried out by using methanol at room temperature for 30-40 min, to give the corresponding alcohols in high yields. The solvent plays an important role in the cleavage reaction; it was found that methanol is the best one among the solvents tested with THP ether of 2-iodo phenol. Methanol gave the best results compared to other solvents like ethanol, isopropyl alcohol, acetone, acetonitrile and THF (Table-1).
Table-1 Deprotection of 2-iodo phenol THP ether in various solvents.\(^a\)

![Deprotection reaction](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time</th>
<th>Yield (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Methanol</td>
<td>30 min</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>Ethanol</td>
<td>60 hr</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>Acetonitrile</td>
<td>3 hr</td>
<td>87</td>
</tr>
<tr>
<td>4</td>
<td>1,4-Dioxane</td>
<td>Incomplete after 10 hr</td>
<td>---</td>
</tr>
<tr>
<td>5</td>
<td>Acetone</td>
<td>Incomplete after 10 hr</td>
<td>---</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>Incomplete after 10 hr</td>
<td>---</td>
</tr>
<tr>
<td>7</td>
<td>CH₂Cl₂</td>
<td>No reaction</td>
<td>---</td>
</tr>
</tbody>
</table>

\(^a\) All Reactions were carried out at room temperature, \(^b\) isolated yield

Scheme-1

![Scheme-1](image)

Table-2 Deprotection of THP ethers by using zinc triflate in methanol at room temperature.\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td><img src="image" alt="Substrate" /></td>
<td><img src="image" alt="Product" /></td>
<td>30</td>
<td>96</td>
</tr>
<tr>
<td>b</td>
<td><img src="image" alt="Substrate" /></td>
<td><img src="image" alt="Product" /></td>
<td>30</td>
<td>95</td>
</tr>
</tbody>
</table>

\(^a\)
A variety of THP ethers with different structures were prepared according to standard procedures. THP ethers were subjected to deprotection with 10 mol% of Zn(OTf)₂ in methanol at room temperature for 30-40 min (Scheme-1). Under such conditions all the THP groups investigated in our study were cleanly and completely removed with in short time and the corresponding alcohols and phenols are isolated in good yields. Various
THP ethers of phenolic, benzylic and allylic alcohols can be deprotected efficiently by using zinc triflate in methanol at room temperature for 30-40 mins and the efficiency of this method is illustrated using the examples shown in the Table-2. The present deprotection method is highly efficient. The THP ethers can be easily cleaved in presence of wide range of functional groups present in phenols and alcohols. Aldehyde, Boc, nitro, nitrile groups, halogens, and methoxy groups are unaffected. Moreover, the conversions occurred at room temperature and therefore the experimental procedure is simple. The structures of generated alcohols were established by direct comparison of their spectral (^1H NMR, 400 MHz) data with that of the authentic alcohols.

2.5 Conclusion

In conclusion, the author had developed a simple, inexpensive and efficient protocol for deprotection of THP ethers using Zn(OTf)₂ at room temperature. The reaction completed within 30-40 min. Experimental simplicity, utilization of cheap, commercially available catalyst and excellent yields are the main advantages of the present procedure. Further, it was shown that substrates such as Aldehyde, Boc, nitro, and methoxy groups are also unaffected by the present reagent system.

2.6 Experimental Section

The ^1H and ^13C NMR were recorded on 400 MHz Varian FT-NMR spectrometer with tetramethylsilane (TMS) as the internal standard. The solvent CDCl₃ was used for NMR analysis. The mass spectra were recorded on Waters ZQ-4000 equipped with ESI and API mass detector. The Carbon, Hydrogen and Nitrogen (CHN) analysis was done on Perkin-Elmer PE 2400 Series II machine. The thin layer chromatography (TLC) was performed either using the Merck precoated TLC plates or on ACME’s silica gel with 13% calcium sulphate (CaSO₄) as binder and the components were visualized under iodine chamber or by UV exposure or by the potassium permanganate (KMnO₄) spray technique. Flash column chromatography was performed using Merck silica gel (100-200 mesh). The chemicals and solvents were purchased from commercial suppliers.
either from Aldrich, Spectrochem, and Sisco research laboratories (SRL), and they were used without purification prior to use. The structures of generated alcohols were established by direct comparison of their spectral (\(^1\)H NMR, 400 MHz) data with that of the authentic alcohols.

**General procedure for deprotection reactions:**

A solution of THP Ether (1.0 mmol) in methanol (10mL) was treated with Zn(OTf)\(_2\) (0.1 mmol) and stirred at room temperature for 30–40 min. After the completion of reaction (TLC analysis), the solvent was removed under reduced pressure and the obtained residue was treated with EtOAc (20mL). The organic layer was washed with water (10mL), brine (10mL), dried (Na\(_2\)SO\(_4\)) and evaporated under reduced pressure to give the crude products. It was purified by flash column chromatography (100–200 mesh silica gel, EtOAc–petroleum ether) to furnish the desired alcohols or phenols in 81–96% yields.

