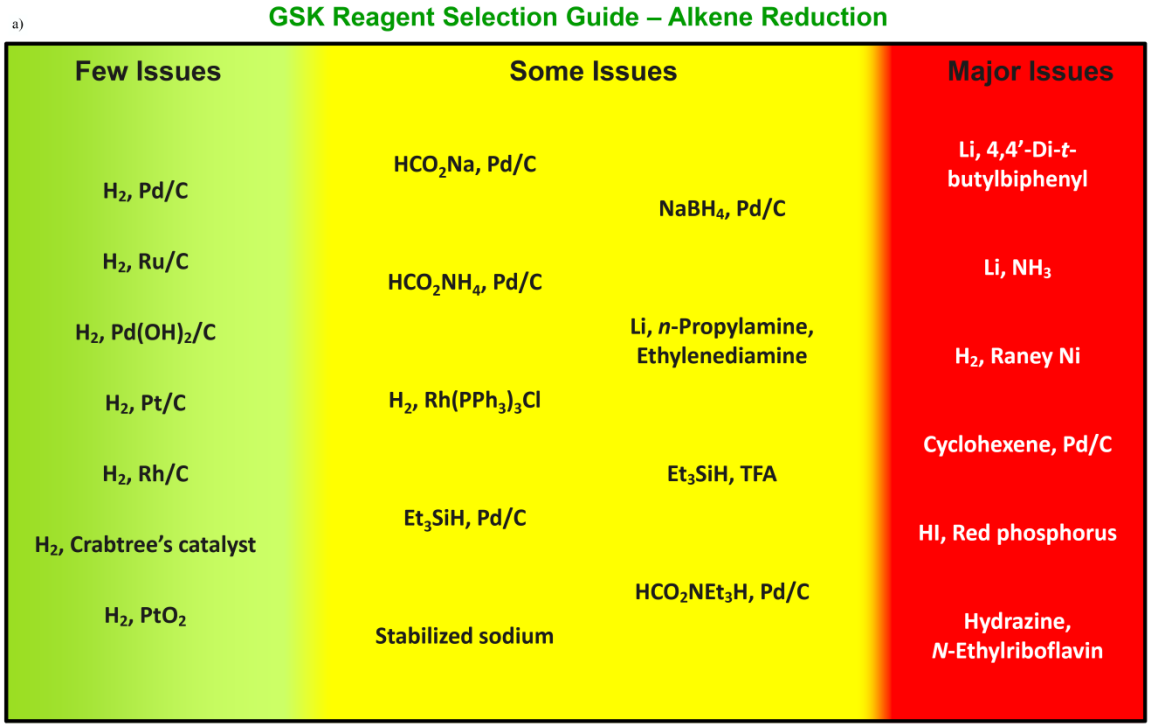
Electronic Supplementary Material (ESI) for Green Chemistry

Supplementary Info:

a)

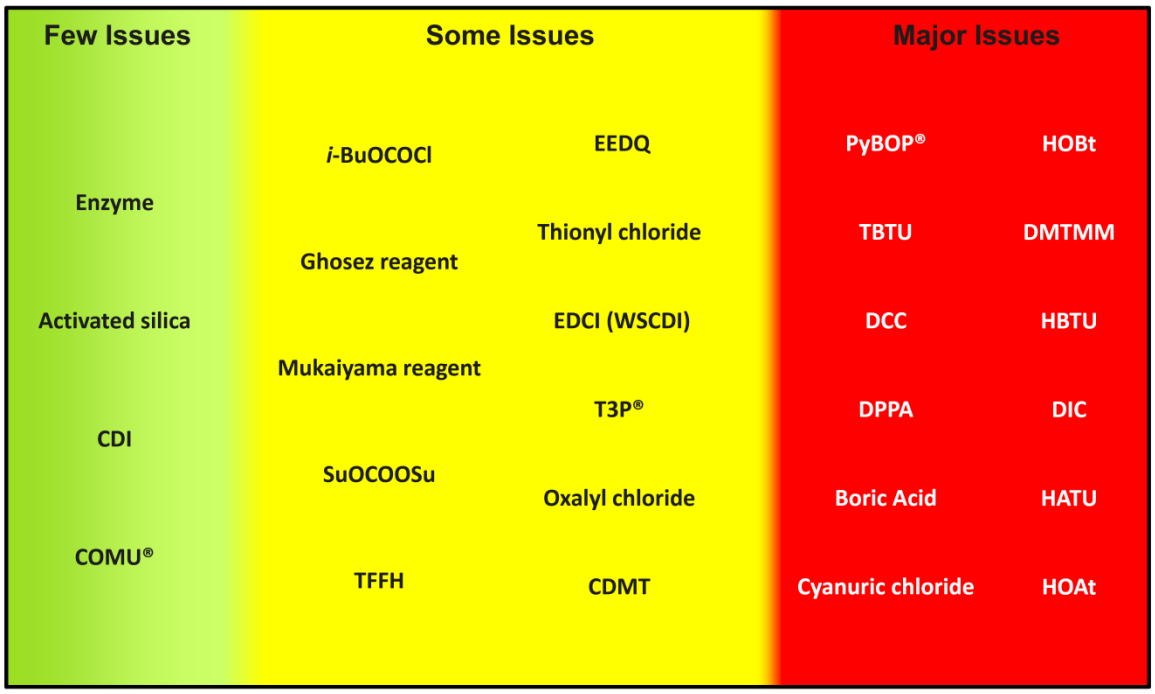


b)

Material	Full name	CAS / MFCD number	EHS	Clean chemistry	Greenness	Comment
H_2, Pd/C	Hydrogen, Palladium on Carbon	1333-74-0/7440-05-3	7	7	7.2	Flammable. Relative cost cheap. Catalyst can be recycled.
H_2, Ru/C	Hydrogen, Ruthenium on Carbon	1333-74-0/7440-18-8	7	7	7.2	Flammable. Relative cost cheap. Catalyst can be recycled.
H_2, $Pd(OH)_2/C$	Hydrogen, Palladium hydroxide	1333-74-0 12135-22-7	7	7	7.2	Flammable. Slightly more expensive than Pd/C. Catalyst can be recycled.
H_2, Pt/C	Hydrogen, Platinum on Carbon	1333-74-0 7440-06-4	7	7	7.2	Flammable. Relative cost expensive. Catalyst can be recycled.
H_2, Rh/C	Hydrogen, Rhodium on Carbon	1333-74-0/7440-16-6	7	7	7.1	Flammable. Relative cost extremely expensive.
H_2, Crabtree's catalyst	Hydrogen, (1,5-Cyclooctadiene)(pyridine) (tricyclohexylphosphine)-iridium(I) hexafluorophosphate	1333-74-0 64536-78-3	7	6	6.8	Flammable. Relative cost of iridium very expensive. Catalyst can be recycled.
H_2, PtO_2	Hydrogen, Platinum oxide	1333-74-0 1314-15-4	5	7	6.1	Flammable. Relative cost expensive. Catalyst can be recycled.
HCO_2Na, Pd/C	Sodium Formate, Palladium on Carbon	141-53-7 7440-05-3	7	5	5.9	Hydrogen transfer. Reaction rates, off-gassing rates may be a concern on some systems.
Ammonium formate, Pd/C	Ammonium Formate, Palladium on Carbon	540-69-2 7440-05-3	7	5	5.8	Hydrogen transfer. Reaction rates, off-gassing rates may be a concern on some systems.
H_2, $Rh(PPh_3)_3Cl$	Hydrogen, Chlorotris(triphenylphosphine)rhodium(I)	1333-74-0/14694-95-2	5	6	5.8	Flammable. Relative cost of rhodium extremely expensive.
Et_3SiH, Pd/C	Triethylsilane, Palladium on Carbon	617-86-7/7440-05-3	7	5	5.5	Hydrogen transfer.
Stabilized sodium	Sodium on Silica gel	MFCD01941718	5	5	5.3	Used in Birch reduction, no need for ammonia.
$NaBH_4$, Pd/C	Sodium borohydride, Palladium on Carbon, Acetic acid	16940-66-2 7440-05-3/64-19-7	5	5	5.3	Acetic acid required.
Li, *n*-Propylamine, $NH_2CH_2CH_2NH_2$	Lithium, *n*-Propylamine, Ethylenediamine	7439-93-2/107-10-8 107-15-3	5	5	5.0	Flammable.
Et_3SiH, TFA	Triethylsilane, Trifluoroacetic acid	617-86-7 76-05-1	5	5	4.9	Higher stoichiometry of Et_3SiH may be required for less electron rich alkenes.
HCO_2NEt_3H, Pd/C	Triethylammonium formate, Palladium on Carbon	585-29-5 7440-05-3	5	4	4.9	Hydrogen transfer. Reaction rates, off-gassing rates may be a concern on some systems.
Li, 4,4'-Di-*t*-butylbiphenyl	Lithium, 4,4'-Di-*tert*-butylbiphenyl	7439-93-2 1625-91-8	5	2	3.5	Causes burns. Reacts violently with water.
Li, NH_3	Lithium, Ammonia	7439-93-2 7664-41-7	4	3	3.3	Causes burns. Very toxic to aquatic organisms. Danger of serious irreversible effects by exposure.
H_2, Raney Ni	Hydrogen, Raney nickel	1333-74-0 7440-02-0	1	6	3.0	Highly flammable. Potential carcinogen and sensitizer.
Cyclohexene, Pd/C	Cyclohexene, Palladium on Carbon	110-83-8 7440-05-3	1	6	3.0	Benzene (known carcinogen) forms as by-product.
HI, Red phosphorus	Hydroiodic acid, Red phosphorus	10034-85-2 7723-14-0	2	3	2.7	Highly flammable. Red phosphorus is a controlled substance.
Hydrazine, *N*-Ethylriboflavin	Hydrazine, *N*-Ethylriboflavin	302-01-2 N/A	1	4	2.4	Hydrazine is a material of concern. May cause cancer.

