Paths of analysis*

L2_DIA

Synthia

October 11, 2022

1 Analysis parameters

Analysis type: Automatic Retrosynthesis

Rules: none selected

Filters: 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

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: 76.25

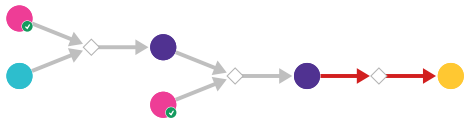
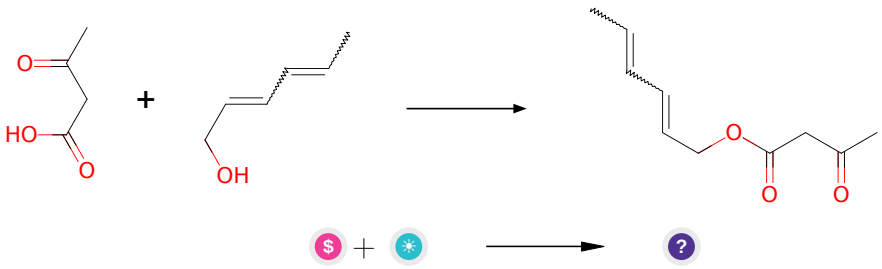


Figure 1: Outline of path 1

2.1.1 Steglich Esterification



Substrates:

1. Lithium acetoacetate - *available at Sigma-Aldrich*
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)CC(C)=O

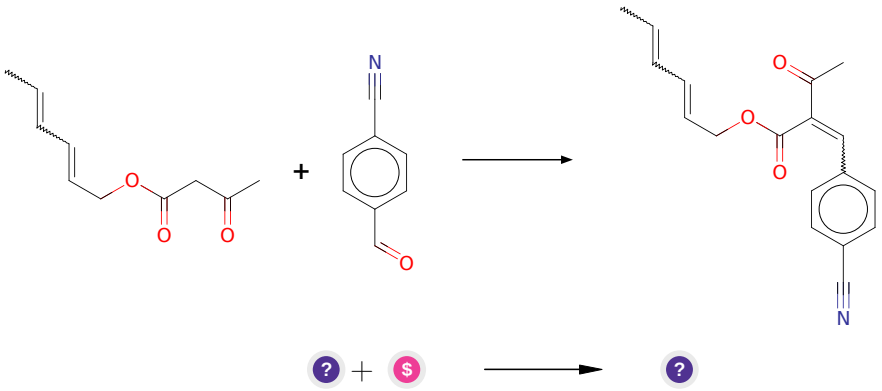
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.1.2 Knoevenagel Condensation



Substrates:

1. CC=CC=CCOC(=O)CC(C)=O
2. 4-Cyanobenzaldehyde - *available at Sigma-Aldrich*

Products:

1. CC=CC=CCOC(=O)C(=Cc1ccc(C#N)cc1)C(C)=O

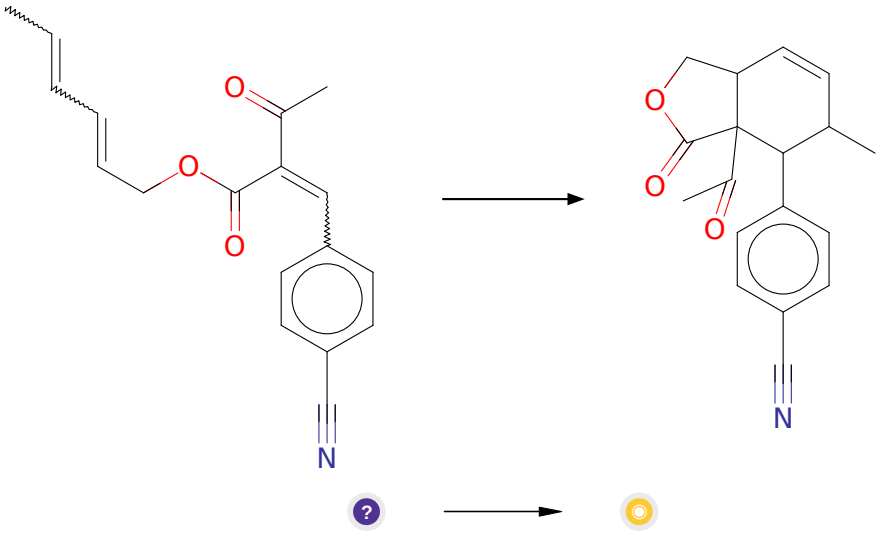
Typical conditions: base e.g.piperidine. solvent

