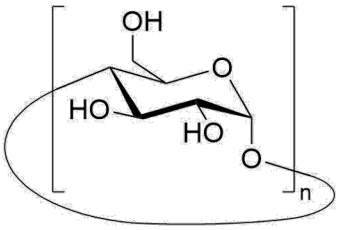
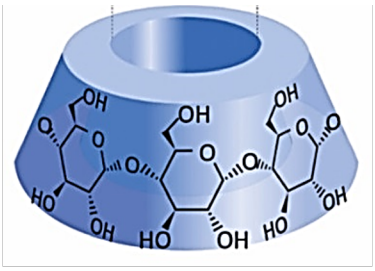
# T9. Cyclodextrin Chemistry

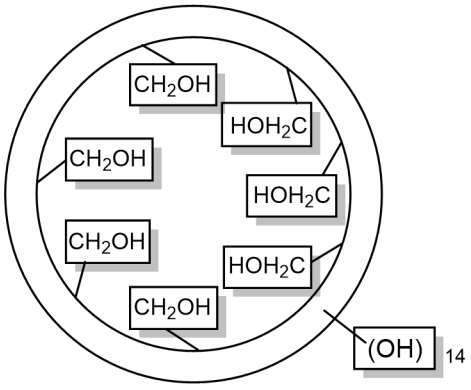
| 7% | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 9.1 | 9.2 | 9.3 | 9.4 | 9.5 | 9.6 | 9.7 | 9.8 | 9.9 | ∑ |
| 2 | 6 | 8 | 3 | 2 | 4 | 6 | 18 | 4 | 53 |

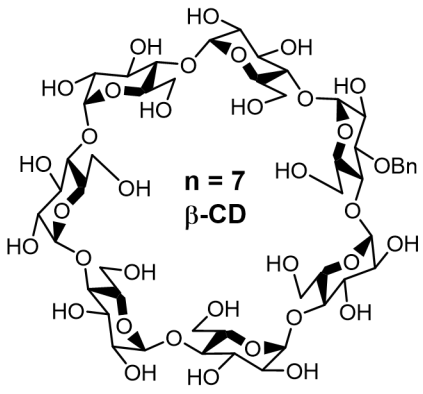
Cyclodextrins (CD) are a family of cyclic oligosaccharides, consisting of glucose subunits joined by α-1,4-glycosidic bonds. The three most common cyclodextrins (α-, β-, γ-cyclodextrin) contain 6, 7, and 8 α-D-glucopyranoside units, respectively.

**9.1** **Calculate** the molar mass of β-CD. **Assume** $M_w$(glucose) = 180.16 g mol$^{-1}$. 2.0 pt

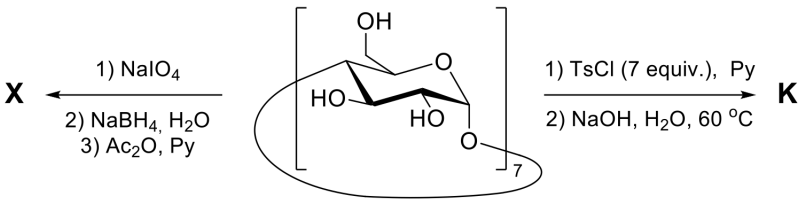


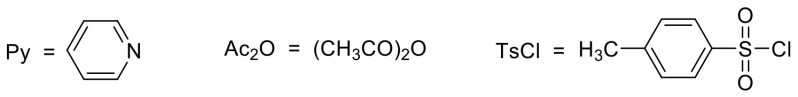





CDs combine macrocyclic properties with glucose chemistry, which was demonstrated in the synthesis of **X**. Primary and secondary hydroxy groups show different reactivity due to being a part of CDs. Stoddart *et al.* synthesised compound **K**, where only one OH group remained free per glucopyranoside unit.




equiv.= equivalent

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| **9.2** | **Tick** the favorable chair conformation and **draw** the structure of **K** by completing the CD template. **Show** stereochemistry unambiguously. | 6.0 pt |