**2.7 Physical, Spectral and Analytical Data of compounds (Table-2)**

**2-(Benzyloxy)tetrahydro-2\(H\)-pyran (Table-2, entry a)**

![2-(Benzyloxy)tetrahydro-2\(H\)-pyran](image)

Colourless liquid; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 7.34-7.25 (m, 5H), 4.79 (d, \(J=13.6\) Hz, 1H), 4.71-4.69 (m, 1H), 4.43 (d, \(J=13.6\) Hz, 1H), 3.90-3.87 (m, 1H), 3.52-3.48 (m, 1H), 1.90-1.50 (m, 6H).
Phenyl methanol (Table-2, entry a)

Yield: 96%, colourless liquid; \(^1\)H NMR (CDCl\(_3\)): \(\delta \) 7.39-7.29 (m, 5H), 4.71 (d, \(J=6\)Hz, 2H), 1.76 (m, 1H).

4-(tetrahydro-2H-pyran-2-yloxy)benzaldehyde (Table-2, entry b)

Colourless gummy solid; \(^1\)H NMR (CDCl\(_3\)): \(\delta \) 9.91 (s, 1H), 7.81 (d, \(J=9.2\) Hz, 2H), 6.97 (d, \(J=9.2\) Hz, 2H), 5.39 (m, 1H), 3.90-3.82 (m, 1H), 3.61-3.56 (m, 1H), 1.98-1.54 (m, 6H).

4-Hydroxybenzaldehyde (Table-2, entry b)

Yield: 95%, off-white solid; m.p: 112-114 °C; \(^1\)H NMR (CDCl\(_3\)): \(\delta \) 9.87 (s, 1H), 7.81 (d, \(J=8.8\) Hz, 2H), 6.96 (d, \(J=8.4\) Hz, 2H), 5.74 (br s, 1H).
2-(2-Iodobenzyloxy)tetrahydro-2\(H\)-pyran (Table-2, entry c)

Colourless gummy compound; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 7.82 (d, \(J= 8\) Hz, 1H), 7.47 (d, \(J= 7.6\) Hz, 1H), 7.35 (t, \(J= 7.2\) Hz, 1H), 6.98 (t, \(J= 7.2\) Hz, 1H), 4.79 (m, 1H), 4.75 (d, \(J= 13.2\) Hz, 1H), 4.48 (d, \(J= 12.8\) Hz, 1H), 3.96-3.87 (m, 1H), 3.59-3.50 (m, 1H), 1.93-1.55 (m, 6H).

(2-Iodophenyl)methanol (Table-2, entry c)

Yield: 96%, off-white solid; m.p: 90-94\(^o\)C; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 7.83 (d, \(J= 8\) Hz, 1H), 7.46 (d, \(J= 7.2\) Hz, 1H), 7.37 (t, \(J= 7.2\) Hz, 1H), 7.01 (t, \(J= 7.2\) Hz, 1H), 4.68 (d, \(J= 6\) Hz, 2H), 2.01 (t, \(J= 6\) Hz, 1H).

2-(4-Chloro-2-iodobenzyloxy)tetrahydro-2\(H\)-pyran (Table-2, entry d)

Colourless gummy compound; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 7.82 (s, 1H), 7.41-7.33 (m, 2H), 4.77-4.75 (m, 1H) 4.71 (d, \(J= 13.2\) Hz, 1H), 4.44 (d, \(J= 13.6\) Hz, 1H), 3.93-3.87 (m, 1H), 3.59-3.53 (m, 1H), 1.92-1.53 (m, 6H); \(^13\)C NMR (CDCl\(_3\), 400 MHz) \(\delta\): 19.26, 25.35, 30.42, 62.22, 72.23, 97.26, 98.42, 128.28, 129.20, 133.51, 138.25, 139.37. Anal. Calcd
for C$_{12}$H$_{14}$ClIO$_2$: C, 40.88; H, 4.00; Cl, 10.05; I, 35.99; O, 9.08; Found C, 40.95; H, 4.15. (LC-MS) m/z: 350.9 [M-H].

(4-Chloro-2-iodophenyl)methanol (Table-2, entry d)

Yield: 95%, off-white solid; m.p: 114-116°C; $^1$H NMR (CDCl$_3$): $\delta$7.87(s, 1H), 7.48-7.44 (m, 2H), 5.52 (t, $J$ = 5.6 Hz, 1H), 4.38 (d, $J$ = 5.6 Hz, 2H). (LC-MS) m/z: 266.9 [M-H].

