Paths of analysis*

BMK2

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

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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: `70.00`

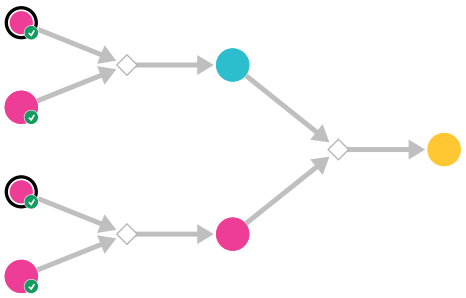
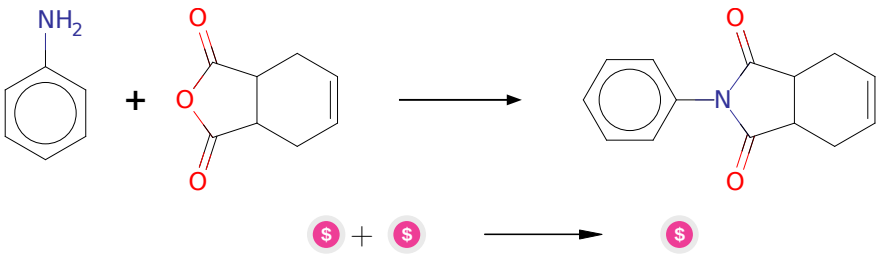


Figure 1: Outline of path 1

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*

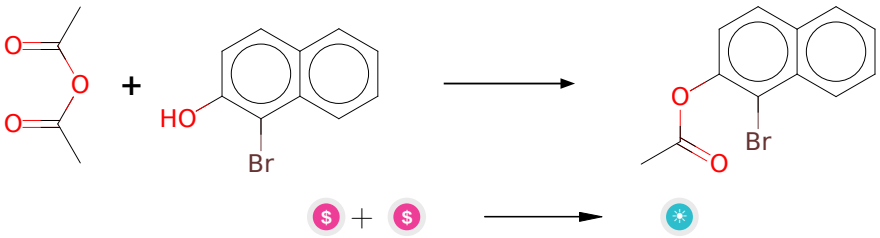
Typical conditions: AcOH

Protections: none

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

Retrosynthesis ID: 8178

2.1.2 Cu(OTf)2 catalyzed acylation of phenols



Substrates:

1. Acetic anhydride - *available at Sigma-Aldrich*
2. 1-Bromo-2-naphthol - *available at Sigma-Aldrich*

Products:

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

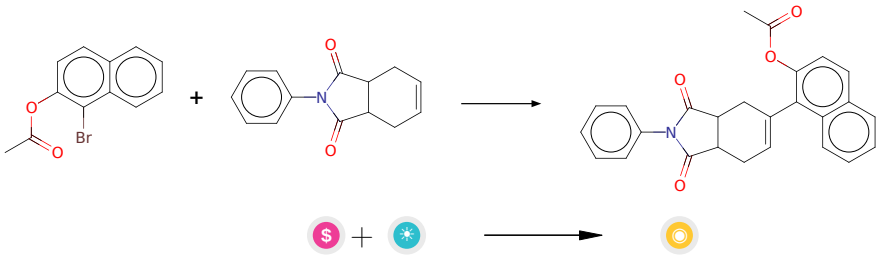
Typical conditions: Cu(II).triflate.DCM.RT

Protections: none

Reference: DOI: *10.1016/S0040-4020(01)01229-7*

Retrosynthesis ID: 11601

2.1.3 Heck Reaction



Substrates:

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

Products:

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

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 Path 2

Score: 76.25

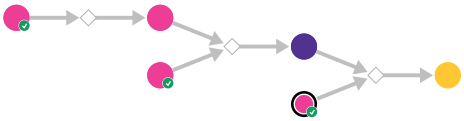
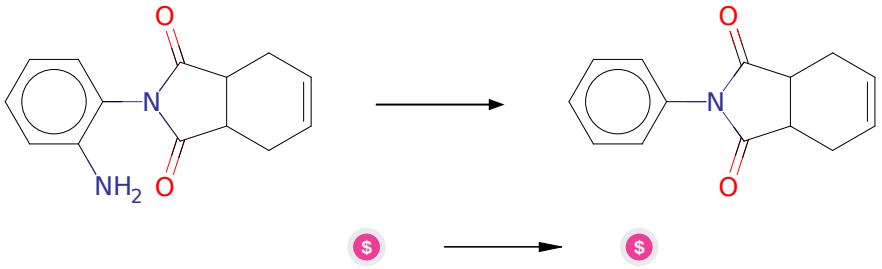


