Paths of analysis*

BMK3

Synthia

October 10, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: Exclude Diastereoselecitve reactions, Tunnels, FGI, FGI with protections

Max. paths returned: 50

Max. iterations: 2000

Commercial:

1. Max. molecular weight - 1000 g/mol
2. Max. price - 1500 $/g

Published:

1. Max. molecular weight - 1000 g/mol
2. Popularity - 5

My Stockroom:

1. Max. molecular weight - 1000 g/mol

Reaction scoring formula: TUNNEL_COEF*FGI_COEF*STEP*20+1000000*(CONFLICT+NON_SELECTIVITY+FILTERS+PROTECT)

Chemical scoring formula: SMALLER^ 3,SMALLER^ 1.5

Min. search width: 400

Max. reactions per product: 60

*The results stated herein were generated using the proprietary platform owned and maintained by Grzybowski Scientific Inventions, Inc., a subsidiary of Merck KGaA, Darmstadt Germany. The results are provided on an as is basis, and shall be used solely in connection with the rights afforded in the license agreement and for no other purpose.

Strategies: none selected

FGI Coeff: 0

Tunnels Coeff: 0

JSON Parameters: {}

2 Paths

5 paths found. *Paths are sorted by score. Reactions are sorted in appearance order for each path.*

2.1 Path 1

Score: `56.25`

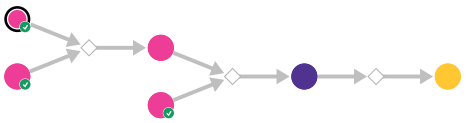
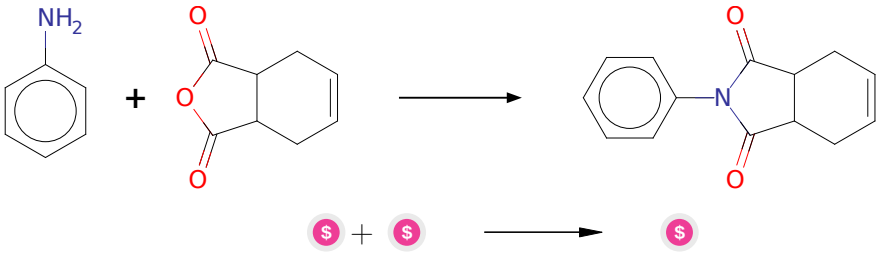


Figure 1: Outline of path 1

2.1.1 Synthesis of imides from anhydrides



Substrates:

1. Aniline - *available at Sigma-Aldrich*
2. 3a,4,7,7a-Tetrahydroisobenzofuran-1,3-dione - *available at Sigma-Aldrich*

Products:

1. 2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *ChemBridgeCorporation*

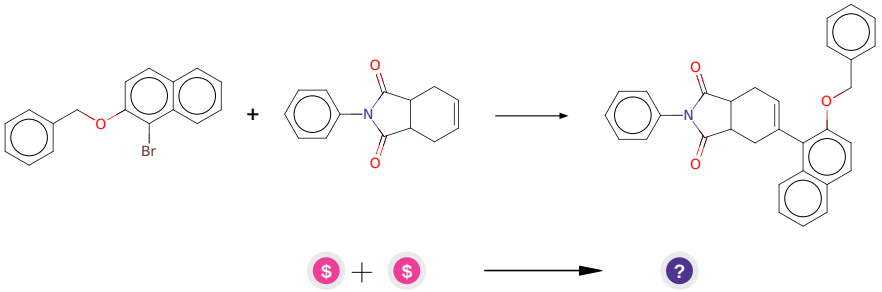
Typical conditions: AcOH

Protections: none

Reference: *10.1080/00397910802474966* and *10.1021/ja9024676* (SI) and *10.1002/ejoc.201402202*

Retrosynthesis ID: 8178

2.1.2 Heck Reaction



Substrates:

1. 2-Benzyloxy-1-bromonaphthalene - *available at Sigma-Aldrich*
2. 2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *ChemBridgeCorporation*

Products:

1. O=C1C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C(=O)N1c1ccccc1

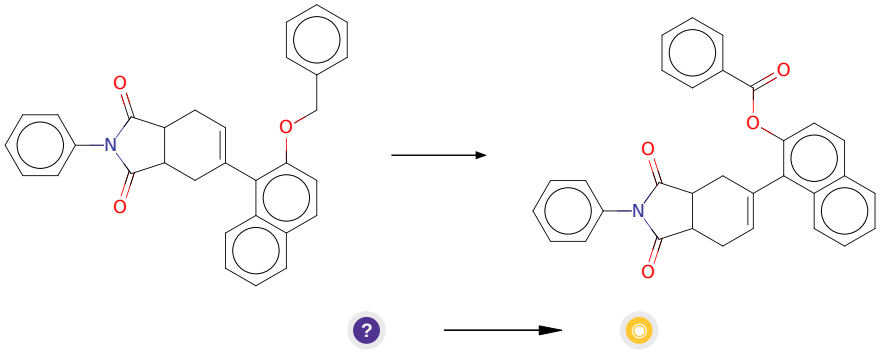
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

Protections: none

Reference: *10.1016/j.tetlet.2013.01.077* or *10.1039/C3GC40493E* *10.1021/ol0360288* or *10.1021/ol702755g* or *10.1055/s-0033-1340319* or *10.1016/j.tet.2004.10.049*

Retrosynthesis ID: 9170

2.1.3 Benzylic oxidation



Substrates:

1. O=C1C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C(=O)N1c1ccccc1

Products:

1. O=C(Oc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1)c1ccccc1

Typical conditions: Oxidant eg. O2 or K2S2O8 or HIO4.solvent

Protections: none

Reference: *10.1039/B404823G* and *10.1055/s-0036-1588429* and *10.1016/j.tetlet.2010.09.021* and *10.1002/chem.201604750* and *10.1016/j.apcata.2014.01.042* and *10.1039/c3nj00045a* and *10.1021/jacs.6b08305*

Retrosynthesis ID: 31019416

2.2 Path 2

Score: `64.06`

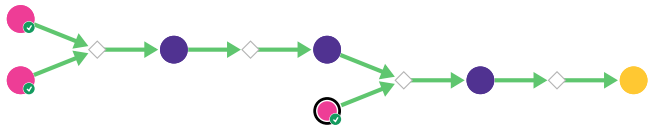
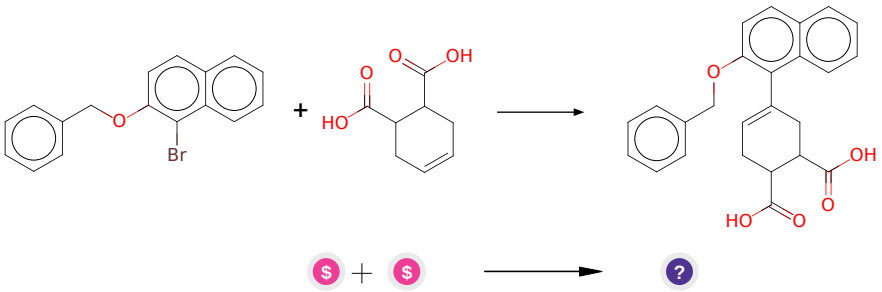


Figure 2: Outline of path 2

2.2.1 Heck Reaction



Substrates:

1. Cyclohex-4-ene-1,2-dicarboxylic acid - *available at Sigma-Aldrich*
2. 2-Benzyloxy-1-bromonaphthalene - *available at Sigma-Aldrich*

Products:

1. O=C(O)C1CC=C(c2c(OCc3ccccc3)ccc3ccccc23)CC1C(=O)O

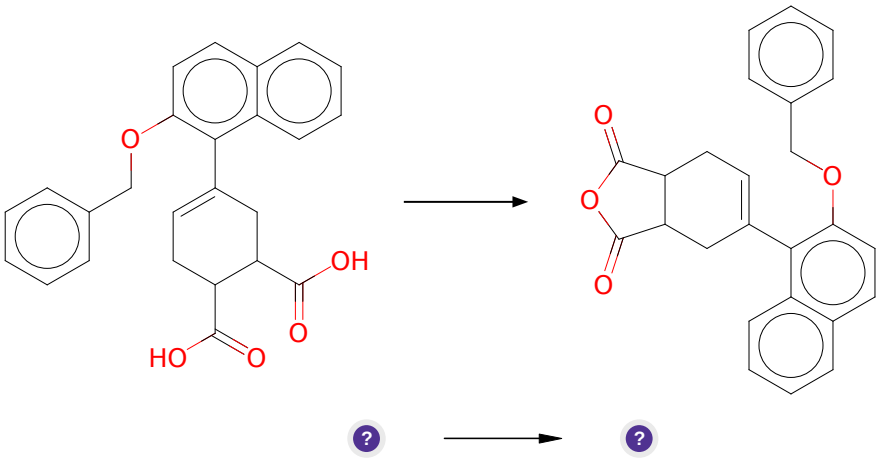
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

