Supplementary Information

A new generation of aprotic yet Brønsted acidic imidazolium salts: Effect of ester/amide groups in the C-2, C-4 and C-5 on antimicrobial toxicity and biodegradation

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Green metrics Lab Book for SYNFLOW Project

User guide

Dr Patrice Ribiere, BRITEST Ltd, 25/07/2011

Introduction

The Green Metrics Lab Book is a Microsoft Excel® spreadsheet aimed to automate reagent and solvent charges calculations and a subsequent set of green metrics.

This documents reflects work carried out by Britest Ltd in the EU FP7 SYNFLOW Project to automate the calculation of the published metrics developed by John Andraos. References to the original publications by John Andraos:

J. Andraos, *Org. Proc. Res. Dev.*, 2005, **9**, 149-163.
J. Andraos, *Org. Proc. Res. Dev.*, 2005, **9**, 404-431.
J. Andraos, *Org. Proc. Res. Dev.*, 2006, **10**, 212-240.
J. Andraos, in *Green chemistry metrics: measuring and monitoring sustainable processes*, eds. A. Lapkin and D. Constable, Blackwell-Wiley, Oxford, 2008, pp. 69-200.
J. Andraos, *Org. Proc. Res. Dev.*, 2009, **13**, 161-185.
J. Andraos, *Pure Appl. Chem.*, 2011, **83**, 1361-1378.

Content

Quick overview

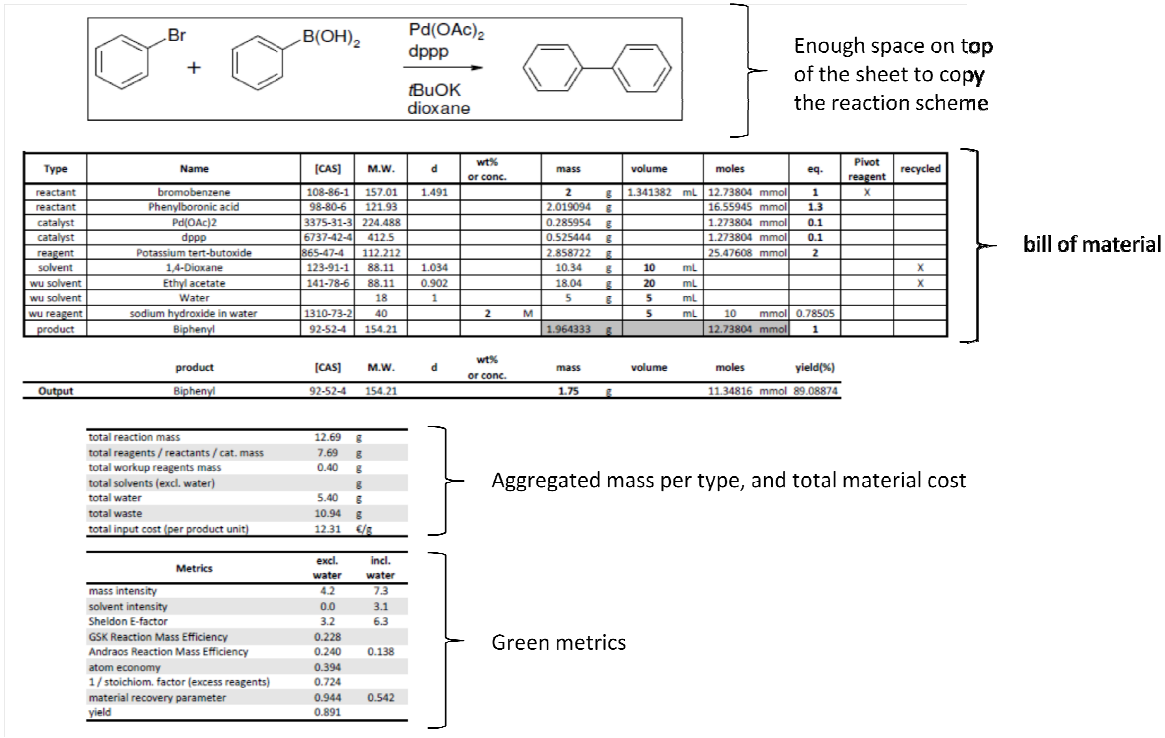
Structure of the Excel file:

The Excel file contains 2 different types of spreadsheets:

- A series of experiment sheets, each one storing data from a single reaction. An experiment is composed of 3 tables: a bill of the materials used in the reaction, a table aggregating the mass of these materials according to their type (reagents, solvents, water, waste...), and a green metrics summary for the reaction. (see picture next page).
- a single sheet called "Chemicals" which can be considered as basic chemical database. (see header next page).

The idea for using an excel file is to be able

- to share easily between partners both the data for an experiment (by copying the sheet of interest) and the chemical database (by merging two "Chemicals" tables together).
- to use macro programming to make automatic and speed-up calculations.



Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	bromobenzene	108-86-1	157.01	1.491		2 g	1.341382 mL	12.73804 mmol	1	X	
reactant	Phenylboronic acid	98-80-6	121.93			2.019094 g		16.55945 mmol	1.3		
catalyst	Pd(OAc)2	3375-31-3	224.488			0.285954 g		1.273804 mmol	0.1		
catalyst	dppp	6737-42-4	412.5			0.525444 g		1.273804 mmol	0.1		
reagent	Potassium tert-butoxide	865-47-4	112.212			2.858722 g		25.47608 mmol	2		
solvent	1,4-Dioxane	123-91-1	88.11	1.034		10.34 g	10 mL				X
wu solvent	Ethyl acetate	141-78-6	88.11	0.902		18.04 g	20 mL				X
wu solvent	Water		18	1		5 g	5 mL				
wu reagent	sodium hydroxide in water	1310-73-2	40		2 M		5 mL	10 mmol	0.78505		
product	Biphenyl	92-52-4	154.21			1.964333 g		12.73804 mmol	1		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	Biphenyl	92-52-4	154.21			1.75 g		11.34816 mmol	89.08874

total reaction mass	12.69	g
total reagents / reactants / cat. mass	7.69	g
total workup reagents mass	0.40	g
total solvents (excl. water)		g
total water	5.40	g
total waste	10.94	g
total input cost (per product unit)	12.31	€/g

Metrics	excl. water	incl. water
mass intensity	4.2	7.3
solvent intensity	0.0	3.1
Sheldon E-factor	3.2	6.3
GSK Reaction Mass Efficiency	0.228	
Andraos Reaction Mass Efficiency	0.240	0.138
atom economy	0.394	
1 / stoichiom. factor (excess reagents)	0.724	
material recovery parameter	0.944	0.542
yield	0.891	

Final aspect of an experiment sheet

Name	[CAS]	M.W. (g/mol)	d	wt% or conc.	unit	solvent name	Price (€/unit)	unit	COSHH	Bp	Mp	Fp	...

Header of the "Chemicals" sheet

Create new Experiment:

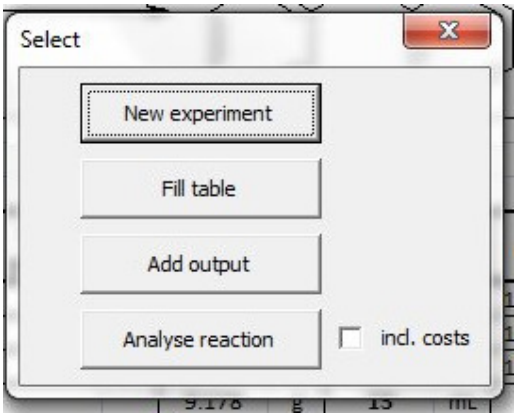
1) Open the "Lab book and Green Metrics" excel file and choose "**enable macro**" (clicking "**option**" in the bar above the worksheet).

2) Each experiment sheet name should have the following format:

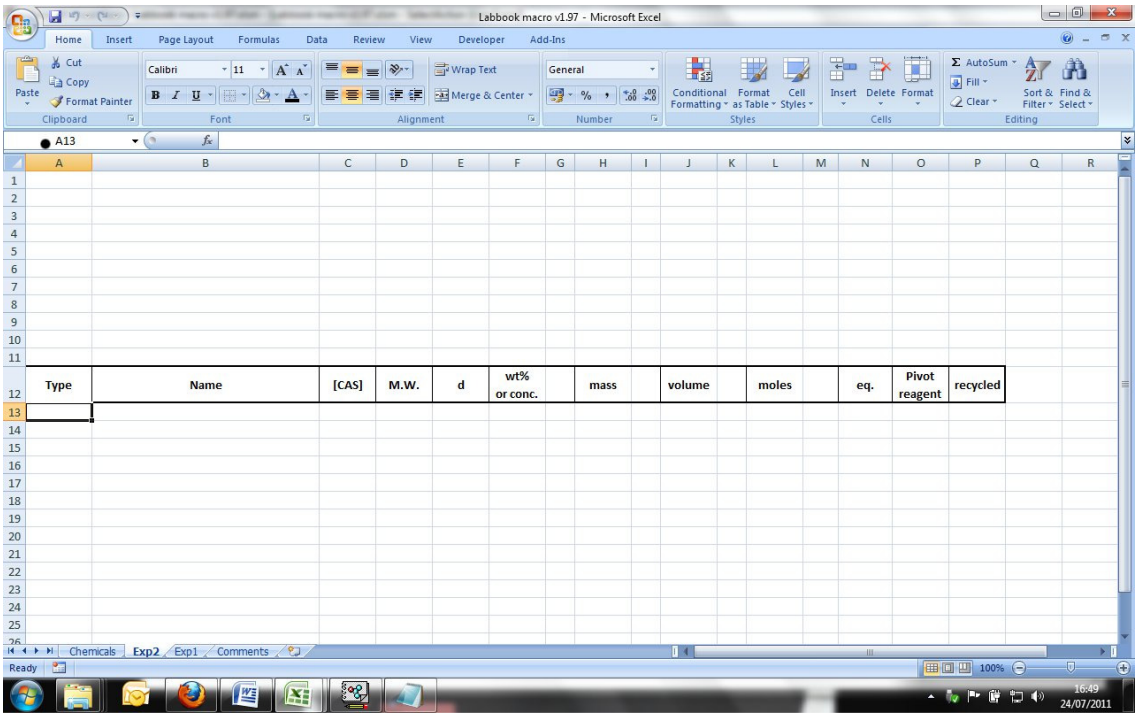
"experimentator's name" followed by the experiment number

e.g. "Exp 01" or "JD 112" or "John Doe25"

Press **Crtl + "M"** to launch the menu window (the macro will work on the current activated spreadsheet)

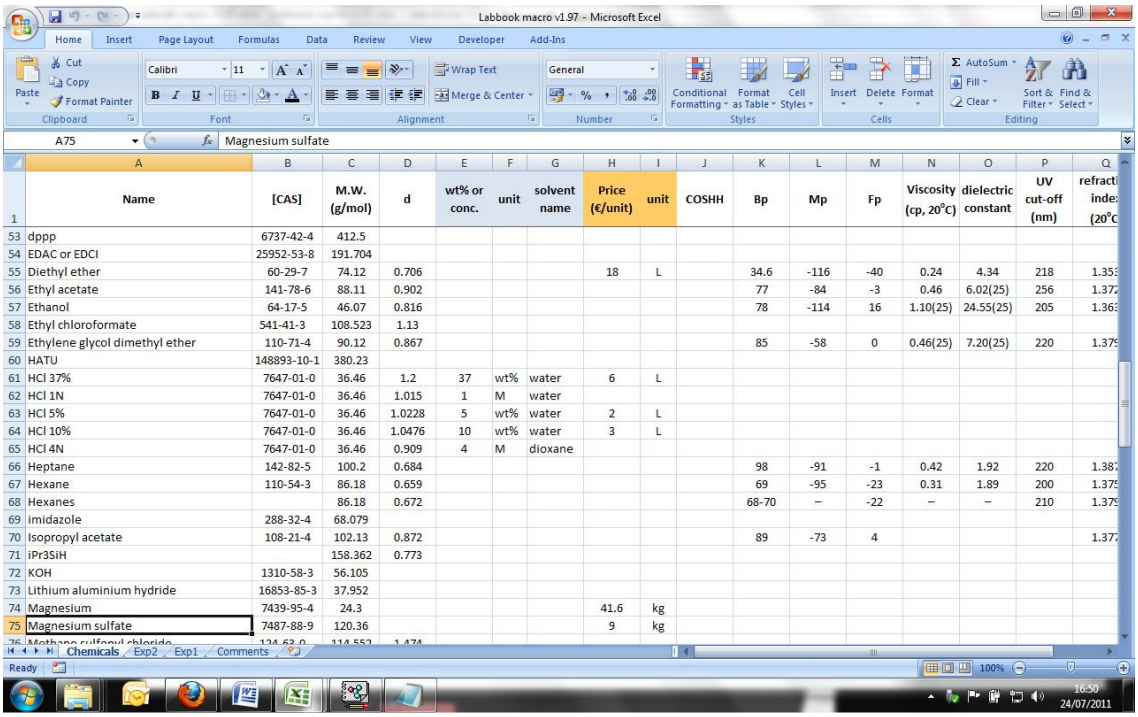


3) Select "New Experiment": a new spreadsheet will be created next to "chemicals" with a name having an incremented experiment number (e.g. "Exp 02" or "JD 113" or "John Doe26"), and the header of the bill of material.



The top of the sheet (row 1 to 11) are left empty to allow space for copying a reaction scheme. **Please remember: the header of the bill of material should always be at the 12th row** (do not insert row above it).

4) In "**Chemicals**", select the reagents, solvents and target product for your reaction. Hold the **Ctrl** key for multiple selection.



	Name	[CAS]	M.W. (g/mol)	d	wt% or conc.	unit	solvent name	Price (€/unit)	unit	COSHH	Bp	Mp	Fp	Viscosity (cp, 20°C)	dielectric constant	UV cut-off (nm)	refract inde (20°C
1																	
53	dppp	6737-42-4	412.5														
54	EDAC or EDCI	25952-53-8	191.704														
55	Diethyl ether	60-29-7	74.12	0.706				18	L		34.6	-116	-40	0.24	4.34	218	1.353
56	Ethyl acetate	141-78-6	88.11	0.902							77	-84	-3	0.46	6.02(25)	256	1.372
57	Ethanol	64-17-5	46.07	0.816							78	-114	16	1.10(25)	24.55(25)	205	1.363
58	Ethyl chloroformate	541-41-3	108.523	1.13													
59	Ethylene glycol dimethyl ether	110-71-4	90.12	0.867							85	-58	0	0.46(25)	7.20(25)	220	1.375
60	HATU	148893-10-1	380.23														
61	HCl 37%	7647-01-0	36.46	1.2	37	wt%	water	6	L								
62	HCl 1N	7647-01-0	36.46	1.015	1	M	water										
63	HCl 5%	7647-01-0	36.46	1.0228	5	wt%	water	2	L								
64	HCl 10%	7647-01-0	36.46	1.0476	10	wt%	water	3	L								
65	HCl 4N	7647-01-0	36.46	0.909	4	M	dioxane										
66	Heptane	142-82-5	100.2	0.684							98	-91	-1	0.42	1.92	220	1.387
67	Hexane	110-54-3	86.18	0.659							69	-95	-23	0.31	1.89	200	1.375
68	Hexanes		86.18	0.672							68-70	–	-22	–	–	210	1.375
69	imidazole	288-32-4	68.079														
70	Isopropyl acetate	108-21-4	102.13	0.872							89	-73	4				1.377
71	iPr3SiH		158.362	0.773													
72	KOH	1310-58-3	56.105														
73	Lithium aluminium hydride	16853-85-3	37.952														
74	Magnesium	7439-95-4	24.3					41.6	kg								
75	Magnesium sulfate	7487-88-9	120.36					9	kg								

5) Press **Crtl + "M"** : the selected chemicals will automatically be transferred to the experiment sheet with the highest experiment number.

	Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
11												
12												
13		1,4-Dioxane	123-91-1	88.11	1.034							
14		bromobenzene	108-86-1	157.01	1.491							
15		Biphenyl	92-52-4	154.21								
16		dppp	6737-42-4	412.5								
17		Pd(OAc)2	3375-31-3	224.488								
18		Phenylboronic acid	98-80-6	121.93								
19		Potassium tert-butoxide	865-47-4	112.212								
20		Ethyl acetate	141-78-6	88.11	0.902							
21		Water		18	1							
22												

You can modify the order of the materials in the table: to move one material a row up, select this material and press **Crtl + "L"**.
You can also add more chemicals to the table simply by going again through **4)-5)**.
A solution transferred to the table will have the following name:

"chemicals" in "solvent" (e.g. "HCl in water" or "HCl in MeOH").

Fill the table:

1) Back to the new experiment sheet, fill the following minimum information in the table:

   - Type of chemicals (from the drop down list): reagent (a molecule for which no part remains in the product of the reaction), reactant (a molecule for which a part remains in the product), catalyst, solvent, wu reagent (work-up reagent), wu solvent (work-up solvent) or product (the product of interest in the reaction).
   - For each material: either a charge (mass, volume, number of mole) **or** a number of equivalent (for reagents/reactants/catalysts/wu reagents). Select the corresponding units from the drop-down lists. This can be either a numerical value, or a formula related to another chemical (e.g. "3 mmol", or for the volume cell: "=5*H14" to charge 5 times more volume of this chemical than the mass of the chemical in row 14).
   - For the **pivot reagent** or reactant (i.e. the material upon which all the other calculations are based), enter a charge **and** the number of equivalent. Enter "**X**" in the corresponding row of the "Pivot reagent" column.
   - For the **product**, enter the number of expected equivalent (100% yield) compared to the pivot reagent. (most of the time, it will be equal to 1, but it would be equal to 0.5 for a dimerisation, or to 2 for the ozonolysis of a symmetrical alkene for example).