Protections: none

Reference: *10.1002/0471264180.or015.02* and *10.13005/ojc/350154*

Retrosynthesis ID: 252

2.1.3 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C(=Cc1ccc(C#N)cc1)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C#N)cc1

Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

Protections: none

Reference: DOI: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z* AND *10.1021/ja062508t*

Retrosynthesis ID: 18116

2.2 Path 2

Score: 76.25

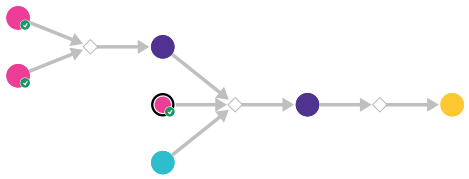
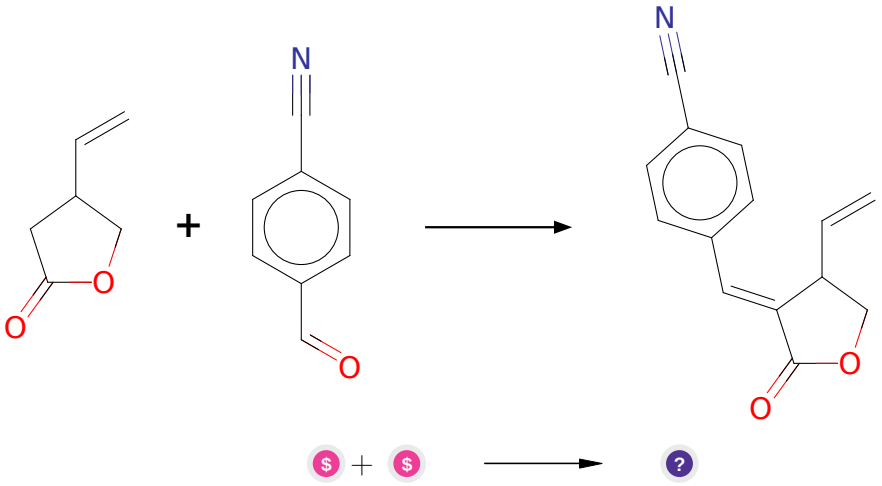


Figure 2: Outline of path 2

2.2.1 Condensation of esters with aldehydes



Substrates:

1. 4-Cyanobenzaldehyde - *available at Sigma-Aldrich*
2. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*

Products:

1. C=CC1COC(=O)/C1=C/c1ccc(C#N)cc1

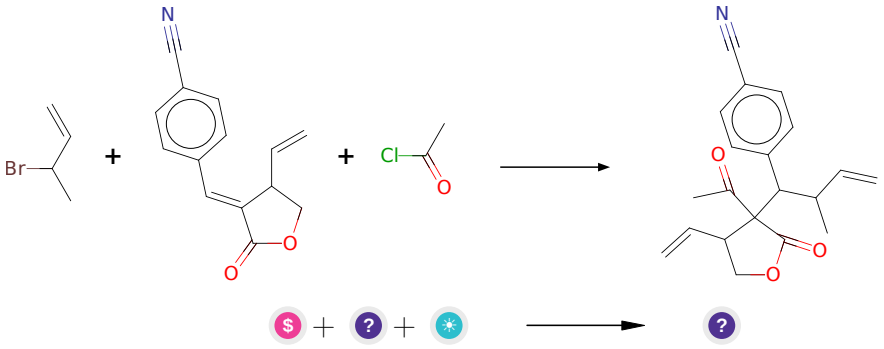
Typical conditions: 1.LDA.2RCHO

Protections: none

Reference: *10.1021/jo970387x* AND *10.1021/jo00076a051* AND *10.1016/S0040-4039(97)10827-9* AND *10.1055/s-2002-25767* AND *10.1039/P19920003277*