Protections: none

Reference: *10.1016/j.tetlet.2013.01.077* or *10.1039/C3GC40493E* *10.1021/ol0360288* or *10.1021/ol702755g* or *10.1055/s-0033-1340319* or *10.1016/j.tet.2004.10.049*

Retrosynthesis ID: 9170

2.2.2 Synthesis of cyclic anhydrides



Substrates:

1. O=C(O)C1CC=C(c2c(OCc3ccccc3)ccc3ccccc23)CC1C(=O)O

Products:

1. O=C1OC(=O)C2CC(c3c(OCc4ccccc4)ccc4ccccc34)=CCC12

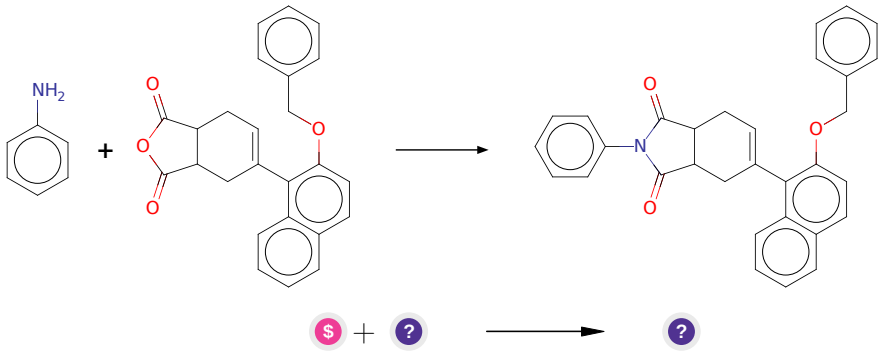
Typical conditions: MgCl2.Boc2O.THF.40C

Protections: none

Reference: DOI:*10.1021/cs501237p*

Retrosynthesis ID: 7263

2.2.3 Synthesis of imides from anhydrides



Substrates:

1. Aniline - *available at Sigma-Aldrich*
2. O=C1OC(=O)C2CC(c3c(OCc4ccccc4)ccc4ccccc34)=CCC12

Products:

1. O=C1C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C(=O)N1c1ccccc1

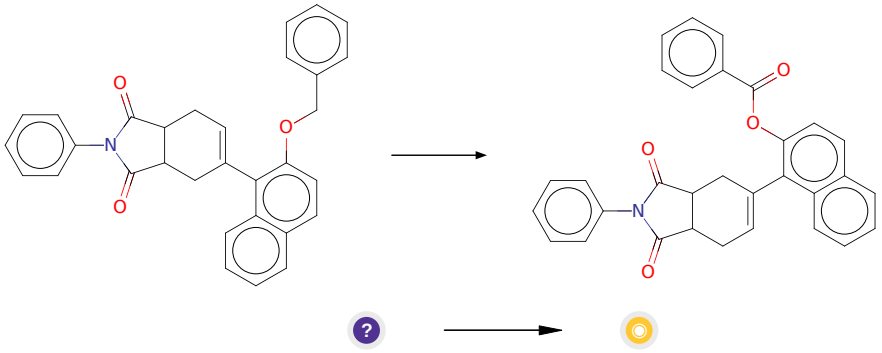
Typical conditions: AcOH

Protections: none

Reference: *10.1080/00397910802474966* and *10.1021/ja9024676* (SI) and *10.1002/ejoc.201402202*

Retrosynthesis ID: 8178

2.2.4 Benzylic oxidation



Substrates:

1. O=C1C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C(=O)N1c1ccccc1

Products:

1. O=C(Oc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1)c1ccccc1

Typical conditions: Oxidant eg. O2 or K2S2O8 or HIO4.solvent

Protections: none

Reference: *10.1039/B404823G* and *10.1055/s-0036-1588429* and *10.1016/j.tetlet.2010.09.021* and *10.1002/chem.201604750* and *10.1016/j.apcata.2014.01.042* and *10.1039/c3nj00045a* and *10.1021/jacs.6b08305*

Retrosynthesis ID: 31019416

2.3 Path 3

Score: `64.06`

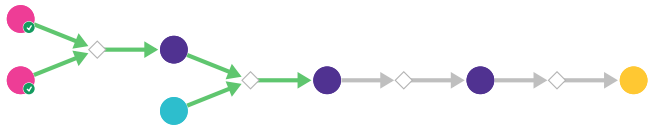
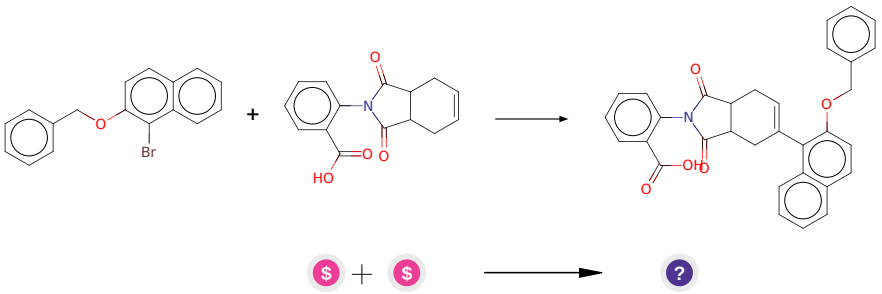


Figure 3: Outline of path 3

2.3.1 Heck Reaction



Substrates:

1. 2-(1,3-dioxo-1,3,3a,4,7,7a-hexahydro-isoindol-2-yl)-benzoic acid - *available at Sigma-Aldrich*
2. 2-Benzyloxy-1-bromonaphthalene - *available at Sigma-Aldrich*

Products:

1. O=C(O)c1ccccc1N1C(=O)C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C1=O

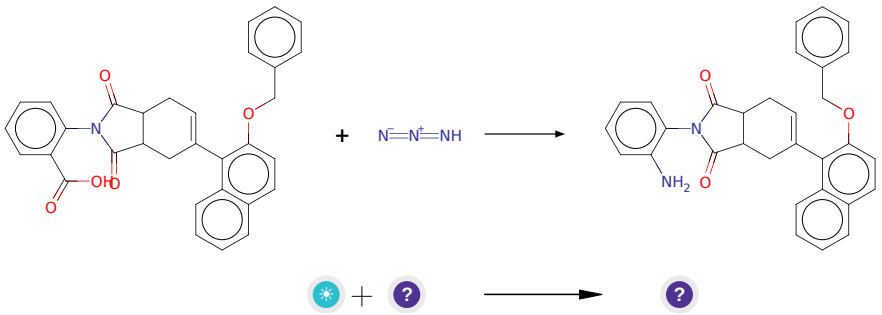
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

Protections: none

Reference: *10.1016/j.tetlet.2013.01.077* or *10.1039/C3GC40493E* *10.1021/ol0360288* or *10.1021/ol702755g* or *10.1055/s-0033-1340319* or *10.1016/j.tet.2004.10.049*

Retrosynthesis ID: 9170

2.3.2 Schmidt Reaction



Substrates:

1. hydrazoic acid
2. O=C(O)c1ccccc1N1C(=O)C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C1=O

Products:

1. Nc1ccccc1N1C(=O)C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C1=O

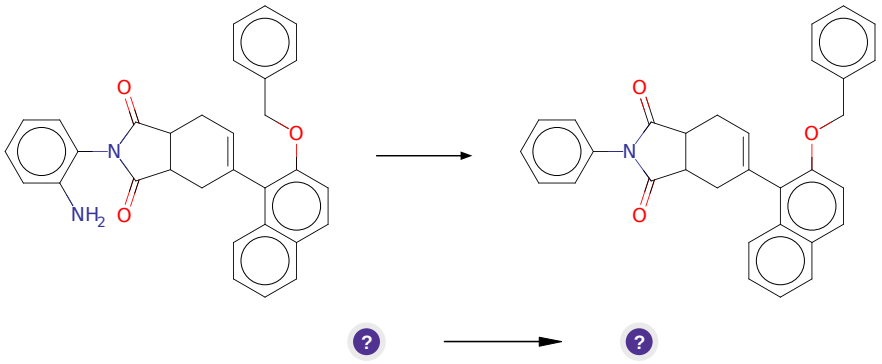
Typical conditions: azide.H+.40C

Protections: none

Reference: *10.1039/B505080D*

Retrosynthesis ID: 10953

2.3.3 Hydrodediazoniation



Substrates:

1. Nc1ccccc1N1C(=O)C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C1=O

Products:

1. O=C1C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C(=O)N1c1ccccc1

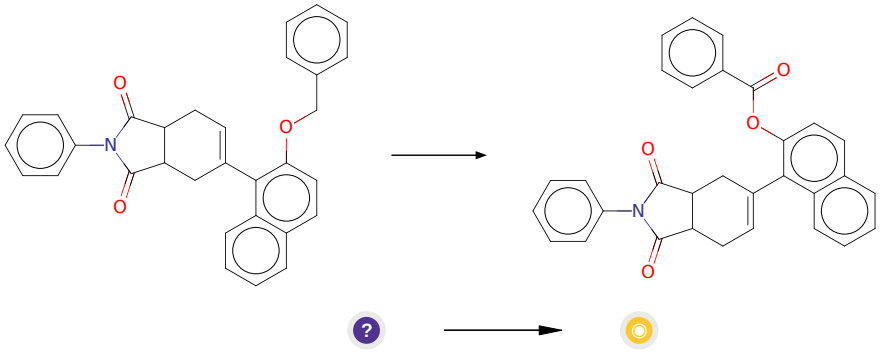
Typical conditions: 1) HCl.NaNO2 2) H3PO2

Protections: none

Reference: *10.1016/j.bmcl.2013.10.058* and *10.1021/jm0004906* and *10.1002/ejoc.200600030* and *10.1016/j.tet.2016.02.011*

Retrosynthesis ID: 9999756

2.3.4 Benzylic oxidation



Substrates:

1. O=C1C2CC=C(c3c(OCc4ccccc4)ccc4ccccc34)CC2C(=O)N1c1ccccc1

Products:

1. O=C(Oc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1)c1ccccc1

Typical conditions: Oxidant eg. O2 or K2S2O8 or HIO4.solvent

Protections: none

Reference: *10.1039/B404823G* and *10.1055/s-0036-1588429* and *10.1016/j.tetlet.2010.09.021* and *10.1002/chem.201604750* and *10.1016/j.apcata.2014.01.042* and *10.1039/c3nj00045a* and *10.1021/jacs.6b08305*

Retrosynthesis ID: 31019416

2.4 Path 4

Score: `70.00`

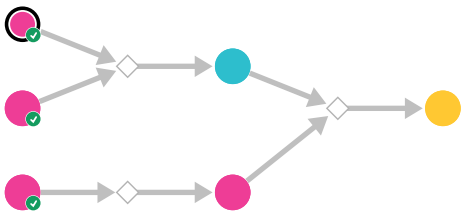
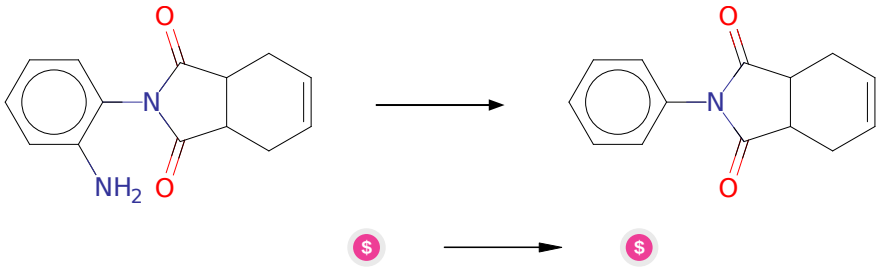


Figure 4: Outline of path 4

2.4.1 Hydrodediazoniation



Substrates:

1. 2-(2-aminophenyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindole-1,3-dione - *available at Sigma-Aldrich*

Products:

1. 2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *ChemBridgeCorporation*

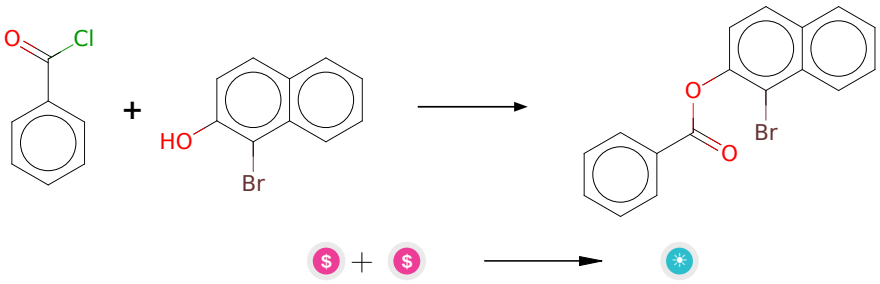
Typical conditions: 1) HCl.NaNO2 2) H3PO2

Protections: none

Reference: *10.1016/j.bmcl.2013.10.058* and *10.1021/jm0004906* and *10.1002/ejoc.200600030* and *10.1016/j.tet.2016.02.011*

Retrosynthesis ID: 9999756

2.4.2 Reaction of acyl chlorides with alcohols and phenols



Substrates:

1. Benzoyl chloride - *available at Sigma-Aldrich*
2. 1-Bromo-2-naphthol - *available at Sigma-Aldrich*

Products:

1. benzoic acid-(1-bromo-[2]naphthyl ester)

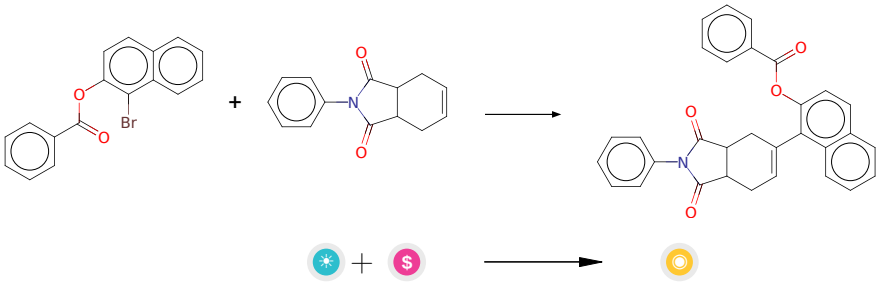
Typical conditions: base.DCM

Protections: none

Reference: *10.1016/j.bmcl.2012.03.021* AND *10.1021/ja026266i* (SI, hydroperoxides) AND *10.1016/j.tetasy.2004.07.044* AND *10.1021/jm1006929* (SI) AND *10.1016/j.tet.2011.05.017* AND *10.1016/j.tetasy.2012.09.002* AND *10.1021/ol016268s* (SI) AND *10.1021/jo801116n* AND *10.1021/jo00279a041* AND WO2013/64518 A1, 2013 (page 102)

Retrosynthesis ID: 28549

2.4.3 Heck Reaction



Substrates:

1. benzoic acid-(1-bromo-[2]naphthyl ester)
2. 2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *ChemBridgeCorporation*

Products:

1. O=C(Oc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1)c1ccccc1

Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

Protections: none

Reference: *10.1016/j.tetlet.2013.01.077* or *10.1039/C3GC40493E* *10.1021/ol0360288* or *10.1021/ol702755g* or *10.1055/s-0033-1340319* or *10.1016/j.tet.2004.10.049*

Retrosynthesis ID: 9170

2.5 Path 5

Score: 70.00

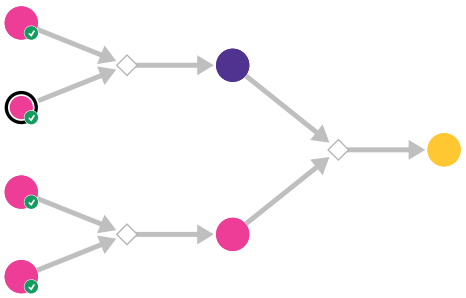
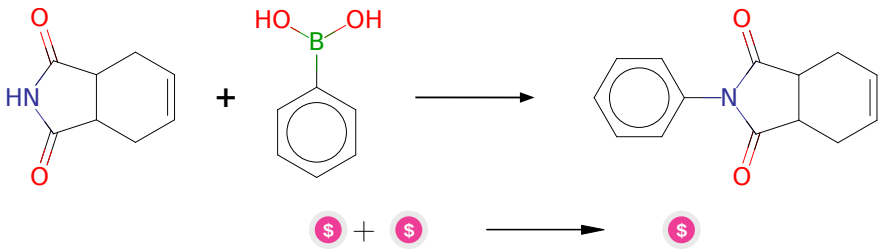