Type	Name	[CAS]	M.W.	d	wt% or conc.		mass		volume		moles		eq.	Pivot reagent	recycled
reactant	bromobenzene	108-86-1	157.01	1.491			2	g					1	X	
reactant	Phenylboronic acid	98-80-6	121.93										1.3		
catalyst	Pd(OAc)2	3375-31-3	224.488										0.1		
catalyst	dppp	6737-42-4	412.5										0.1		
reagent	Potassium tert-butoxide	865-47-4	112.212										2		
solvent	1,4-Dioxane	123-91-1	88.11	1.034					10	mL					
wu solvent	Ethyl acetate	141-78-6	88.11	0.902					20	mL					
wu solvent	Water		18	1					5	mL					
wu reagent	sodium hydroxide in water	1310-73-2	40		2	M			5	mL					
product	Biphenyl	92-52-4	154.21										1		

Please remember: Values of mass and volume represent what is actually charged, i.e. if the concentration is given, the mass and volume values will be for the solution to be charged, not for the pure material. Same wise, in this case the density value is expected to be for the mixture not the pure product.

2) Press **Crtl + "M"** to launch the menu window, and select "**Fill table**". The rest of the values in the table will be automatically calculated. Their units will be initially selected by default, but the user can choose in advance a specific unit from the drop-down menu prior to the calculations.

Type	Name	[CAS]	M.W.	d	wt% or conc.		mass		volume		moles		eq.	Pivot reagent	recycled
reactant	bromobenzene	108-86-1	157.01	1.491			**2**	g	1.341382	mL	12.73804	mmol	**1**	X	
reactant	Phenylboronic acid	98-80-6	121.93				2.019094	g			16.55945	mmol	**1.3**		
catalyst	Pd(OAc)2	3375-31-3	224.488				0.285954	g			1.273804	mmol	**0.1**		
catalyst	dppp	6737-42-4	412.5				0.525444	g			1.273804	mmol	**0.1**		
reagent	Potassium tert-butoxide	865-47-4	112.212				2.858722	g			25.47608	mmol	**2**		
solvent	1,4-Dioxane	123-91-1	88.11	1.034			10.34	g	**10**	mL					
wu solvent	Ethyl acetate	141-78-6	88.11	0.902			18.04	g	**20**	mL					
wu solvent	Water		18	1			5	g	**5**	mL					
wu reagent	sodium hydroxide in water	1310-73-2	40		**2**	M			**5**	mL	10	mmol	0.78505		
product	Biphenyl	92-52-4	154.21				1.964333	g			12.73804	mmol	**1**		

The charge or equivalent values entered by the user will now be in bold. As the rest of the values are calculated through excel formula system, the user can change his own (bold) data, and the rest of the calculation will change accordingly.

Please remember: Values (in grey) for the product are maximum output (100% yield).

Add Output:

1) Press **Crtl + "M"** to launch the menu window, and select "**Add output**". A new row is created.

Type	Name	[CAS]	M.W.	d	wt% or conc.		mass		volume		moles		eq.	Pivot reagent	recycled
reactant	bromobenzene	108-86-1	157.01	1.491			2	g	1.341382	mL	12.73804	mmol	1	X	
reactant	Phenylboronic acid	98-80-6	121.93				2.019094	g			16.55945	mmol	1.3		
catalyst	Pd(OAc)2	3375-31-3	224.488				0.285954	g			1.273804	mmol	0.1		
catalyst	dppp	6737-42-4	412.5				0.525444	g			1.273804	mmol	0.1		
reagent	Potassium tert-butoxide	865-47-4	112.212				2.858722	g			25.47608	mmol	2		
solvent	1,4-Dioxane	123-91-1	88.11	1.034			10.34	g	10	mL					
wu solvent	Ethyl acetate	141-78-6	88.11	0.902			18.04	g	20	mL					
wu solvent	Water		18	1			5	g	5	mL					
wu reagent	sodium hydroxide in water	1310-73-2	40		2	M			5	mL	10	mmol	0.78505		
product	Biphenyl	92-52-4	154.21				1.964333	g			12.73804	mmol	1		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		yield(%)
Output	Biphenyl	92-52-4	154.21				g				mmol	

2) Enter a discharge value (mass, volume or mole).

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		yield(%)
Output	Biphenyl	92-52-4	154.21			1.75	g				mmol	

It is possible to have the product as a solution (a concentration input is then needed).

Analysis the reaction:

1) If any material is recycled, enter "X" in the corresponding cell of the "recycled" column of the bill of material. This material won't be taken into account for the following calculations (mass, cost, metrics).

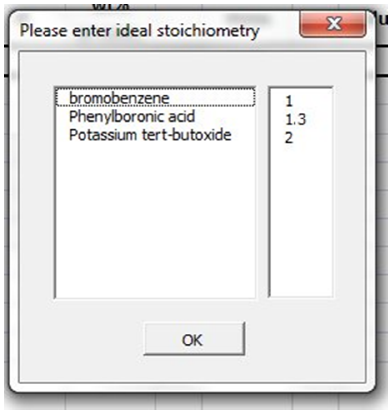
Type	Name	[CAS]	M.W.	d	wt% or conc.		mass		volume		moles		eq.	Pivot reagent	recycled
reactant	bromobenzene	108-86-1	157.01	1.491			2	g	1.341382	mL	12.73804	mmol	1	X	
reactant	Phenylboronic acid	98-80-6	121.93				2.019094	g			16.55945	mmol	1.3		
catalyst	Pd(OAc)2	3375-31-3	224.488				0.285954	g			1.273804	mmol	0.1		
catalyst	dppp	6737-42-4	412.5				0.525444	g			1.273804	mmol	0.1		
reagent	Potassium tert-butoxide	865-47-4	112.212				2.858722	g			25.47608	mmol	2		
solvent	1,4-Dioxane	123-91-1	88.11	1.034			10.34	g	10	mL					X
wu solvent	Ethyl acetate	141-78-6	88.11	0.902			18.04	g	20	mL					X
wu solvent	Water		18	1			5	g	5	mL					
wu reagent	sodium hydroxide in water	1310-73-2	40		2	M			5	mL	10	mmol	0.78505		
product	Biphenyl	92-52-4	154.21				1.964333	g			12.73804	mmol	1		

2) Press **Crtl + "M"** to launch the menu window, and select "**Analyse reaction**" from the menu.

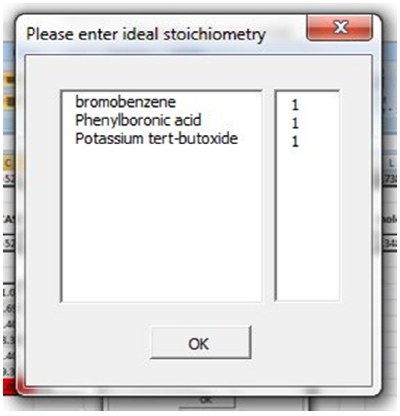
The user can include the calculation of raw material cost in the analysis. If the program cannot find a material, its concentration, or its cost in the "Chemical" sheet,

a window will list the missing chemicals and the reason why it was excluded of the cost calculation. In that case the cost result cell will be coloured in red.

3) Enter the ideal stoichiometry of the reaction in the new window.



Original stoichiometry (reagents used in excess from the bill of material)



ideal stoichiometry

This data from this window will be used in the calculation of two of the green metrics: the atom economy, and the stoichiometric factor.

4) Two new tables will be added. The first one will extract and aggregate the mass of materials according to different categories.

- total reaction mass
- total reagents / reactants / cat. mass
- total workup reagents mass
- total solvents (excl. water)
- total water
- total waste
- total raw material cost (€/mass unit)

5) The second table will provide the following green metrics:

- **Mass intensity** (both excluding and including water):

$$Mass\ intensity = \frac{total\ mass\ of\ raw\ materials\ (incl. workup)}{mass\ of\ product\ recovered}$$

- **Solvent intensity** (both excluding and including water):

$$Solvent\ intensity = \frac{total\ mass\ of\ solvents\ (incl. workup)}{mass\ of\ product\ recovered}$$

- **Sheldon Environmental impact factor, E-Factor** (both excluding and including water):

$$E - Factor = \frac{total\ mass\ of\ wastes}{mass\ of\ product\ recovered}$$

$$E - Factor = \frac{total\ mass\ of\ raw\ materials - mass\ of\ product\ recovered}{mass\ of\ product\ recovered}$$

- **GSK Reaction Mass Efficiency**:

$$GSK\ RME = \frac{mass\ of\ product\ recovered}{total\ mass\ of\ reagents/reactants/catalysts}$$

- **Andraos Reaction Mass Efficiency**:

$$Andraos\ RME = \frac{mass\ of\ product\ recovered}{total\ mass\ of\ raw\ materials} = \frac{1}{mass\ intensity}$$

$$Andraos\ RME = \frac{1}{1 + E - factor}$$

$$Andraos\ RME = \frac{yield\ \times Atom\ Economy\ \times material\ recovery\ parameter}{Stoichiometric\ Factor}$$

- **Atom Economy**:

$$AE = \frac{eq_{product} \times\ MW_{product}}{\sum(eq._i^0 \times MW_i)}$$

where $eq._i^0$ is the ideal stoichiometry of reagent i for the reaction, and MW_i is the molecular weight of reagent i.

- **Stoichiometric Factor**:

$$SF = \frac{\sum mass_{total\ reagents}}{\sum mass_{stoichiometric\ reagents}} = 1 + \frac{\sum mass_{excess\ reagents}}{\sum mass_{stoiciometric\ reagents}}$$

and calculated as:

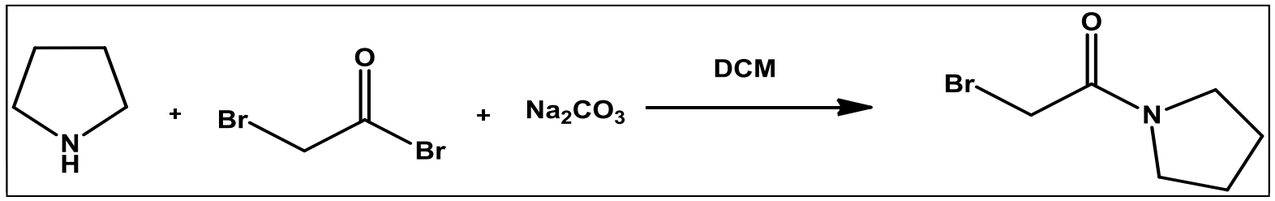
$$SF = \frac{\sum(eq._i \times MW_i)}{\sum(eq._i^0 \times MW_i)}$$

where $eq._i$ is the stoichiometry of reagent i in the current reaction.

- **Material recovery parameter**:

$$material\ recovery\ parameter\ = \frac{Andraos\ RME\ \times Stoichiometric\ Factor}{yield\ \times Atom\ Economy}$$

- **Yield**.



Type	Name	[CAS]	M.W.	d	wt% or conc.		mass		volume		moles		eq.	Pivot reagent	recycled
reactant	bromoacetyl bromide	598-21-0	201.84	2.317			**28.46**	g	12.28312	mL	141.0028	mmol	1.0028117		
reactant	pyrrolidine	123-75-1	71.12	0.852			**10**	g	11.73709	mL	140.6074	mmol	**1**	X	
reagent	sodium carbonate	497-19-8	105.99				**14.94**	g			140.9567	mmol	1.002484		
solvent	Dichloromethane	75-09-2	84.93	1.325			159	g	**120**	mL					
wu solvent	Water		18	1			100	g	**100**	mL					
product	N-(Bromoacetyl)pyrrolidine	90892-09-4	192.05				27.00366	g			140.6074	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	N-(Bromoacetyl)pyrrolidine	90892-09-4	192.05			**10.51**	g		54.72533	mmol	38.920656

total reaction mass	312.40	g
total reagents / reactants / cat. mass	53.40	g
total workup reagents mass		g
total solvents (excl. water)	159.00	g
total water	100.00	g
total waste	301.89	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	20.2	29.7
solvent intensity	15.1	24.6
Sheldon E-factor	19.2	28.7
GSK Reaction Mass Efficiency	0.197	
Andraos Reaction Mass Efficiency	0.049	0.034
atom economy	0.506	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	0.251	0.171
yield	0.389	

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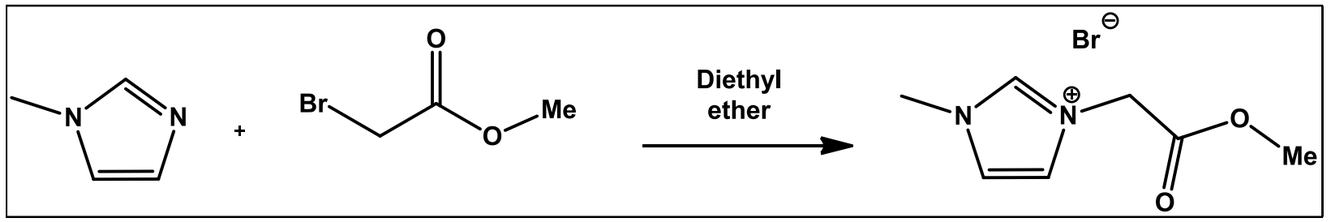

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	N-Methylimidazole	616-47-7	82.105	1.04		5.152697 g	4.954516 mL	62.7574 mmol	**1.2**		
reactant	Methyl bromoacetate	96-32-2	152.97	1.616		**8** g	4.950495 mL	52.29784 mmol	**1**	X	
solvent	Diethyl ether	60-29-7	74.12	0.706		35.3 g	**50** mL				
wu solvent	Diethyl ether	60-29-7	74.12	0.706		141.2 g	**200** mL				
product	1H-Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, bromide	109833-17-2	235.078			12.29407 g		52.29784 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1H-Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, bromide	109833-17-2	235.078			**11.8** g		50.19611 mmol	95.98123

total reaction mass	189.65	g
total reagents / reactants / cat. mass	13.15	g
total workup reagents mass		g
total solvents (excl. water)	176.50	g
total water		g
total waste	177.85	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	16.1	16.1
solvent intensity	15.0	15.0
Sheldon E-factor	15.1	15.1
GSK Reaction Mass Efficiency	0.897	
Andraos Reaction Mass Efficiency	0.062	0.062
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.935	
material recovery parameter	0.069	0.069
yield	0.960	

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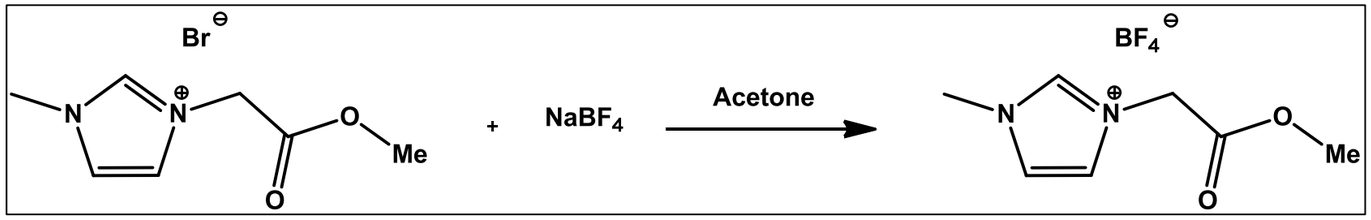

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1*H* -Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, bromide	109833-17-2	235.078			**500** mg		2.126954 mmol	**1**	X	
reactant	Sodium tetrafluoroborate	13755-29-8	109.79			233.5182 mg		2.126954 mmol	**1**		
solvent	Acetone	67-64-1	58.08	0.791		3164 mg	**4** mL				
wu solvent	Acetone	67-64-1	58.08	0.791		6328 mg	**8** mL				
product	1*H* -Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, tetrafluoroborate	503439-28-9	241.979			514.6781 mg		2.126954 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1*H* -Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, tetrafluoroborate	503439-28-9	241.979			**492** mg		2.033234 mmol	95.59373

total reaction mass	10225.52	mg
total reagents / reactants / cat. mass	733.52	mg
total workup reagents mass		mg
total solvents (excl. water)	9492.00	mg
total water		mg
total waste	9733.52	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	20.8	20.8
solvent intensity	19.3	19.3
Sheldon E-factor	19.8	19.8
GSK Reaction Mass Efficiency	0.671	
Andraos Reaction Mass Efficiency	0.048	0.048
atom economy	0.702	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	0.072	0.072
yield	0.956	

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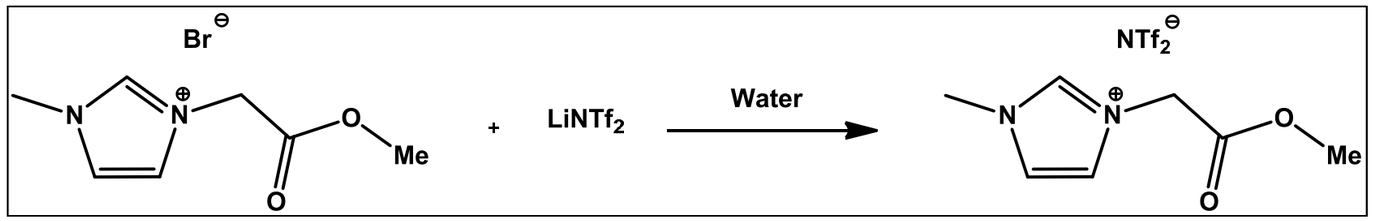

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, bromide	109833-17-2	235.078			**500** mg		2.126954 mmol	**1**	X	
reactant	Lithium bis(trifluoromethanesulfonimide)	90076-65-6	287.09			732.7525 mg		2.552344 mmol	**1.2**		
solvent	Water		18	1		4000 mg	**4** mL				
wu solvent	Water		18	1		9000 mg	**9** mL				
product	1H-Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, bis(trifluoromethanesulfonimide)	503439-61-0	435.32			925.9054 mg		2.126954 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1H-Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, bis(trifluoromethanesulfonimide)	503439-61-0	435.32			**650** mg		1.493154 mmol	70.20155

total reaction mass	14232.75	mg
total reagents / reactants / cat. mass	1232.75	mg
total workup reagents mass		mg
total solvents (excl. water)		mg
total water	13000.00	mg
total waste	13582.75	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	1.9	21.9
solvent intensity	0.0	20.0
Sheldon E-factor	0.9	20.9
GSK Reaction Mass Efficiency	0.527	
Andraos Reaction Mass Efficiency	0.527	0.046
atom economy	0.834	
1 / stoichiom. factor (excess reagents)	0.901	
material recovery parameter	1.000	0.087
yield	0.702	