Figure 2: Outline of path 2

2.2.1 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*

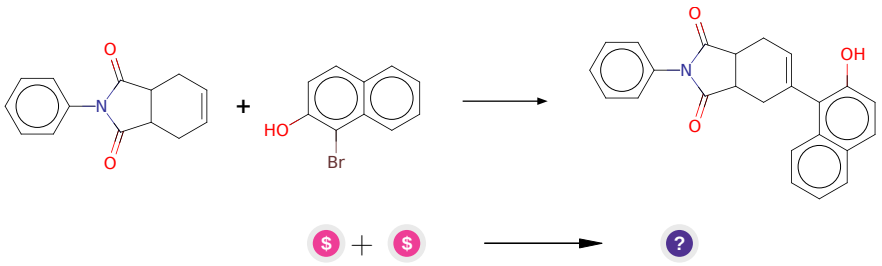
Typical conditions: 1) HCl.NaNO2 2) H3PO2

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

2.2.2 Heck Reaction



Substrates:

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

Products:

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

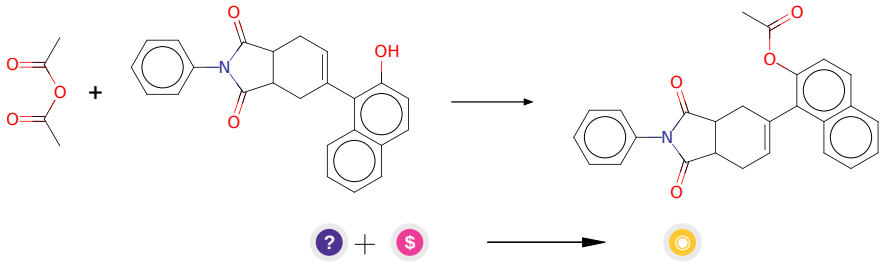
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

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

2.2.3 Cu(OTf)2 catalyzed acylation of phenols



Substrates:

1. O=C1C2CC=C(c3c(O)ccc4ccccc34)CC2C(=O)N1c1ccccc1
2. Acetic anhydride - *available at Sigma-Aldrich*

Products:

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

Typical conditions: Cu(II).triflate.DCM.RT

Protections: none

Reference: DOI: *10.1016/S0040-4020(01)01229-7*

Retrosynthesis ID: 11601

2.3 Path 3

Score: 76.25

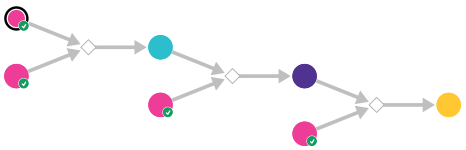
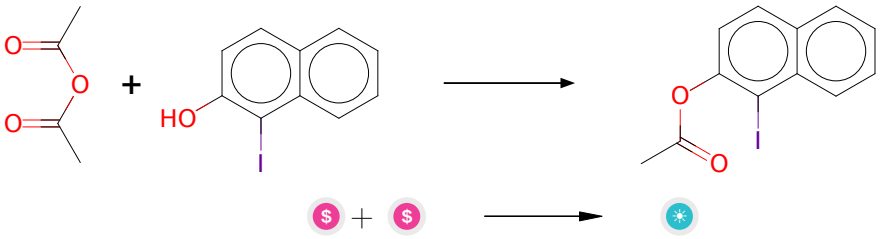


Figure 3: Outline of path 3

2.3.1 Cu(OTf)2 catalyzed acylation of phenols



Substrates:

1. Acetic anhydride - *available at Sigma-Aldrich*
2. 1-Iodo-2-naphthol - *available at Sigma-Aldrich*

Products:

1. acetic acid-(1-iodo-[2]naphthyl ester)