Figure S1: GSK Alkene Reduction Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)



This guide should only be used by the expert trained chemist. Before using any reagent listed on this guide, a complete risk assessment must be carried out.

b)

Material	Full Name	CAS number	EHS	Clean Chemistry	Greenness	Comments
Enzyme	Enzyme	N/A	10	8	8.8	
Activated silica	Thermally activated Kieselgel 60	7631-86-9	10	8	8.7	Activated at > 600 °C.
CDI	1,1-Carbonyl diimidazole	530-62-1	7	7	6.5	Gaseous and water soluble byproducts.
COMU®	(1-Cyano-2-ethoxy-2-oxoethylidenaminooxy)dimethylamino morpholino-carbenium hexafluorophosphate	1075198-30-9	10	4	6.5	Water soluble byproduct.
i-BuOCOCl	Isobutyl chloroformate	543-27-1	7	6	6.4	Lachrymator, gaseous byproducts. Recommended storage at +4 °C. Activated species forms quickly.
Ghosez reagent	1-Chloro-*N*,*N*,2-trimethyl-1-propenylamine	26189-59-3	7	6	6.4	Recommended storage at +4 °C.
Mukaiyama reagent	2-Chloro-1-methylpyridinium iodide	14338-32-0	10	4	6.3	Recommended storage at +4 °C.
SuOCOOSu	*N*,*N*′-Disuccinimidyl carbonate	74124-79-1	9	4	6.3	Water sensitive. Recommended storage at +4 °C.
TFFH	Fluoro-*N*,*N*,*N*′,*N*′-tetramethylformamidinium hexafluorophosphate	164298-23-1	10	4	6.0	Fluoride byproduct may limit vessel choice. Avoid acidic work-up.
EEDQ	2-Ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline	16357-59-8	9	4	5.6	Odour. Recommended storage at +4 °C
Thionyl chloride	Thionyl chloride	7719-09-7	5	6	5.5	Lachrymator. Gaseous byproducts .
EDCI (WSCDI)	[1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride]	25952-53-8	7	4	5.3	Water soluble byproducts. Recommended storage at +4 °C. Known to test AMES positive, potential mutagen.
T3P®	2-Propanephosphonic acid anhydride	68957-94-8	5	5	5.3	Regulated chemical. Usage as 50% in EtOAc preferable to DMF solution
Oxalyl chloride	Oxalyl chloride	79-37-8	5	5	5.2	Lachrymator. Gaseous byproducts. Scored for usage on own, usage with DMF not recommended as DMCC carcinogen may be produced.
CDMT	2-Chloro-4,6-dimethoxy-1,3,5-triazine	3140-73-6	5	5	5.0	Sensitizer. Toxic to aquatic organisms.
PyBOP®	Benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate	128625-52-5	10	3	5.2	Cytotoxic urea byproduct.
TBTU	*O*-Benzotriazol-1-yl-*N*,*N*,*N*′,*N*′-tetramethyluronium tetrafluoroborate	125700-67-6	3	6	4.5	Risk of explosion. Urea byproduct difficult to remove.
DCC	*N*,*N*′-Dicyclohexylcarbodiimide	538-75-0	7	3	4.4	Urea byproduct is a sensitizer, also difficult to remove.
DPPA	Diphenylphosphoryl azide	26386-88-9	5	3	4.2	May form explosive hydrogen azide on contact with moisture.
Boric acid	Boric acid	10043-35-3	2	9	4.1	May damage fertility. May damage the unborn child.
Cyanuric chloride	2,4,6-Trichloro-1,3,5-triazine	108-77-0	3	6	3.8	Reacts violently with water. Causes burns. Toxic by inhalation.
HOBt	1-Hydroxybenzotriazole hydrate	123333-53-9	3	4	3.7	May cause explosion. Cytotoxic urea byproduct.
DMTMM	4-Dimethoxy-1,3,5,triazin-2-yl)-4-methyl morpholinium chloride	3945-69-5	3	5	3.6	Causes burns.
HBTU	*N*,*N*,*N*′,*N*′-Tetramethyl-*O*-(benzotriazol-1-yl)uronium hexafluorophosphate	94790-37-1	3	4	3.5	Cytotoxic urea byproduct.
DIC	Diisopropyl carbodiimide	693-13-0	3	4	3.5	Flammable. Toxic by inhalation.
HATU	1-[Bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate	148893-10-1	3	4	3.3	Cytotoxic urea byproduct.
HOAt	1-Hydroxy-7-azabenzotriazole	39968-33-7	2	5	2.9	May cause explosion. Cytotoxic urea byproduct. Currently only available as DMF solution - may cause harm to the unborn child.

Figure S2: GSK Amide Formation Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)

GSK Reagent Selection Guide – C-H Bromination

Few Issues	Some Issues	Major Issues
Enzyme	HBr, H_2O_2 ‡	$NaBr, NaBrO_3$
NBS	$PhNMe_3Br_3$	Br_2
KBr, H_2O_2 ‡	$Py \cdot HBr_3$	$LiBr, O_2$, Cu catalyst
	NaBr or NH_4Br, Oxone®	HBr, O_2, Cu catalyst
	HBr, Oxone®	Dibromodimethylhydantoin
		NaBr, TCCA

‡ Use of ≤30% H_2O_2 is required for these procedures to not fall into the "Major Issues" category.

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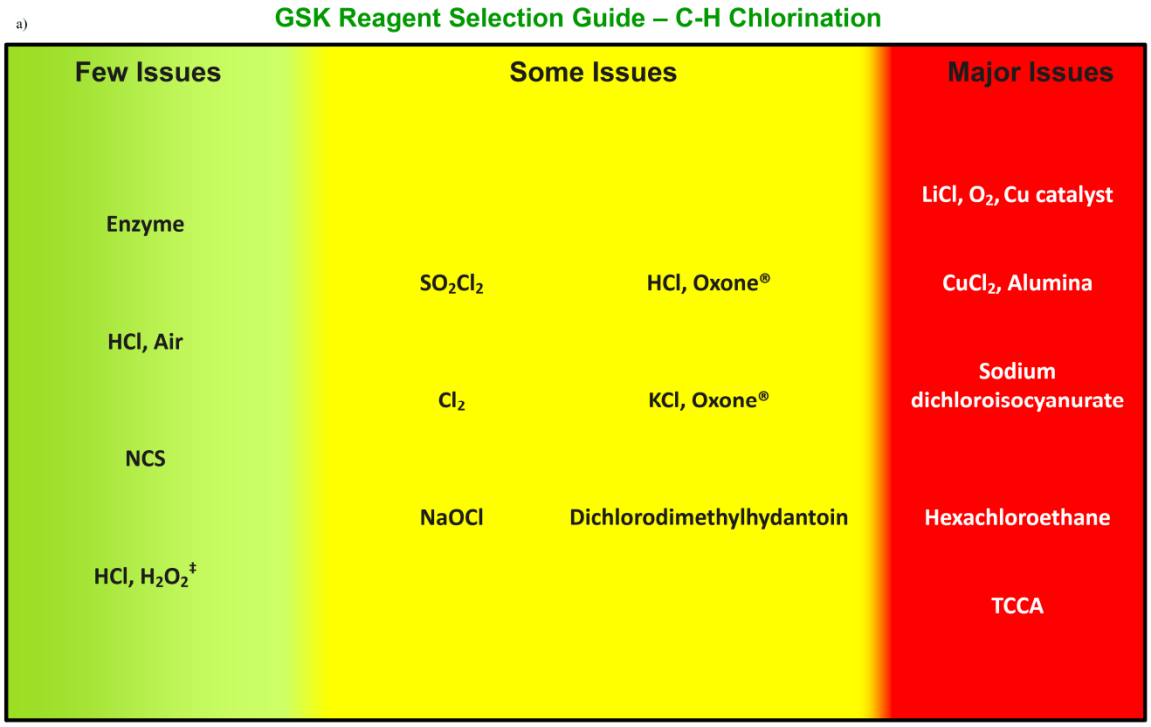
b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
Enzyme	Enzyme	N/A	10	9	9.3	
NBS	*N*-Bromosuccinimide	128-08-5	7	7	7.3	
KBr, H_2O_2	Potassium bromide, Hydrogen peroxide (≤30%)	7758-02-3 7722-84-1	7	7	7.3	
HBr, H_2O_2	Hydrogen bromide, Hydrogen peroxide (≤30%)	10035-10-6 7722-84-1	7	6	6.7	Causes burns.
$PhNMe_3Br_3$	Phenyltrimethylammonium tribromide	4207-56-1	7	5	6.3	Causes burns.
$Py{\cdot}HBr_3$	Pyridinium hydrobromide perbromide	39416-48-3	7	5	6.1	Causes burns.
NaBr or NH_4Br, Oxone®	Sodium bromide or Ammonium bromide, Potassium monoperoxysulfate	7647-15-6 or 70693-62-8 37222-66-5	5	4	4.9	Causes burns. Oxone is highly exothermic and less stable above pH 7. May be unstable in the presence of water above 70 °C.
HBr, Oxone®	Hydrogen bromide, Potassium monoperoxysulfate	10035-10-6 37222-66-5	5	4	4.6	Causes burns. Oxone is highly exothermic and less stable above pH 7. May be unstable in the presence of water above 70 °C.
$NaBr, NaBrO_3$	Sodium bromide, Sodium bromate	7647-15-6 7789-38-0	3	8	4.8	May cause fire.
Br_2	Bromine	7726-95-6	3	8	4.5	Causes severe burns, very toxic by inhalation.
$LiBr, O_2$, Cu catalyst	Lithium bromide, Oxygen, Copper catalyst	7550-35-8	3	6	4.3	Copper catalyst is very toxic to aquatic environment. Solvent selection should take oxygen atmosphere into account.
HBr, O_2, Cu catalyst	Hydrogen bromide, Oxygen, Copper catalyst	10035-10-6	2	7	3.7	Copper catalyst is very toxic to aquatic environment. Causes burns. Solvent selection should take oxygen atmosphere into account.
Dibromodimethylhydantoin	1,3-Dibromo-5,5-dimethylhydantoin	77-48-5	2	5	3.2	May cause fire.
NaBr, TCCA	Sodium bromide, Trichloroisocyanuric acid	7647-15-6 87-90-1	2	4	3.1	May cause explosion.

Figure S3: GSK C-H Bromination Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)



‡ Use of ≤30% H_2O_2 is required for these procedures to not fall into the "Major Issues" category.