Retrosynthesis ID: 14981

2.2.2 Conjugated addition of organocuprate-acylation of enones and enoate esters



Substrates:

1. Acetyl chloride - *available at Sigma-Aldrich*
2. C=CC1COC(=O)/C1=C/c1ccc(C#N)cc1
3. 3-brom-but-1-en

Products:

1. C=CC(C)C(c1ccc(C#N)cc1)C1(C(C)=O)C(=O)OCC1C=C

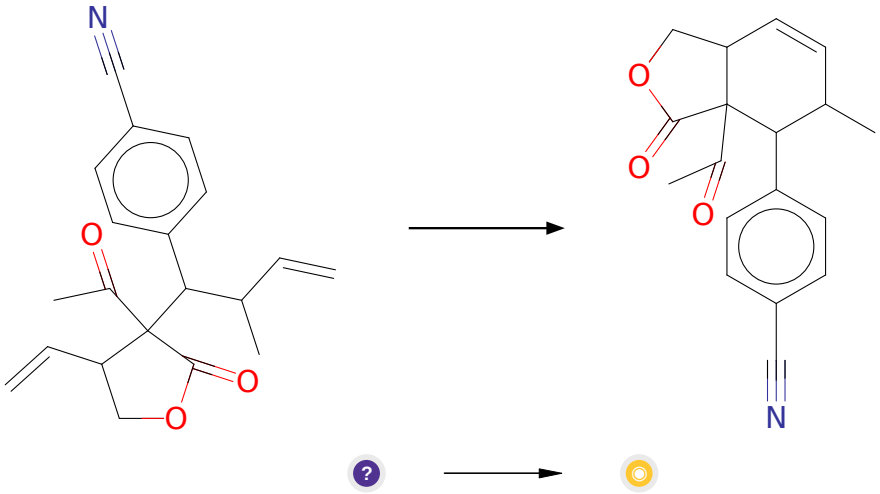
Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.3987/COM-99-S143* AND *10.1021/ja00148a023* AND *10.1016/S0040-4039(01)80891-1*

Retrosynthesis ID: 20523

2.2.3 Ring-Closing Metathesis



Substrates:

1. C=CC(C)C(c1ccc(C#N)cc1)C1(C(C)=O)C(=O)OCC1C=C

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C#N)cc1

Typical conditions: catalyst e.g. Hoveyda-Grubbs . solvent e.g. CH2Cl2

Protections: none

Reference: DOI: *10.1002/anie.200800693* and *10.1021/acs.orglett.8b04003* and *10.1021/jo0264729* and *10.1021/ja072334v* and *10.1002/ejoc.201001102*

Retrosynthesis ID: 31014187

2.3 Path 3

Score: 76.25

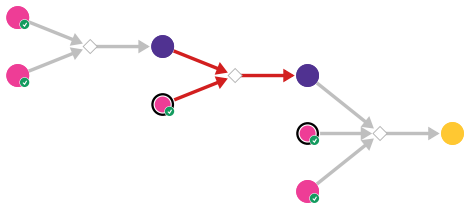
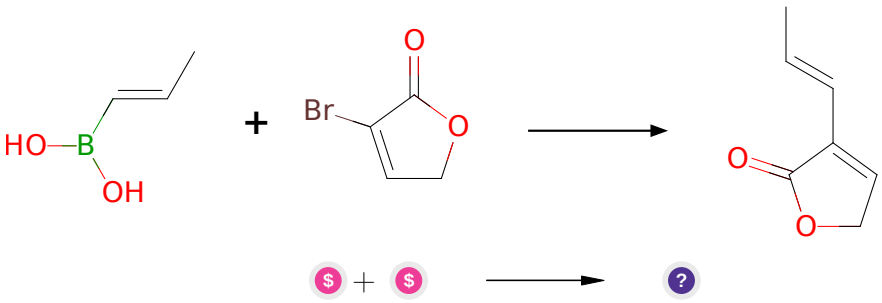