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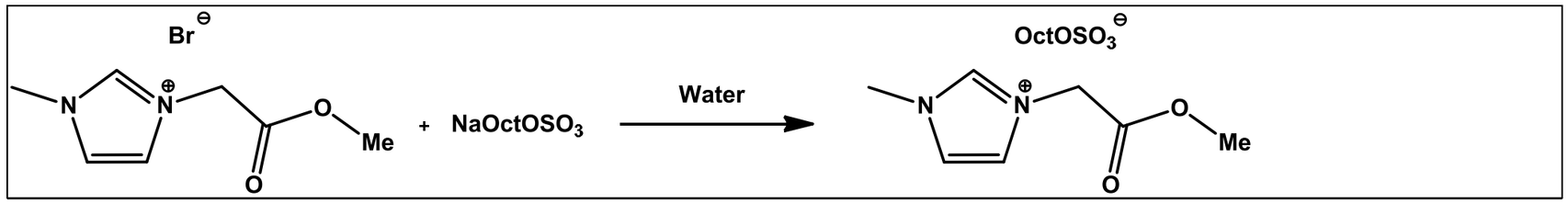

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, bromide	109833-17-2	235.078			**2** g		8.507814 mmol	**1**	X	
reactant	Sodium octyl sulfate	142-31-4	232.27			1.97611 g		8.507814 mmol	**1**		
solvent	Water		18	1		15 g	**15** mL				
wu solvent	Dichloromethane	75-09-2	84.93	1.325		19.875 g	**15** mL				
product	1H-Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, octyl sulfate	1239486-26-0	364.46			3.100758 g		8.507814 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1H-Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, octyl sulfate	1239486-26-0	364.46			**1.91** g		5.24063 mmol	61.59784

total reaction mass	38.85	g
total reagents / reactants / cat. mass	3.98	g
total workup reagents mass		g
total solvents (excl. water)	19.88	g
total water	15.00	g
total waste	36.94	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	12.5	20.3
solvent intensity	10.4	18.3
Sheldon E-factor	11.5	19.3
GSK Reaction Mass Efficiency	0.480	
Andraos Reaction Mass Efficiency	0.080	0.049
atom economy	0.780	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	0.167	0.102
yield	0.616	

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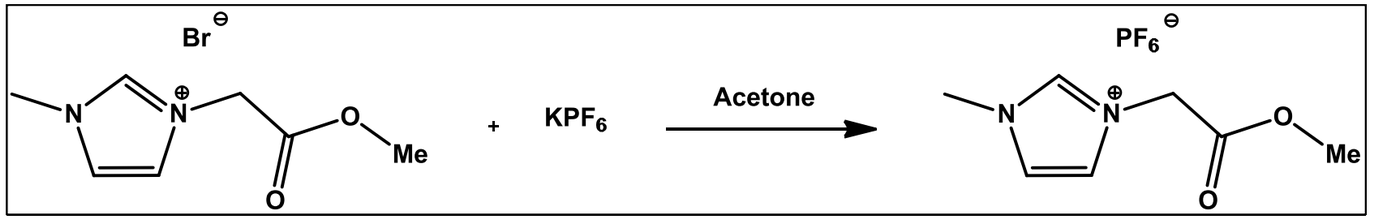

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, bromide	109833-17-2	235.078			**500** mg		2.126954 mmol	**1**	X	
reactant	Potassium hexafluorophosphate	17084-13-8	184.06			**600** mg		3.259807 mmol	1.532618		
solvent	Acetone	67-64-1	58.08	0.791		3164 mg	**4** mL				
wu solvent	Acetone	67-64-1	58.08	0.791		6328 mg	**8** mL				
product	1H-Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, hexafluorophosphate	503439-48-3	300.14			638.3839 mg		2.126954 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1H-Imidazolium, 3-(2-methoxy-2-oxoethyl)-1-methyl-, hexafluorophosphate	503439-48-3	300.14			**605** mg		2.015726 mmol	94.77057

total reaction mass	10592.00	mg
total reagents / reactants / cat. mass	1100.00	mg
total workup reagents mass		mg
total solvents (excl. water)	9492.00	mg
total water		mg
total waste	9987.00	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	17.5	17.5
solvent intensity	15.7	15.7
Sheldon E-factor	16.5	16.5
GSK Reaction Mass Efficiency	0.550	
Andraos Reaction Mass Efficiency	0.057	0.057
atom economy	0.716	
1 / stoichiom. factor (excess reagents)	0.810	
material recovery parameter	0.104	0.104
yield	0.948	

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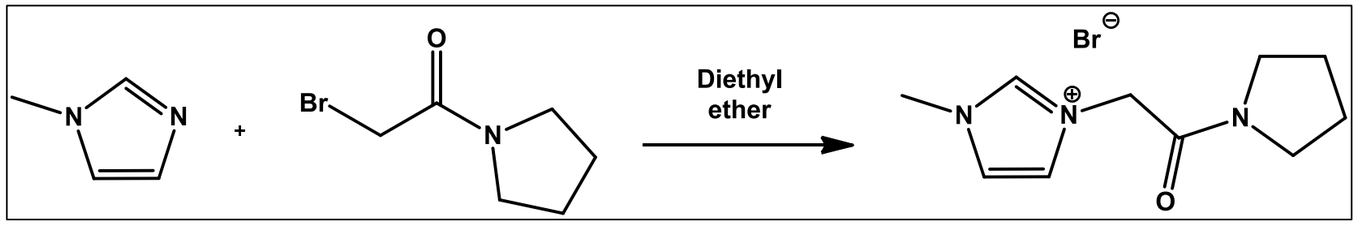

Type	Name	[CAS]	M.W.	d	wt% or conc.		mass		volume		moles		eq.	Pivot reagent	recycled
reactant	N-Methylimidazole	616-47-7	82.105	1.04			**6.4**	g	6.153846	mL	77.94897	mmol	0.998007		
reactant	N-(Bromoacetyl)pyrrolidine	90892-09-4	192.05				**15**	g			78.10466	mmol	**1**	X	
solvent	Diethyl ether	60-29-7	74.12	0.706			282.4	g	**400**	mL					
wu solvent	Diethyl ether	60-29-7	74.12	0.706			353	g	**500**	mL					
product	1H-Imidazolium, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, bromide	1188502-49-9	274.157				21.41294	g			78.10466	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	1H-Imidazolium, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, bromide	1188502-49-9	274.157			**17.32**	g		63.17548	mmol	80.88567

total reaction mass	656.80	g
total reagents / reactants / cat. mass	21.40	g
total workup reagents mass		g
total solvents (excl. water)	635.40	g
total water		g
total waste	639.48	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	37.9	37.9
solvent intensity	36.7	36.7
Sheldon E-factor	36.9	36.9
GSK Reaction Mass Efficiency	0.809	
Andraos Reaction Mass Efficiency	0.026	0.026
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	1.001	
material recovery parameter	0.033	0.033
yield	0.809	

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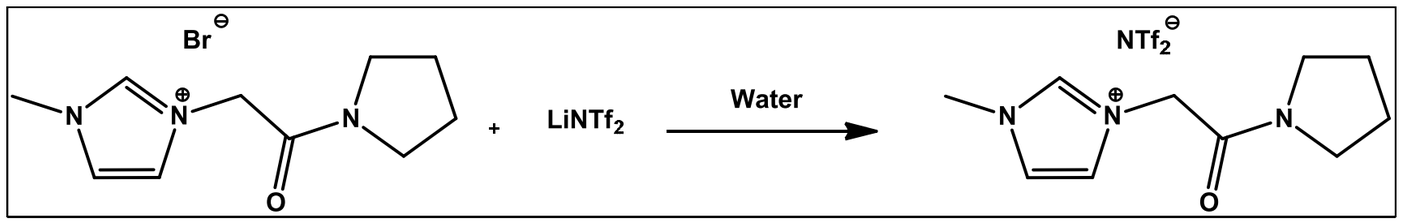

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	1H-Imidazolium, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, bromide	1188502-49-9	274.157			**11**	g			40.123	mmol	**1**	X	
reactant	Lithium bis(trifluoromethanesulfonimide)	90076-65-6	287.09			11.51891	g			40.123	mmol	**1**		
solvent	Water		18					**40**	mL					
wu solvent	Water		18	1		120	g	**120**	mL					
product	1*H* -Imidazolium, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, bis(trifluoromethanesulfonimide)	1239486-27-1	474.399			19.03431	g			40.123	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	1*H* -Imidazolium, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, bis(trifluoromethanesulfonimide)	1239486-27-1	474.399			**13.15**	g		27.71928	mmol	69.08578

total reaction mass	142.52	g
total reagents / reactants / cat. mass	22.52	g
total workup reagents mass		g
total solvents (excl. water)		g
total water	120.00	g
total waste	129.37	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	1.7	10.8
solvent intensity	0.0	9.1
Sheldon E-factor	0.7	9.8
GSK Reaction Mass Efficiency	0.584	
Andraos Reaction Mass Efficiency	0.584	0.092
atom economy	0.845	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	1.000	0.158
yield	0.691	

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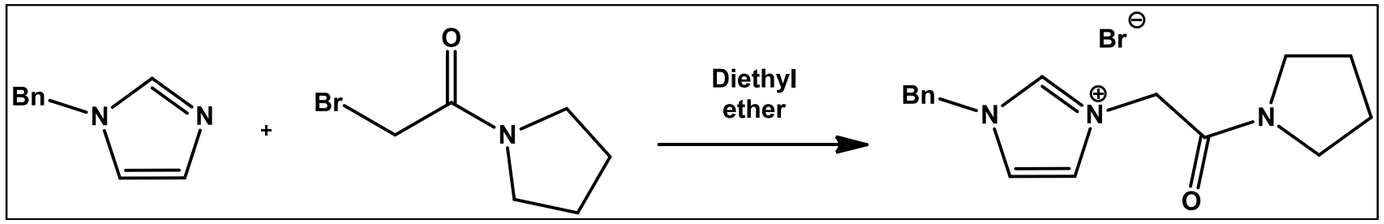

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	1-Benzylimidazole	4238-71-5	158.2			**2**	g			12.64223	mmol	**1**	X	
reactant	N-(Bromoacetyl)pyrrolidine	90892-09-4	192.05			2.427939	g			12.64223	mmol	**1**		
solvent	Diethyl ether	60-29-7	74.12	0.706		70.6	g	**100**	mL					
wu solvent	Diethyl ether	60-29-7	74.12	0.706		176.5	g	**250**	mL					
product	1*H* -Imidazolium, 3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-1-(phenylmethyl)-, bromide	1239486-29-3	350.25			4.427939	g			12.64223	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	1*H* -Imidazolium, 3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-1-(phenylmethyl)-, bromide	1239486-29-3	350.25			**2.78**	g		7.937188	mmol	62.78315

total reaction mass	251.53	g
total reagents / reactants / cat. mass	4.43	g
total workup reagents mass		g
total solvents (excl. water)	247.10	g
total water		g
total waste	248.75	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	90.5	90.5
solvent intensity	88.9	88.9
Sheldon E-factor	89.5	89.5
GSK Reaction Mass Efficiency	0.628	
Andraos Reaction Mass Efficiency	0.011	0.011
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	0.018	0.018
yield	0.628	

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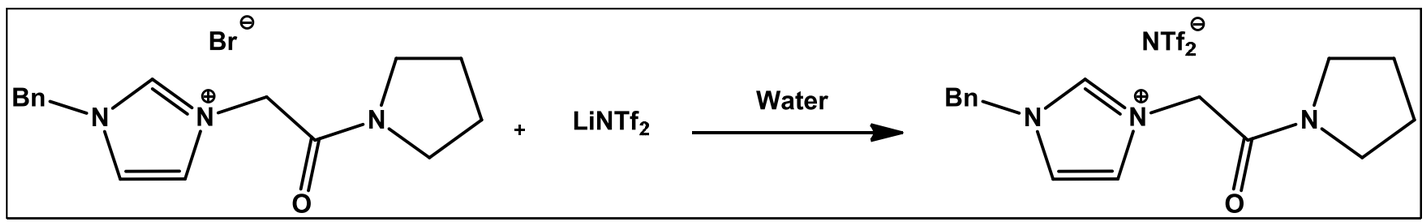

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazolium, 3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-1-(phenylmethyl)-, bromide	1239486-29-3	350.25			**200** mg		0.571021 mmol	**1**	X	
reactant	Lithium bis(trifluoromethanesulfonimide)	90076-65-6	287.09			163.9343 mg		0.571021 mmol	**1**		
solvent	Water		18	1		4000 mg	**4** mL				
wu solvent	Water		18	1		12000 mg	**12** mL				
product	1H-Imidazolium, 3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-1-(phenylmethyl)-, bis(trifluoromethanesulfonimide)	1239486-31-7	550.078			314.1059 mg		0.571021 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1H-Imidazolium, 3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-1-(phenylmethyl)-, bis(trifluoromethanesulfonimide)	1239486-31-7	550.078			**271** mg		0.492657 mmol	86.27663

total reaction mass	16363.93	mg
total reagents / reactants / cat. mass	363.93	mg
total workup reagents mass		mg
total solvents (excl. water)		mg
total water	16000.00	mg
total waste	16092.93	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	1.3	60.4
solvent intensity	0.0	59.0
Sheldon E-factor	0.3	59.4
GSK Reaction Mass Efficiency	0.745	
Andraos Reaction Mass Efficiency	0.745	0.017
atom economy	0.863	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	1.000	0.022
yield	0.863	

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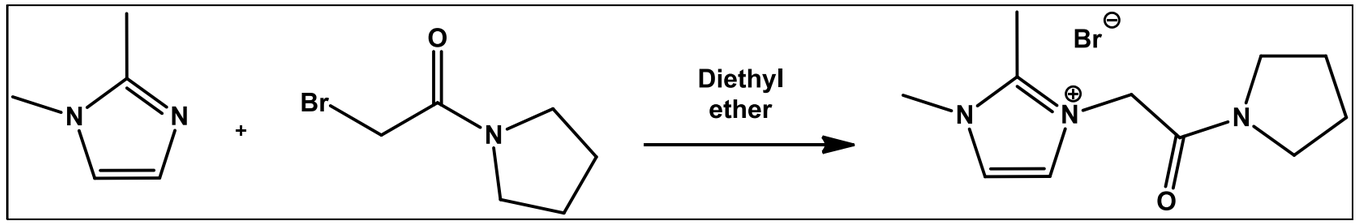

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	1,2-Dimethylimidazole	1739-84-0	96.13			**3.84**	g			39.94591	mmol	**1**	X	
reactant	N-(Bromoacetyl)pyrrolidine	90892-09-4	192.05			**8.06**	g			41.96824	mmol	1.050627		
solvent	Diethyl ether	60-29-7	74.12	0.706		70.6	g	**100**	mL					
wu solvent	Diethyl ether	60-29-7	74.12	0.706		141.2	g	**200**	mL					
product	**18**	1188502-55-7	288.184			11.51177	g			39.94591	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	**18**	1188502-55-7	288.184			**9.41**	g		32.65275	mmol	81.74242

total reaction mass	223.70	g
total reagents / reactants / cat. mass	11.90	g
total workup reagents mass		g
total solvents (excl. water)	211.80	g
total water		g
total waste	214.29	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	23.8	23.8
solvent intensity	22.5	22.5
Sheldon E-factor	22.8	22.8
GSK Reaction Mass Efficiency	0.791	
Andraos Reaction Mass Efficiency	0.042	0.042
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.967	
material recovery parameter	0.053	0.053
yield	0.817	

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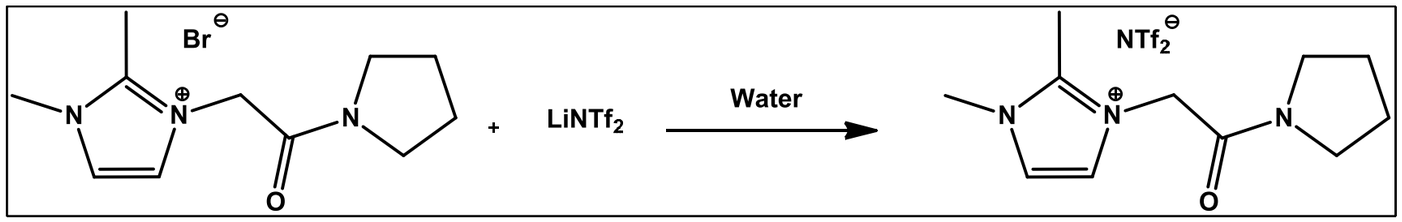
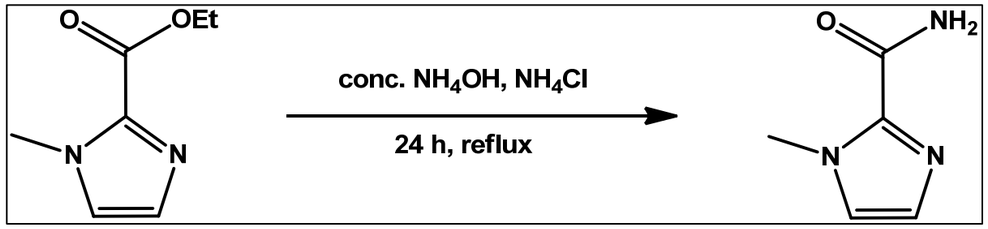


Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	1H-Imidazolium, 1,2-dimethyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, bromide	1188502-55-7	288.184			**11**	g			38.17006	mmol	**1**	X	
reactant	Lithium bis(trifluoromethanesulfonimide)	90076-65-6	287.09			10.95824	g			38.17006	mmol	**1**		
solvent	Water		18	1		40	g	**40**	mL					
wu solvent	Water		18	1		150	g	**150**	mL					
product	1H-Imidazolium, 1,2-dimethyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, bis(trifluoromethanesulfonimide)	1239486-32-8	488.426			18.64325	g			38.17006	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		yield(%)
Output	1H-Imidazolium, 1,2-dimethyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, bis(trifluoromethanesulfonimide)	1239486-32-8	488.426			**14.13**	g			28.92966	mmol	75.79151

total reaction mass	211.96	g
total reagents / reactants / cat. mass	21.96	g
total workup reagents mass		g
total solvents (excl. water)		g
total water	190.00	g
total waste	197.83	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	1.6	15.0
solvent intensity	0.0	13.4
Sheldon E-factor	0.6	14.0
GSK Reaction Mass Efficiency	0.643	
Andraos Reaction Mass Efficiency	0.643	0.067
atom economy	0.849	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	1.000	0.104
yield	0.758	