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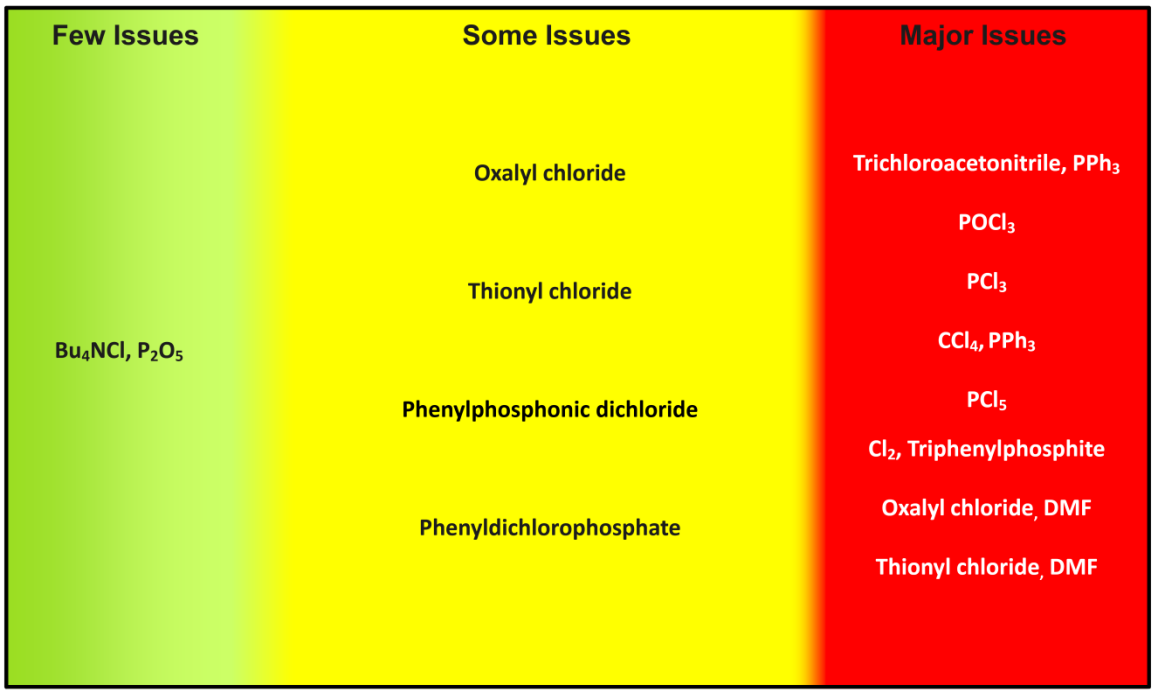
b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
Enzyme	Enzyme	N/A	10	9	9.3	
HCl, air	Hydrochloric acid, Air	7647-01-0	7	7	7.2	Solvent selection should take oxygen atmosphere into account.
NCS	*N*-Chlorosuccinimide	128-09-6	7	7	7.2	
HCl, H_2O_2	Hydrochloric acid, Hydrogen peroxide (≤30%)	7647-01-0 7722-84-1	7	6	6.8	Possible generation of chlorine and/or oxygen gas.
SO_2Cl_2	Sulfuryl chloride	7791-25-5	5	6	5.8	Can generate elemental sulfur and SO_2, will likely need scrubbing.
Cl_2	Chlorine	7782-50-5	5	6	5.8	Handling gases, co-catalyst may be required. Acid/base extractions may be an issue on larger scale.
NaOCl	Sodium hypochlorite	7681-52-9	4	8	5.5	
HCl, Oxone®	Hydrochloric acid, Potassium monoperoxysulfate	7647-01-0 37222-66-5	5	5	5.2	Possible generation of chlorine and/or oxygen. Can be voluminous when large excesses of Oxone® required.
KCl, Oxone®	Potassium chloride, Potassium monoperoxysulfate	7447-40-7 37222-66-5	5	5	5.2	Possible generation of chlorine and/or oxygen. Can be voluminous when large excesses of Oxone® required.
Dichlorodimethylhydantoin	Dichlorodimethylhydantoin	118-52-5	4	6	5.0	Both halogens present may react, although rates of reaction may vary in each case.
$LiCl, O_2$, Cu catalyst	Lithium chloride, Oxygen, Copper catalyst	7447-41-8	3	6	4.0	Solvent selection should take oxygen atmosphere into account. Very toxic to aquatic organisms.
$CuCl_2$, Alumina	Copper chloride, Alumina	7447-39-4	3	6	3.8	Very toxic to aquatic organisms.
Sodium dichloroisocyanurate	Sodium dichloroisocyanurate	2893-78-9	2	7	3.3	Risk of explosion. May cause fire. Both halogens present may react, although rates of reaction may vary in each case.
Hexachloroethane	Hexachloroethane	67-72-1	3	4	3.2	Limited evidence of a carcinogenic effect.
TCCA	Trichloroisocyanuric acid	87-90-1	2	4	3.1	Very toxic to aquatic organisms. All halogens present may react, although rates of reaction may vary in each case.

Figure S4: GSK C-H Chlorination Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)



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b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
Bu_4NCl, P_2O_5	Tetrabutylammonium chloride Phosphorus pentoxide	1112-67-0 1314-56-3	7	6	6.5	Limited examples.
Oxalyl chloride	Oxalyl chloride	79-37-8	5	6	5.8	Lachrymator. Gaseous byproducts.
Thionyl chloride	Thionyl chloride	7719-09-7	5	5	5.3	Lachrymator. Gaseous byproducts.
Phenylphosphonic dichloride	Phenylphosphonic dichloride	824-72-6	5	5	5.0	Possible high temperatures needed.
Phenyldichlorophosphate	Phenyldichlorophosphate	770-12-7	5	5	5.0	Limited examples.
Trichloroacetonitrile, PPh_3	Trichloroacetonitrile Triphenylphosphine	545-06-2 603-35-0	5	3	4.2	Danger of serious damage to health by prolonged exposure through inhalation. PPh_3 is a material of concern, future regulatory impact possible.
$POCl_3$	Phosphorus oxychloride	10025-87-3	3	6	3.8	Danger of serious damage to health by prolonged exposure through inhalation.
PCl_3	Phosphorus trichloride	7719-12-2	3	5	3.7	Danger of serious damage to health by prolonged exposure through inhalation.
CCl_4, PPh_3	Carbon tetrachloride Triphenylphosphine	56-23-5 603-35-0	3	5	3.6	Limited evidence of carcinogenic effect. Dangerous for the ozone layer, PPh_3 is a material of concern, future regulatory impact possible.
PCl_5	Phosphorus pentachloride	10026-13-8	3	5	3.4	Danger of serious damage to health by prolonged exposure through inhalation.
Cl_2, Triphenylphosphite,	Chlorine, Triphenylphosphite	101-02-0 7782-50-5	3	4	3.2	Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment.
Oxalyl chloride, DMF	Oxalyl chloride, Dimethylformamide catalyst	79-37-8 68-12-2	1	5	2.5	DMF typically used in catalytic amounts. DMCC carcinogen may be formed if used in conjunction with DMF.
Thionyl chloride, DMF	Thionyl chloride, Dimethylformamide catalyst	7719-09-7 68-12-2	1	5	2.5	DMF typically used in catalytic amounts. Risk to unborn child.

Figure S5: GSK Deoxychlorination Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)

GSK Reagent Selection Guide – Epoxide Formation from Olefin

Few Issues	Some Issues		Major Issues
Enzyme	H_2O_2,‡ WO_3 or $NaWO_4$	H_2O_2,‡ $RuCl_3$	*m*-CPBA
MMPP	H_2O_2,‡ $FeCl_3 \cdot 6H_2O$	Sodium percarbonate	H_2O_2 (>30%), Base
H_2O_2,‡ Base	O_2, Isobutyraldehyde	Oxone®, Acetone	Peracetic acid
H_2O_2,‡ Diketal catalyst	H_2O_2,‡ $MeReO_3$	Urea-Hydrogen peroxide	Cumene hydroperoxide
H_2O_2,‡ poly-Leucine	H_2O_2,‡ $MnSO_4 \cdot H_2O$	NaOCl, Mn(III) salen complex	Sodium Perborate
	H_2O_2,‡ $Fe(acac)_3$		Trichloroisocyanuric acid
			tert-Butyl hydroperoxide
			Sharpless Epoxidation

‡ Use of ≤30% H_2O_2 is required for these procedures to not fall into the "Major Issues" category.