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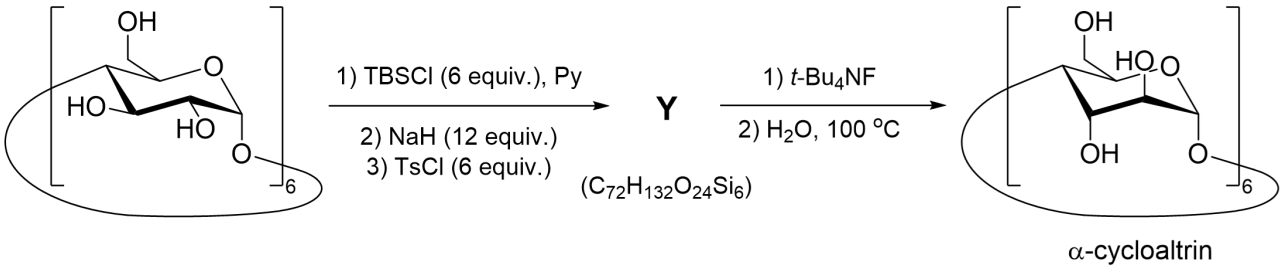
| **9.3** | **Determine** the ring size, $rs$, of macrocycle **X**. **Give** the number of stereocentres, $sc$, in **X.** | 8.0 pt |

α-Cycloaltrin, a synthetic analogue of α-CD, was synthesised as follows.





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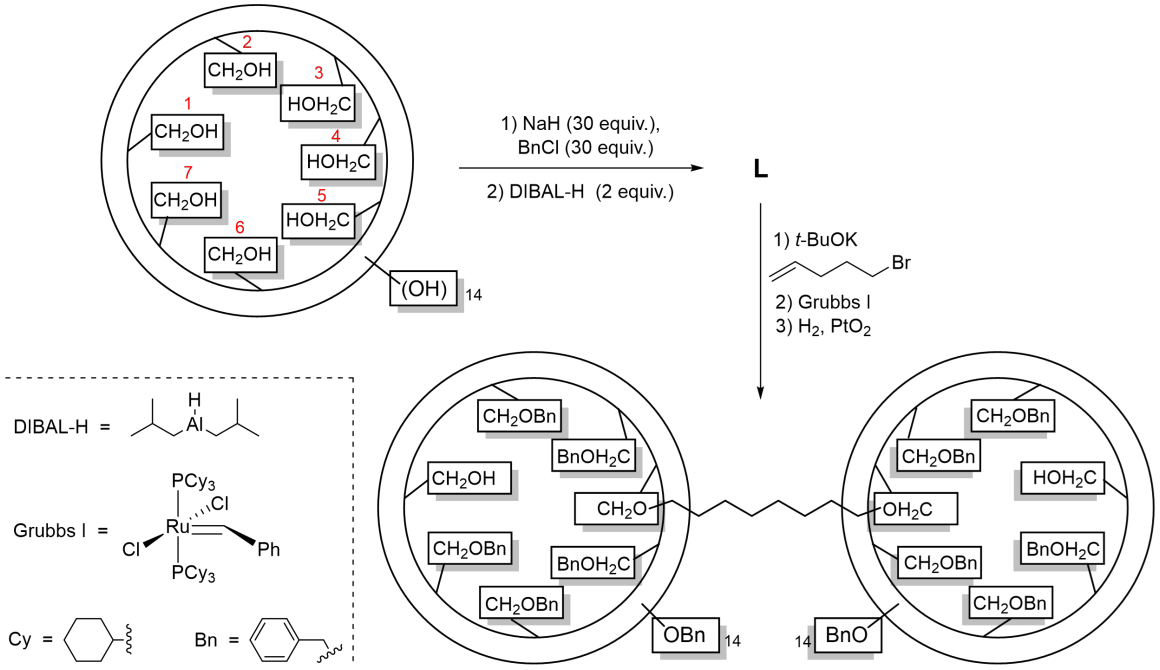
| **9.4** | **Draw** the structure of **Y** with stereochemistry by completing the CD template. | 3.0 pt |

In 2000, Sinay *et al.* demonstrated that a single protic group (NH and OH) at unit 1 directs the **next** reductive debenzylation of a primary OH group to unit 4 in the macrocyclic ring (or to unit 3 if the unit 4 position is not available). This allowed the synthesis of the following β-CD dimer as a mixture of constitutional linkage isomers.