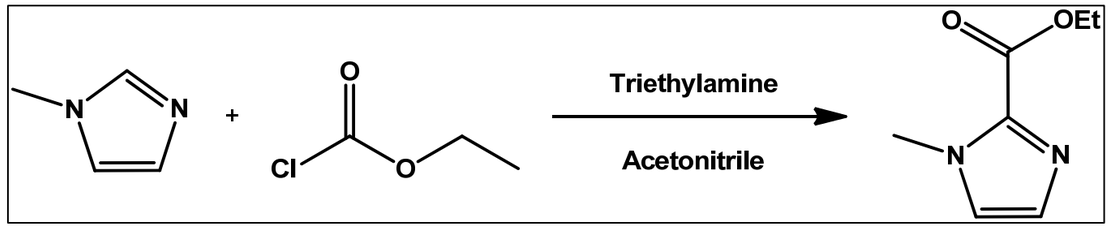


Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazole-2-carboxylic acid, 1-methyl-, ethyl ester	30148-21-1	154.17	1.14		**6** g	5.263158 mL	38.91808 mmol	**1**	X	
reactant	Ammonium hydroxide solution in Water	1336-21-6	35.05	0.88	**0.3** wt%	88 g	**100** mL	7.532097 mmol	0.193537		
catalyst	Ammonium chloride	12125-02-9	53.49			**0.2** g		3.739017 mmol	0.096074		
product	1H-Imidazole-2-carboxamide, 1-methyl-	20062-51-5	125.13			4.869819 g		38.91808 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1H-Imidazole-2-carboxamide, 1-methyl-	20062-51-5	125.13			**3.21** g		25.65332 mmol	65.91621

total reaction mass	94.20	g
total reagents / reactants / cat. mass	6.46	g
total workup reagents mass		g
total solvents (excl. water)		g
total water	87.74	g
total waste	90.99	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	2.0	29.3
solvent intensity	0.0	27.3
Sheldon E-factor	1.0	28.3
GSK Reaction Mass Efficiency	0.497	
Andraos Reaction Mass Efficiency	0.497	0.034
atom economy	0.661	
1 / stoichiom. factor (excess reagents)	1.176	
material recovery parameter	0.969	0.066
yield	0.659	



Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	1-Methylimidazole	616-47-7	82.105	1.04		**10**	g	9.615385	mL	121.7953	mmol	**1**	X	
reactant	Ethyl chloroformate	541-41-3	108.523	1.13		24.45254	g	21.63941	mL	225.3212	mmol	**1.85**		
reagent	Triethylamine	121-44-8	101.2	0.726		21.93971	g	30.21999	mL	216.7956	mmol	**1.78**		
solvent	Acetonitrile	75-05-8	41.05	0.786		78.6	g	**100**	mL					
wu solvent	Water		18	1		100	g	**100**	mL					
wu solvent	Chloroform	67-66-3	119.38	1.492		149.2	g	**100**	mL					
product	1*H* -Imidazole-2-carboxylic acid, 1-methyl-, ethyl ester	30148-21-1	154.17	1.14		18.77718	g	16.47121	mL	121.7953	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		yield(%)
Output	1H-Imidazole-2-carboxylic acid, 1-methyl-, ethyl ester	30148-21-1	154.17	1.14		**9.82**	g	8.614035	mL	63.69592	mmol	52.29754

total reaction mass	384.19	g
total reagents / reactants / cat. mass	56.39	g
total workup reagents mass		g
total solvents (excl. water)	227.80	g
total water	100.00	g
total waste	374.37	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	28.9	39.1
solvent intensity	23.2	33.4
Sheldon E-factor	27.9	38.1
GSK Reaction Mass Efficiency	0.174	
Andraos Reaction Mass Efficiency	0.035	0.026
atom economy	0.528	
1 / stoichiom. factor (excess reagents)	0.630	
material recovery parameter	0.198	0.147
yield	0.523	

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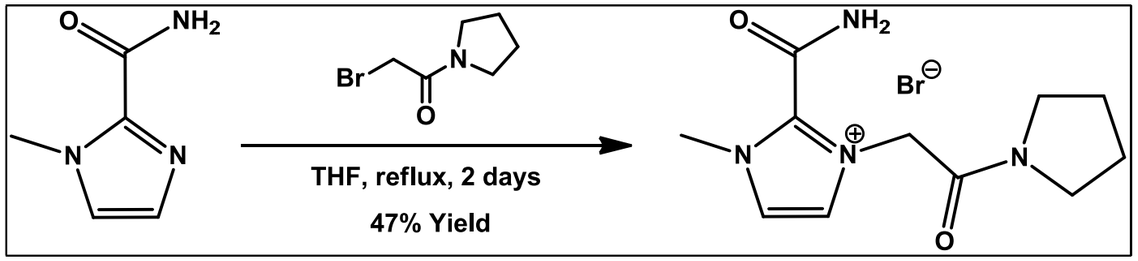

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	1H-Imidazole-2-carboxamide, 1-methyl-	20062-51-5	125.13			**2**	g			15.98338	mmol	**1**	X	
reactant	N-(Bromoacetyl)pyrrolidine	90892-09-4	192.05			**3.07**	g			15.98542	mmol	1.000128		
solvent	Tetrahydrofuran	109-99-9	72.11	0.889		88.9	g	**100**	mL					
wu solvent	Tetrahydrofuran	109-99-9	72.11	0.889		222.25	g	**250**	mL					
product	1H-Imidazolium-2-carboxamide, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, Bromide		317.18			5.069608	g			15.98338	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	1H-Imidazolium-2-carboxamide, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, Bromide		317.18			**2.35**	g		7.409042	mmol	46.35467

total reaction mass	316.22	g
total reagents / reactants / cat. mass	5.07	g
total workup reagents mass		g
total solvents (excl. water)	311.15	g
total water		g
total waste	313.87	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	134.6	134.6
solvent intensity	132.4	132.4
Sheldon E-factor	133.6	133.6
GSK Reaction Mass Efficiency	0.464	
Andraos Reaction Mass Efficiency	0.007	0.007
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	0.016	0.016
yield	0.464	

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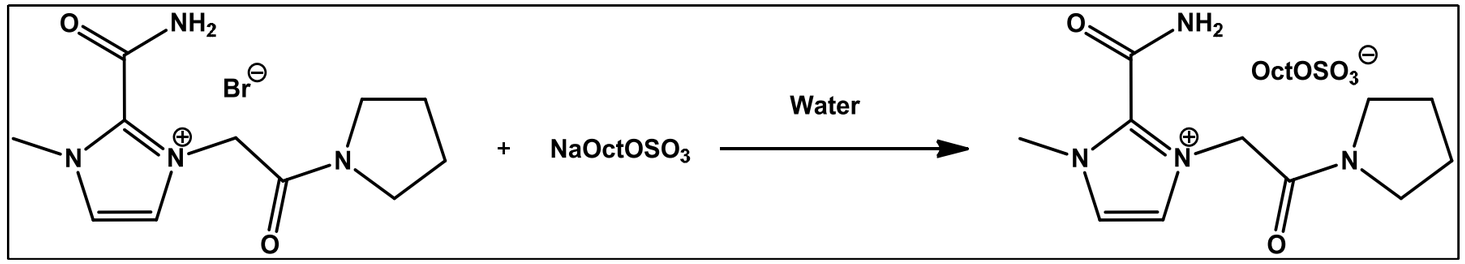

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	1H-Imidazolium-2-carboxamide, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, Bromide		317.18			**1**	g			3.152784	mmol	**1**	X	
reactant	Sodium octyl sulfate	142-31-4	232.27			**0.731**	g			3.147199	mmol	0.998229		
solvent	Water		18	1		20	g	**20**	mL					
wu solvent	Dichloromethane	75-09-2	84.93	1.325		26.5	g	**20**	mL					
product	1H-Imidazolium-2-carboxamide, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, octylsulfate		446.56			1.407907	g			3.152784	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		yield(%)
Output	1H-Imidazolium-2-carboxamide, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, octylsulfate		446.56			**0.649**	g			1.453332	mmol	46.09679

total reaction mass	48.23	g
total reagents / reactants / cat. mass	1.73	g
total workup reagents mass		g
total solvents (excl. water)	26.50	g
total water	20.00	g
total waste	47.58	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	43.5	74.3
solvent intensity	40.8	71.6
Sheldon E-factor	42.5	73.3
GSK Reaction Mass Efficiency	0.375	
Andraos Reaction Mass Efficiency	0.023	0.013
atom economy	0.813	
1 / stoichiom. factor (excess reagents)	1.001	
material recovery parameter	0.061	0.036
yield	0.461	

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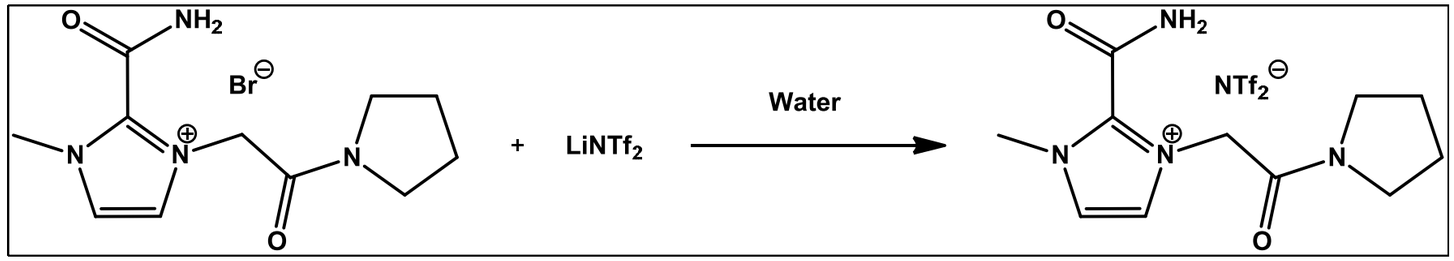

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazolium-2-carboxamide, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, Bromide		317.18			**1** g		3.152784 mmol	**1**	X	
reactant	Lithium bis(trifluoromethanesulfonimide)	90076-65-6	287.09			0.905133 g		3.152784 mmol	**1**		
solvent	Water		18	1		10 g	**10** mL				
wu solvent	Water		18	1		30 g	**30** mL				
product	1H-Imidazolium-2-carboxamide, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, bis(trifluoromethanesulfonimide)		517.42			1.631313 g		3.152784 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1H-Imidazolium-2-carboxamide, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, bis(trifluoromethanesulfonimide)		517.42			**1.205** g		2.328862 mmol	73.86686

total reaction mass	41.91	g
total reagents / reactants / cat. mass	1.91	g
total workup reagents mass		g
total solvents (excl. water)		g
total water	40.00	g
total waste	40.70	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	1.6	34.8
solvent intensity	0.0	33.2
Sheldon E-factor	0.6	33.8
GSK Reaction Mass Efficiency	0.633	
Andraos Reaction Mass Efficiency	0.633	0.029
atom economy	0.856	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	1.000	0.045
yield	0.739	

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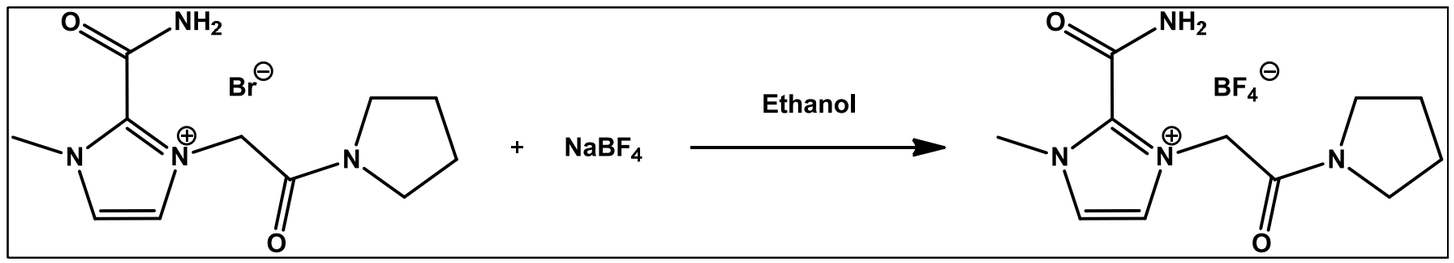

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazolium-2-carboxamide, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, Bromide		317.18			**1.2** g		3.783341 mmol	**1**	X	
reactant	Sodium tetrafluoroborate	13755-29-8	109.79			0.415373 g		3.783341 mmol	**1**		
solvent	Ethanol	64-17-5	46.07	0.816		48.96 g	**60** mL				
product	1H-Imidazolium-2-carboxamide, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, tetrafluoroborate		324.08			1.226105 g		3.783341 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1H-Imidazolium-2-carboxamide, 1-methyl-3-[2-oxo-2-(1-pyrrolidinyl)ethyl]-, tetrafluoroborate		324.08			**0.764** g		2.357443 mmol	62.31114

total reaction mass	50.58	g
total reagents / reactants / cat. mass	1.62	g
total workup reagents mass		g
total solvents (excl. water)	48.96	g
total water		g
total waste	49.81	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	66.2	66.2
solvent intensity	64.1	64.1
Sheldon E-factor	65.2	65.2
GSK Reaction Mass Efficiency	0.473	
Andraos Reaction Mass Efficiency	0.015	0.015
atom economy	0.759	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	0.032	0.032
yield	0.623	

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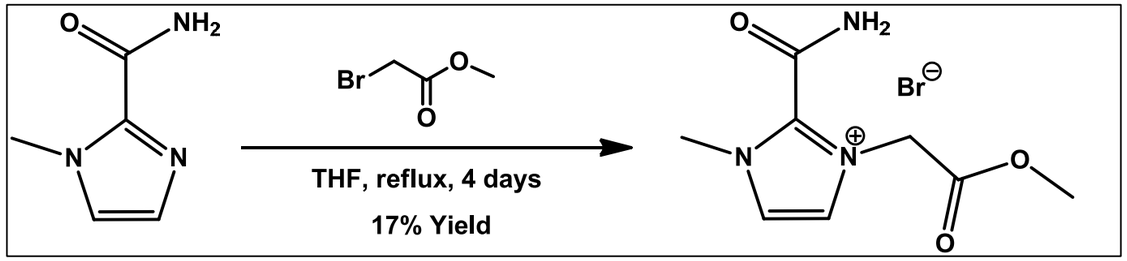
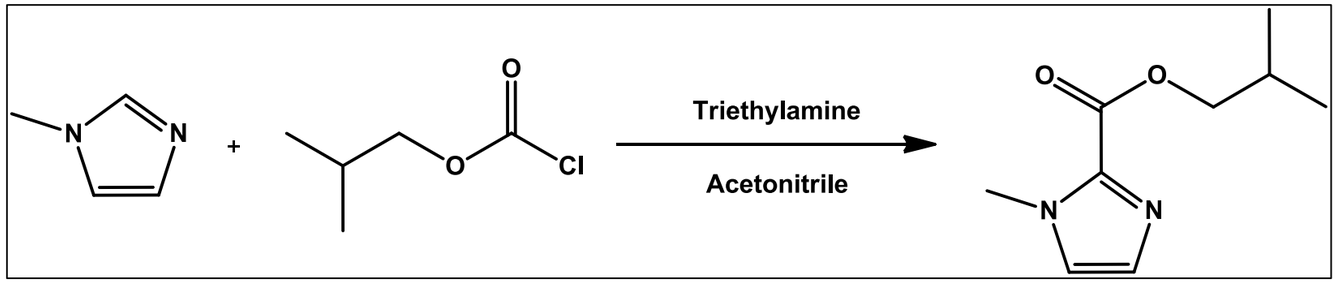


Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazole-2-carboxamide, 1-methyl-	20062-51-5	125.13			**500** mg		3.995844 mmol	**1**	X	
reactant	Methyl bromoacetate	96-32-2	152.97	1.616		**612** mg	0.378713 mL	4.000784 mmol	1.001236		
solvent	Tetrahydrofuran	109-99-9	72.11	0.889		17780 mg	**20** mL				
wu solvent	Tetrahydrofuran	109-99-9	72.11	0.889		17780 mg	**20** mL				
product	1H-Imidazolium-2-carboxamide,3-(2-methoxy-2-oxoethyl)-1-methyl-, Bromide		278.1			1111.244 mg		3.995844 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1H-Imidazolium-2-carboxamide,3-(2-methoxy-2-oxoethyl)-1-methyl-, Bromide		278.1			**189** mg		0.679612 mmol	17.00796

total reaction mass	36672.00	mg
total reagents / reactants / cat. mass	1112.00	mg
total workup reagents mass		mg
total solvents (excl. water)	35560.00	mg
total water		mg
total waste	36483.00	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	194.0	194.0
solvent intensity	188.1	188.1
Sheldon E-factor	193.0	193.0
GSK Reaction Mass Efficiency	0.170	
Andraos Reaction Mass Efficiency	0.005	0.005
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.999	
material recovery parameter	0.030	0.030
yield	0.170	



Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	1-Methylimidazole	616-47-7	82.105	1.04		**3.3**	g	3.173077	mL	40.19244	mmol	**1**	X	
reactant	Isobutyl chloroformate	543-27-1	136.58	1.053		10.15554	g	9.644391	mL	74.35601	mmol	**1.85**		
reagent	Triethylamine	121-44-8	101.2	0.726		7.240105	g	9.972596	mL	71.54254	mmol	**1.78**		
solvent	Acetonitrile	75-05-8	41.05	0.786		23.58	g	**30**	mL					
wu solvent	Water		18	1		30	g	**30**	mL					
product	Isobutyl 1-methylimidazole-2-carboxylate	154475-19-1	182.22	1.1		7.323866	g	6.65806	mL	40.19244	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		yield(%)
Output	Isobutyl 1-methylimidazole-2-carboxylate	154475-19-1	182.22	1.1		**3.99**	g	3.627273	mL	21.89661	mmol	54.47943

total reaction mass	74.28	g
total reagents / reactants / cat. mass	20.70	g
total workup reagents mass		g
total solvents (excl. water)	23.58	g
total water	30.00	g
total waste	70.29	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	11.1	18.6
solvent intensity	5.9	13.4
Sheldon E-factor	10.1	17.6
GSK Reaction Mass Efficiency	0.193	
Andraos Reaction Mass Efficiency	0.090	0.054
atom economy	0.570	
1 / stoichiom. factor (excess reagents)	0.621	
material recovery parameter	0.467	0.279
yield	0.545	

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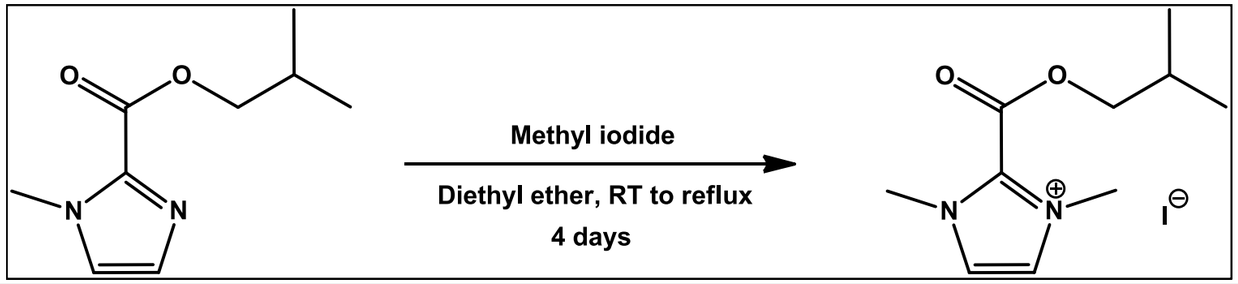

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	Isobutyl 1-methylimidazole-2-carboxylate	154475-19-1	182.22	1.1		**2**	g	1.818182	mL	10.97574	mmol	**1**	X	
reactant	Iodomethane	74-88-4	141.94	2.28		**6.24**	g	2.736842	mL	43.96224	mmol	4.005399		
solvent	Diethyl ether	60-29-7	74.12	0.706		70.6	g	**100**	mL					
wu solvent	Diethyl ether	60-29-7	74.12	0.706		70.6	g	**100**	mL					
product	1H-Imidazolium, 1,3-dimethyl-2-[(2-methylpropoxy)carbonyl]-, Iodide		324.16			3.557897	g			10.97574	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	1H-Imidazolium, 1,3-dimethyl-2-[(2-methylpropoxy)carbonyl]-, Iodide		324.16			**2.21**	g		6.817621	mmol	62.11534

total reaction mass	149.44	g
total reagents / reactants / cat. mass	8.24	g
total workup reagents mass		g
total solvents (excl. water)	141.20	g
total water		g
total waste	147.23	g
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	67.6	67.6
solvent intensity	63.9	63.9
Sheldon E-factor	66.6	66.6
GSK Reaction Mass Efficiency	0.268	
Andraos Reaction Mass Efficiency	0.015	0.015
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.432	
material recovery parameter	0.055	0.055
yield	0.621	

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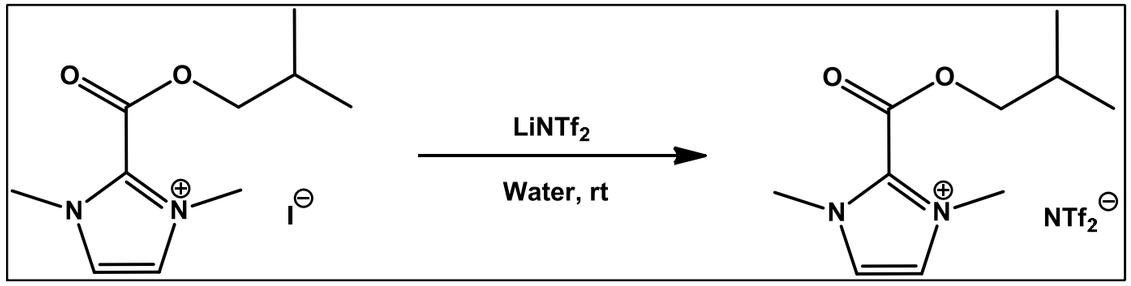

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazolium, 1,3-dimethyl-2-[(2-methylpropoxy)carbonyl]-, Iodide		324.16			**500** mg		1.542448 mmol	**1**	X	
reactant	Lithium bis(trifluoromethanesulfonimide)	90076-65-6	287.09			**443** mg		1.54307 mmol	1.000403		
solvent	Water		18	1		4000 mg	**4** mL				
wu solvent	Water		18	1		12000 mg	**12** mL				
product	1H-Imidazolium, 1,3-dimethyl-2-[(2-methylpropoxy)carbonyl]-, bis(trifluoromethanesulfonimide)		477.4			736.3648 mg		1.542448 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1H-Imidazolium, 1,3-dimethyl-2-[(2-methylpropoxy)carbonyl]-, bis(trifluoromethanesulfonimide)		477.4			**630** mg		1.319648 mmol	85.55543

total reaction mass	16943.00	mg
total reagents / reactants / cat. mass	943.00	mg
total workup reagents mass		mg
total solvents (excl. water)		mg
total water	16000.00	mg
total waste	16313.00	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	1.5	26.9
solvent intensity	0.0	25.4
Sheldon E-factor	0.5	25.9
GSK Reaction Mass Efficiency	0.668	
Andraos Reaction Mass Efficiency	0.668	0.037
atom economy	0.781	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	1.000	0.056
yield	0.856	

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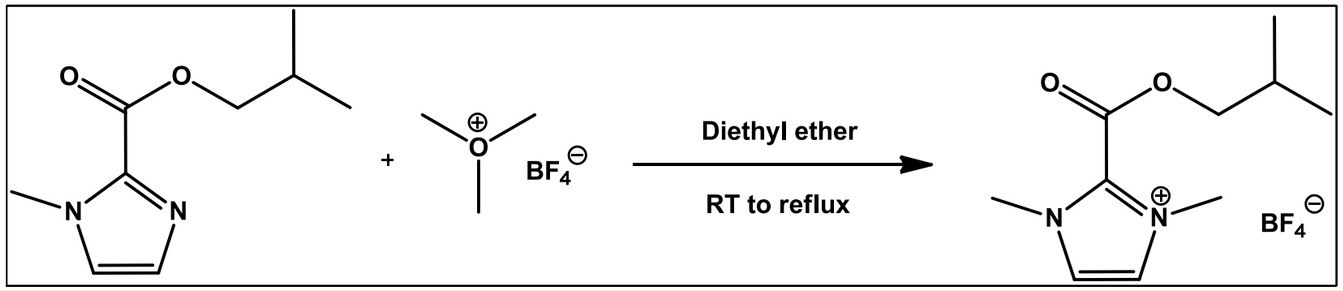

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	Isobutyl 1-methylimidazole-2-carboxylate	154475-19-1	182.22	1.1		**200**	mg	0.181818	mL	1.097574	mmol	**1**	X	
reactant	Trimethyloxonium tetrafluoroborate	420-37-1	147.91			**162**	mg			1.095261	mmol	0.997892		
solvent	Diethyl ether	60-29-7	74.12	0.706		7060	mg	**10**	mL					
wu solvent	Diethyl ether	60-29-7	74.12	0.706		14120	mg	**20**	mL					
product	1H-Imidazolium, 1,3-dimethyl-2-[(2-methylpropoxy)carbonyl]-, tetrafluoroborate		284.06			311.777	mg			1.097574	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	1H-Imidazolium, 1,3-dimethyl-2-[(2-methylpropoxy)carbonyl]-, tetrafluoroborate		284.06			**302**	mg		1.063156	mmol	96.86411

total reaction mass	21542.00	mg
total reagents / reactants / cat. mass	362.00	mg
total workup reagents mass		mg
total solvents (excl. water)	21180.00	mg
total water		mg
total waste	21240.00	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	71.3	71.3
solvent intensity	70.1	70.1
Sheldon E-factor	70.3	70.3
GSK Reaction Mass Efficiency	0.834	
Andraos Reaction Mass Efficiency	0.014	0.014
atom economy	0.860	
1 / stoichiom. factor (excess reagents)	1.001	
material recovery parameter	0.017	0.017
yield	0.969	

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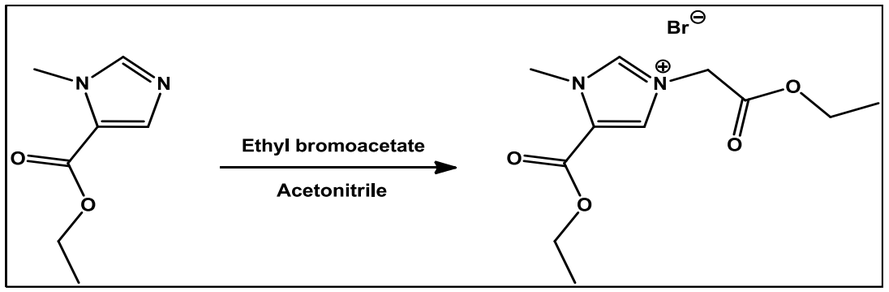

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	Ethyl 1-methyl-1H-imidazole-5-carboxylate		154.17			**200**	mg			1.297269	mmol	**1**	X	
reactant	Ethyl bromoacetate	105-36-2	167	1.506		481.92	mg	**320**	µL	2.885749	mmol	2.224479		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572	mg	**2**	mL					
wu solvent	Diethyl ether	60-29-7	74.12	0.706		21180	mg	**30**	mL					
product	3,5-bis(ethoxycarbonyl)-1-methyl-1H-imidazol-3-ium, bromide (30)		321.17			416.644	mg			1.297269	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	3,5-bis(ethoxycarbonyl)-1-methyl-1H-imidazol-3-ium, bromide		321.17			**370**	mg		1.152038	mmol	88.80484

total reaction mass	23433.92	mg
total reagents / reactants / cat. mass	681.92	mg
total workup reagents mass		mg
total solvents (excl. water)	22752.00	mg
total water		mg
total waste	23063.92	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	63.3	63.3
solvent intensity	61.5	61.5
Sheldon E-factor	62.3	62.3
GSK Reaction Mass Efficiency	0.543	
Andraos Reaction Mass Efficiency	0.016	0.016
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.611	
material recovery parameter	0.029	0.029
yield	0.888	

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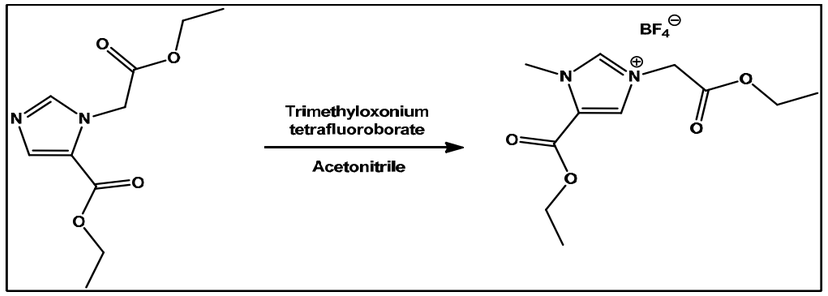

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	Diethyl 1H-imidazole-1,5-dicarboxylate		226.23			**150**	mg			0.663042	mmol	**1**	X	
reactant	Trimethyloxonium tetrafluoroborate	420-37-1	147.91			**103**	mg			0.696369	mmol	1.050264		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572	mg	**2**	mL					
product	3,5-bis(ethoxycarbonyl)-1-methyl-1H-imidazol-3-ium, tetrafluoroborate		328.07			217.5242	mg			0.663042	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	3,5-bis(ethoxycarbonyl)-1-methyl-1H-imidazol-3-ium, tetrafluoroborate		328.07			**197**	mg		0.600482	mmol	90.56464

total reaction mass	1825.00	mg
total reagents / reactants / cat. mass	253.00	mg
total workup reagents mass		mg
total solvents (excl. water)	1572.00	mg
total water		mg
total waste	1628.00	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	9.3	9.3
solvent intensity	8.0	8.0
Sheldon E-factor	8.3	8.3
GSK Reaction Mass Efficiency	0.779	
Andraos Reaction Mass Efficiency	0.108	0.108
atom economy	0.877	
1 / stoichiom. factor (excess reagents)	0.981	
material recovery parameter	0.139	0.139
yield	0.906	

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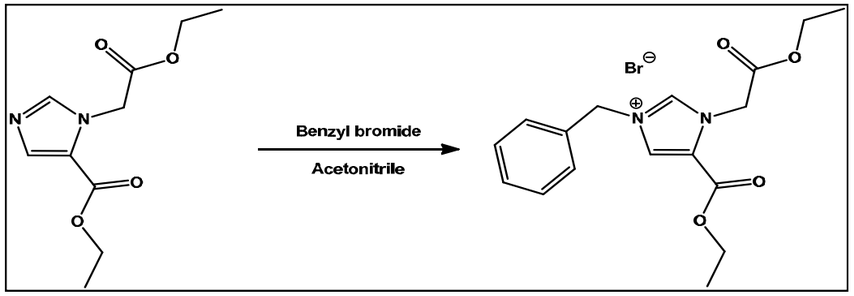

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	Diethyl 1H-imidazole-1,5-dicarboxylate		226.23			**150**	mg			0.663042	mmol	**1**	X	
reactant	Benzyl bromide	100-39-0	171.03	1.438		461.598	mg	**321**	µL	2.69893	mmol	4.070526		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572	mg	**2**	mL					
wu solvent	Diethyl ether	60-29-7	74.12	0.706		14120	mg	**20**	mL					
product	3-benzyl-1,5-bis(ethoxycarbonyl)-1H-imidazol-3-ium, bromide		397.26			263.4001	mg			0.663042	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	3-benzyl-1,5-bis(ethoxycarbonyl)-1H-imidazol-3-ium, bromide		397.26			**174**	mg		0.438	mmol	66.05921

total reaction mass	16303.60	mg
total reagents / reactants / cat. mass	611.60	mg
total workup reagents mass		mg
total solvents (excl. water)	15692.00	mg
total water		mg
total waste	16129.60	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	93.7	93.7
solvent intensity	90.2	90.2
Sheldon E-factor	92.7	92.7
GSK Reaction Mass Efficiency	0.285	
Andraos Reaction Mass Efficiency	0.011	0.011
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.431	
material recovery parameter	0.038	0.038
yield	0.661	

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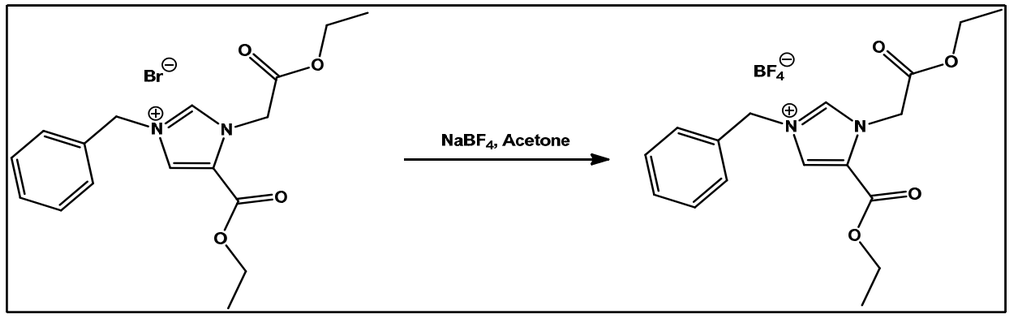

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	3-benzyl-1,5-bis(ethoxycarbonyl)-1H-imidazol-3-ium, bromide		397.26			**150** mg		0.377586 mmol	**1**	X	
reactant	Sodium tetrafluoroborate	13755-29-8	109.79			**75** mg		0.683122 mmol	1.809181		
solvent	Acetone	67-64-1	58.08	0.791		7910 mg	**10** mL				
wu solvent	Acetone	67-64-1	58.08	0.791		7910 mg	**10** mL				
product	3-benzyl-1,5-bis(ethoxycarbonyl)-1H-imidazol-3-ium, tetrafluoroborate		404.16			152.6053 mg		0.377586 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	3-benzyl-1,5-bis(ethoxycarbonyl)-1H-imidazol-3-ium, tetrafluoroborate		404.16			**146** mg		0.361243 mmol	95.67162

total reaction mass	16045.00	mg
total reagents / reactants / cat. mass	225.00	mg
total workup reagents mass		mg
total solvents (excl. water)	15820.00	mg
total water		mg
total waste	15899.00	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	109.9	109.9
solvent intensity	108.4	108.4
Sheldon E-factor	108.9	108.9
GSK Reaction Mass Efficiency	0.649	
Andraos Reaction Mass Efficiency	0.009	0.009
atom economy	0.797	
1 / stoichiom. factor (excess reagents)	0.851	
material recovery parameter	0.014	0.014
yield	0.957	

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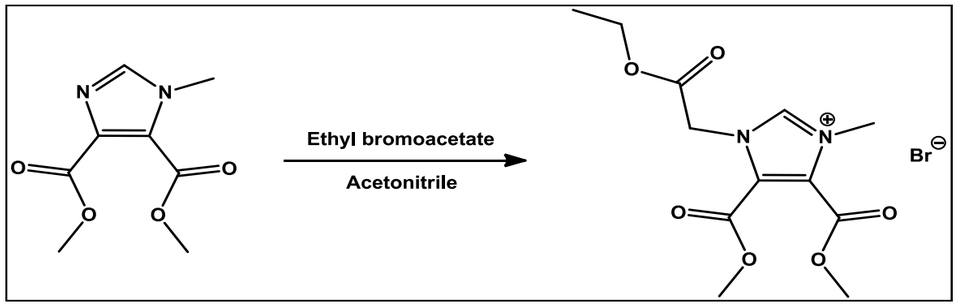