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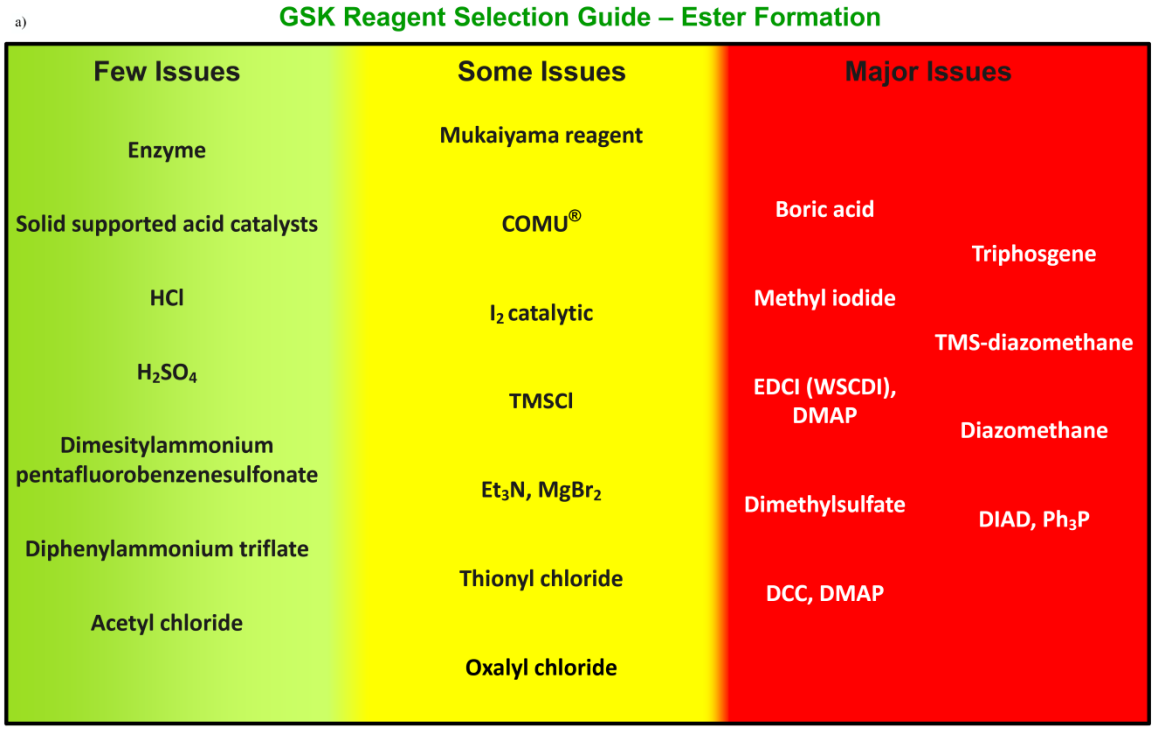
b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
Enzyme	Enzyme	N/A	10	9	9.6	
MMPP	Magnesium monoperoxyphthalate hexahydrate	84665-66-7	10	5	7.4	
H_2O_2, Base	Hydrogen peroxide (≤30%), Base (e.g. NaOH, $NaHCO_3$)	7722-84-1	7	6	6.8	
H_2O_2, Diketal catalyst	Hydrogen peroxide (≤30%), 1,2:4,5-di-*O*-Isopropylidene-β-D-erythro-2,3-hexodiulo-2,6-pyranose	7722-84-1 18422-53-2	7	6	6.8	
H_2O_2, poly-Leucine	Hydrogen peroxide (≤30%), poly-Leucine	7722-84-1/25322-63-8	7	6	6.8	
H_2O_2, WO_3 or $NaWO_4$	Hydrogen peroxide (≤30%), Tungstic acid or Sodium pertungstate	7722-84-1 7783-03-1 or 10213-10-2	7	6	6.8	Potential explosion hazard from mixture of hydrogen peroxide with transition metal salt.
H_2O_2, $FeCl_3 \cdot 6H_2O$	Hydrogen peroxide (≤30%), Iron(III) chloride hexahydrate	7722-84-1 10025-77-1	7	6	6.5	Potential explosion hazard from mixture of hydrogen peroxide with transition metal salt.
O_2, Isobutyraldehyde	Oxygen, Isobutyraldehyde	78-84-2	7	6	6.5	Enriched oxygen atmosphere could be safety hazard, especially at elevated temperatures.
H_2O_2, $MeReO_3$	Hydrogen peroxide (≤30%), Methyltrioxorhenium	7722-84-1 70197-13-6	7	6	6.5	Potential explosion hazard from mixture of hydrogen peroxide with transition metal salt.
H_2O_2, $MnSO_4 \cdot H_2O$	Hydrogen peroxide (≤30%), Manganese(II) sulfate monohydrate	7722-84-1 10034-96-5	5	7	6.0	Potential explosion hazard from mixture of hydrogen peroxide with transition metal salt.
H_2O_2, $Fe(acac)_3$	Hydrogen peroxide (≤30%), Ferric acetylacetonate	7722-84-1 10025-77-1	7	5	5.8	Potential explosion hazard from mixture of hydrogen peroxide with transition metal salt.
H_2O_2, $RuCl_3$	Hydrogen peroxide (≤30%), Ruthenium(III) chloride (unsolvated or hydrate)	7722-84-1, 10049-08-8 or 14898-67-0 or 815-94-6	7	5	5.6	Potential explosion hazard from mixture of hydrogen peroxide with transition metal salt.
Sodium percarbonate	Sodium percarbonate	15630-89-4	5	5	5.4	
Oxone®, Acetone	Potassium monoperoxysulfate, Acetone	37222-66-5/67-64-1	5	5	5.1	Oxone is highly exothermic & less stable above pH 7. May be unstable in the presence of H_2O above 70 °C.
Urea-Hydrogen peroxide	Urea-Hydrogen peroxide	124-43-6	5	5	5.0	
NaOCl, Mn(III) salen complex	Sodium hypochlorite, *N,N'*-bis(3,5-Di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminomanganese(III) chloride	7681-52-9 135620-04-1	4	6	4.8	
m-CPBA	*meta*-Chloroperoxybenzoic acid	937-14-4	3	7	4.3	Heating may cause explosion.
H_2O_2 (>30%), Base	Hydrogen peroxide (>30%), Base	7722-84-1	5	3	4.1	Explosive risk.
Peracetic acid	Peracetic acid	79-21-0	2	7	3.7	Causes severe burns. May cause fire. Reacts violently with water.
Cumene hydroperoxide	α,α-Dimethylbenzyl hydroperoxide	80-15-9	2	6	3.4	Causes burns. May cause fire.
$NaBO_3$	Sodium perborate	10486-00-7 or 7632-04-4	1	7	3.1	Contact with combustible material may cause fire. Risk of impaired fertility. Possible harm to the unborn child.
TCCA	Trichloroisocyanuric acid	87-90-1	2	4	3.0	Very toxic to aquatic organisms.
tert-Butyl hydroperoxide	*tert*-Butyl hydroperoxide	75-91-2	1	7	2.7	Sensitive to shocks, sparks. May react explosively with reducing agents.
Sharpless epoxidation	*tert*-Butyl hydroperoxide, Diisopropyl L-tartrate, Titanium(IV) isopropoxide,	75-91-2/2217-15-4 546-68-9	1	6	2.5	*t*-BuOOH is sensitive to shocks, sparks. May react explosively with reducing agents.

Figure S6: GSK Epoxide Formation From Olefin Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)



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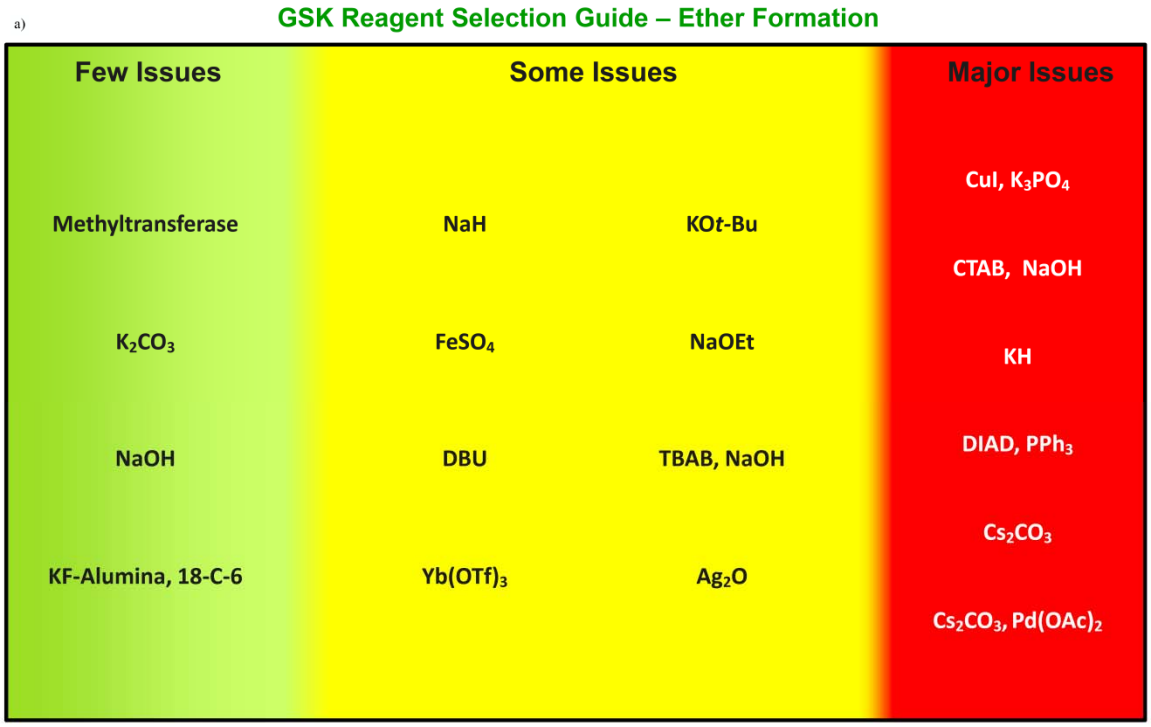
b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
Enzyme	Enzyme	N/A	10	9	9.6	
Solid supported acid catalysts	Smopex-101 catalyst, Amberlyst 15, Dowex	N/A	10	6	9.6	
HCl	Hydrogen chloride	7647-01-0	7	9	8.3	Corrosive gas.
H_2SO_4	Sulfuric acid	7664-93-9	7	9	8.3	Highly corrosive.
Dimesitylammonium pentafluorobenzenesulfonate	Dimesitylammonium pentafluorobenzenesulfonate	850629-65-1	10	6	7.7	
Diphenylammonium triflate	Diphenylammonium trifluoromethanesulfonate	164411-06-7	10	6	7.7	
Acetyl chloride	Acetyl chloride	75-36-5	5	9	7.1	Exothermic reaction.
Mukaiyama reagent	2-Chloro-1-methylpyridinium iodide	14338-32-0	10	4	6.5	Recommended storage at +4 °C.
COMU®	(1-Cyano-2-ethoxy-2-oxoethylidenaminooxy)dimethylaminomorpholino carbenium hexafluorophosphate	1075198-30-9	10	4	6.5	Water soluble byproduct.
I_2 catalytic	Iodine	7553-56-2	7	6	6.4	Very toxic to aquatic organisms.
TMSCl	Trimethylsilyl chloride	75-77-4	5	7	6.3	Corrosive. Flammable.
Et_3N, $MgBr_2$	Triethylamine, Magnesium bromide	121-44-8 13446-53-2	5	6	5.8	Reaction between alcohols, anhydrides.
Thionyl chloride	Thionyl chloride	7719-09-7	5	6	5.5	Lachrymator. Gaseous byproducts.
Oxalyl chloride	Oxalyl chloride	79-37-8	5	5	5.0	Lachrymator. Gaseous byproducts. Scored for usage on own, usage with DMF not recommended as DMCC carcinogen may be produced.
Boric acid	Boric acid	10043-35-3	2	9	4.1	May damage fertility. May damage the unborn child.
Methyl iodide	Methyl iodide	74-88-4	3	6	4.0	Limited evidence of carcinogenic effect.
EDCI (WSCDI), DMAP	[1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride], Dimethylaminopyridine	25952-53-8 1122-58-3	3	5	4.0	Water soluble byproduct . EDCI known to be Ames positive.
Dimethylsulfate	Dimethylsulfate	77-78-1	2	7	3.6	Material of concern. May cause cancer.
DCC, DMAP	*N,N'*-Dicyclohexylcarbodiimide, Dimethylaminopyridine	538-75-0 1122-58-3	3	3	3.3	DCC is a material of concern. Risk of serious damage to the eyes.
Triphosgene	Bis(trichloromethyl) carbonate	32315-10-9	3	3	2.8	Substitution recommended. Contact with water forms phosgene.
TMS-diazomethane	Trimethylsilyldiazomethane	18107-18-1	1	5	2.6	Has been implicated in fatalities.
Diazomethane	Diazomethane	334-88-3	1	5	2.6	An extremely sensitive explosive gas.
DIAD, Ph_3P	Diisopropylazodicarboxylate, Triphenylphosphine	2446-83-5 603-35-0	3	2	2.5	Triphenyl phosphine is a material of concern. DIAD has limited evidence of carcinogenic effect.