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| **9.5** | **Draw** the structure of **L** on the β-CD template. **Fill in** all the boxes. | 2.0 pt |

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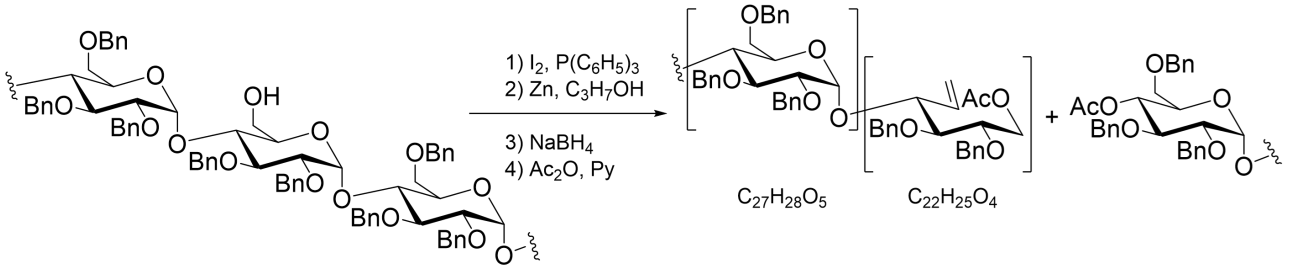
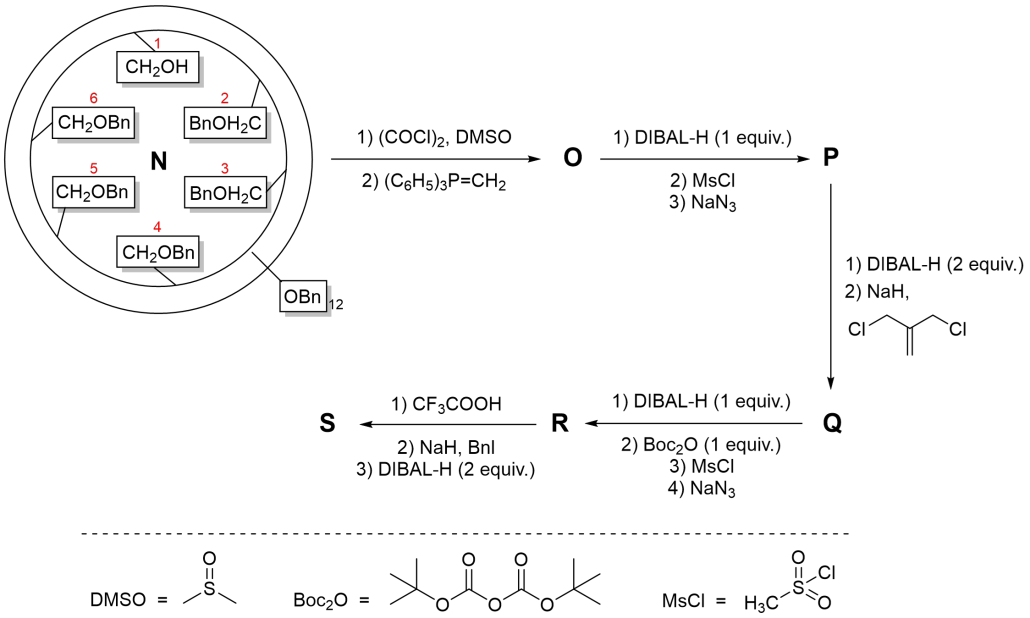
| **9.6** | **Determine** the number of isomers of the β-CD dimer that can form during the synthesis by *Sinay et. al.* | 4.0 pt |

To confirm the positions of debenzylation, **L** was subjected to the "hexo-5-enose degradation" reaction, as shown below. The products were then analysed by mass spectrometry.




**9.7** **Calculate** the $m/z$ value for the two $[M+Na]^+$ peaks that were observed for the degradation products from **L**. **Use** integer values of atomic mass. 6.0 pt

Later, Sollogoub *et al.* applied the ability of alkenes to direct the debenzylation to the "*ortho*"-glucopyranose unit for the synthesis of hexadifferentiated α-CD **S**:




**9.8** **Draw** the structures of **O-S** on the α-CD templates. **Fill in** all the boxes. You may draw structures outside the boxes if appropriate. **Assume** 1,2-unit modification happens **clockwise**, while 1,3-unit modification happens **counterclockwise**. Protic groups have stronger directing effects than alkenes. 18.0 pt

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| **9.9** | **Determine** the number of all possible arrangements of the functional groups on a hexadifferentiated α-CD (**assume** only the $CH_2OH$ groups have been modified). | 4.0 pt |