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazole-4,5-dicarboxylic acid, 1-methyl-, 4,5-dimethyl ester	42545-22-2	198.18			**250** mg		1.261479 mmol	**1**	X	
reactant	Ethyl bromoacetate	105-36-2	167	1.506		417.162 mg	**277** µL	2.497976 mmol	1.980196		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572 mg	**2** mL				
wu solvent	Diethyl ether	60-29-7	74.12	0.706		14120 mg	**20** mL				
product	1-(2-ethoxy-2-oxoethyl)-4,5-bis(methoxycarbonyl)-3-methyl-1H-imidazol-3-ium, bromide		365.18			460.6671 mg		1.261479 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1-(2-ethoxy-2-oxoethyl)-4,5-bis(methoxycarbonyl)-3-methyl-1H-imidazol-3-ium, bromide		365.18			**408** mg		1.117257 mmol	88.56722

total reaction mass	16359.16	mg
total reagents / reactants / cat. mass	667.16	mg
total workup reagents mass		mg
total solvents (excl. water)	15692.00	mg
total water		mg
total waste	15951.16	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	40.1	40.1
solvent intensity	38.5	38.5
Sheldon E-factor	39.1	39.1
GSK Reaction Mass Efficiency	0.612	
Andraos Reaction Mass Efficiency	0.025	0.025
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.690	
material recovery parameter	0.041	0.041
yield	0.886	

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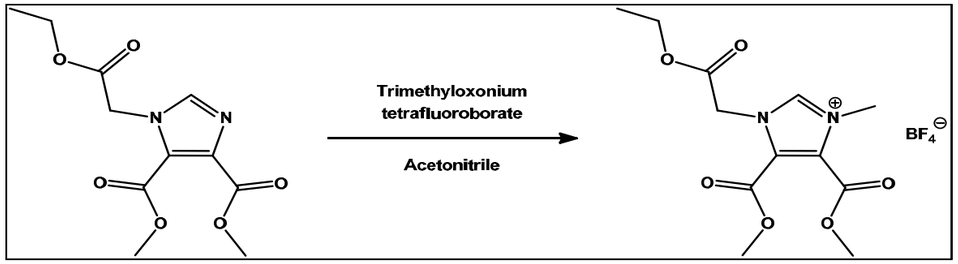

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	Dimethyl 1-(2-ethoxy-2-oxoethyl)-1H-imidazole-4,5-dicarboxylate		270.24			**250** mg		0.925104 mmol	**1**	X	
reactant	Trimethyloxonium tetrafluoroborate	420-37-1	147.91			**137** mg		0.926239 mmol	1.001227		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572 mg	**2** mL				
product	1-(2-ethoxy-2-oxoethyl)-4,5-bis(methoxycarbonyl)-3-methyl-1H-imidazol-3-ium, tetrafluoroborate		372.08			344.2126 mg		0.925104 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1-(2-ethoxy-2-oxoethyl)-4,5-bis(methoxycarbonyl)-3-methyl-1H-imidazol-3-ium, tetrafluoroborate		372.08			**318** mg		0.854655 mmol	92.38478

total reaction mass	1959.00	mg
total reagents / reactants / cat. mass	387.00	mg
total workup reagents mass		mg
total solvents (excl. water)	1572.00	mg
total water		mg
total waste	1641.00	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	6.2	6.2
solvent intensity	4.9	4.9
Sheldon E-factor	5.2	5.2
GSK Reaction Mass Efficiency	0.822	
Andraos Reaction Mass Efficiency	0.162	0.162
atom economy	0.890	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	0.198	0.198
yield	0.924	

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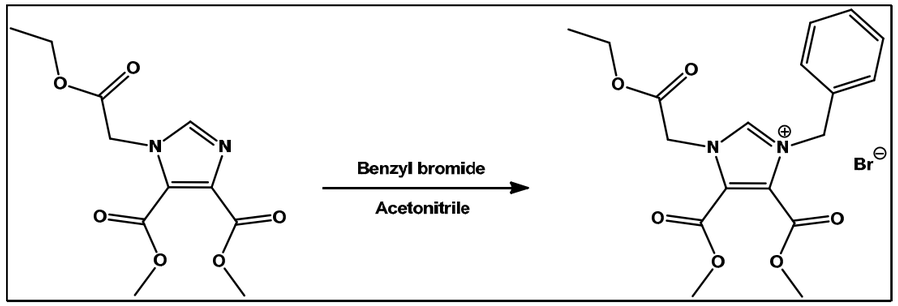

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	Dimethyl 1-(2-ethoxy-2-oxoethyl)-1H-imidazole-4,5-dicarboxylate		270.24			**500**	mg			1.9	mmol	**1**	X	
reactant	Benzyl bromide	100-39-0	171.03	1.438		649.914	mg	0.451957	mL	3.8	mmol	**2**		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572	mg	**2**	mL					
wu solvent	Diethyl ether	60-29-7	74.12	0.706		10590	mg	**15**	mL					
product	3-benzyl-1-(2-ethoxy-2-oxoethyl)-4,5-bis(methoxycarbonyl)-1H-imidazol-3-ium bromide		441.27			838.413	mg			1.9	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	3-benzyl-1-(2-ethoxy-2-oxoethyl)-4,5-bis(methoxycarbonyl)-1H-imidazol-3-ium bromide		441.27			**620**	mg		1.405035	mmol	73.94924

total reaction mass	13311.91	mg
total reagents / reactants / cat. mass	1149.91	mg
total workup reagents mass		mg
total solvents (excl. water)	12162.00	mg
total water		mg
total waste	12691.91	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	21.5	21.5
solvent intensity	19.6	19.6
Sheldon E-factor	20.5	20.5
GSK Reaction Mass Efficiency	0.539	
Andraos Reaction Mass Efficiency	0.047	0.047
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.721	
material recovery parameter	0.087	0.087
yield	0.739	

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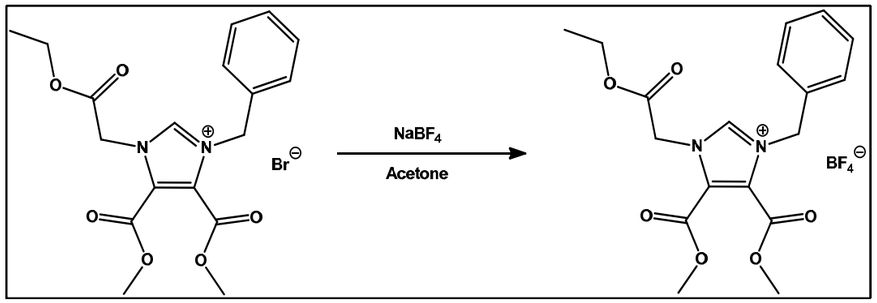

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	3-benzyl-1-(2-ethoxy-2-oxoethyl)-4,5-bis(methoxycarbonyl)-1H-imidazol-3-ium bromide		441.27			**250** mg		0.566547 mmol	**1**	X	
reactant	Sodium tetrafluoroborate	13755-29-8	109.79			**74.8** mg		0.681301 mmol	1.20255		
solvent	Acetone	67-64-1	58.08	0.791		7910 mg	**10** mL				
wu solvent	Acetone	67-64-1	58.08	0.791		7910 mg	**10** mL				
product	3-benzyl-1-(2-ethoxy-2-oxoethyl)-4,5-bis(methoxycarbonyl)-1H-imidazol-3-ium tetrafluoroborate		448.17			253.9092 mg		0.566547 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	3-benzyl-1-(2-ethoxy-2-oxoethyl)-4,5-bis(methoxycarbonyl)-1H-imidazol-3-ium tetrafluoroborate		448.17			**249** mg		0.555593 mmol	98.06656

total reaction mass	16144.80	mg
total reagents / reactants / cat. mass	324.80	mg
total workup reagents mass		mg
total solvents (excl. water)	15820.00	mg
total water		mg
total waste	15895.80	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	64.8	64.8
solvent intensity	63.5	63.5
Sheldon E-factor	63.8	63.8
GSK Reaction Mass Efficiency	0.767	
Andraos Reaction Mass Efficiency	0.015	0.015
atom economy	0.813	
1 / stoichiom. factor (excess reagents)	0.961	
material recovery parameter	0.020	0.020
yield	0.981	

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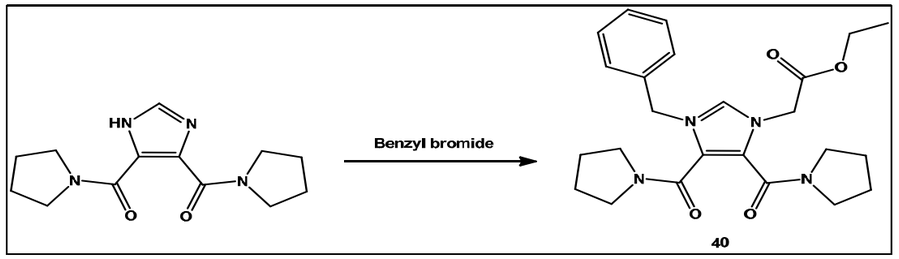

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	(40a)		348.39			**332.04**	mg			953.0698	µmol	**1**	X	
reactant	Benzyl bromide	100-39-0	171.03	1.438		0.649976	g	**0.452**	mL	3.800363	mmol	3.987496		
wu solvent	Diethyl ether	60-29-7	74.12	0.706		10.59	g	**15**	mL					
product	1-Benzyl-3-(2-ethoxy-2-oxoethyl)-4,5-bis(pyrrolidine-1-carbonyl)-1H-imidazol-3-ium bromide (40)		519.43			495.0531	mg			953.0698	µmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	1-Benzyl-3-(2-ethoxy-2-oxoethyl)-4,5-bis(pyrrolidine-1-carbonyl)-1H-imidazol-3-ium bromide (40)		519.43			**355**	mg		683.4415	µmol	71.70948

total reaction mass	11572.02	mg
total reagents / reactants / cat. mass	982.02	mg
total workup reagents mass		mg
total solvents (excl. water)	10590.00	mg
total water		mg
total waste	11217.02	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	32.6	32.6
solvent intensity	29.8	29.8
Sheldon E-factor	31.6	31.6
GSK Reaction Mass Efficiency	0.362	
Andraos Reaction Mass Efficiency	0.031	0.031
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.504	
material recovery parameter	0.085	0.085
yield	0.717	

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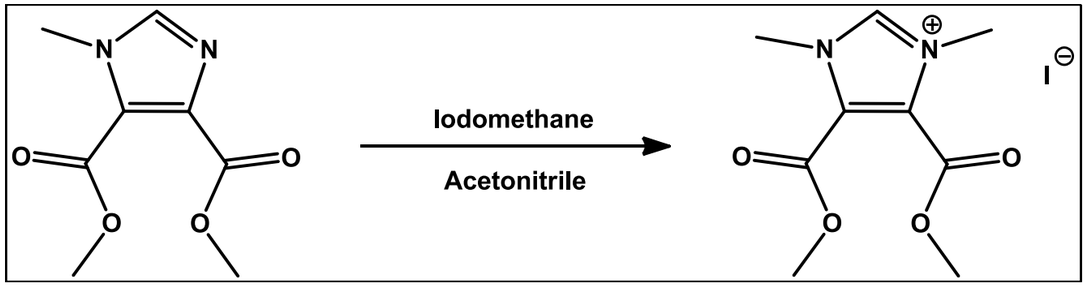

Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazole-4,5-dicarboxylic acid, 1-methyl-, 4,5-dimethyl ester	42545-22-2	198.18			**250** mg		1.261479 mmol	**1**	X	
reactant	Iodomethane	74-88-4	141.94	2.28		180.12 mg	**79** µL	1.268987 mmol	1.005951		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572 mg	**2** mL				
product	4,5-bis(methoxycarbonyl)-1,3-dimethyl-1H-imidazol-3-ium, iodide		340.12			429.0544 mg		1.261479 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	4,5-bis(methoxycarbonyl)-1,3-dimethyl-1H-imidazol-3-ium, iodide		340.12			**368** mg		1.081971 mmol	85.77001

total reaction mass	2002.12	mg
total reagents / reactants / cat. mass	430.12	mg
total workup reagents mass		mg
total solvents (excl. water)	1572.00	mg
total water		mg
total waste	1634.12	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	5.4	5.4
solvent intensity	4.3	4.3
Sheldon E-factor	4.4	4.4
GSK Reaction Mass Efficiency	0.856	
Andraos Reaction Mass Efficiency	0.184	0.184
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.998	
material recovery parameter	0.215	0.215
yield	0.858	

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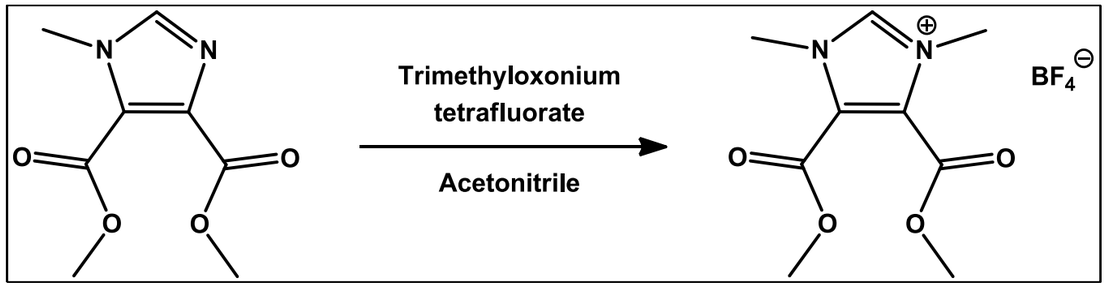


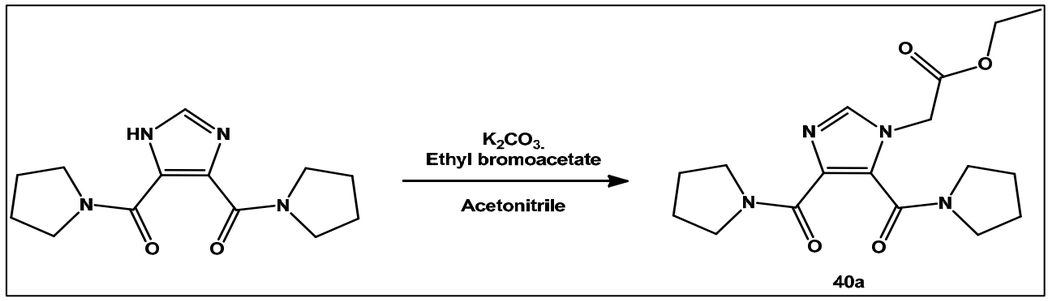
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	1H-Imidazole-4,5-dicarboxylic acid, 1-methyl-, 4,5-dimethyl ester	42545-22-2	198.18			**250** mg		1.261479 mmol	**1**	X	
reactant	Trimethyloxonium tetrafluoroborate	420-37-1	147.91			**240** mg		1.622608 mmol	1.286274		
solvent	Acetonitrile	75-05-8	41.05	0.786		1.572 g	**2** mL				
product	4,5-bis(methoxycarbonyl)-1,3-dimethyl-1H-imidazol-3-ium, tetrafluoroborate		300.02			378.4691 mg		1.261479 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	4,5-bis(methoxycarbonyl)-1,3-dimethyl-1H-imidazol-3-ium, tetrafluoroborate		300.02			**344** mg		1.14659 mmol	90.8925

total reaction mass	2062.00	mg
total reagents / reactants / cat. mass	490.00	mg
total workup reagents mass		mg
total solvents (excl. water)	1572.00	mg
total water		mg
total waste	1718.00	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	6.0	6.0
solvent intensity	4.6	4.6
Sheldon E-factor	5.0	5.0
GSK Reaction Mass Efficiency	0.702	
Andraos Reaction Mass Efficiency	0.167	0.167
atom economy	0.867	
1 / stoichiom. factor (excess reagents)	0.891	
material recovery parameter	0.238	0.238
yield	0.909	

40a



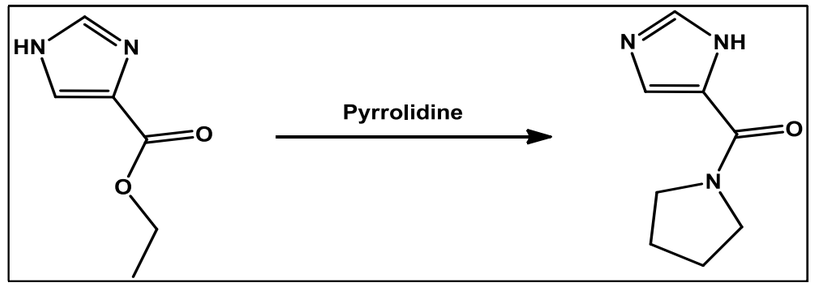
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	(1H-imidazole-4,5-diyl)bis(pyrrolidin-1-ylmethanone) (24a)		262.31			**250**	mg			0.953071	mmol	**1**	X	
reagent	Potassium carbonate	584-08-7	138.204			**135**	mg			0.976817	mmol	1.024915		
reactant	Ethyl bromoacetate	105-36-2	167	1.506		634.026	mg	**421**	µL	3.796563	mmol	3.983506		
solvent	Acetonitrile	75-05-8	41.05	0.786		3930	mg	**5**	mL					
wu solvent	Dichloromethane	75-09-2	84.93	1.325		6625	mg	**5**	mL					
product	(40a)		348.39			332.0403	mg			0.953071	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	(40a)		348.39			**332.04**	mg		0.95307	mmol	99.9999

total reaction mass	11574.03	mg
total reagents / reactants / cat. mass	1019.03	mg
total workup reagents mass		mg
total solvents (excl. water)	10555.00	mg
total water		mg
total waste	11241.99	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	34.9	34.9
solvent intensity	31.8	31.8
Sheldon E-factor	33.9	33.9
GSK Reaction Mass Efficiency	0.326	
Andraos Reaction Mass Efficiency	0.029	0.029
atom economy	0.614	
1 / stoichiom. factor (excess reagents)	0.531	
material recovery parameter	0.088	0.088
yield	1.000	