Figure S7: GSK Ester Formation Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)



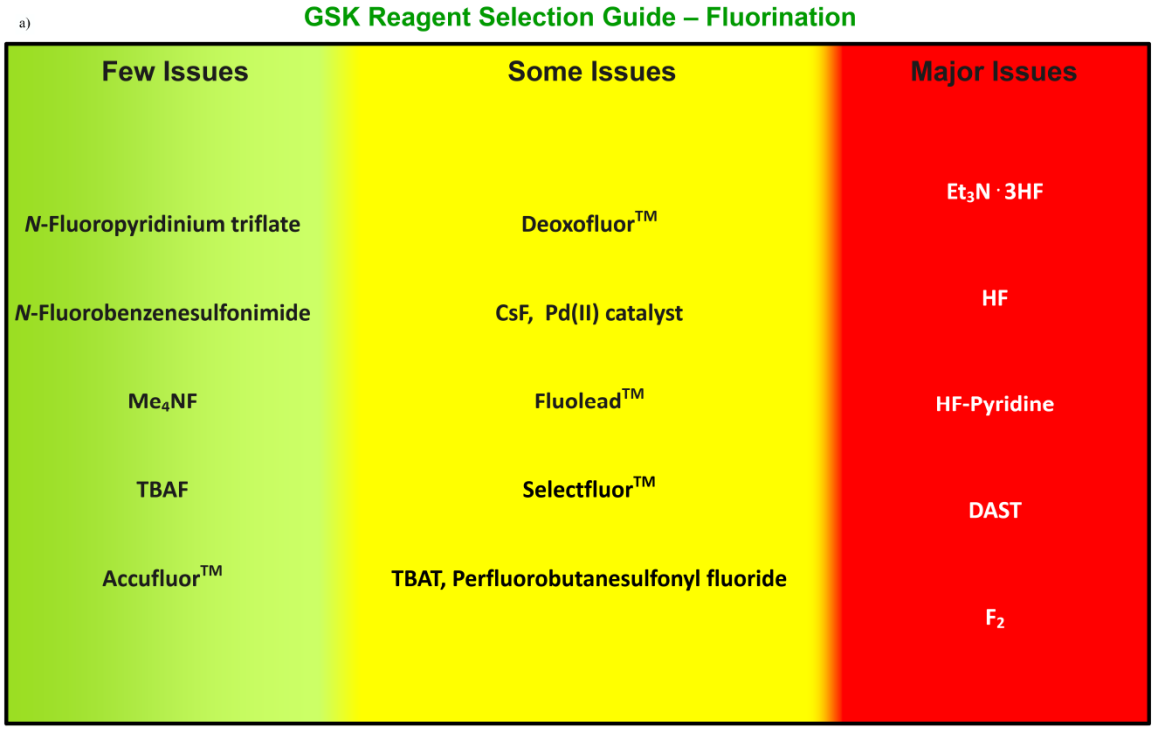
This guide should only be used by the expert trained chemist. Before using any reagent listed on this guide, a complete risk assessment must be carried out.

b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
Methyltransferase	Methyltransferase enzyme	N/A	10	8	9.0	
K_2CO_3	Potassium carbonate	584-08-7	9	7	8.1	
NaOH	Sodium hydroxide	1310-73-2	7	8	7.7	
KF-Alumina, 18-C-6	Potassium fluoride-Alumina, 18-Crown-6	7789-23-2 17445-13-9	7	8	7.4	Phenol with aryl halide. KF on alumina may not be compatible with glass vessels.
NaH	Sodium hydride	7646-60-7	7	7	7.1	Use of 60% mineral oil dispersion in THF or 2-MeTHF is preferred over DMF or DMA.
$FeSO_4$	Iron(II) sulfate	7782-63-0 or 15244-10-7	9	5	7.0	Benzyl halide with primary, secondary, or benzyl alcohol. No base or co-solvent needed.
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene	6674-22-2	7	7	6.8	Phenol with alkyl or benzyl halide.
$Yb(OTf)_3$	Ytterbium triflate	54761-04-5	7	6	6.6	Condensation of benzyl alcohol (having a group which can stabilize the benzyl cation intermediate) with alkyl alcohol.
KO*t*-Bu	Potassium *tert*-butoxide	865-47-4	5	8	6.6	
NaOEt	Sodium ethoxide	141-52-6	5	8	6.4	
TBAB, NaOH	Tetrabutylammonium bromide, Sodium hydroxide	1643-19-2 1310-73-2	7	5	6.0	Phase transfer conditions.
Ag_2O	Silver(I) oxide	20667-12-3	5	7	6.0	Benzyl bromide with alcohol.
CuI, K_3PO_4	Copper(I) iodide, Potassium phosphate tribasic	7681-65-4 7778-53-2	3	6	4.0	Very toxic to aquatic organisms. Risk of serious damage to the eyes.
CTAB, NaOH	Cetyltrimethylammonium bromide, Sodium hydroxide	57-09-0 1310-73-2	3	5	3.4	Very toxic to aquatic organisms. Causes severe burns.
KH	Potassium hydride	7693-26-7	1	8	3.4	Base oil is a potential carcinogen (R45), depending on supplier. If supplied in a non-R45 base oil, KH would score closer to NaH.
DIAD, PPh_3	Diisopropylazodicarboxylate, Triphenylphosphine	2446-83-5 603-35-0	3	4	3.0	Triphenylphosphine is a material of concern, DIAD has limited evidence of a carcinogenic effect.
Cs_2CO_3	Cesium carbonate	534-17-8	2	5	2.9	Possible risk of irreversible effects.
Cs_2CO_3, $Pd(OAc)_2$	Cesium carbonate Palladium(II) acetate	534-17-8 3375-31-3	2	5	2.9	Possible risk of irreversible effects.

Figure S8: GSK Ether Formation Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)



b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
N-Fluoropyridinium triflate	*N*-Fluoropyridinium triflate	107263-95-6	9	6	7.3	C-H fluorination. Causes severe burns.
NFSI	*N*-Fluorobenzenesulfonimide	133745-75-2	10	4	6.5	C-H fluorination.
Me_4NF	Tetramethylammonium fluoride	373-68-2	9	5	6.4	Halogen exchange and fluorodenitration.
TBAF	Tetrabutylammonium fluoride	429-41-4	7	5	6.1	Deoxyfluorination. Causes burns.
Accufluor ™	1-Fluoro-4-hydroxy-1,4-diazabicyclo[2.2.2]octane bis(tetrafluoroborate)	162241-33-0	7	5	6.1	C-H fluorination. Danger of serious damage to health by prolonged exposure.
Deoxofluor ™	Bis(2-methoxyethyl)aminosulfur trifluoride	202289-38-1	5	6	5.8	Deoxyfluorination. Causes severe burns. Reacts violently with water.
CsF, Pd(II) catalyst	Cesium fluoride, Palladium (II) catalyst	13400-13-0	7	4	5.4	Deoxyfluorination.
Fluolead ™	4-*tert*-Butyl-2,6-dimethylphenylsulfur trifluoride	947725-04-4	5	5	5.3	Deoxyfluorination. Causes burns.
Selectfluor ™	1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate)	140681-55-6	7	4	4.8	Incompatible with DMF and DMSO.
TBAT, Perfluorobutanesulfonyl fluoride	Tetrabutylammonium difluorotriphenylsilicate, Nonafluorobutanesulfonyl fluoride	163931-61-1 375-72-4	5	4	4.6	Deoxyfluorination. Causes burns.
$Et_3N \cdot 3HF$	Triethylamine trihydrofluoride	73602-61-6	3	6	4.5	Causes severe burns.
HF	Hydrogen fluoride	7664-39-3	3	5	3.8	Extremely corrosive. Special vessel necessary; avoid contact with glass.
HF-Pyridine	HF-Pyridine complex (70:30)	62778-11-4	3	4	3.7	Causes severe burns. Special vessel necessary; avoid contact with glass.
DAST	Diethylaminosulfur trifluoride	38078-09-0	3	5	3.5	Deoxyfluorination. Causes severe burns. May explode upon heating.
F_2	Fluorine	7782-41-4	2	5	3.0	Extremely corrosive. Special vessel necessary.

Figure S9: GSK Fluorination Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)

GSK Reagent Selection Guide – Iodination

Few Issues	Some Issues		Major Issues
	ICl	NaI, Chloramine-T	NaI, MsCl
	Benzyltrimethylammonium dichloroiodate	NaI, Tosyl chloride	Diiododimethylhydantoin
HI	Pyridinium ICl	NaI, NaOCl	TICA, Acid
	KI, H_2O_2‡	I_2, KIO_3	I_2, $(Bu_4N)_2S_2O_8$
KI, HI, NCS	KI, Ammonium peroxydisulfate	I_2, Urea-Hydrogen peroxide	I_2, PPh_3
NIS, Acid	TMADCl, H_2SO_4	I_2, H_2O_2‡	I_2, $AgNO_3$
	NaI, H_2O_2‡	I_2, Knochel-Hauser base	I_2, *n*-BuLi
	KI, Oxone®	NaI, Tf_2O, Pyridine	

‡ Use of ≤30% H_2O_2 is required for these procedures to not fall into the "Major Issues" category.

This guide should only be used by the expert trained chemist. Before using any reagent listed on this guide, a complete risk assessment must be carried out.

