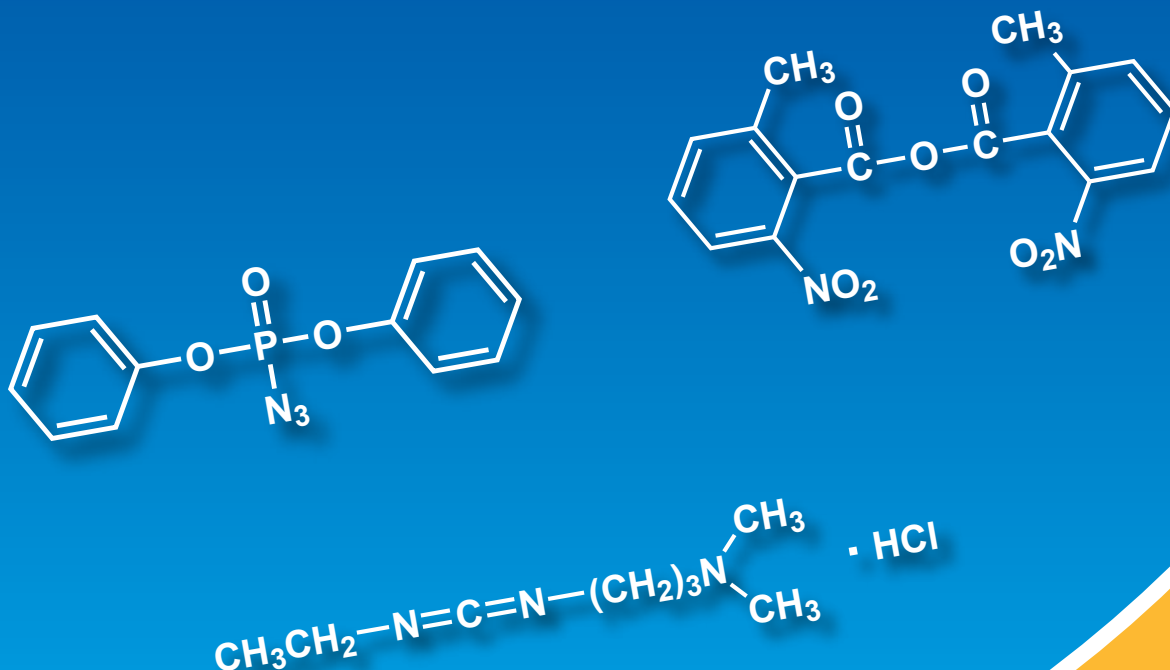


Condensing Agents



Active Esters, Additives

Carbodiimides

Carbonyldiimidazoles

Phosgene Derivatives

Phosphonium Salts, Uronium Salts, Formamidinium Salts

Condensation Organocatalysts

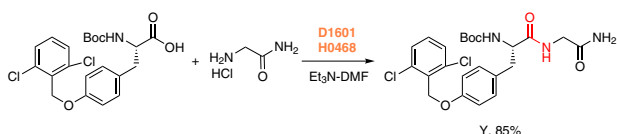
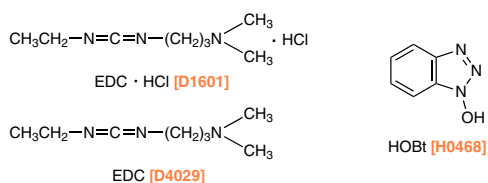
Others

Condensing Agents

Esterification and amidation have been regarded as one of the most basic reactions in organic chemistry. Among them, esterification under an acidic conditions has been known for more than 100 years,¹⁾ the conditions of which being dependent on Le Chatelier's principle. To drive the reaction to completion, water is removed as the reaction progresses, usually via a Dean-Stark trap or a dehydrating reagent. However, this method is often ineffective when applied to thermally unstable materials. Milder conditions and condensing agents have been developed to surmount this problem. For amidation, the activation of a carboxylic acid is key with the amide bond formed through the nucleophilic addition of amines to an activated carboxylic acid. However, if the reactivity of the activated carboxy group is too high, epimerization at α -position can occur. Reagents that do not impart epimerization have since been developed to avoid this potential issue. With significant research into esterification and amidation having been conducted for many years, many condensing agents which have both high reactivity and control of epimerization are readily available. Furthermore, many reviews of these methods and reagents have been reported.²⁾ Applications and references for these varied methods are available on each of TCI's product pages.

● EDC + HOBt

Since the first report of a condensation reaction utilizing *N,N'*-dicyclohexylcarbodiimide (DCC) [D0436] in 1950's,³⁾ many carbodiimide reagents have been developed. Among them, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC) [D1601], and [D4029] are favored as the byproducts are easily removed by partition. EDC can be used together with 1-hydroxybenzotriazole (HOBt)⁴⁾ [H0468] which is one of the most used conditions for condensations.

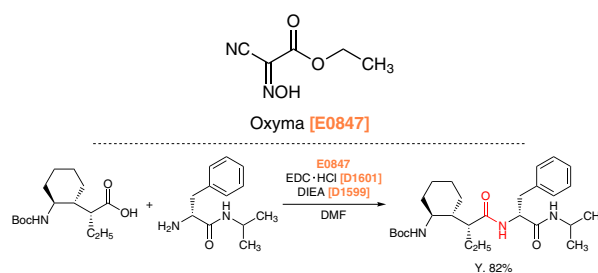


● PS-DCC

It often becomes troublesome to remove byproducts when applying to condensing agents. Removal of byproducts from condensation reactions is one of the more troublesome aspects of the reactions. Dicyclohexylurea, a byproduct from DCC, is notoriously difficult to remove. However, polymer supported PS-DCC [C2141] has the advantage of easily removal by simple filtration and is often employed in the total synthesis of natural products.⁵⁾

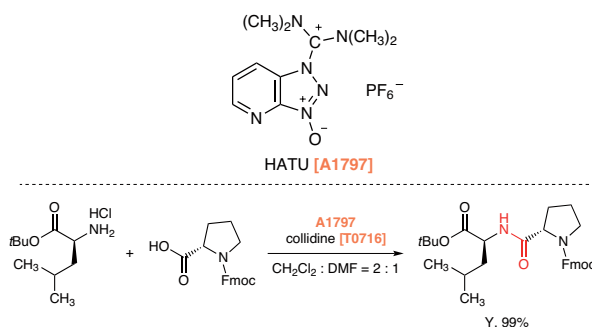
● Oxyma

1,2,3-Triazol derivatives are utilized in the synthesis of active esters and are frequently used with carbodiimides, but are potentially explosive if dried. The reagent oxyma [E0847] bears the same reactivity to that of triazoles with a minimized explosion risk.⁶⁻⁸⁾



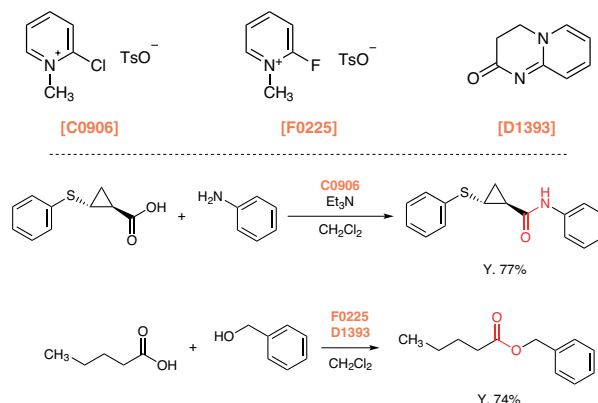
● HATU

Uronium salts represented by HATU [A1797] have been known as condensing agents with both high reactivity and suppressed epimerization.^{9,10)}



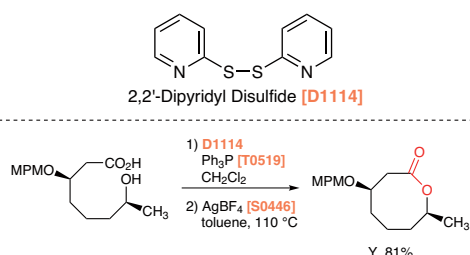
● Mukaiyama Condensing Agents

Mukaiyama *et al.* reported 2-chloro-1-methylpyridinium *p*-toluenesulfonate [C0906] and 2-fluoro-1-methylpyridinium *p*-toluenesulfonate [F0225] which were utilized in condensation reactions.^{11,12)} In this reaction, either conventional organic bases such as triethylamine or acid captor H [D1393] can be used as an acid sequesterant.



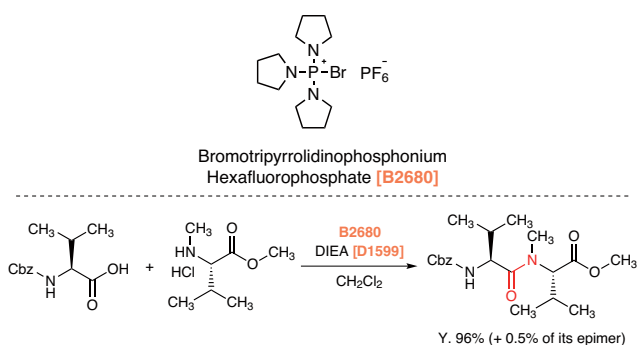
Corey-Nicolaou macrolactonization

2,2'-Dipyridyl disulfide [D1114] is useful for the lactonization and is conducted under mild conditions. Corey and Nicolaou have reported this method in several total syntheses making use of this reagent.^{13,14}



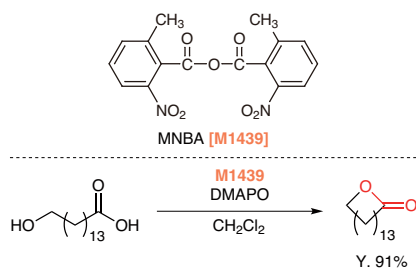
Bromotripyrrolidinophosphonium Hexafluorophosphate

Phosphonium salts such as bromotripyrrolidinophosphonium hexafluorophosphate [B2680] also have utility in condensation reactions.¹⁵ When using these salts, additives like HOBT are not necessary. Furthermore, the rate of epimerization is low and N-methyl amino acid derivatives, which are difficult to impart reactivity on, are applicable. In this way, these salts are anticipated to be used more frequently in further research.



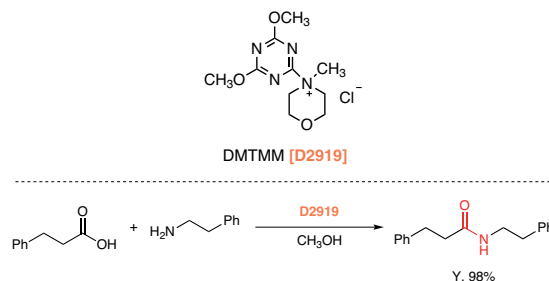
Shiina Macrolactonization

Shiina *et al.* have reported that 2-methyl-6-nitrobenzoic anhydride (MNBA) [M1439] affords esters or amides in high yields from mostly equimolar carboxylic acid and alcohols or amines under basic conditions.^{16,17} This method is also utilized in macrolactonizations.



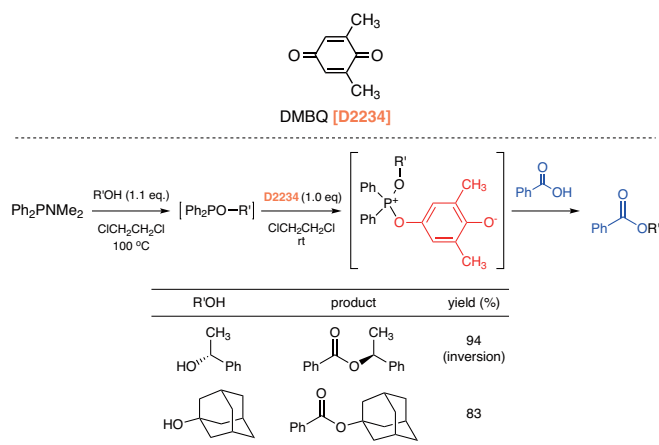
DMTMM

Kunishima *et al.* have reported the utility of 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMTMM) [D2919] as a condensing reagent.^{18,19} This reagent has some advantages: amidation proceeds selectively even in alcohol solvent and the byproducts are easy to remove. D2919 can be used as a powerful condensing reagent.²⁰



Mukaiyama Redox Condensation

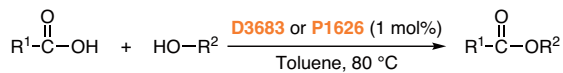
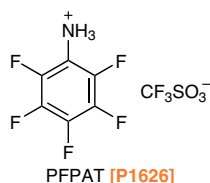
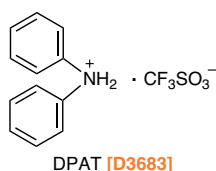
Mukaiyama *et al.* have reported a redox condensation reaction using dihydroquinone derivatives such as 2,6-dimethyl-1,4-benzoquinone (DMBQ) [D2234].^{21,22} In this reaction, tertiary alcohols with high steric hindrance can react and afford products with stereoinversion. Furthermore, this reaction is even applicable to 1-adamantanol, the structure of which being highly resistant to stereoinversion.



Organocatalysts for Condensation Reactions

DPAT [D3683] is a useful esterification catalyst developed by Tanabe *et al.* affording esters in high yields from equimolar amounts of carboxylic acids and alcohols under mild reaction condition.^{23,24} In this case, desired esters can be obtained by simple operation without addition of dehydrating agent and azeotropic water removal. There is also a report using fluorosolvent, in which DPAT is useful for the substrate with high steric hindrance.²⁵

PFPAT [P1626] shows higher activity than DPAT and it can be applied widely to esterification and lactonization.²⁴ Furthermore, PFPAT can be removed after work-up; washing with NaOH aqueous solution removed CF₃SO₃H, followed by distillation of C₆F₅NH₂.

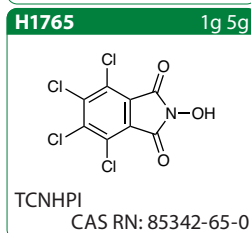
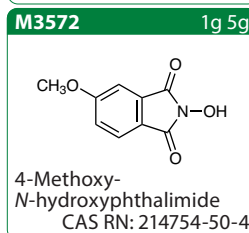
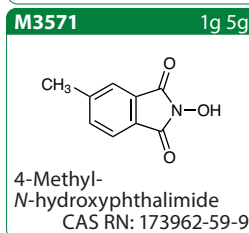
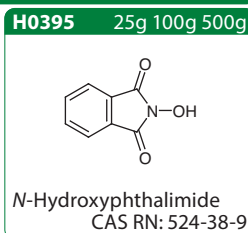
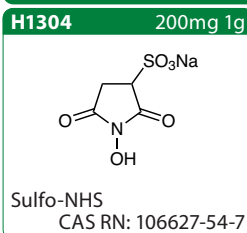
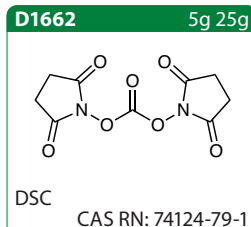
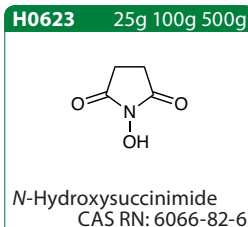
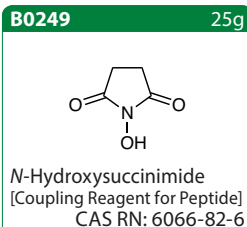


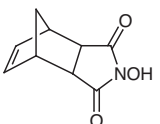
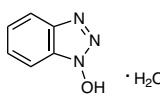
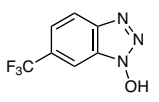
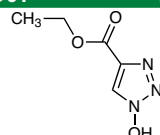
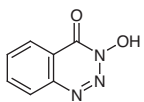
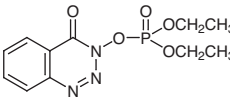
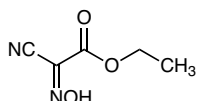
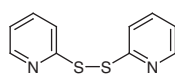
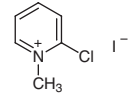
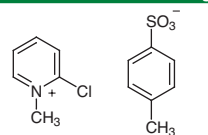
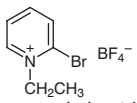
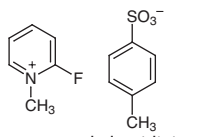

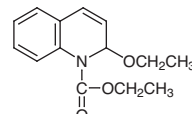
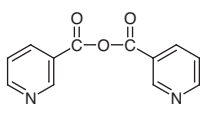
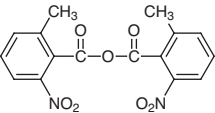
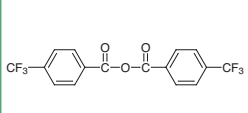
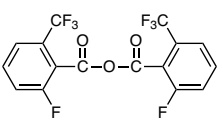
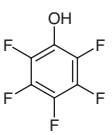
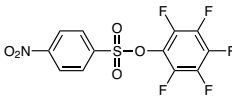
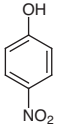
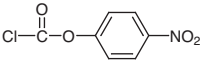
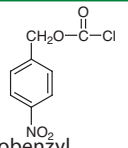
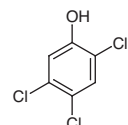
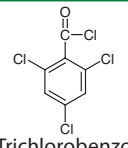
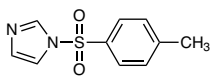
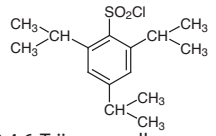
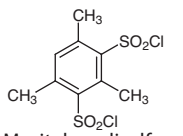
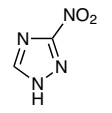
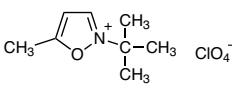
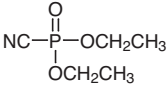
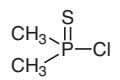
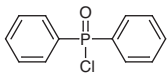
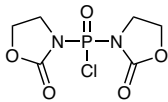
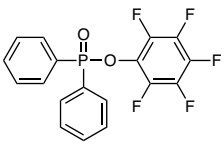
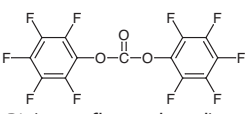
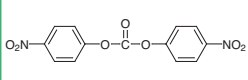
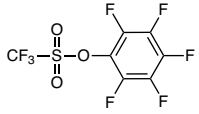
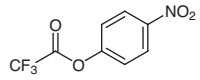
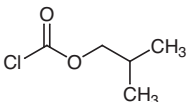
R ¹	R ²	catalyst	time (h)	Y. (%)
PhCH ₂ CH ₂ —	CH ₂ =CH(CH ₂) ₈ —	D3683	8	96
PhCH ₂ CH ₂ —	CH ₂ =CH(CH ₂) ₈ —	P1626	3	96
^t Bu—	CH ₃ (CH ₂) ₇ —	D3683	24	92
^t Bu—	CH ₃ (CH ₂) ₇ —	P1626	6	90

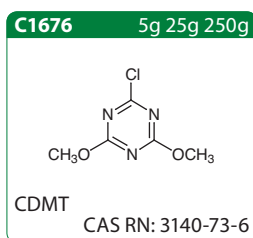
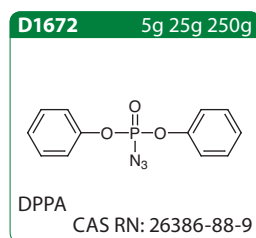
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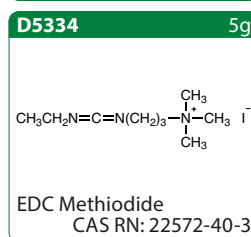
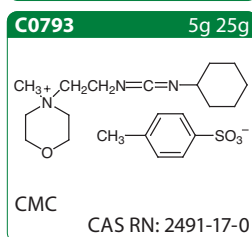
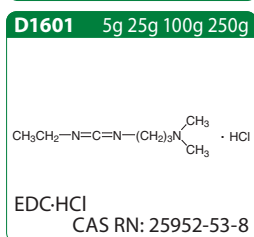
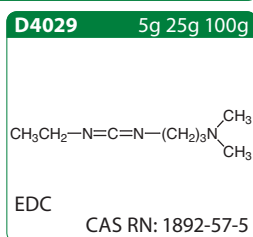
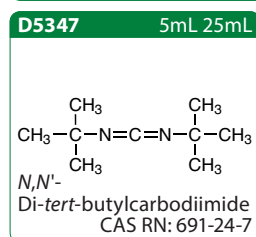
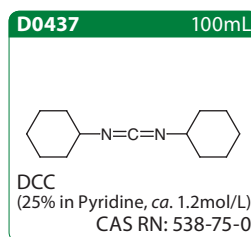
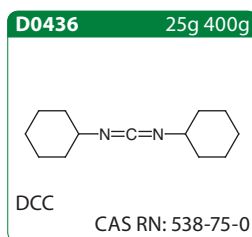
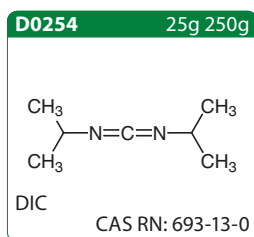
Active Esters, Additives



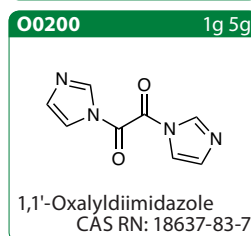
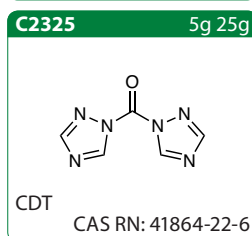
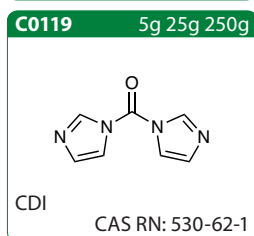
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D3262 5g  DEPBT CAS RN: 165534-43-0	E0847 25g 100g  Oxyma CAS RN: 3849-21-6	D1114 5g 25g 250g  2,2'-Dithiodipyridine CAS RN: 2127-03-9	C0903 25g  2-Chloro-1-methylpyridinium iodide CAS RN: 14338-32-0	C0906 25g  2-Chloro-1-methylpyridinium <i>p</i> -Toluenesulfonate CAS RN: 7403-46-5
B1036 5g 25g  2-Bromo-1-ethylpyridinium Tetrafluoroborate CAS RN: 878-23-9	F0225 5g 25g  2-Fluoro-1-methylpyridinium <i>p</i> -Toluenesulfonate CAS RN: 58086-67-2	H0672 25g  2-Hydroxypyridine <i>N</i> -Oxide CAS RN: 13161-30-3	E0363 25g  EEDQ CAS RN: 16357-59-8	P1768 1g 5g  Nicotinic Anhydride CAS RN: 16837-38-0
M1439 1g 5g 25g  MNBA CAS RN: 434935-69-0	T1593 10g  TFBA CAS RN: 25753-16-6	F1184 1g  FTFBA CAS RN: 2118332-08-2	P0919 10g 25g  Pentafluorophenol CAS RN: 771-61-9	P2231 1g 5g  Pentafluorophenyl 4-Nitrobenzenesulfonate CAS RN: 244633-31-6
N0220 5g 25g 100g 500g  4-Nitrophenol CAS RN: 100-02-7	C1400 25g 100g 250g  4-Nitrophenyl Chloroformate CAS RN: 7693-46-1	C1077 25g  4-Nitrobenzyl Chloroformate CAS RN: 4457-32-3	T0389 25g 500g  2,4,5-Trichlorophenol CAS RN: 95-95-4	T1413 5g 25g  2,4,6-Trichlorobenzoyl Chloride CAS RN: 4136-95-2
T1985 5g 25g  1-Tosylimidazole CAS RN: 2232-08-8	T0459 25g 100g 500g  2,4,6-Triisopropylbenzenesulfonyl Chloride CAS RN: 6553-96-4	M1186 5g 25g  2,4-Mesitylenedisulfonyl Dichloride CAS RN: 68985-08-0	N0477 1g 5g  3-Nitro-1,2,4-triazole CAS RN: 24807-55-4	B0832 1g 5g  Woodward's Reagent L CAS RN: 10513-45-8
C1242 5g 25g  Diethyl Cyanophosphonate CAS RN: 2942-58-7	D2159 1g 5g  Dimethylthiophosphinoyl Chloride CAS RN: 993-12-4	C1415 5g 10g 25g  Diphenylphosphinic Chloride CAS RN: 1499-21-4	B1213 5g 25g  BOP-Cl CAS RN: 68641-49-6	P2726 1g 5g  FDPP CAS RN: 138687-69-1
B3604 5g  Bis(pentafluorophenyl) Carbonate CAS RN: 59483-84-0	C1481 5g 25g  Bis(4-nitrophenyl) Carbonate CAS RN: 5070-13-3	P2188 200mg 1g  Pentafluorophenyl Triflate CAS RN: 60129-85-3	T0681 5g 25g  4-Nitrophenyl Trifluoroacetate CAS RN: 658-78-6	C0178 25g 100g 500g  IBCF CAS RN: 543-27-1



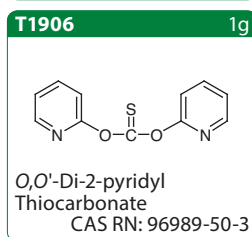
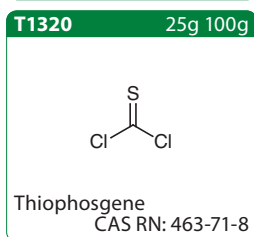
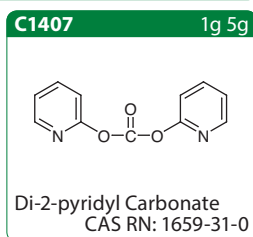
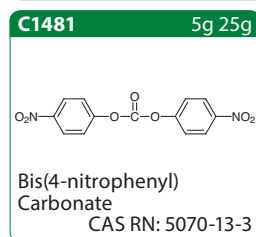
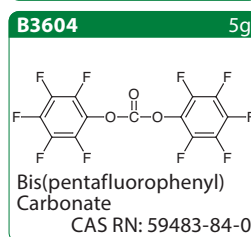
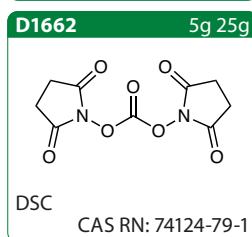
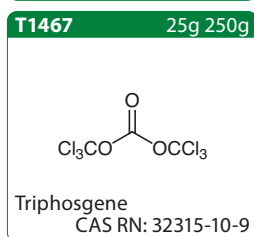
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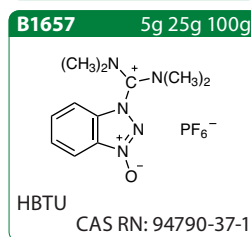
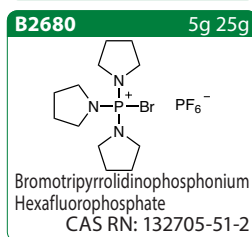
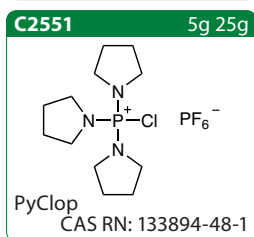
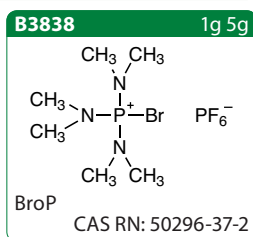
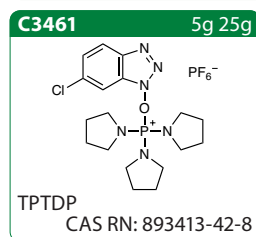
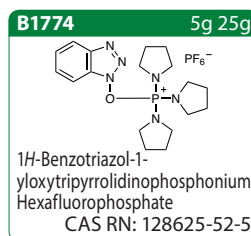
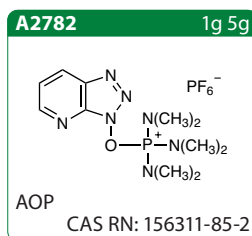
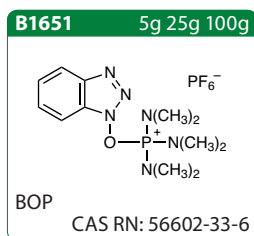
Carbonyldiimidazoles



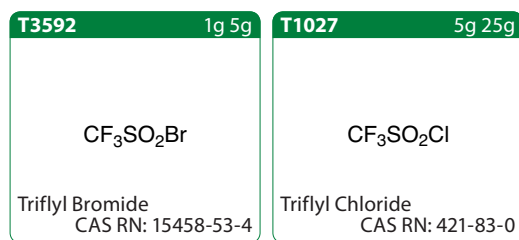
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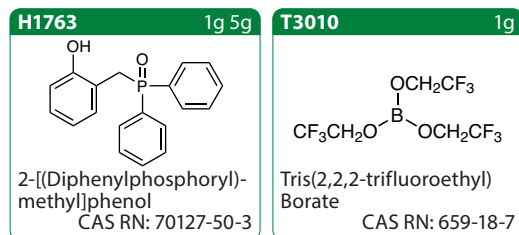
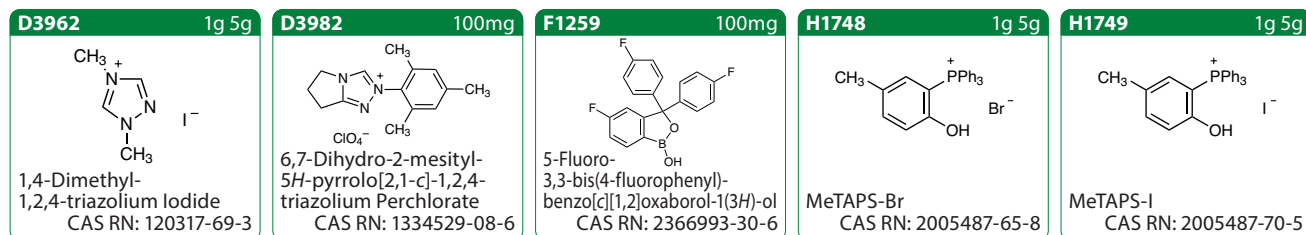
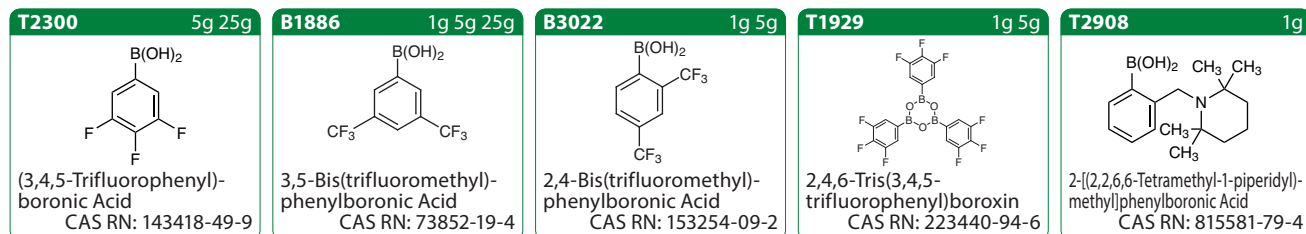
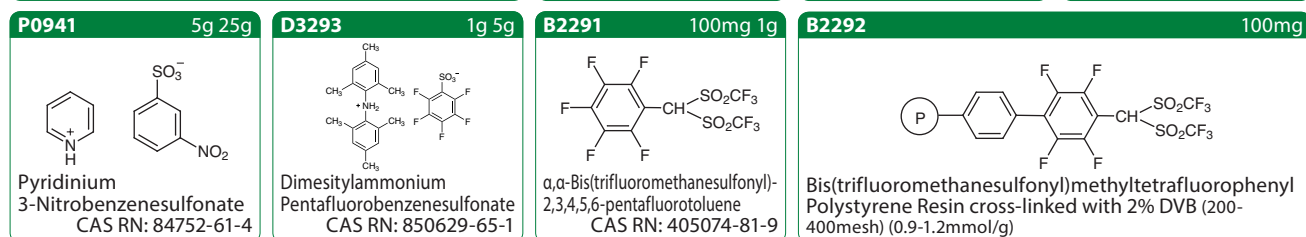
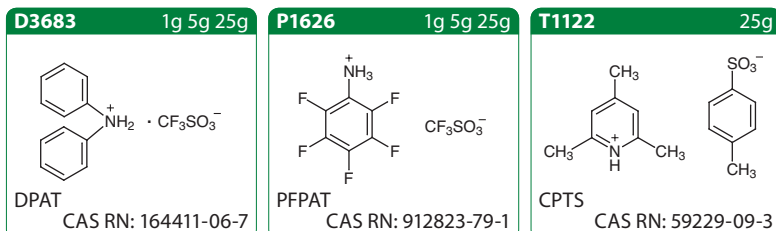
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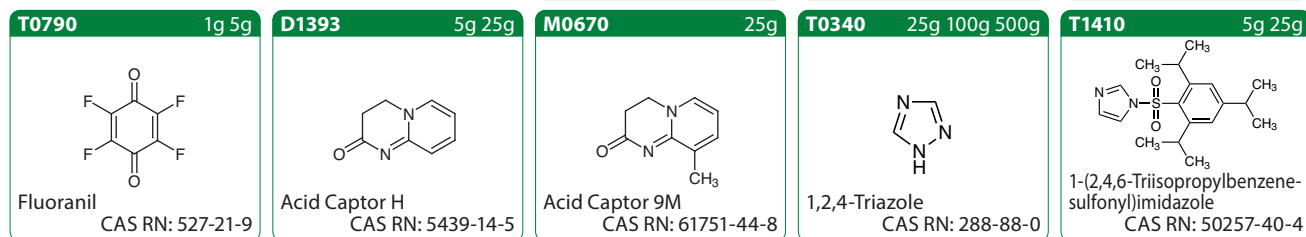
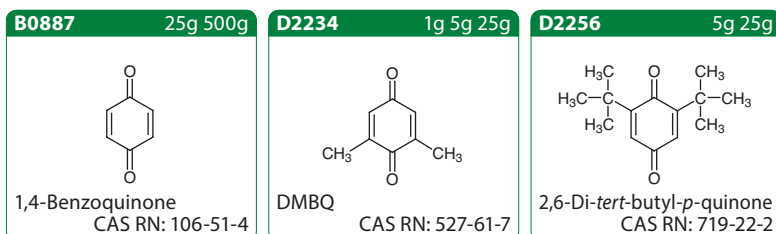
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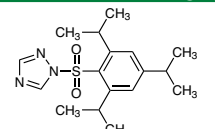
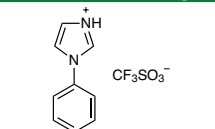
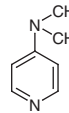
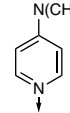
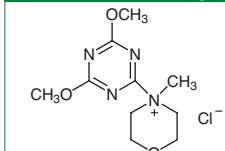
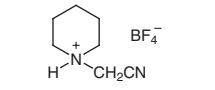
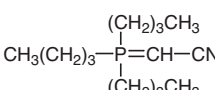


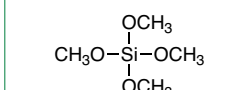
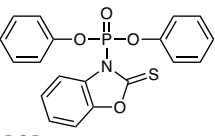
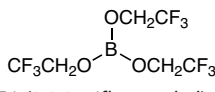


Condensation Organocatalysts



Others



<p>T2951 1g 5g</p>  <p>1-(2,4,6-Trisopropylbenzenesulfonyl)-1,2,4-triazole CAS RN: 54230-60-3</p>	<p>P2822 5g 25g</p>  <p>1-Phenyl-1H-imidazol-3-ium Triflate CAS RN: 361447-81-6</p>	<p>D1450 25g 100g 500g</p>  <p>DMAP CAS RN: 1122-58-3</p>	<p>D3220 1g 5g</p>  <p>DMAPO CAS RN: 1005-31-8</p>	<p>D2919 5g 25g</p>  <p>DMTMM CAS RN: 3945-69-5</p>
<p>C2421 5g</p>  <p>1-(Cyanomethyl)piperidinium Tetrafluoroborate CAS RN: 434937-12-9</p>	<p>C1500 1g 5g 25g</p>  <p>Tsunoda Reagent CAS RN: 157141-27-0</p>	<p>C0597 25g 100g 500g</p>  <p>Chlorodiphenylphosphine CAS RN: 1079-66-9</p>	<p>I0865 1g</p>  <p>Iodosodilactone CAS RN: 2902-68-3</p>	<p>T0588 25g 100g 500g</p>  <p>TMOS CAS RN: 681-84-5</p>
<p>D2038 5g 25g</p>  <p>DBOP CAS RN: 111160-56-6</p>	<p>T3010 1g</p>  <p>Tris(2,2,2-trifluoroethyl) Borate CAS RN: 659-18-7</p>	<p>R0274 10each</p> <p>Reagents for Condensation Reactions (EDCI-HCl, HOBt-H₂O) (HPMC encapsulated)</p>		

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