2-(2-Iodophenoxy)tetrahydro-2H-pyran (Table-2, entry e)

Brown colour gummy solid; $^1$H NMR (CDCl$_3$): $\delta$7.77 (d dt, $J$ = 6.4 Hz, 1H), 7.29-7.26 (m, 1H), 7.08 (d, $J$ = 8.4 Hz, 1H), 6.73 (t, $J$ = 6.4 Hz, 1H), 5.54 (m, 1H), 3.91-3.84 (m, 1H), 3.61-3.59 (m, 1H), 2.20-1.54 (m, 6H).

2-Iodophenol (Table-2, entry e)

Yield: 96%, light brown solid; m.p: 44-45°C; $^1$H NMR (CDCl$_3$): $\delta$ 7.70 (d, $J$ = 6.4 Hz, 1H), 7.20 (t, $J$ = 6.4 Hz, 1H), 6.98 (d, $J$ = 8.2 Hz, 1H), 6.67 (t, $J$ = 6.4 Hz, 1H), 5.22 (s, 1H).
2-(4-Iodophenoxy)tetrahydro-2\(H\)-pyran (Table-2, entry f)

Brown colour gummy solid; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 7.55 (d, \(J = 9.2\) Hz, 2H), 6.83 (d, \(J = 9.2\) Hz, 2H), 5.37 (m, 1H), 3.89-3.82 (m, 1H), 3.61-3.56 (m, 1H), 1.98-1.54 (m, 6H).

4-Iodophenol (Table-2, entry f)

Yield: 92\%, light brown solid; m.p: 94-97°C; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 7.51 (d, \(J = 8.8\) Hz, 2H), 6.62 (d, \(J = 8.8\) Hz, 2H), 4.86 (s, 1H).

2-(4-Methoxybenzyloxy)tetrahydro-2\(H\)-pyran (Table-2, entry g)

Colourless liquid; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 7.30 (d, \(J = 8.4\) Hz, 2H), 6.91 (d, \(J = 8.4\) Hz, 2H), 4.79-4.70 (m, 2H), 4.42 (d, \(J = 13.6\) Hz, 1H), 3.96-3.92 (m, 1H), 3.80 (s, 3H), 3.58-3.51 (m, 1H), 1.90-1.50 (m, 6H).
(4-Methoxyphenyl)methanol (Table-2, entry g)

Yield: 95%, colourless liquid; $^1$H NMR (CDCl$_3$): $\delta$ 7.30 (d, $J=8.8$ Hz, 2H), 6.88 (d, $J=8.8$ Hz, 2H), 4.81 (d, $J=5.6$ Hz, 2H), 3.80 (s, 3H), 1.62 (m, 1H).

2-(4-Nitrobenzyloxy)tetrahydro-2H-pyran (Table-2, entry h)

Pale yellow colour liquid; $^1$H NMR (CDCl$_3$): $\delta$ 8.21 (d, $J=8.8$ Hz, 2H), 7.53 (d, $J=8.4$ Hz, 2H), 4.88 (d, $J=14$ Hz, 1H), 4.73 (m, 1H), 4.60 (d, $J=13.6$ Hz, 1H), 3.91-3.85 (m, 1H), 3.58-3.55 (m, 1H), 1.89-1.56 (m, 6H).

(4-Nitrophenyl)methanol (Table-2, entry h)

Yield: 90%, pale yellow solid; m.p: 90-92 °C $^1$H NMR (CDCl$_3$): $\delta$ 8.22 (d, $J=8.8$ Hz, 2H), 7.53 (d, $J=8.8$ Hz, 2H), 4.84 (d, $J=5.6$ Hz, 2H), 1.91 (t, $J=5.6$ Hz, 1H).
** tert-Butyl 3-(tetrahydro-2H-pyran-2-yloxy)propylcarbamate (Table-2, entry i)**

![Chemical Structure](image1)

Colourless gummy compound; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 4.92 (s, 1H), 4.57-4.56 (m, 1H), 3.85-3.78 (m, 2H), 3.51-3.43 (m, 2H), 3.25-3.24 (m, 2H), 1.84-1.46 (m, 8H), 1.43 (s, 9H); \(^{13}\)C NMR (CDCl\(_3\), 400 MHz) \(\delta\): 19.40, 25.34, 28.35, 29.57, 30.55, 38.61, 62.20, 65.70, 78.82, 98.81, 155.95; Anal. Calcd for C\(_{13}\)H\(_{25}\)NO\(_4\): C, 60.21; H, 9.72; N, 5.40; O, 24.68; Found C, 60.44; H, 9.98; N, 5.45.