b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
HI	Hydrogen iodide	10034-85-2	7	7	7.1	Deoxyiodination.
KI, HI, NCS	Potassium iodide, Hydroiodic acid *N*-Chlorosuccinimide	7681-11-0 /10034-85-2 128-09-6	7	7	7.0	Forms NIS *in situ.*
NIS, Acid	*N*-Iodosuccinimide, Acid	516-12-1	9	6	7.0	Examples include deactivated arenes.
ICl	Iodine Monochloride	7790-99-0	7	6	6.6	
Benzyltrimethylammonium Dichloroiodiate	Benzyltrimethylammonium dichloroiodate	114971-52-7	10	4	6.3	
Pyridinium ICl	Pyridinium iodochloride (Pyr·ICl)	6643-90-0	5	7	6.3	
KI, H_2O_2	Potassium iodide, Hydrogen peroxide (≤30%)	7681-11-0 7722-84-1	5	6	5.8	KI will react with hydrogen peroxide with the evolution of significant heat, possibly oxygen. These reactions can proceed with violent force, may be highly hazardous.
KI, Ammonium peroxydisulfate	Potassium iodide, Ammonium peroxydisulfate	7681-11-0 7727-54-0	5	6	5.8	KI can potentially react with oxidants to evolve heat, oxygen with hazardous consequences.
TMADCl, H_2SO_4	Tetramethylammonium dichloroiodate, Sulfuric acid	1838-41-1/7664-93-9	7	4	5.7	Examples include deactivated arenes.
NaI, H_2O_2	Sodium iodide, Hydrogen peroxide (≤30%)	7681-82-5 7722-84-1	5	6	5.6	NaI will react with hydrogen peroxide with the evolution of significant heat, possibly oxygen. These reactions can proceed with violent force, may be highly hazardous.
KI, Oxone®	Potassium iodide, Potassium monoperoxysulfate	7681-11-0 37222-66-5	5	6	5.6	KI can potentially react with oxidants to evolve heat & O_2 with hazardous consequences. Oxone is highly exothermic & less stable above pH 7. May be unstable in the presence of H_2O above 70 °C.
NaI, Chloramine-T	Sodium iodide, Chloramine-T	7681-82-5/7080-50-4	5	5	5.3	Examples include deactivated arenes.
NaI, Tosyl chloride	Sodium iodide, *p*-Toluenesulfonyl chloride	7681-82-5/98-59-9	5	5	5.3	Deoxyiodination.
NaI, NaOCl	Sodium iodide, Sodium hypochlorite	7681-52-9	4	7	5.2	NaI can potentially react with oxidants to evolve heat, oxygen with hazardous consequences.
I_2, KIO_3	Iodine, Potassium iodate	7553-56-2 7758-05-6	5	5	5.0	Iodine can potentially react with oxidants to evolve heat, oxygen with hazardous consequences.
I_2, Urea-Hydrogen peroxide	Iodine, Urea-Hydrogen peroxide	124-73-6/7553-56-2	4	6	4.8	Examples include deactivated arenes.
I_2, H_2O_2	Iodine, Hydrogen peroxide (≤30%)	7553-56-2 7722-84-1	4	5	4.4	Iodine will react with hydrogen peroxide with the evolution of significant heat, possibly oxygen. These reactions can proceed with violent force, may be highly hazardous.
I_2, Knochel-Hauser base	Iodine, 2,2,6,6-Tetramethylpiperidinyl magnesium chloride-Lithium chloride complex	7553-56-2 898838-07-8	4	5	4.4	
NaI, Tf_2O, Pyridine	Sodium iodide, Triflic anhydride, Pyridine	7681-82-5/358-23-6 110-86-1	4	4	4.1	
NaI, MsCl	Sodium iodide, Methanesulfonyl chloride	7681-82-5 124-63-0	3	5	3.6	Deoxyiodination. May causes sensitization.
Diiododimethylhydantoin	Diiododimethylhydantoin	2232-12-4	2	5	3.2	Causes severe burns. Very toxic to aquatic organisms.
TICA, Acid	Triiodoisocyanuric acid in Acid	27694-85-5	2	4	3.1	Very toxic to aquatic organisms. Not commercially available.
I_2, $(Bu_4N)_2S_2O_8$	Iodine, Bis(tetrabutylammonium) peroxydisulfate	7553-56-2 88505-29-7	2	4	3.1	May cause fire. Iodine can potentially react with oxidants to evolve heat, oxygen with hazardous consequences.
I_2, PPh_3	Iodine, Triphenylphosphine	7553-56-2/603-35-0	3	4	3.0	Deoxyiodination. Toxic to aquatic organisms. PPh_3 is a material of concern, future regulatory impact possible.
I_2, $AgNO_3$	Iodine, Silver nitrate	7553-56-2/7761-88-8	2	5	3.0	Causes burns. Very toxic to aquatic organisms.
I_2, *n*-BuLi	Iodine, *n*-Butyllithium	7553-56-2 109-72-8	1	4	2.4	Very toxic to aquatic organisms. Possible risk of impaired fertility. Very flammable. Causes burns.

Figure S10: GSK Iodination Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)

GSK Reagent Selection Guide – Ketone Reduction

Few Issues	Some Issues		Major Issues
Ketone reductase	$LiBH_4$	Catecholborane	$LiEt_3BH$
Zeolite-beta MPV catalyst	Borane-THF	Et_3SiH, TFA	Sodium dithionite
Baker's yeast	$NaBH_4$	Red Al	DIBAL
H_2, Pd/C	$LiAlH_4$	Bu_4NBH_4	Nickel boride
H_2, Pt/C	Ammonium formate, Pd/C	$Na(OAc)_3BH$	$Zn(BH_4)_2$
H_2, Ir	$Al(Oi\text{-}Pr)_3$		H_2, Raney Ni
PPh_3- Copper hydride, PMHS			$NaBH_3CN$
H_2, Rh/Al_2O_3			

This guide should only be used by the expert trained chemist. Before using any reagent listed on this guide, a complete risk assessment must be carried out.

b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
KRED	Ketone reductase enzyme	N/A	10	9	9.3	
Zeolite-beta MPV catalyst	Zeolite-beta MPV catalyst	N/A	10	9	9.3	Heterogeneous catalyst for MPV reaction.
Baker's yeast	Baker's yeast enzyme	N/A	10	8	8.7	Whole cell and purified reductase conditions known.
H_2, Pd/C	Hydrogen, Palladium on Carbon	1333-74-0/7440-05-3	7	7	7.2	Flammable. Relative cost cheap. Catalyst can be recycled.
H_2, Pt/C	Hydrogen, Platinum on Carbon	1333-74-0/7440-06-4	7	7	7.2	Flammable. Expensive. Catalyst can be recycled.
H_2, Ir	Hydrogen, Iridium	1333-74-0/7439-88-5	7	7	7.1	Flammable. Expensive. Catalyst can be recycled.
PPh_3-Copper hydride, PMHS	Triphenylphosphine-Copper hydride hexamer, PMHS	33636-93-0 63148-57-2	10	5	7.0	
H_2, Rh/Al_2O_3	Hydrogen, Rh on Aluminum oxide	1333-74-0 7440-16-6	7	6	6.8	Flammable. Extremely expensive. Other groups susceptible to reduction.
$LiBH_4$	Lithium borohydride	16949-15-8	5	8	6.6	Intermediate reactivity between $NaBH_4$ and LAH.
Borane-THF	Borane-Tetrahydrofuran	14044-65-6	5	8	6.6	Flammable.
$NaBH_4$	Sodium borohydride	16940-66-2	5	8	6.6	
$LiAlH_4$	Lithium aluminum hydride	16853-85-3	5	7	6.1	Other groups susceptible to reduction.
Ammonium formate, Pd/C	Ammonium formate, Palladium on Carbon	540-69-2 7440-05-3	7	5	5.8	Hydrogen transfer. Reaction rates and off-gassing rates may be a concern on some systems.
$Al(Oi\text{-}Pr)_3$	Aluminum isopropoxide	555-31-7	5	6	5.8	
Catecholborane	Catecholborane	274-07-7	5	6	5.6	Flammable.
Et_3SiH, TFA	Triethylsilane, Trifluoroacetic acid	617-86-7/76-05-1	5	6	5.5	Flammable. Corrosive.
Red Al	Sodium bis(2-methoxyethoxy) aluminum dihydride	22722-98-1	4	7	5.2	Flammable. Causes burns. Danger of serious health damage by prolonged exposure. Currently only available in toluene – poses possible risk to the unborn child.
Bu_4NBH_4	Tetrabutylammonium borohydride	33745-74-5	5	5	5.0	Reduces ketones in aprotic solvent
$Na(OAc)_3BH$	Sodium triacetoxyborohydride	56553-60-7	5	5	5.0	Limited scope for ketone reduction.
$LiEt_3BH$	Lithium triethylborohydride	22560-16-3	3	9	4.7	Super Hydride. Spontaneously flammable in air.
Sodium dithionite	Sodium dithionite	7775-14-6	3	5	3.8	May cause fire. Contact with acids liberates toxic gas.
DIBAL	Diisobutylaluminum hydride	1191-15-7	2	7	3.7	Spontaneously flammable in air. Reacts violently with water to liberate extremely flammable gases.
Nickel boride	Nickel boride	12007-01-1	2	7	3.6	May cause cancer.
$Zn(BH_4)_2$	Zinc borohydride	17611-70-0	2	5	3.3	Prepared from $NaBH_4$ and $ZnCl_2$. Causes burns. Very toxic to aquatic organisms.
H_2, Raney Ni	Hydrogen, Raney nickel	1333-74-0 7440-02-0	1	6	3.0	Highly flammable. Potential carcinogen and sensitizer.
$NaBH_3CN$	Sodium cyanoborohydride	25895-60-7	1	5	2.3	Explosive when mixed with oxidizing substances. Very toxic. Contact with acid liberates very toxic gas.

Figure S11: GSK Ketone Reduction Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)

GSK Reagent Selection Guide – Nitro Reduction

Few Issues	Some Issues		Major Issues
Nitroreductase			$Na_2S_2O_4$
H_2, Pt/V on C	Fe, NH_4Cl	Et_3SiH, Pd/C	Zn, NH_4Cl
H_2, Pd/C			Zn, AcOH
H_2, $Pd(OH)_2/C$	$NaBH_4$, Pd/C	Fe, AcOH	Hydrazine, Metal
H_2, Pt/C			H_2, Raney Ni
Fe, $CaCl_2$	Ammonium formate, Pd/C	Fe, HCl	Zn, HCl
HI			Cyclohexene, Pd/C
$NaHS{\cdot}H_2O$	$SnCl_2$	$Na_2S{\cdot}9H_2O$	$NaBH_4$, $NiCl_2$
H_2, PtO_2			

This guide should only be used by the expert trained chemist. Before using any reagent listed on this guide, a complete risk assessment must be carried out.