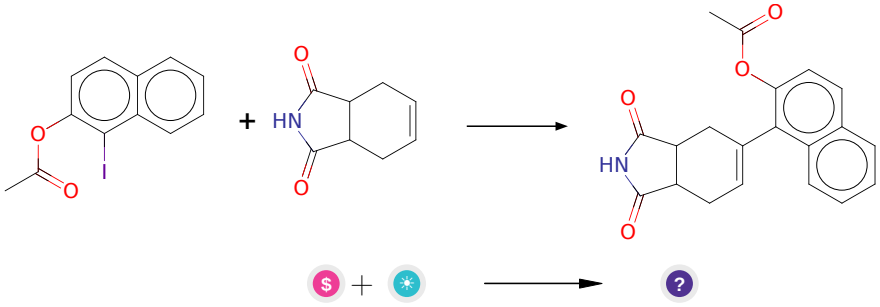
Typical conditions: Cu(II).triflate.DCM.RT

Protections: none

Reference: DOI: *10.1016/S0040-4020(01)01229-7*

Retrosynthesis ID: 11601

2.3.2 Heck Reaction



Substrates:

1. Tetrahydrophthalimide - *available at Sigma-Aldrich*
2. acetic acid-(1-iodo-[2]naphthyl ester)

Products:

1. CC(=O)Oc1ccc2ccccc2c1C1=CCC2C(=O)NC(=O)C2C1

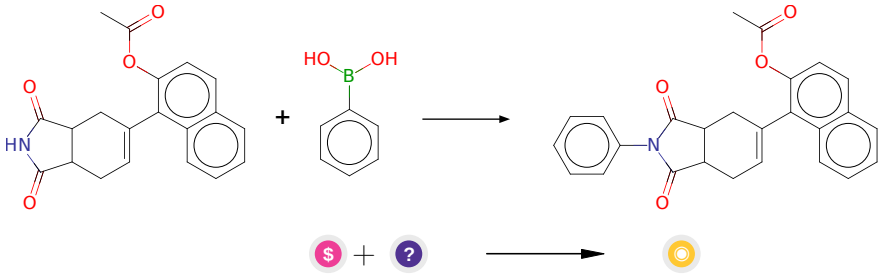
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

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

2.3.3 Chan-Lam Coupling



Substrates:

1. Phenylboric acid - *available at Sigma-Aldrich*
2. CC(=O)Oc1ccc2ccccc2c1C1=CCC2C(=O)NC(=O)C2C1

Products:

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

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

2.4 Path 4

Score: `90.31`

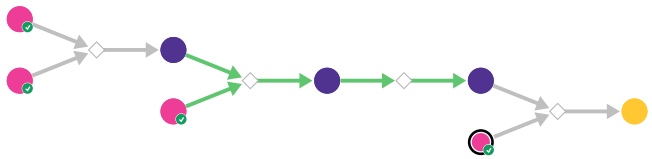
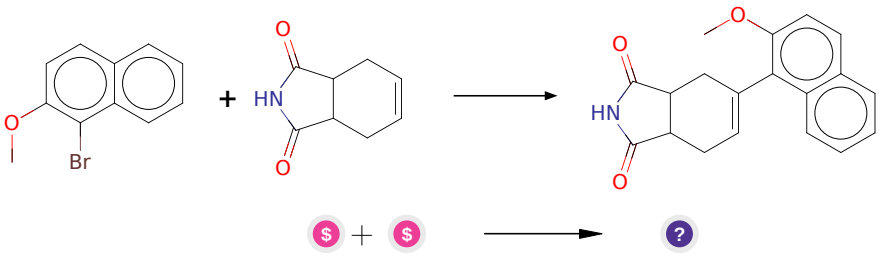


Figure 4: Outline of path 4

2.4.1 Heck Reaction



Substrates:

1. 1-Bromo-2-methoxynaphthalene - *available at Sigma-Aldrich*
2. Tetrahydrophthalimide - *available at Sigma-Aldrich*

Products:

1. COc1ccc2ccccc2c1C1=CCC2C(=O)NC(=O)C2C1

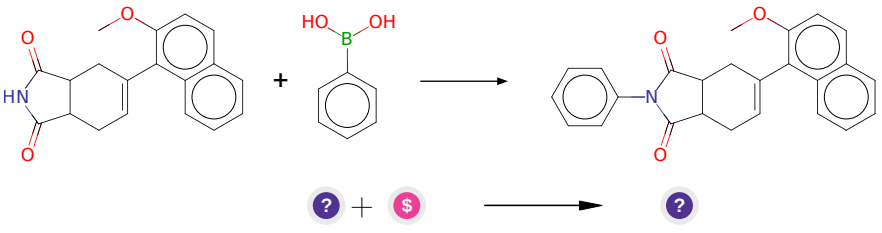
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