(1H-imidazol-5-yl)(pyrrolidin-1-yl)methanone



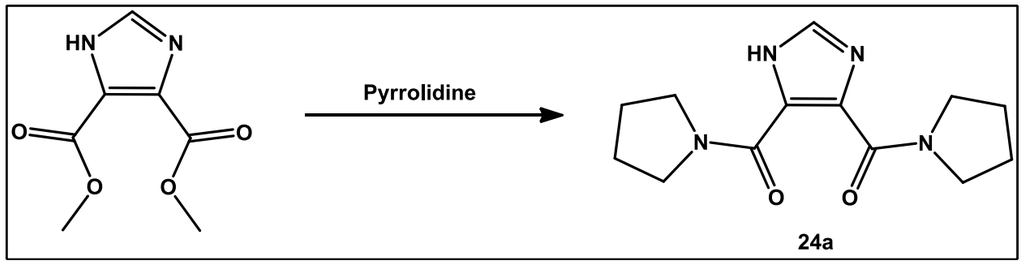
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	Ethyl 1H-imidazole-4-carboxylate	23785-21-9	140.14			**250**	mg			1.78393	mmol	**1**	X	
reactant	Pyrrolidine	123-75-1	71.12	0.852		1022.4	mg	**1.2**	mL	14.3757	mmol	8.058444		
wu solvent	Methanol	67-56-1	32.04	0.791		19775	mg	**25**	mL					
wu solvent	Dichloromethane	75-09-2	84.93	1.325		430625	mg	**325**	mL					
product	(1H-imidazol-5-yl)(pyrrolidin-1-yl)methanone		165.19			294.6875	mg			1.78393	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	(1H-imidazol-5-yl)(pyrrolidin-1-yl)methanone		165.19			**217**	mg		1.313639	mmol	73.63734

total reaction mass	451672.40	mg
total reagents / reactants / cat. mass	1272.40	mg
total workup reagents mass		mg
total solvents (excl. water)	450400.00	mg
total water		mg
total waste	451455.40	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	2081.4	2081.4
solvent intensity	2075.6	2075.6
Sheldon E-factor	2080.4	2080.4
GSK Reaction Mass Efficiency	0.171	
Andraos Reaction Mass Efficiency	0.000	0.000
atom economy	0.782	
1 / stoichiom. factor (excess reagents)	0.296	
material recovery parameter	0.003	0.003
yield	0.736	

(1H-imidazole-4,5-diyl)bis(pyrrolidin-1-ylmethanone)



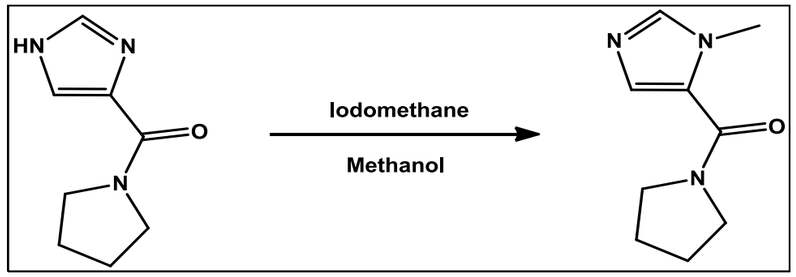
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	Dimethyl 1H-imidazole-4,5-dicarboxylate	3304-70-9	184.15			**500**	mg			2.715178	mmol	**1**	X	
reactant	Pyrrolidine	123-75-1	71.12	0.852		1022.4	mg	**1.2**	mL	14.3757	mmol	5.294571		
wu solvent	Methanol	67-56-1	32.04	0.791		23730	mg	**30**	mL					
wu solvent	Dichloromethane	75-09-2	84.93	1.325		490250	mg	**370**	mL					
product	(1H-imidazole-4,5-diyl)bis(pyrrolidin-1-ylmethanone)		262.31			712.2183	mg			2.715178	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	(1H-imidazole-4,5-diyl)bis(pyrrolidin-1-ylmethanone)		262.31			**338**	mg		1.288552	mmol	47.45736

total reaction mass	515502.40	mg
total reagents / reactants / cat. mass	1522.40	mg
total workup reagents mass		mg
total solvents (excl. water)	513980.00	mg
total water		mg
total waste	515164.40	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	1525.2	1525.2
solvent intensity	1520.7	1520.7
Sheldon E-factor	1524.2	1524.2
GSK Reaction Mass Efficiency	0.222	
Andraos Reaction Mass Efficiency	0.001	0.001
atom economy	0.804	
1 / stoichiom. factor (excess reagents)	0.582	
material recovery parameter	0.003	0.003
yield	0.475	

(1-methyl-1H-imidazol-5-yl)(pyrrolidin-1-yl)methanone



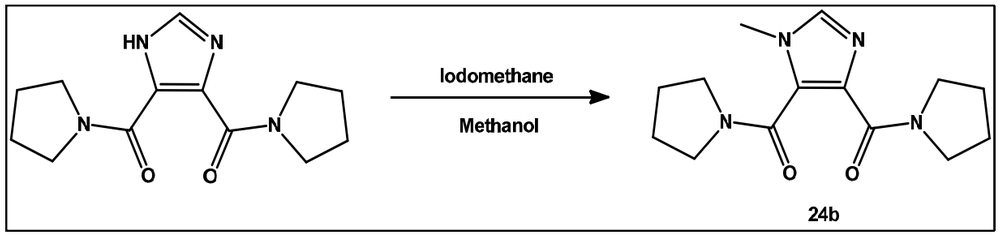
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	(1H-imidazol-5-yl)(pyrrolidin-1-yl)methanone		165.19			**150**	mg			0.908045	mmol	**1**	X	
reactant	Iodomethane	74-88-4	141.94	2.28		383.04	mg	**168**	µL	2.698605	mmol	2.971884		
solvent	Methanol	67-56-1	32.04	0.791		7830.9	mg	**9.9**	mL					
wu solvent	Methanol	67-56-1	32.04	0.791		15820	mg	**20**	mL					
wu solvent	Chloroform	67-66-3	119.38	1.492		566960	mg	**380**	mL					
product	(1-methyl-1H-imidazol-5-yl)(pyrrolidin-1-yl)methanone		179.22			162.7399	mg			0.908045	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	(1-methyl-1H-imidazol-5-yl)(pyrrolidin-1-yl)methanone		179.22			**104**	mg		0.580292	mmol	63.90567

total reaction mass	591143.94	mg
total reagents / reactants / cat. mass	533.04	mg
total workup reagents mass		mg
total solvents (excl. water)	590610.90	mg
total water		mg
total waste	591039.94	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	5684.1	5684.1
solvent intensity	5679.0	5679.0
Sheldon E-factor	5683.1	5683.1
GSK Reaction Mass Efficiency	0.195	
Andraos Reaction Mass Efficiency	0.000	0.000
atom economy	0.584	
1 / stoichiom. factor (excess reagents)	0.523	
material recovery parameter	0.001	0.001
yield	0.639	

1H-imidazole-1-methyl-(4,5-diyl)*bis* (pyrrolidin-1-ylmethanone)



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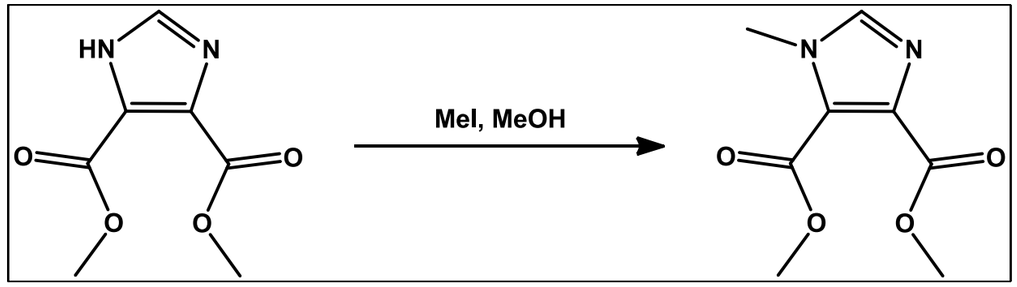
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	(1H-imidazole-4,5-diyl)bis(pyrrolidin-1-ylmethanone)		262.31			**250**	mg			0.953071	mmol	**1**	X	
reactant	Iodomethane	74-88-4	141.94	2.28		328.32	mg	**144**	µL	2.31309	mmol	2.426987		
solvent	Methanol	67-56-1	32.04	0.791		5.537	g	**7**	mL					
wu solvent	Dichloromethane	75-09-2	84.93	1.325		13.25	g	**10**	mL					
wu solvent	Water		18	1		15	g	**15**	mL					
product	1H-imidazole-1-methyl-(4,5-diyl)bis(pyrrolidin-1-ylmethanone)		276.33			263.3621	mg			0.953071	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	1H-imidazole-1-methyl-(4,5-diyl)bis(pyrrolidin-1-ylmethanone)		276.33			**220**	mg		0.79615	mmol	83.53519

total reaction mass	34365.32	mg
total reagents / reactants / cat. mass	578.32	mg
total workup reagents mass		mg
total solvents (excl. water)	18787.00	mg
total water	15000.00	mg
total waste	34145.32	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	88.0	156.2
solvent intensity	85.4	153.6
Sheldon E-factor	87.0	155.2
GSK Reaction Mass Efficiency	0.380	
Andraos Reaction Mass Efficiency	0.011	0.006
atom economy	0.684	
1 / stoichiom. factor (excess reagents)	0.666	
material recovery parameter	0.030	0.017
yield	0.835	

1*H*-Imidazole-4,5-dicarboxylic acid, 1-methyl-, 4,5-dimethyl ester



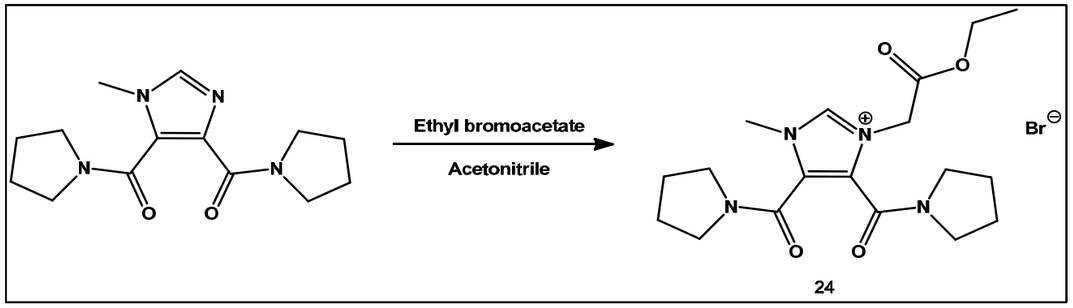
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	Dimethyl 1H-imidazole-4,5-dicarboxylate	3304-70-9	184.15			**300** mg		1.629107 mmol	**1**	X	
reactant	Iodomethane	74-88-4	141.94	2.28		0.42582 g	0.186763 mL	**3** mmol	1.8415		
solvent	Methanol	67-56-1	32.04	0.791		5.537 g	**7** mL				
wu solvent	Dichloromethane	75-09-2	84.93	1.325		13.25 g	**10** mL				
wu solvent	Water		18				**15** mL				
product	1H-Imidazole-4,5-dicarboxylic acid, 1-methyl-, 4,5-dimethyl ester	42545-22-2	198.18			322.8564 mg		1.629107 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	1H-Imidazole-4,5-dicarboxylic acid, 1-methyl-, 4,5-dimethyl ester	42545-22-2	198.18			**273** mg		1.377536 mmol	84.55773

total reaction mass	19512.82	mg
total reagents / reactants / cat. mass	725.82	mg
total workup reagents mass		mg
total solvents (excl. water)	18787.00	mg
total water		mg
total waste	19239.82	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	71.5	71.5
solvent intensity	68.8	68.8
Sheldon E-factor	70.5	70.5
GSK Reaction Mass Efficiency	0.376	
Andraos Reaction Mass Efficiency	0.014	0.014
atom economy	0.608	
1 / stoichiom. factor (excess reagents)	0.732	
material recovery parameter	0.037	0.037
yield	0.846	

3-(2-methoxyacetyl)-1-methyl-4,5-bis[(pyrrolidin-1-yl)carbonyl]-1H-imidazol-3-ium bromide



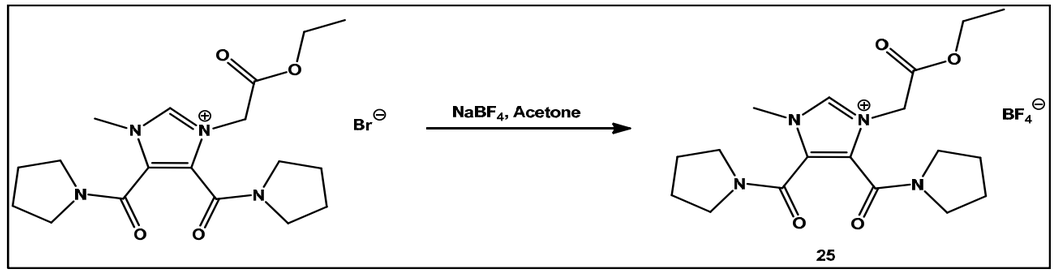
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	(1H-imidazole-4,5-diyl)bis(pyrrolidin-1-ylmethanone)		276.33			**200** mg		0.723772 mmol	**1**	X	
reactant	Ethyl bromoacetate	105-36-2	167	1.506		481.92 mg	**320** µL	2.885749 mmol	3.987094		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572 mg	**2** mL				
wu solvent	Diethyl ether	60-29-7	74.12	0.706		17650 mg	**25** mL				
product	3-(2-methoxyacetyl)-1-methyl-4,5-bis[(pyrrolidin-1-yl)carbonyl]-1H-imidazol-3-ium bromide		443.34			320.8772 mg		0.723772 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	3-(2-methoxyacetyl)-1-methyl-4,5-bis[(pyrrolidin-1-yl)carbonyl]-1H-imidazol-3-ium bromide		443.34			**282** mg		0.636081 mmol	87.88408

total reaction mass	19903.92	mg
total reagents / reactants / cat. mass	681.92	mg
total workup reagents mass		mg
total solvents (excl. water)	19222.00	mg
total water		mg
total waste	19621.92	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	70.6	70.6
solvent intensity	68.2	68.2
Sheldon E-factor	69.6	69.6
GSK Reaction Mass Efficiency	0.414	
Andraos Reaction Mass Efficiency	0.014	0.014
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.471	
material recovery parameter	0.034	0.034
yield	0.879	

3-(2-methoxyacetyl)-1-methyl-4,5-bis[(pyrrolidin-1-yl)carbonyl]-1H-imidazol-3-ium, tetrafluoroborate



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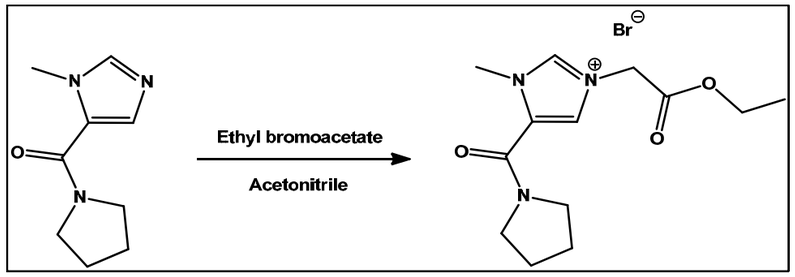
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	3-(2-methoxyacetyl)-1-methyl-4,5-bis[(pyrrolidin-1-yl)carbonyl]-1H-imidazol-3-ium, bromide		443.34			**250** mg		0.563901 mmol	**1**	X	
reactant	Sodium tetrafluoroborate	13755-29-8	109.79			**74.8** mg		0.681301 mmol	1.208191		
solvent	Acetone	67-64-1	58.08	0.791		7910 mg	**10** mL				
wu solvent	Acetone	67-64-1	58.08	0.791		7910 mg	**10** mL				
product	3-(2-methoxyacetyl)-1-methyl-4,5-bis[(pyrrolidin-1-yl)carbonyl]-1H-imidazol-3-ium, tetrafluoroborate		450.24			253.8909 mg		0.563901 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	3-(2-methoxyacetyl)-1-methyl-4,5-bis[(pyrrolidin-1-yl)carbonyl]-1H-imidazol-3-ium, tetrafluoroborate		450.24			**241** mg		0.53527 mmol	94.92265

total reaction mass	16144.80	mg
total reagents / reactants / cat. mass	324.80	mg
total workup reagents mass		mg
total solvents (excl. water)	15820.00	mg
total water		mg
total waste	15903.80	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	67.0	67.0
solvent intensity	65.6	65.6
Sheldon E-factor	66.0	66.0
GSK Reaction Mass Efficiency	0.742	
Andraos Reaction Mass Efficiency	0.015	0.015
atom economy	0.814	
1 / stoichiom. factor (excess reagents)	0.960	
material recovery parameter	0.020	0.020
yield	0.949	

3-(ethoxycarbonyl)-1-methyl-5-(pyrrolidine-1-carbonyl)-1H-imidazol-3-ium, bromide