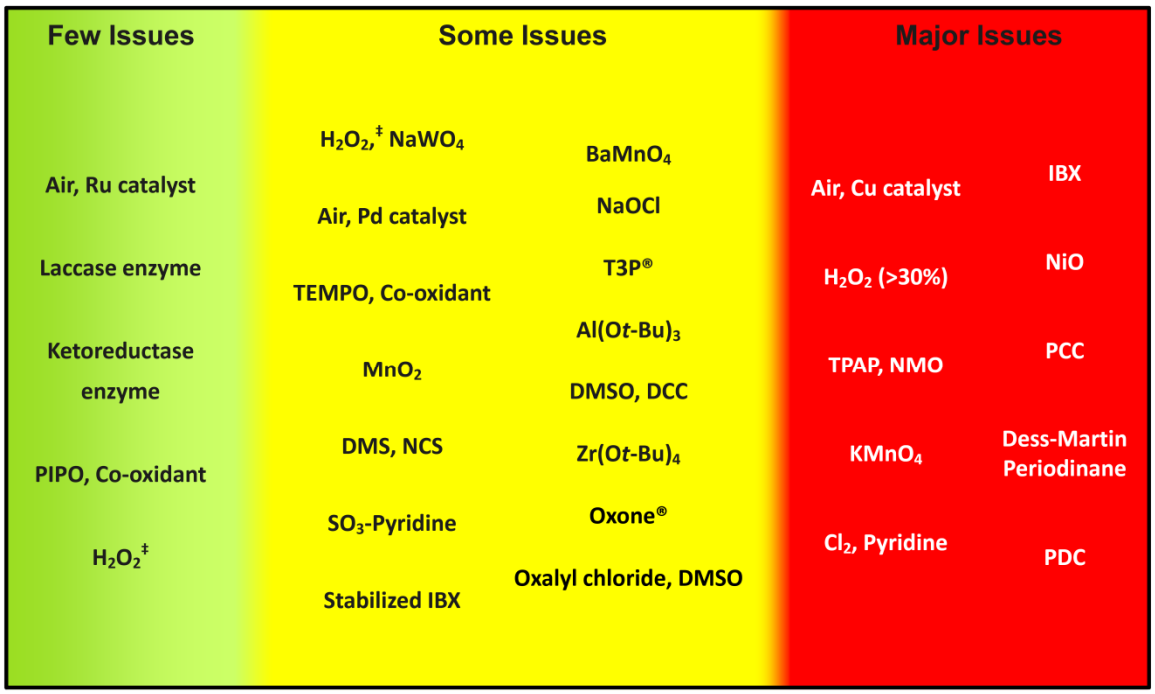
b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
Nitroreductase	Nitroreductase enzyme	N/A	10	8	9.0	
H_2, Pt/V on C	Hydrogen, Platinum/Vanadium on Carbon	1333-74-0 7440-62-2/7440-06-4	7	8	7.5	Flammable. Relative cost expensive. Catalyst can be recycled.
H_2, Pd/C	Hydrogen, Palladium on Carbon	1333-74-0/7440-05-3	7	7	7.2	Flammable. Relative cost cheap. Catalyst can be recycled.
H_2, $Pd(OH)_2/C$	Hydrogen, Palladium hydroxide on Carbon	1333-74-0/12135-22-7	7	7	7.2	Flammable. Slightly more expensive than Pd/C, can be recycled.
H_2, Pt/C	Hydrogen, Platinum on Carbon	1333-74-0/7440-6-4	7	7	7.2	Flammable. Relative cost expensive. Catalyst can be recycled.
Fe, $CaCl_2$	Iron, Calcium chloride	7439-89-6/10043-52-4	7	7	7.1	Dissolving metal reduction with potential exotherm.
HI	Hydroiodic acid	10034-85-2	7	5	6.3	Selective reduction of nitro in presence of other functionality.
$NaHS{\cdot}H_2O$	Sodium hydrogen sulfide hydrate	207683-19-0	5	7	6.3	Contact with acids liberates toxic gas.
H_2, PtO_2	Hydrogen, Platinum oxide	1333-74-0/1314-15-4	5	7	6.1	Flammable. Relative cost expensive. Catalyst can be recycled.
Fe, NH_4Cl	Iron, Ammonium chloride	7439-89-6/12125-02-9	7	5	6.0	Aliphatic or aromatic nitro groups can be reduced.
$NaBH_4$, Pd/C	Sodium Borohydride, Palladium on Carbon	16940-66-2/7440-05-3	5	6	5.9	Contact with water liberates extremely flammable gases.
Ammonium formate, Pd/C	Ammonium formate, Palladium on Carbon	540-69-2/7440-05-3	7	5	5.8	Hydrogen transfer. Reaction rates, off-gassing may be a concern.
$SnCl_2$	Tin(II) chloride dihydrate	10025-69-1	7	5	5.8	Possible sensitizer.
Et_3SiH, Pd/C	Triethylsilane, Palladium on Carbon	617-86-7/7440-05-3	7	5	5.5	Hydrogen transfer.
Fe, AcOH	Iron in Acetic acid	7439-89-6/64-19-7	5	5	5.2	Causes severe burns.
Fe, HCl	Iron in Hydrochloric acid	7439-89-6/7647-01-0	5	5	5.0	Aliphatic or aromatic nitro groups can be reduced.
$Na_2S{\cdot}9H_2O$	Sodium sulfide nonahydrate	1313-84-4	4	5	4.3	Contact with acids liberates toxic gas. Very toxic to aquatic organisms.
$Na_2S_2O_4$	Sodium dithionite	7775-14-6	3	5	3.6	May cause fire. Contact with acids liberates toxic gas.
Zn, NH_4Cl	Zinc, Ammonium chloride	7440-66-6/12125-02-9	3	5	3.4	Very toxic to aquatic organisms.
Zn, AcOH	Zinc in Acetic acid	7440-66-6/64-19-7	2	5	3.4	Very toxic to aquatic organisms. Causes severe burns.
Hydrazine, Metal	Hydrazine, Metal	7803-57-8	2	7	3.3	Hydrazine is a material of concern, possible carcinogen.
H_2, Raney Ni	Hydrogen, Raney nickel	1333-74-0/7440-02-0	1	7	3.2	Highly flammable. Potential carcinogen and sensitizer.
Zn, HCl	Zinc in Hydrochloric acid	7440-66-6/7647-01-0	3	4	3.0	Very toxic to aquatic organisms.
Cyclohexene, Pd/C	Cyclohexene, Palladium on Carbon	110-83-8/7440-05-3	1	6	3.0	Benzene (known carcinogen) forms as byproduct.
$NaBH_4$, $NiCl_2$	Sodium Borohydride, Nickel(II) chloride	16940-66-2/7791-20-0 OR 7718-54-9 OR 69098-15-3	1	5	2.7	$NiCl_2$ has many severe risk phrases, including possible carcinogen.

Figure S12: GSK Nitro Reduction Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)

GSK Reagent Selection Guide – Oxidation to Aldehydes and Ketones



‡ Use of ≤30% H_2O_2 is required for these procedures to not fall into the "Major Issues" category.

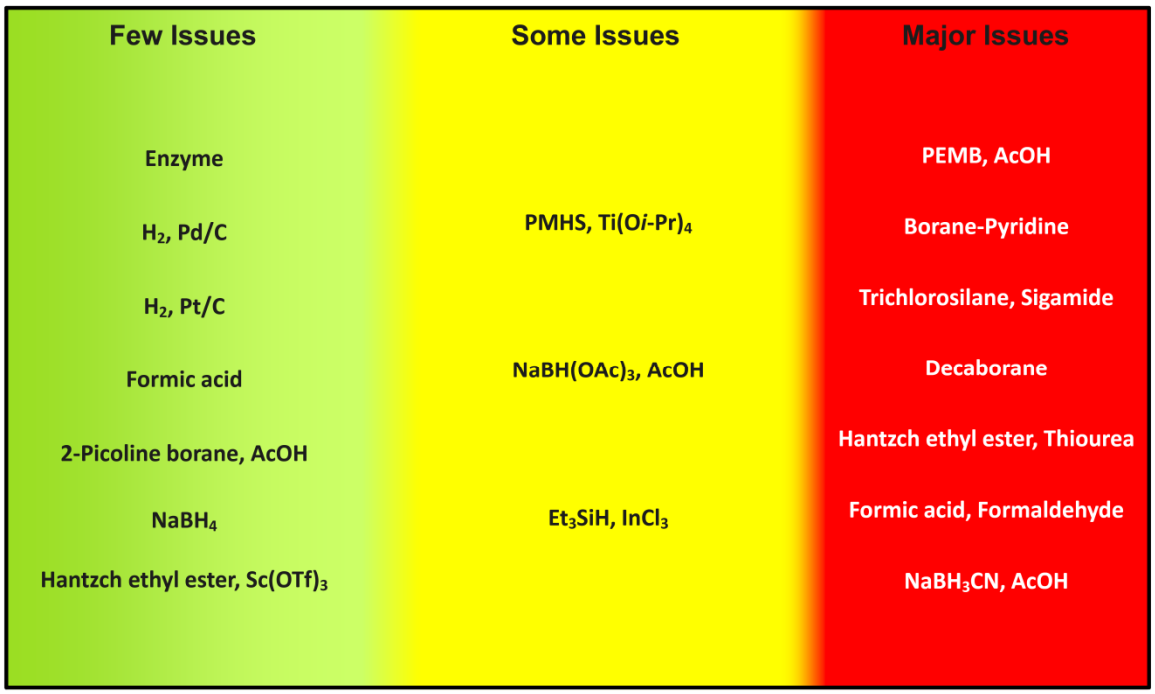
This guide should only be used by the expert trained chemist. Before using any reagent listed on this guide, a complete risk assessment must be carried out.

b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
Air, Ruthenium catalyst	Air with a ruthenium catalyst (RuO_2 in Zeolite)	12036-10-1	10	8	9.0	Heterogeneous catalyst. Solvent selection should take oxygen atmosphere into account.
Laccase enzyme	e.g. Laccase, from *Trametes versicolor*	80498-15-3	10	7	8.3	
Ketoreductase enzyme	Ketoreducase or alcohol dehydrogenase	9028-12-0	10	7	8.3	
PIPO, Co-oxidant	Polymer-immobilized TEMPO on Chimassorb® 944, Co-oxidant	91993-31-6	10	6	7.8	
H_2O_2	Hydrogen peroxide (≤30%)	7722-84-1	7	7	7.2	
H_2O_2, $NaWO_4$	Hydrogen peroxide (≤30%), Sodium tungstate	7722-84-1 10213-10-2	7	6	6.7	Potential explosion hazard from mixture of hydrogen peroxide with transition metal salt.
Air, Pd catalyst	Air, Palladium catalyst	3375-31-3	7	6	6.3	Homogeneous catalyst, requires ligand. Solvent selection should take oxygen atmosphere into account.
TEMPO, Co-oxidant	2,2,6,6-Tetramethylpiperidine 1-oxyl, co-oxidant	7789-45-9	7	5	6.1	Needs catalytic co-oxidant *e.g.*KBr, NaBr, NaOCl or air on small scale. Solvent selection should take potential oxygen atmosphere into account.
MnO_2	Manganese dioxide	1313-13-9	9	4	5.8	Ensure "activated" manganese dioxide is used.
DMS, NCS	Dimethyl sulfide, *N*-Chlorosuccinimide	75-18-3 128-09-6	5	6	5.8	DMS stench. Low temp (-25 °C) necessary.
SO_3-Pyridine	Sulfur trioxide-Pyridine	26412-87-3	7	4	5.6	
Stabilized IBX	Stabilized 2-Iodoxybenzoic acid	61717-82-6	7	4	5.4	
$BaMnO_4$	Barium manganate	7787-35-1	7	4	5.4	
NaOCl	Sodium hypochlorite	7681-52-9	4	7	5.3	
T3P®	Propylphosphonic anhydride	68957-94-8	5	5	5.3	Regulated chemical. Usage of commercial solution in ethyl acetate preferred instead of DMF solution.
$Al(Ot\text{-}Bu)_3$	Aluminium *tert*-butoxide	556-91-2	5	5	5.3	MPV catalyst, ketone coreagent .
DMSO, DCC	Dimethyl sulfoxide, *N,N'*-Dicyclohexylcarbodiimide	67-68-5 538-75-0	7	4	5.1	
$Zr(Ot\text{-}Bu)_4$	Zirconium *tert*-butoxide	2081-12-1	5	5	5.1	MPV catalyst, ketone coreagent .
Oxone®	Potassium monoperoxysulfate	37222-66-5	5	4	4.7	Oxone is highly exothermic & less stable above pH 7. May be unstable in the presence of water above 70 °C.
Oxalyl chloride, DMSO	Oxalyl chloride, Dimethyl sulfoxide	79-37-8 67-68-5	5	4	4.5	Lachrymator, gaseous byproducts, DMS stench. Low temperature (-75 °C) necessary.
Air, Cu catalyst	Air, Copper catalyst	7758-89-6	3	8	4.5	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment. Solvent selection should account for oxygen atmosphere.
H_2O_2 (>30%)	Hydrogen peroxide (>30%)	7722-84-1	5	3	4.1	Explosive risk.
TPAP, NMO	Tetrapropylammonium perruthenate, *N*-Methylmorpholine-*N*-Oxide	114615-82-6 7529-22-8	3	5	3.8	NMO generates toxic by-product.
$KMnO_4$	Potassium permanganate	7722-64-7	2	6	3.6	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Cl_2, Pyridine	Chlorine, Pyridine	7782-50-5	4	3	3.4	Highly flammable. Very toxic to aquatic organisms.
IBX	2-Iodoxybenzoic acid	61717-82-6	3	4	3.3	Severe explosive risk.
NiO	Nickel (II) oxide	1313-99-1	2	5	2.9	Damaging to lungs, may cause cancer.
PCC	Pyridinium chlorochromate	26299-14-9	1	6	2.9	May cause cancer.
Dess-Martin periodinane	(1,1,1-Trisacetoxy)-1,1-dihydro-1,2-benziodoxol-3-(1H)-one	87413-09-0	1	4	2.5	Explosive risk.
PDC	Pyridinium dichromate	20039-37-6	1	4	2.5	May cause cancer. Very toxic to aquatic organisms.