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

2.4.2 Chan-Lam Coupling



Substrates:

1. COc1ccc2ccccc2c1C1=CCC2C(=O)NC(=O)C2C1
2. Phenylboric acid - *available at Sigma-Aldrich*

Products:

1. COc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1

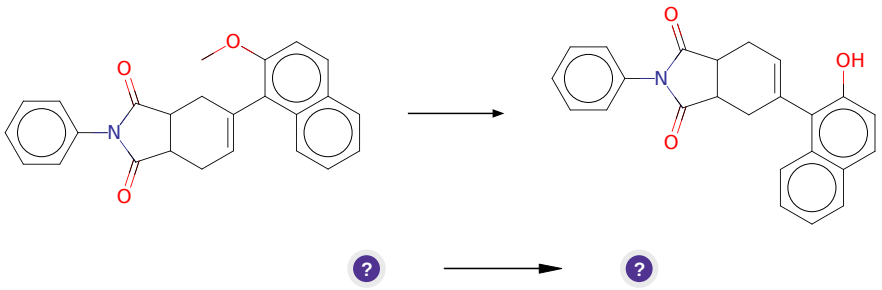
Typical conditions: Cu(Oac)2.Et3N.DCM

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

2.4.3 Demethylation of Phenols



Substrates:

1. COc1ccc2ccccc2c1C1=CCC2C(=O)N(c3ccccc3)C(=O)C2C1

Products:

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

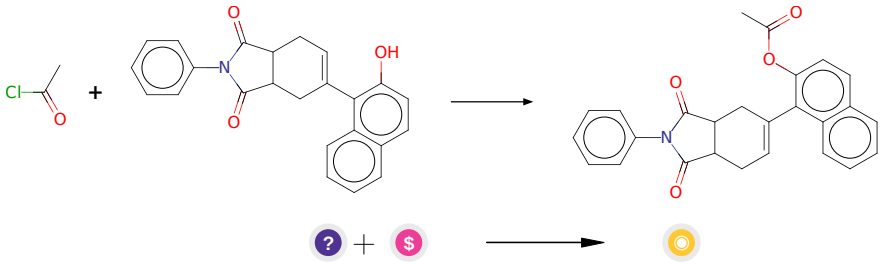
Typical conditions: BBr3.CH2Cl2

Protections: none

Reference: DOI: *10.1021/ja00105a021* and *10.1021/jm00176a011* and *10.1021/jm970277i* and *10.1021/ja0106164* and Patent: US2010/16298, 2010, A1, page 185

Retrosynthesis ID: 10011837

2.4.4 Reaction of acyl chlorides with alcohols and phenols



Substrates:

1. O=C1C2CC=C(c3c(O)ccc4ccccc34)CC2C(=O)N1c1ccccc1
2. Acetyl chloride - *available at Sigma-Aldrich*

Products:

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

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 Path 5

Score: `101.25`

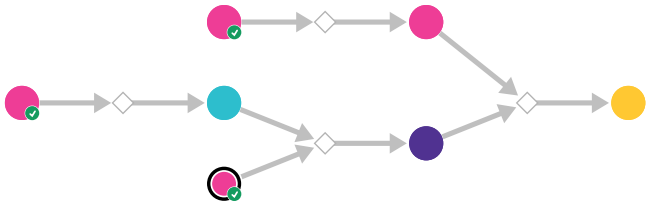
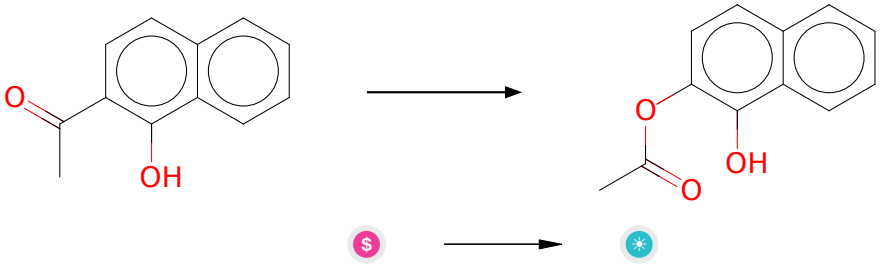