Figure 3: Outline of path 3

2.3.1 Suzuki coupling of vinyl bromides with alkenyl boronic acids



Substrates:

1. trans-Propenylboronic acid - *available at Sigma-Aldrich*
2. 3-bromo-2,5-dihydrofuran-2-one - *available at Sigma-Aldrich*

Products:

1. C/C=C/C1=CCOC1=O

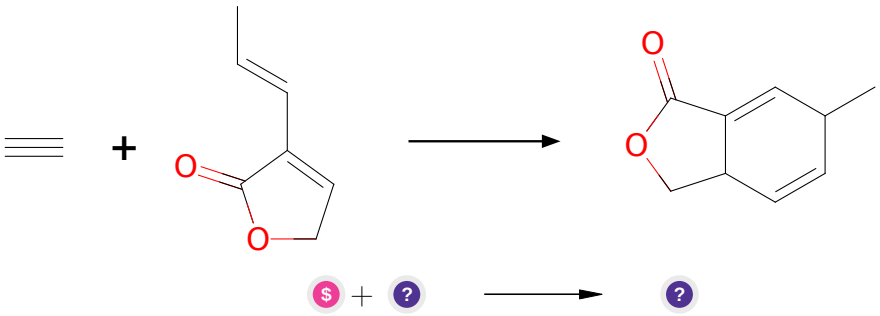
Typical conditions: Pd catalyst.base.solvent

Protections: none

Reference: *10.1021/cr00039a007* and *10.1007/3418_2012_32* and *10.1021/cr0505268* and *10.1016/j.jfluchem.2016.01.018* and *10.1039/C3CS60197H*

Retrosynthesis ID: 24937

2.3.2 Diels-Alder



Substrates:

1. Calcium carbide - *available at Sigma-Aldrich*
2. C/C=C/C1=CCOC1=O

Products:

1. CC1C=CC2COC(=O)C2=C1

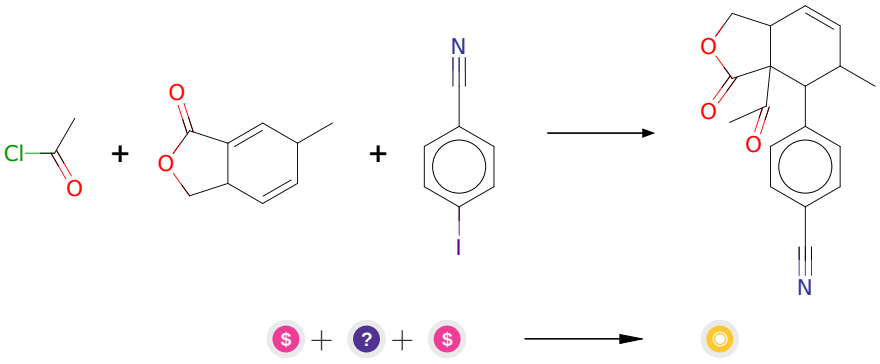
Typical conditions: H2O.MeOH.EtOH.isooctane

Protections: none

Reference: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z*

Retrosynthesis ID: 10557

2.3.3 Conjugated addition of organocuprate-acylation of enones and enoate esters



Substrates:

1. Acetyl chloride - *available at Sigma-Aldrich*

2. CC1C=CC2COC(=O)C2=C1
3. 4-Iodobenzonitrile - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C#N)cc1

Typical conditions: 1.RCuLi.2.AcCl.HMPA

Protections: none

Reference: *10.3987/COM-99-S143* AND *10.1021/ja00148a023* AND *10.1016/S0040-4039(01)80891-1*