Figure S13: GSK Oxidation to Aldehydes and Ketones Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)



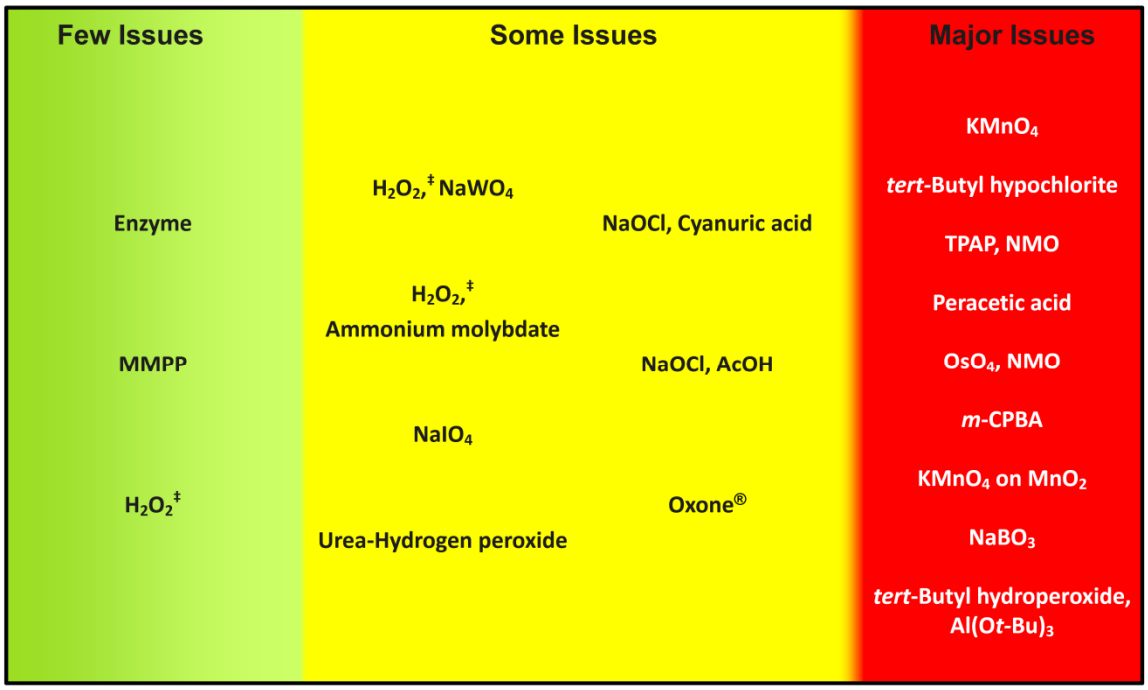
This guide should only be used by the expert trained chemist. Before using any reagent listed on this guide, a complete risk assessment must be carried out.

b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
Enzyme	Enzyme	N/A	10	8	9.0	
H_2, Pd/C	Hydrogen, Palladium on Carbon	1333-74-0 7440-05-3	7	7	7.2	Flammable. Relative cost cheap. Catalyst can be recycled.
H_2, Pt/C	Hydrogen, Platinum on Carbon	1333-74-0 7440-6-4	7	7	7.2	Flammable. Relative cost expensive. Catalyst can be recycled.
Formic acid	Formic acid	64-18-6	7	7	6.9	Causes severe burns.
2-Picoline borane, AcOH	2-Picoline borane complex Acetic acid	3999-38-0 64-19-7	5	8	6.6	Broad scope claimed in literature.
$NaBH_4$	Sodium borohydride	16940-66-2	5	8	6.4	
Hantzch ethyl ester, $Sc(OTf)_3$	Diethyl 1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate, Scandium triflate	1149-23-1 144026-79-9	7	5	6.1	Preferred over Hantzsch ethyl ester/thiourea conditions
PMHS, $Ti(Oi\text{-}Pr)_4$	Poly(methylhydrosiloxane), Titanium(IV) isopropoxide	9004-73-3 546-68-9	8	4	5.8	Scope depends on catalyst used for imine formation.
$NaBH(OAc)_3$, AcOH	Sodium triacetoxyborohydride, Acetic acid	56553-60-7 64-19-7	5	6	5.8	Many examples. Granular $NaBH(OAc)_3$ preferred on scale.
Et_3SiH, $InCl_3$	Triethylsilane, Indium chloride	617-86-7 10025-82-8	5	7	5.7	Broad scope claimed in literature, mild conditions.
PEMB, AcOH	5-Ethyl-2-methylpyridineborane, Acetic acid	1014979-56-6 64-19-7	3	8	4.8	Very toxic by inhalation and in contact with skin. Pic-BH_3 should be considered instead.
Borane-Pyridine	Borane-Pyridine	110-51-0	3	9	4.7	Contact with water liberates extremely flammable gases. Very toxic by inhalation. Pic-BH_3 should be considered instead.
Trichlorosilane, Sigamide	Trichlorosilane, *S*-*N*-(3,5-Di-*tert*-butylphenyl)-3-methyl-2-(*N*-formyl-*N*-methylamino)butanamide	10025-78-2 928789-96-2	3	7	4.1	Reacts violently with water. Spontaneously flammable in air. Contact with water liberates toxic gas.
Decaborane	Decaborane	17702-41-9	2	9	3.9	Heating may cause an explosion. Very toxic by inhalation.
Hantzch ethyl ester, Thiourea	Diethyl 1,4-dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate, Thiourea	1149-23-1 62-56-6	3	5	3.5	Thiourea has limited evidence of a carcinogenic effect, is toxic to aquatic organisms, and risks harm to the unborn child. Use of Hantzch ethyl ester with $Sc(OTf)_3$ is preferred.
Formic acid, Formaldehyde	Formic acid, Formaldehyde	64-18-6 50-00-0	2	5	3.3	May cause cancer. Potential skin sensitizer. Danger of serious irreversible effects.
$NaBH_3CN$, AcOH	Sodium cyanoborohydride, Acetic acid	25895-60-7 64-19-7	1	8	2.7	Explosive when mixed with oxidizing substances. Very toxic. Contact with acid liberates very toxic gas.

Figure S14: GSK Reductive Amination Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.

a)



‡ Use of ≤30% H_2O_2 is required for these procedures to not fall into the "Major Issues" category.

This guide should only be used by the expert trained chemist. Before using any reagent listed on this guide, a complete risk assessment must be carried out.

b)

Material	Full name	CAS number	EHS	Clean chemistry	Greenness	Comments
Enzyme	Enzyme	N/A	10	9	9.6	
MMPP	Magnesium monoperoxyphthalate hexahydrate	84665-66-7	10	5	6.8	
H_2O_2	Hydrogen peroxide (≤30 wt%)	7722-84-1	7	6	6.7	
H_2O_2, $NaWO_4$	Hydrogen peroxide (≤30 wt%), Sodium tungstate	7722-84-1 10213-10-2	7	5	6.1	Potential explosion hazard from mixture of hydrogen peroxide with transition metal salt.
H_2O_2, Ammonium molybdate	Hydrogen peroxide (≤30 wt%), Ammonium molybdate tetrahydrate	7722-84-1 12027-67-7	7	5	6.0	Potential explosion hazard from mixture of hydrogen peroxide with transition metal salt.
$NaIO_4$	Sodium periodate	7790-28-5	7	5	5.5	
Urea-Hydrogen peroxide	Urea-Hydrogen peroxide	124-43-6	5	5	5.3	
NaOCl, Cyanuric acid	Sodium hypochlorite, Cyanuric acid	7681-52-9 108-80-5	4	7	5.2	
NaOCl, AcOH	Sodium hypochlorite, Acetic acid	7681-52-9 64-19-7	4	6	4.9	
Oxone®	Potassium monoperoxysulfate	37222-66-5	5	4	4.8	Oxone is highly exothermic and less stable above pH 7. May be unstable in the presence of water above 70 °C.
$KMnO_4$	Potassium permanganate	7722-64-7	2	7	3.9	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
tert-Butyl hypochlorite	*tert*-Butyl hypochlorite	507-40-4	3	6	3.9	Heating may cause explosion. Causes burns. Spontaneously flammable.
TPAP, NMO	Tetrapropylammonium perruthenate, *N*-Methylmorpholine *N*-oxide	114615-82-6 7529-22-8	3	5	3.9	Heating may cause explosion.
Peracetic acid	Peracetic acid	79-21-0	2	7	3.8	Causes severe burns. May cause fire.
OsO_4, NMO	Osmium tetroxide *N*-Methylmorpholine *N*-oxide	20816-12-0 7529-22-8	3	4	3.7	OsO_4 vapors are highly toxic (high vapor pressure).
m-CPBA	*meta*-Chloroperoxybenzoic acid	937-14-4	3	5	3.6	Heating may cause explosion.
$KMnO_4$ on MnO_2	Manganese dioxide supported Potassium permanganate	1313-13-9 7722-64-7	2	5	3.3	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
$NaBO_3$	Sodium perborate	10486-00-7 or 7632-04-4	1	7	3.2	May cause fire. May cause infertility.
tert-Butyl hydroperoxide, $Al(Ot\text{-}Bu)_3$	*tert*-Butyl hydroperoxide Aluminum *tert*-butoxide	75-91-2 556-91-2	1	6	2.5	Sensitive to shocks, sparks. May react violently with reducing agents.

Figure S15: GSK Oxidation to Sulfones Green Reagent Guide. a) Front of guide with overview, b) Reverse of guide with more detail.