Figure 5: Outline of path 5

2.5.1 Chan-Lam Coupling



Substrates:

1. Phenylboric acid - *available at Sigma-Aldrich*
2. Tetrahydrophthalimide - *available at Sigma-Aldrich*

Products:

1. 2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *ChemBridgeCorporation*

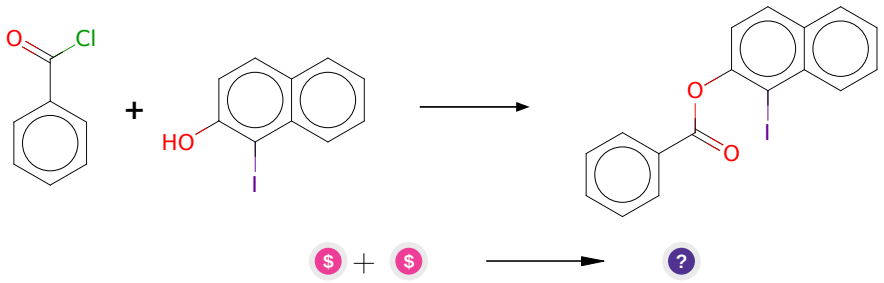
Typical conditions: Cu(Oac)2.Et3N.DCM

Protections: none

Reference: *10.1055/s-2004-820059* and *10.1055/s-2006-949638* and *10.1021/jo0481351* and *10.1016/S0040-4039(98)00503-6*

Retrosynthesis ID: 31015963

2.5.2 Reaction of acyl chlorides with alcohols and phenols



Substrates:

1. 1-Iodo-2-naphthol - *available at Sigma-Aldrich*
2. Benzoyl chloride - *available at Sigma-Aldrich*

Products:

1. O=C(Oc1ccc2ccccc2c1I)c1ccccc1

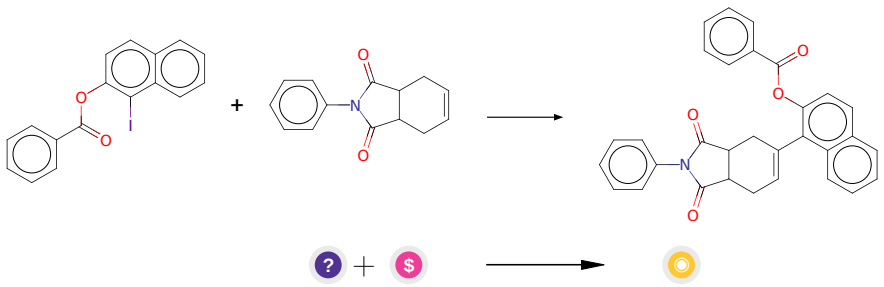
Typical conditions: base.DCM

Protections: none

Reference: *10.1016/j.bmcl.2012.03.021* AND *10.1021/ja026266i* (SI, hydroperoxides) AND *10.1016/j.tetasy.2004.07.044* AND *10.1021/jm1006929* (SI) AND *10.1016/j.tet.2011.05.017* AND *10.1016/j.tetasy.2012.09.002* AND *10.1021/ol016268s* (SI) AND *10.1021/jo801116n* AND *10.1021/jo00279a041* AND WO2013/64518 A1, 2013 (page 102)

Retrosynthesis ID: 28549

2.5.3 Heck Reaction



Substrates:

1. O=C(Oc1ccc2ccccc2c1I)c1ccccc1

2. 2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *ChemBridgeCorporation*

Products:

1. O=C(Oc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1)c1ccccc1

Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

Protections: none

Reference: *10.1016/j.tetlet.2013.01.077* or *10.1002/9780470716076* or *10.1021/op050106k* or *10.1021/ol0360288* or *10.1021/ol702755g* or *10.1055/s-0033-1340319* or *10.1016/j.tet.2004.10.049*

Retrosynthesis ID: 9186