Retrosynthesis ID: 12521

2.4 Path 4

Score: 84.06

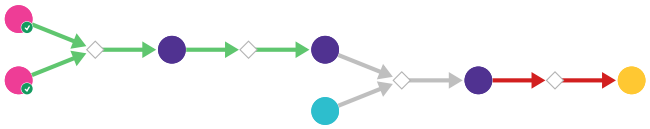
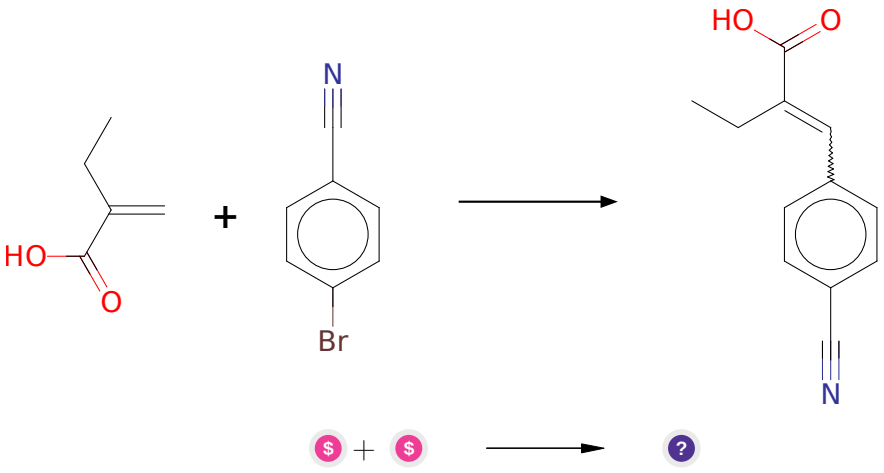


Figure 4: Outline of path 4

2.4.1 Heck Reaction



Substrates:

1. 2-Ethylacrylic acid - *available at Sigma-Aldrich*
2. 4-Bromobenzonitrile - *available at Sigma-Aldrich*

Products:

1. CCC(=Cc1ccc(C#N)cc1)C(=O)O

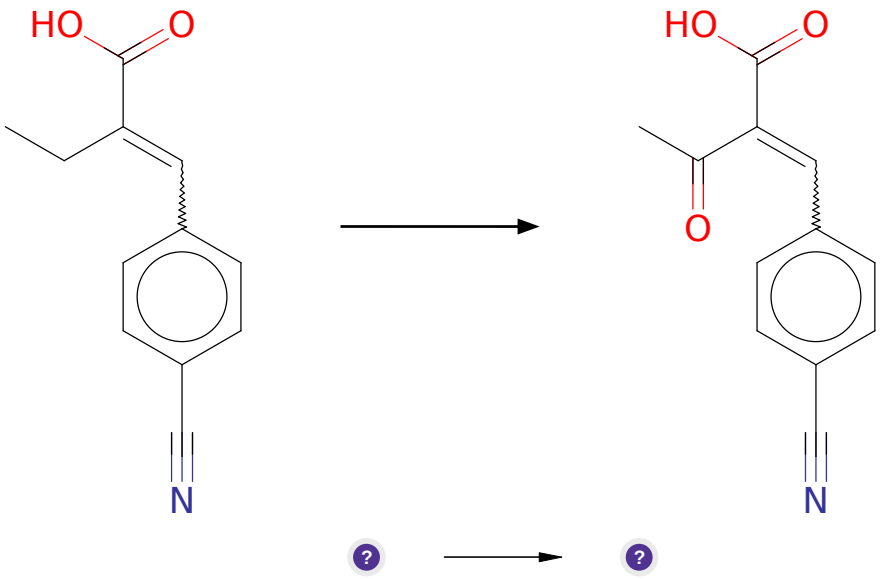
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

Protections: none

Reference: *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: 9177

2.4.2 Allylic Oxidation of Alkenes



Substrates:

1. CCC(=Cc1ccc(C#N)cc1)C(=O)O

Products:

1. CC(=O)C(=Cc1ccc(C#N)cc1)C(=O)O

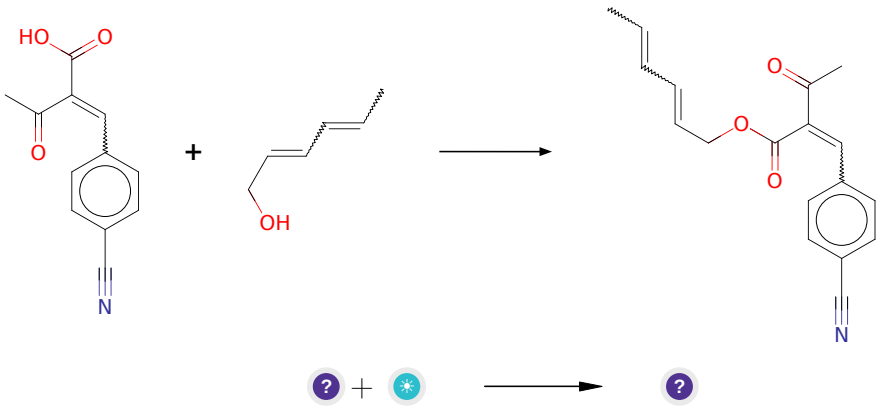
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

Reference: *10.1021/ja0340735* and *10.1021/ol100603q* and *10.1016/j.tetlet.2016.05.063* (Scheme 2)

Retrosynthesis ID: 2583

2.4.3 Steglich Esterification



Substrates:

1. CC(=O)C(=Cc1ccc(C#N)cc1)C(=O)O
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)C(=Cc1ccc(C#N)cc1)C(C)=O

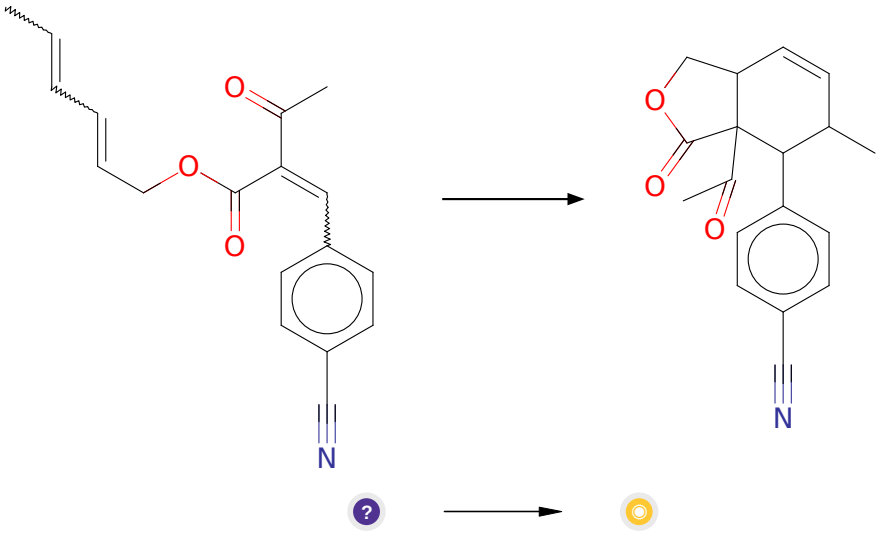
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: *10.1002/anie.197805221*

Retrosynthesis ID: 10171

2.4.4 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C(=Cc1ccc(C#N)cc1)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C#N)cc1

Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

Protections: none

Reference: DOI: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z* AND *10.1021/ja062508t*