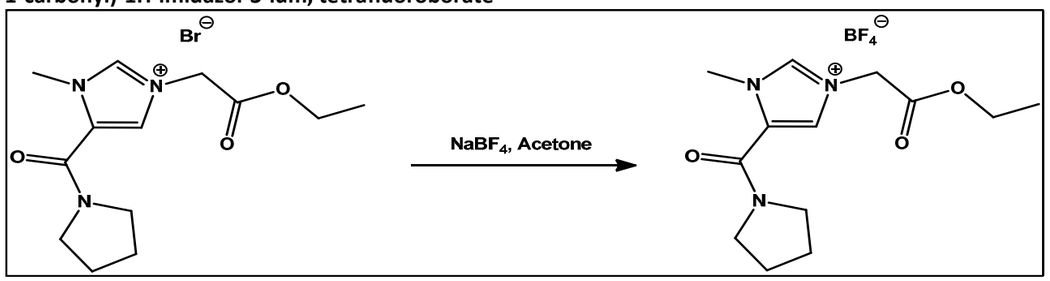
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	(1-methyl-1H-imidazol-5-yl)(pyrrolidin-1-yl)methanone		179.22			**100**	mg			0.557973	mmol	**1**	X	
reactant	Ethyl bromoacetate	105-36-2	167	1.506		371.982	mg	**247**	µL	2.227437	mmol	3.992013		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572	mg	**2**	mL					
wu solvent	Diethyl ether	60-29-7	74.12	0.706		21180	mg	**30**	mL					
product	3-(ethoxycarbonyl)-1-methyl-5-(pyrrolidine-1-carbonyl)-1H-imidazol-3-ium, bromide		346.22			193.1816	mg			0.557973	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	3-(ethoxycarbonyl)-1-methyl-5-(pyrrolidine-1-carbonyl)-1H-imidazol-3-ium, bromide		346.22			**133**	mg		0.384149	mmol	68.84715

total reaction mass	23223.98	mg
total reagents / reactants / cat. mass	471.98	mg
total workup reagents mass		mg
total solvents (excl. water)	22752.00	mg
total water		mg
total waste	23090.98	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	174.6	174.6
solvent intensity	171.1	171.1
Sheldon E-factor	173.6	173.6
GSK Reaction Mass Efficiency	0.282	
Andraos Reaction Mass Efficiency	0.006	0.006
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.409	
material recovery parameter	0.020	0.020
yield	0.688	

3-(ethoxycarbonyl)-1-methyl-5-(pyrrolidine-1-carbonyl)-1H-imidazol-3-ium, tetrafluoroborate



Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	3-(ethoxycarbonyl)-1-methyl-5-(pyrrolidine-1-carbonyl)-1H-imidazol-3-ium, bromide (18)		346.22			**100**	mg			0.288834	mmol	**1**	X	
reactant	Sodium tetrafluoroborate	13755-29-8	109.79			**70**	mg			0.637581	mmol	2.207432		
solvent	Acetone	67-64-1	58.08	0.791		7910	mg	**10**	mL					
wu solvent	Acetone	67-64-1	58.08	0.791		7910	mg	**10**	mL					
product	3-(ethoxycarbonyl)-1-methyl-5-(pyrrolidine-1-carbonyl)-1H-imidazol-3-ium, tetrafluoroborate (19)		353.12			101.993	mg			0.288834	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	3-(ethoxycarbonyl)-1-methyl-5-(pyrrolidine-1-carbonyl)-1H-imidazol-3-ium, tetrafluoroborate (19)		353.12			**100**	mg		0.28319	mmol	98.04599

total reaction mass	15990.00	mg
total reagents / reactants / cat. mass	170.00	mg
total workup reagents mass		mg
total solvents (excl. water)	15820.00	mg
total water		mg
total waste	15890.00	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	159.9	159.9
solvent intensity	158.2	158.2
Sheldon E-factor	158.9	158.9
GSK Reaction Mass Efficiency	0.588	
Andraos Reaction Mass Efficiency	0.006	0.006
atom economy	0.774	
1 / stoichiom. factor (excess reagents)	0.775	
material recovery parameter	0.011	0.011
yield	0.980	

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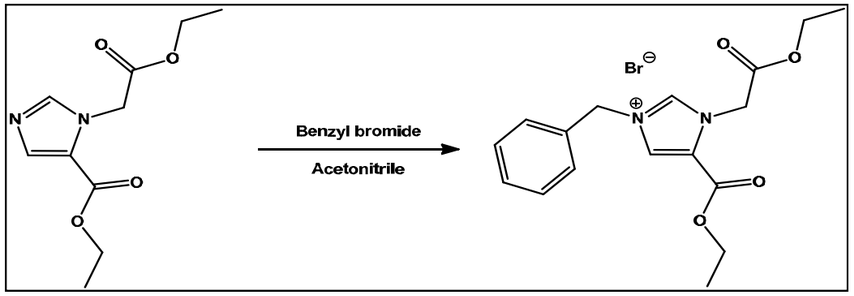


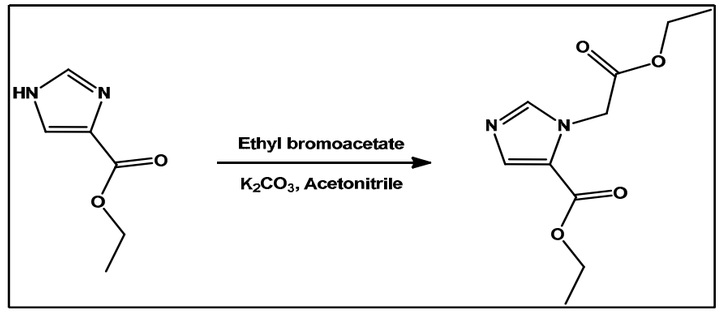
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	Diethyl 1H-imidazole-1,5-dicarboxylate		226.23			**150**	mg			0.663042	mmol	**1**	X	
reactant	Benzyl bromide	100-39-0	171.03	1.438		461.598	mg	**321**	µL	2.69893	mmol	4.070526		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572	mg	**2**	mL					
wu solvent	Diethyl ether	60-29-7	74.12	0.706		14120	mg	**20**	mL					
product	3-benzyl-1,5-bis(ethoxycarbonyl)-1H-imidazol-3-ium, bromide		397.26			263.4001	mg			0.663042	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	3-benzyl-1,5-bis(ethoxycarbonyl)-1H-imidazol-3-ium, bromide		397.26			**174**	mg		0.438	mmol	66.05921

total reaction mass	16303.60	mg
total reagents / reactants / cat. mass	611.60	mg
total workup reagents mass		mg
total solvents (excl. water)	15692.00	mg
total water		mg
total waste	16129.60	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	93.7	93.7
solvent intensity	90.2	90.2
Sheldon E-factor	92.7	92.7
GSK Reaction Mass Efficiency	0.285	
Andraos Reaction Mass Efficiency	0.011	0.011
atom economy	1.000	
1 / stoichiom. factor (excess reagents)	0.431	
material recovery parameter	0.038	0.038
yield	0.661	

Diethyl 1H-imidazole-1,5-dicarboxylate



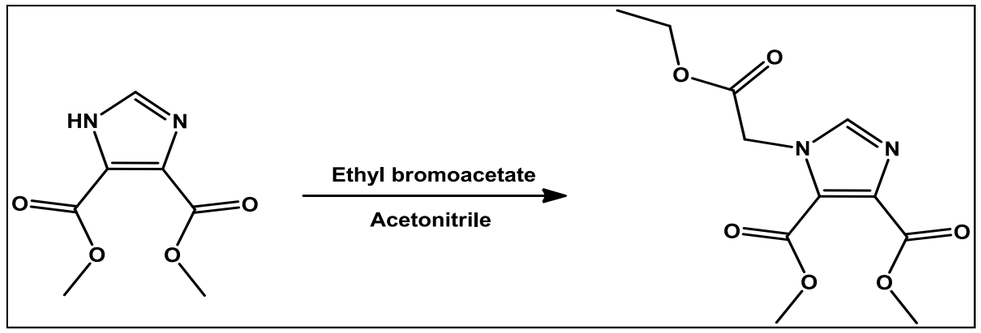
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	Ethyl 1H-imidazole-4-carboxylate	23785-21-9	140.14			**150** mg		1.070358 mmol	**1**	X	
reactant	Ethyl bromoacetate	105-36-2	167	1.506		323.79 mg	**215** µL	1.938862 mmol	1.811414		
reagent	Potassium carbonate	584-08-7	138.204			**145** mg		1.049174 mmol	0.980208		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572 mg	**2** mL				
wu solvent	Dichloromethane	75-09-2	84.93	1.325		26500 mg	**20** mL				
wu solvent	Water		18	1		15000 mg	**15** mL				
wu solvent	Diethyl ether	60-29-7	74.12	0.706		14120 mg	**20** mL				
wu solvent	Methanol	67-56-1	32.04	0.791		23730 mg	**30** mL				
wu solvent	Chloroform	67-66-3	119.38	1.492		402840 mg	**270** mL				
product	Diethyl 1H-imidazole-1,5-dicarboxylate		226.23			242.1471 mg		1.070358 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	Diethyl 1H-imidazole-1,5-dicarboxylate		226.23			**161** mg		0.711665 mmol	66.4885

total reaction mass	484380.79	mg
total reagents / reactants / cat. mass	618.79	mg
total workup reagents mass		mg
total solvents (excl. water)	468762.00	mg
total water	15000.00	mg
total waste	484219.79	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	2915.4	3008.6
solvent intensity	2911.6	3004.7
Sheldon E-factor	2914.4	3007.6
GSK Reaction Mass Efficiency	0.260	
Andraos Reaction Mass Efficiency	0.000	0.000
atom economy	0.508	
1 / stoichiom. factor (excess reagents)	0.770	
material recovery parameter	0.001	0.001
yield	0.665	

Dimethyl 1-(2-ethoxy-2-oxoethyl)-1H-imidazole-4,5-dicarboxylate



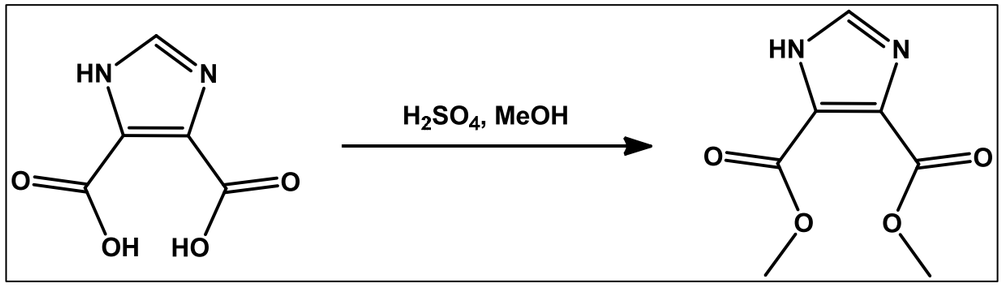
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	Dimethyl 1H-imidazole-4,5-dicarboxylate	3304-70-9	184.15			**500** mg		2.715178 mmol	**1**	X	
reactant	Ethyl bromoacetate	105-36-2	167	1.506		906.8694 mg	0.602171 mL	5.430356 mmol	**2**		
reagent	Potassium carbonate	584-08-7	138.204			375.2484 mg		2.715178 mmol	**1**		
solvent	Acetonitrile	75-05-8	41.05	0.786		1572 mg	**2** mL				
wu solvent	Dichloromethane	75-09-2	84.93	1.325		13250 mg	**10** mL				
wu solvent	Water		18				**20** mL				
product	Dimethyl 1-(2-ethoxy-2-oxoethyl)-1H-imidazole-4,5-dicarboxylate		270.24			733.7497 mg		2.715178 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	Dimethyl 1-(2-ethoxy-2-oxoethyl)-1H-imidazole-4,5-dicarboxylate		270.24			**597** mg		2.209147 mmol	81.3629

total reaction mass	16604.12	mg
total reagents / reactants / cat. mass	1782.12	mg
total workup reagents mass		mg
total solvents (excl. water)	14822.00	mg
total water		mg
total waste	16007.12	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	27.8	27.8
solvent intensity	24.8	24.8
Sheldon E-factor	26.8	26.8
GSK Reaction Mass Efficiency	0.335	
Andraos Reaction Mass Efficiency	0.036	0.036
atom economy	0.552	
1 / stoichiom. factor (excess reagents)	0.746	
material recovery parameter	0.107	0.107
yield	0.814	

Dimethyl 1*H* -imidazole-4,5-dicarboxylate



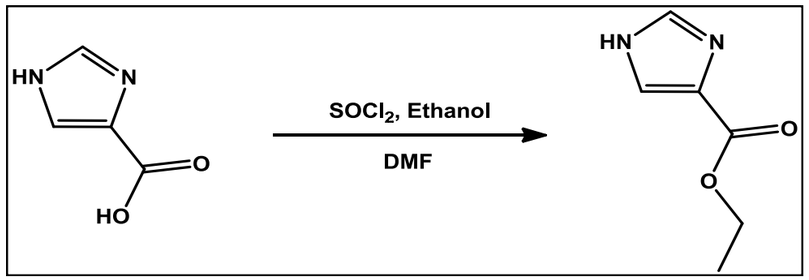
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	4,5-Imidazoledicarboxylic acid	570-22-9	156.1			**500** mg		3.203075 mmol	**1**	X	
reactant	Sulfuric acid	7664-93-9	98.0778			628.3011 mg		6.40615 mmol	**2**		
solvent	Methanol	67-56-1	32.04	0.791		7910 mg	**10** mL				
wu solvent	Water		18				**20** mL				
wu solvent	Ethyl acetate	141-78-6	88.11	0.902		18040 mg	**20** mL				
product	Dimethyl 1H-imidazole-4,5-dicarboxylate	3304-70-9	184.15			589.8463 mg		3.203075 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	Dimethyl 1H-imidazole-4,5-dicarboxylate	3304-70-9	184.15			**456** mg		2.476242 mmol	77.30828

total reaction mass	27078.30	mg
total reagents / reactants / cat. mass	1128.30	mg
total workup reagents mass		mg
total solvents (excl. water)	25950.00	mg
total water		mg
total waste	26622.30	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	59.4	59.4
solvent intensity	56.9	56.9
Sheldon E-factor	58.4	58.4
GSK Reaction Mass Efficiency	0.404	
Andraos Reaction Mass Efficiency	0.017	0.017
atom economy	0.523	
1 / stoichiom. factor (excess reagents)	1.000	
material recovery parameter	0.042	0.042
yield	0.773	

Ethyl 1H-imidazole-4-carboxylate



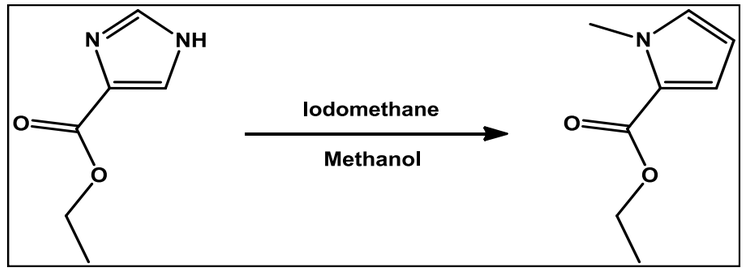
Type	Name	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	eq.	Pivot reagent	recycled
reactant	4-Imidazolecarboxylic acid	1072-84-0	112.09			**250** mg		2.230351 mmol	**1**	X	
reagent	Thionyl Chloride	7719-09-7	118.971	1.373		803.205 mg	**585** µL	6.751267 mmol	3.026998		
reactant	Ethanol	64-17-5	46.07	0.816		4080 mg	**5** mL	88.56089 mmol	39.70716		
catalyst	N,N-Dimethylformamide (DMF)	68-12-2	73.09	0.944		18.88 mg	**20** µL	0.258312 mmol	0.115817		
wu reagent	Sodium hydroxide in water	1310-73-2	40	1.1	**2** M	3300 mg	**3** mL	6 mmol	2.69016		
wu solvent	Ethyl acetate	141-78-6	88.11	0.902		18040 mg	**20** mL				
wu solvent	Water		18	1		30000 mg	**30** mL				
product	Ethyl 1H-imidazole-4-carboxylate	23785-21-9	140.14			312.5613 mg		2.230351 mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass	volume	moles	yield(%)
Output	Ethyl 1H-imidazole-4-carboxylate	23785-21-9	140.14			**155** mg		1.106037 mmol	49.59027

total reaction mass	56492.09	mg
total reagents / reactants / cat. mass	5152.09	mg
total workup reagents mass	240.00	mg
total solvents (excl. water)	18040.00	mg
total water	33060.00	mg
total waste	56337.09	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	151.2	364.5
solvent intensity	116.4	329.7
Sheldon E-factor	150.2	363.5
GSK Reaction Mass Efficiency	0.030	
Andraos Reaction Mass Efficiency	0.007	0.003
atom economy	0.531	
1 / stoichiom. factor (excess reagents)	0.115	
material recovery parameter	0.219	0.091
yield	0.496	

Ethyl 1-methyl-1H-imidazole-5-carboxylate



Type	Name	[CAS]	M.W.	d	wt% or conc.	mass		volume		moles		eq.	Pivot reagent	recycled
reactant	Ethyl 1H-imidazole-4-carboxylate	23785-21-9	140.14			**120**	mg			0.856287	mmol	**1**	X	
reactant	Iodomethane	74-88-4	141.94	2.28		360.24	mg	**158**	µL	2.537974	mmol	2.96393		
solvent	Methanol	67-56-1	32.04	0.791		7830.9	mg	**9.9**	mL					
wu solvent	Methanol	67-56-1	32.04	0.791		3559.5	mg	**4.5**	mL					
wu solvent	Chloroform	67-66-3	119.38	1.492		440886	mg	**295.5**	mL					
product	Ethyl 1-methyl-1H-imidazole-5-carboxylate		154.17			132.0137	mg			0.856287	mmol	**1**		

	product	[CAS]	M.W.	d	wt% or conc.	mass		volume	moles		yield(%)
Output	Ethyl 1-methyl-1H-imidazole-5-carboxylate		154.17			**87**	mg		0.564312	mmol	65.90225

total reaction mass	452756.64	mg
total reagents / reactants / cat. mass	480.24	mg
total workup reagents mass		mg
total solvents (excl. water)	452276.40	mg
total water		mg
total waste	452669.64	mg
total raw material cost		

Metrics	excl. water	incl. water
mass intensity	5204.1	5204.1
solvent intensity	5198.6	5198.6
Sheldon E-factor	5203.1	5203.1
GSK Reaction Mass Efficiency	0.181	
Andraos Reaction Mass Efficiency	0.000	0.000
atom economy	0.547	
1 / stoichiom. factor (excess reagents)	0.503	
material recovery parameter	0.001	0.001
yield	0.659	