KAHNE GLYCOSIDATION

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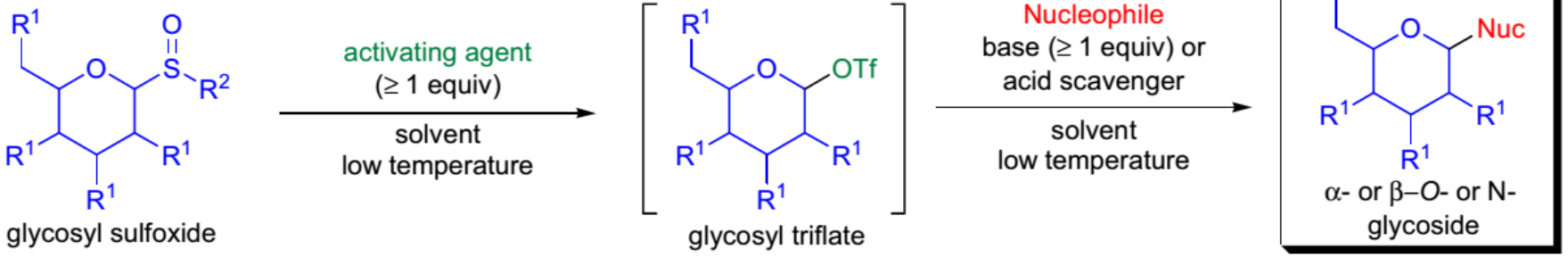
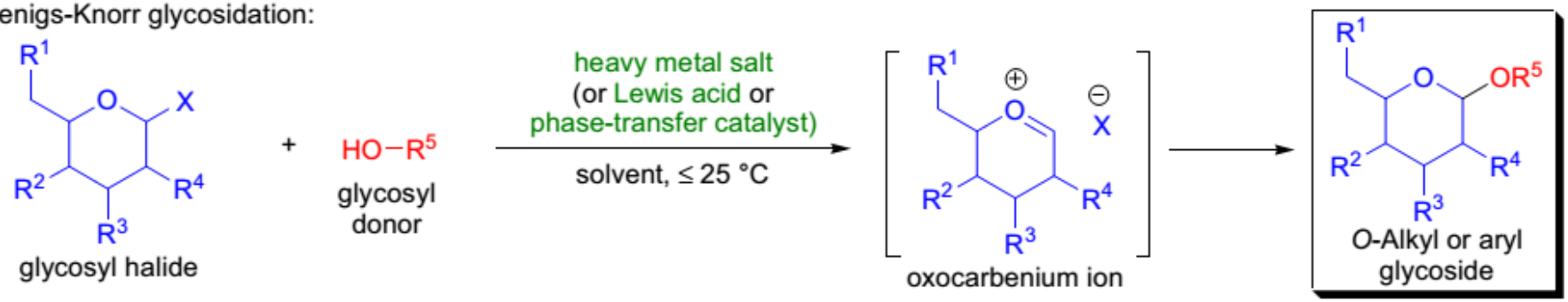
Kahne glycosidation (sulfoxide method):



R^1 = *O*-alkyl, *O*-aryl, *O*-acyl; R^2 = alkyl, aryl; triflate activator: Tf_2O, TMSOTf, TfOH; solvent: toluene, CH_2Cl_2, Et_2O, EtOAc, EtCN; base: DTBMP, DTBP, TTBP; acid scavenger: methyl propiolate, allyl-1,2-dimethoxybenzene, $P(OMe)_3$, $P(OEt)_3$; Nucleophile: 1°, 2° and 3° alcohols, phenols, thiols, silylated amides, *O*-trialkylstannyl phenols

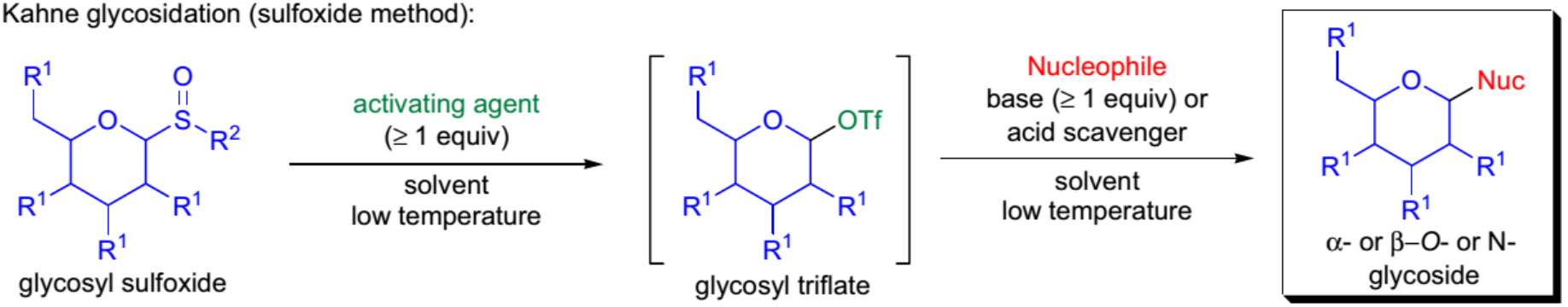
Koenigs-Knorr glycosidation:



R^{1-4} = *O*-alkyl, *O*-acyl, alkyl ,aryl; X = Cl, Br, I; R^5 = alkyl, aryl, heteroaryl; heavy metal salts: AgOTf, Ag_2O, Ag_2CO_3, $AgNO_3$, $AgClO_4$, HgI_2, $HgCl_2$, $HgBr_2$, $Hg(CN)_2$; Lewis acids: $Sn(OTf)_2$, $Sn(OTf)_2$-collidine, $Sn(OTf)_2$-TMU, $SnCl_4$, TrCl-$ZnCl_2$; Phase-transfer catalysts: $(Bu_4N)Br$, $(Et_3NCH_2Ph)Br$, $(Et_3NCH_2Ph)Cl$; solvent: DCM, cyclohexane, petroleum ether, etc.