** tert-Butyl 3-hydroxypropylcarbamate (Table-2, entry i)**

![Chemical Structure](image2)

Yield: 88%, colourless gummy compound; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 4.77 (s, 1H), 3.64-3.68 (m, 2H), 3.27-3.31 (m, 2H), 3.01 (t, \(J=6\)Hz, 1H), 1.66-1.69 (m, 2H), 1.44 (s, 9H).

** tert-Butyl 6-(tetrahydro-2H-pyran-2-yloxy)hexylcarbamate (Table-2, entry j)**

![Chemical Structure](image3)

Colourless gummy compound; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 4.57-4.55 (m, 1H), 4.51 (s, 1H), 3.89-3.87 (m, 1H), 3.76-3.70 (m, 1H), 3.52-3.50 (m, 1H), 3.39-3.36 (m, 1H),
3.13-3.08 (m, 2H), 1.85-1.64 (m, 3H), 1.61-1.33 (m, 11H), 1.44 (s, 9H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 400 MHz) \delta: 19.63, 25.40, 25.87, 26.55, 28.35, 29.57, 29.94, 30.69, 40.45, 62.30, 67.40, 78.89, 98.80, 155.91; IR (DCM film, cm\textsuperscript{-1}): 3355, 2936, 2865, 1702, 1523, 1365, 1251, 1169, 1033, 868; Anal. Caled for C\textsubscript{16}H\textsubscript{31}NO\textsubscript{4}: C, 63.75; H, 10.37; N, 4.65; O, 21.33; Found C, 64.01; H, 10.45; N, 4.72. (LC-MS) m/z: 302.1 [M+H]\textsuperscript{+}

\textit{tert}-Butyl 6-hydroxyhexylcarbamate (Table-2, entry j)

Yield: 89%, colourless gummy compound; \textsuperscript{1}H NMR (CDCl\textsubscript{3}): \delta 4.49 (s, 1H), 3.62-3.65 (m, 2H), 3.10-3.12 (m, 2H), 1.33-1.56 (m, 9H), 1.44 (s, 9H).

3-(Tetrahydro-2\textit{H}-pyran-2-yloxy)propanenitrile (Table-2, entry k)

Colourless liquid; \textsuperscript{1}H NMR (CDCl\textsubscript{3}): \delta 4.82 (m, 1H), 3.94-3.81 (m, 1H), 3.70 (m, 2H), 3.58-3.42 (m, 1H), 2.62 (t, J= 6Hz, 2H), 1.92-1.41 (m, 6H).

3-Hydroxypropanenitrile (Table-2, entry k)

Yield: 81%, colourless liquid; \textsuperscript{1}H NMR (CDCl\textsubscript{3}): \delta 3.88 (t, J= 5.6 Hz, 2H), 2.73 (br s, 1H), 2.61 (t, J= 6 Hz, 2H).
2-(But-3-ynyloxy)tetrahydro-2H-pyran (Table-2, entry 1)

![Structure](image)

Colourless liquid; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 4.65 (m, 1H), 3.91-3.81 (m, 2H), 3.60-3.49 (m, 2H), 2.52-2.48 (m, 2H), 1.98 (s, 1H), 1.89-1.42 (m, 6H).

**But-3-yn-1-ol (Table-2, entry 1)**

![Structure](image)

Yield: 87%, colourless liquid; \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 3.75 (q, J = 6.4 Hz, 2H), 2.49-2.45 (m, 2H), 2.05 (m, 1H), 1.86 (t, J = 6 Hz, 1H).
$^1$H NMR Spectrum of 4-Hydroxybenzaldehyde
$^1$H NMR Spectrum of 2-(4-Chloro-2-iodobenzyloxy)tetrahydro-2$H$-pyran
$^{13}$C NMR Spectrum of 2-(4-Chloro-2-iodobenzyloxy)tetrahydro-2H-pyran
$^1$H NMR Spectrum of (4-Chloro-2-iodophenyl)methanol
$^1$H NMR Spectrum of 2-(4-Nitrobenzylxyloxy)tetrahydro-2H-pyran
$^1$H NMR Spectrum of (4-Nitrophenyl)methanol
$^1$H NMR Spectrum of tert-Butyl 3-(tetrahydro-$2H$-pyran-2-yl oxy)propylcarbamate
$^{13}$C NMR Spectrum of tert-Butyl 3-(tetrahydro-2H-pyran-2-yloxy)propylcarbamate
$^1$H NMR Spectrum of tert-Butyl 3-hydroxypropylcarbamate
$^1$H NMR Spectrum of tert-Butyl 6-(tetrahydro-2H-pyran-2-ylxy)hexylcarbamate
$^{13}$C NMR Spectrum of tert-Butyl 6-(tetrahydro-2H-pyran-2-yloxy)hexylcarbamate
$^1$H NMR Spectrum of tert-Butyl 6-hydroxyhexylcarbamate
2.8 References