Figure 5: Outline of path 5

2.5.1 Bayer-Villiger oxidation



Substrates:

1. 2-Acetyl-1-naphthol - *available at Sigma-Aldrich*

Products:

1. 2-acetoxy-naphthol-(1)

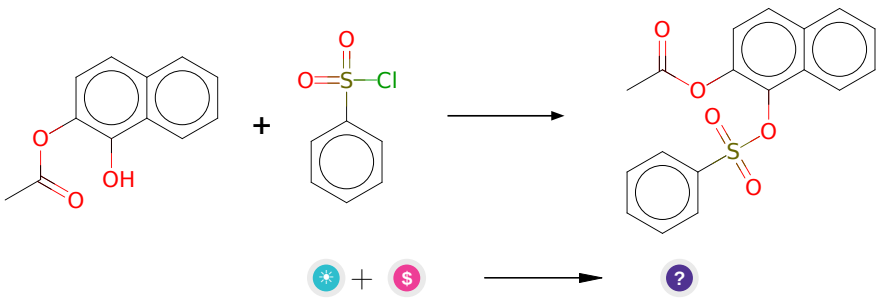
Typical conditions: mCPBA.NaHCO3.DCM

Protections: none

Reference: *10.1021/ol702571c* and *10.1021/ja00272a051* and *10.1080/00397910801997835*

Retrosynthesis ID: 4811

2.5.2 Sulfonylation of hydroxyl group



Substrates:

1. 2-acetoxy-naphthol-(1)
2. Benzenesulfonyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(=O)Oc1ccc2ccccc2c1OS(=O)(=O)c1ccccc1

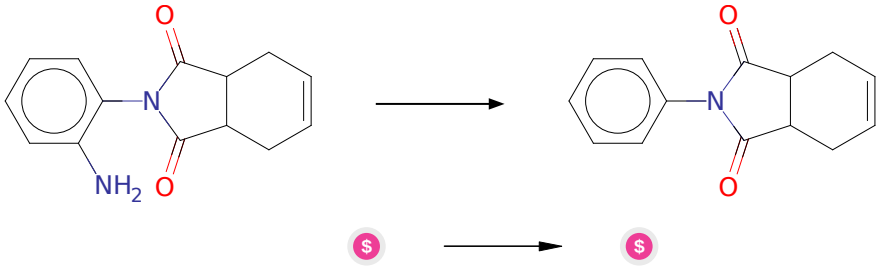
Typical conditions: TEA.THF.0 C

Protections: none

Reference: *10.1016/j.ejmech.2020.112889* p. 4, 11 and *10.1016/j.bmc.2019.04.031* p. 2743, 2750

Retrosynthesis ID: 50428

2.5.3 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*

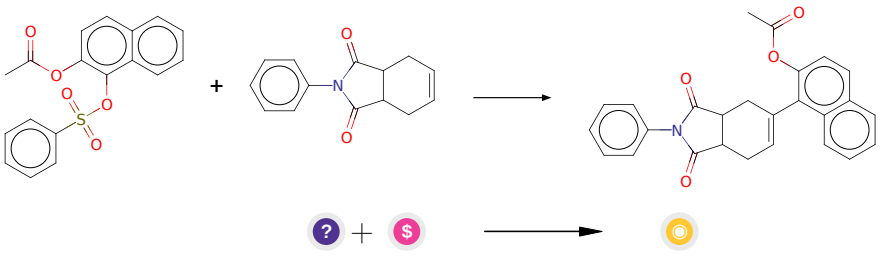
Typical conditions: 1) HCl.NaNO2 2) H3PO2

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

2.5.4 Heck Reaction



Substrates:

1. CC(=O)Oc1ccc2ccccc2c1OS(=O)(=O)c1ccccc1
2. 2-phenyl-3a,4,7,7a-tetrahydro-isoindole-1,3-dione - *ChemBridgeCorporation*

Products:

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

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

Protections: none

Reference: *10.1016/j.tetlet.2013.10.076* or *10.1021/jm060369k* or *10.1021/jo00078a016* or *10.1002/9780470716076*

Retrosynthesis ID: 9269