Features of Kahne Glycosidation

Kahne glycosidation (sulfoxide method):



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1) the sulfoxides are usually prepared via the oxidation of the corresponding thioglycosides;
2) the most common oxidizing agents are mCPBA and MMPP;
3) both alkyl and aryl sulfoxides can be used as substrates;
4) the reactivity of aryl glycosyl sulfoxides can be modulated by placing electron-donating or electron-withdrawing substituents on the aromatic ring;

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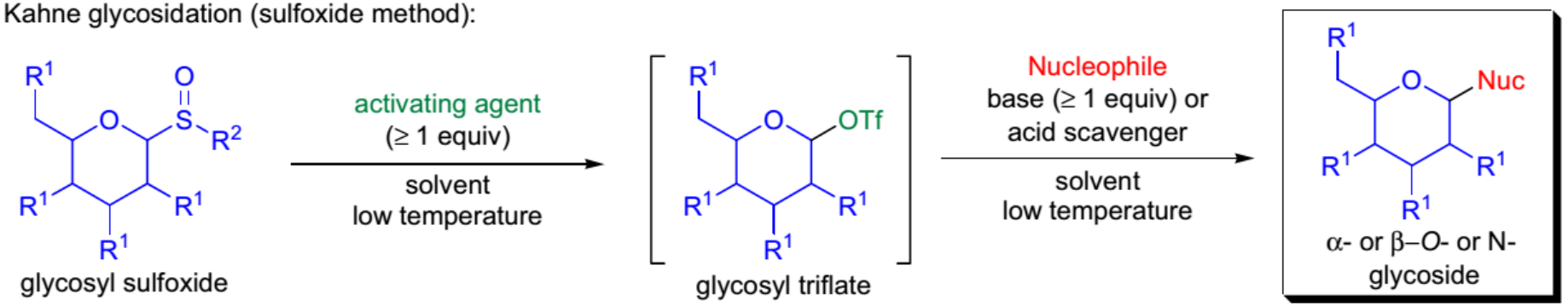

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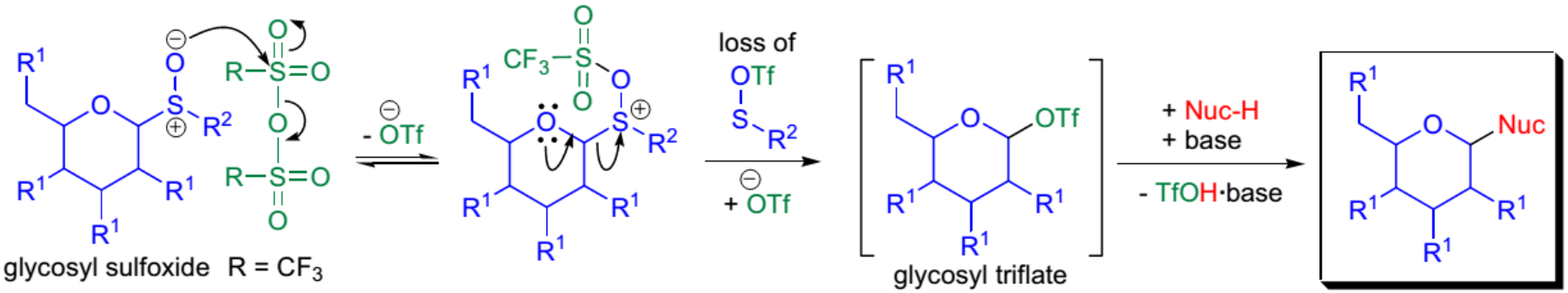
5) the most common activating agent is triflic anhydride (Tf2O) and trimethylsilyl triflate(TMSOTf), but occasionally Lewis acids (e.g., Cp2ZrCl2/AgClO4) and mineral acids can be used as activating agents;
6) since triflic acid or phenylsulfenyl triflate is generated in the reaction, the use of a hindered, nonnucleophilic base to buffer the reaction mixture is recommended (sometimes the use of a base results in the formation of an orthoester instead of a glycoside, a problem that is resolved by simply omitting the base);
7) primary-,secondary and tertiary alcohols, phenols, trialkylstannylated phenols, silylated amides can be used as nucleophiles;
8) the reaction is conducted at low temperatures and is usually complete in a matter of minutes or a few hours.

Mechanism:


glycosyl sulfoxide R = CF3
- OTf
loss of
OTf
+ OTf
glycosyl triflate
+ Nuc-H
+ base
- TfOH·base
Nuc

Synthetic Applications: