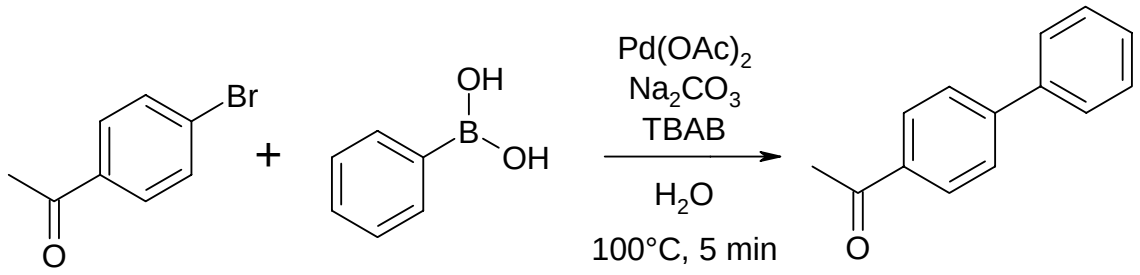
Biotage Summer Program at the University of Richmond - Reactions

1a. Suzuki



MW = 196.25 g/mol

Chemical name	MW (g/mol)	Amount needed (mmol)	Theoretical Weight/Volume	Real Weight/Volume
4-Br-acetophenone	199.05	1.0	199 mg	
Phenylboronic acid	121.93	1.0	122 mg	
Palladium acetate	224.49	0.004	1 mg	
Sodium carbonate	105.99	3.0	318 mg	
Tetrabutylammonium bromide (TBAB)	322.38	1.0	322 mg	
Water			2 ml	

Weigh out all chemicals into a 2-5 ml reaction vial. Add water and a magnetic stir bar. Heat as described using the Initiator, the Absorption level should be set to "High" and Fixed Hold Time should be used. In order to analyze the reaction mixture, you need to extract it (e g with dichloromethane) and take an analysis sample from the organic phase.

Observations:

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Name of analysis sample:

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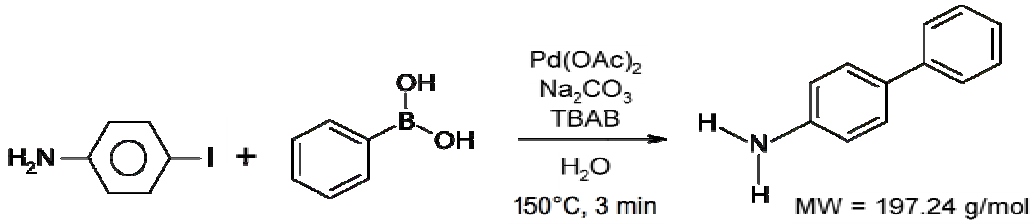
Leadbeater, N. E. and Marco, M. *Journal of Organic Chemistry* **2003**; *68*(3); 888-892

1b. Suzuki



Chemical name	MW (g/mol)	Amount needed (mmol)	Teoretical Weight/Volume	Real Weight/Volume
4-Iodoaniline	219	1.0	219 mg	
Phenylboronic acid	121.93	1.0	122 mg	
Palladium acetate	224.49	0.004	1 mg	
Sodium carbonate	105.99	3.0	318 mg	
Tetrabutylammonium bromide	322.38	1.0	322 mg	
Water			2 ml	

Weigh out all chemicals into a 2-5 ml reaction vial. Add water and a magnetic stir bar. Heat as described using the Initiator, the Absorption level should be set to “High” and Fixed Hold Time should be used. In order to analyse the reaction mixture, you need to extract it (e g with dichloromethane) and take an analysis sample from the organic phase. For this specific substrate combination, you may need to heat the mixture to make the phases separate.

Observations:

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Name of analysis sample:

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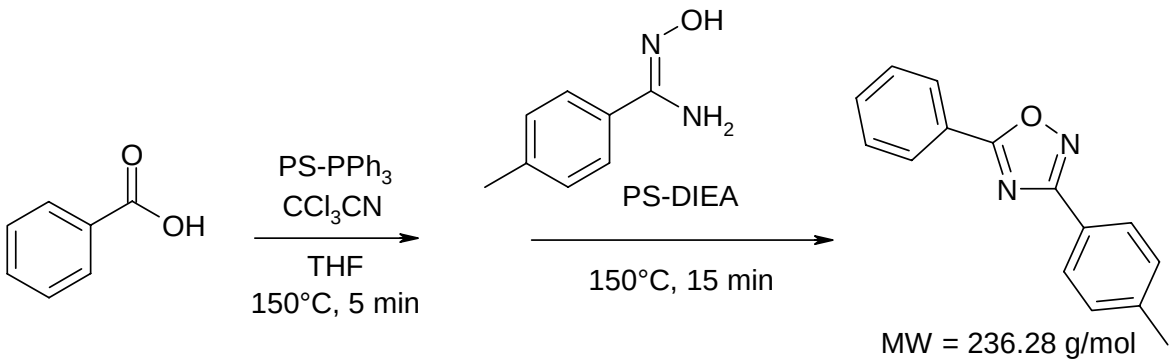
Leadbeater, N. E. and Marco, M. *Journal of Organic Chemistry* **2003**; *68*(3); 888-892

2a. 1,2,4-Oxadiazoles



MW = 236.28 g/mol

Chemical name	MW (g/mol)	Amount needed (mmol)	Theoretical Weight/Volume	Real Weight/Volume
Benzoic acid	122.12	0.1	12 mg	
PS-PPh_3	2.23 mmol/g	0.3	135 mg	
Trichloroacetonitrile	144.39	0.15	21.7 mg, 15 µl	
THF			2 ml	
4-methylbenzamide oxime	150.18	0.11	17 mg	
PS-DIEA	3.56 mmol/g	0.2	56 mg	

Weigh out benzoic acid and the solid-supported triphenyl phosphine into a 0.5-2 ml reaction vial. Add THF, trichloroacetonitrile and a magnetic stir bar. Heat as described for the first step using the Initiator, the Absorption level should be set to “Normal” and Fixed Hold Time should be activated. After the heating is completed, add the 4-methylbenzamide oxime and the solid supported DIEA. Reseal the vial and heat it again as in step two above.

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Name of analysis sample:

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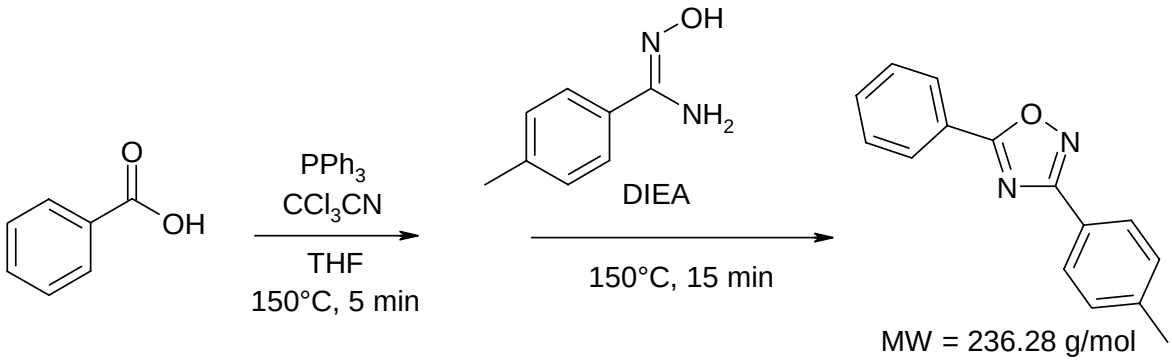
Wang, Y.; Miller, R. L.; Sauer, D. R.; Djuric, S. W. *Organic Letters* **2005**, *7*(5), 925-928

2b. 1,2,4-Oxadiazoles



MW = 236.28 g/mol

Chemical name	MW (g/mol)	Amount needed (mmol)	Theoretical Weight/Volume	Real Weight/Volume
Benzoic acid	122.12	0.1	12 mg	
PPh_3	262.29	0.3	79 mg	
Trichloroacetonitrile	144.39	0.15	21.7 mg, 15 µl	
THF			2 ml	
4-methylbenzamide oxime	150.18	0.11	17 mg	
DIEA	129.24	0.2	25.8 mg, 35 µl	

Weigh out benzoic acid and the triphenyl phosphine into a 0.5-2 ml reaction vial. Add THF, trichloroacetonitrile and a magnetic stir bar. Heat as described for the first step using the Initiator, the Absorption level should be set to “Normal” and Fixed Hold Time should be activated. After the heating is completed, add the 4-methylbenzamide oxime and the DIEA. Reseal the vial and heat it again as in step two above.

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Name of analysis sample:

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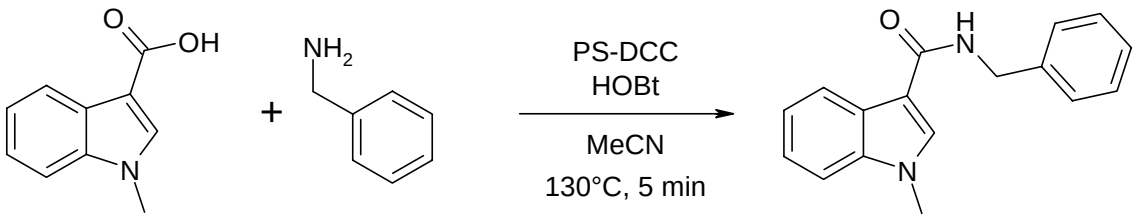
Wang, Y.; Miller, R. L.; Sauer, D. R.; Djuric, S. W. *Organic Letters* **2005**, *7*(5), 925-928

3a. Amide Coupling



MW = 264.33 g/mol

Chemical name	MW (g/mol)	Amount needed (mmol)	Theoretical Weight/Volume	Real Weight/Volume
1-methylindole-3-carboxylic acid	175.19	0.12	21 mg	
Benzylamine	107.15	0.12	12.9 mg, 13 µl	
PS-DCC (Biotage)	1.42 mmol/g	0.28	200 mg	
HOBt	135.12	0.12	16 mg	
Acetonitrile			2.1 ml	

Weigh out 1-methylindole-3-carboxylic acid, HOBt and solid-supported DCC into a 2-5 ml reaction vial. Add benzyl amine, acetonitrile and a magnetic stir bar. Heat as described, using the Initiator. The Absorption level should be set to “Normal” and Fixed Hold Time should be on.

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Name of analysis sample:

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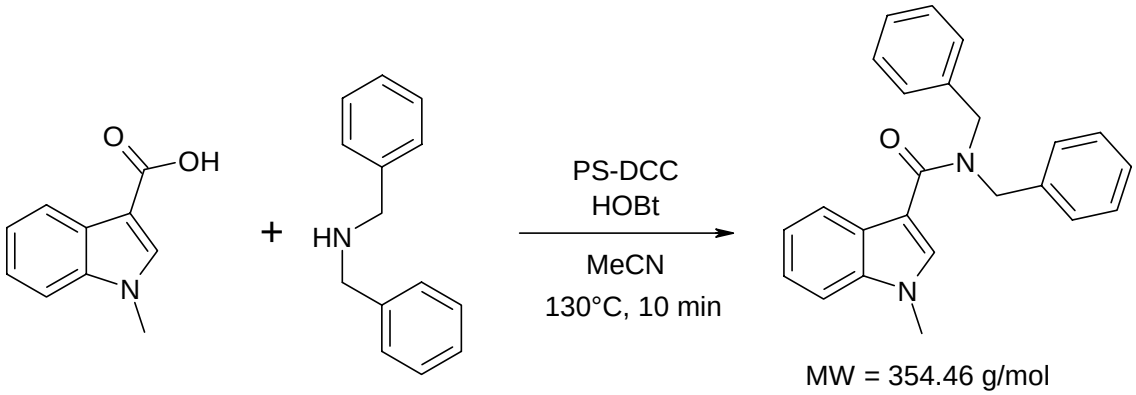
Sauer, D. R.; Kalvin, D. and Phelan, K. *Organic Letters* **2003**, *5*(24), 4721-4724

3b. Amide Coupling



MW = 354.46 g/mol

Chemical name	MW (g/mol)	Amount needed (mmol)	Theoretical Weight/Volume	Real Weight/Volume
1-methylindole-3-carboxylic acid	175.19	0.12	21 mg	
Dibenzylamine	197.28	0.12	23.7 mg, 23 µl	
PS-DCC (Biotage)	1.42 mmol/g	0.28	200 mg	
HOBt	135.12	0.12	16 mg	
Acetonitrile			2.1 ml	

Weigh out 1-methylindole-3-carboxylic acid, HOBt and solid-supported DCC into a 2-5 ml reaction vial. Add benzyl amine, acetonitrile and a magnetic stir bar. Heat as described, using the Initiator. The Absorption level should be set to “Normal” and Fixed Hold Time should be on. This product will be purified using the SP4 system, so you need to find a good TLC system for it. Write down the system you choose (using ethyl acetate and heptane) and the Rf values of your product and impurities and bring your reaction adsorbed onto 1 g of loose silica to the SP instrument.

Observations:

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Name of analysis sample:

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Sauer, D. R.; Kalvin, D. and Phelan, K. *Organic Letters* **2003**, *5*(24), 4721-4724