Retrosynthesis ID: 18116

2.5 Path 5

Score: `84.06`

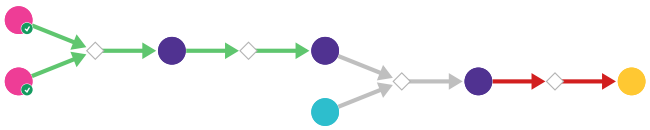
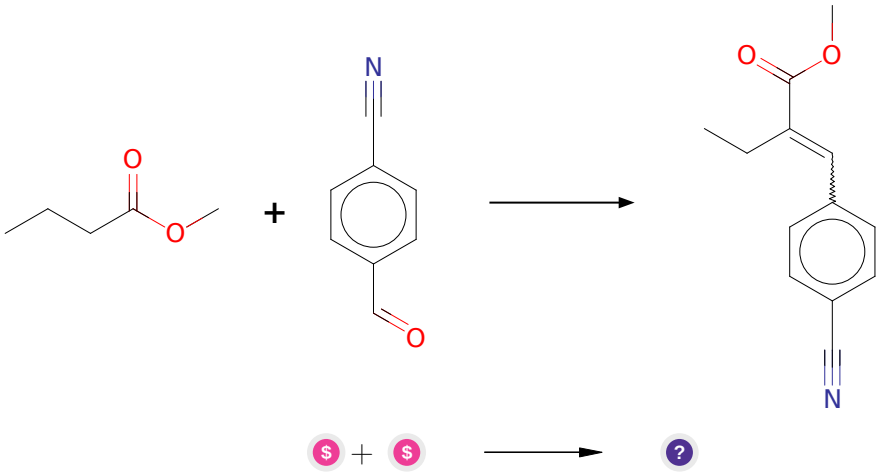


Figure 5: Outline of path 5

2.5.1 Condensation of esters with aldehydes/ketones



Substrates:

1. 4-Cyanobenzaldehyde - *available at Sigma-Aldrich*
2. Methyl butyrate - *available at Sigma-Aldrich*

Products:

1. CCC(=Cc1ccc(C#N)cc1)C(=O)OC

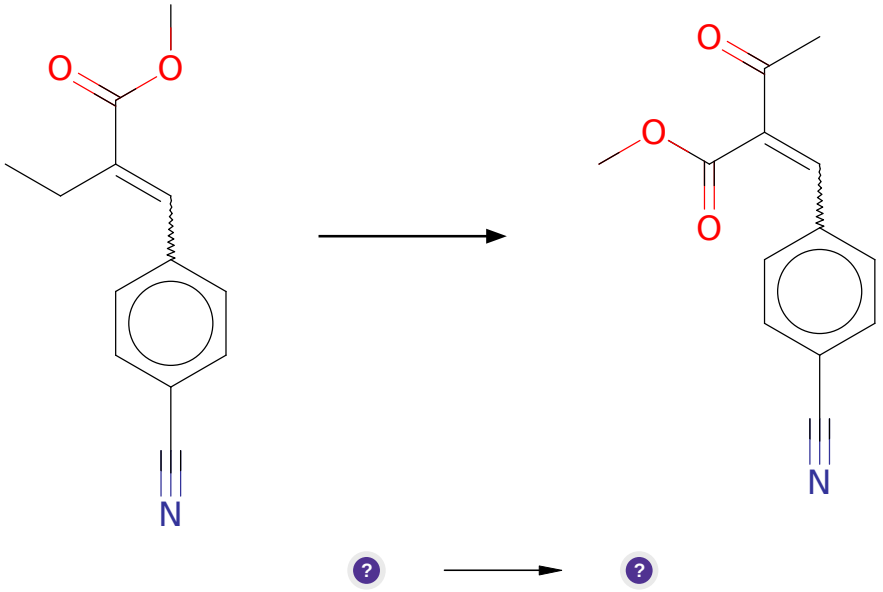
Typical conditions: LDA.THF

Protections: none

Reference: *10.1021/op040006z* AND *10.1016/j.bmcl.2005.10.104* AND

Retrosynthesis ID: 14983

2.5.2 Allylic Oxidation of Alkenes



Substrates:

1. CCC(=Cc1ccc(C#N)cc1)C(=O)OC

Products:

1. COC(=O)C(=Cc1ccc(C#N)cc1)C(C)=O

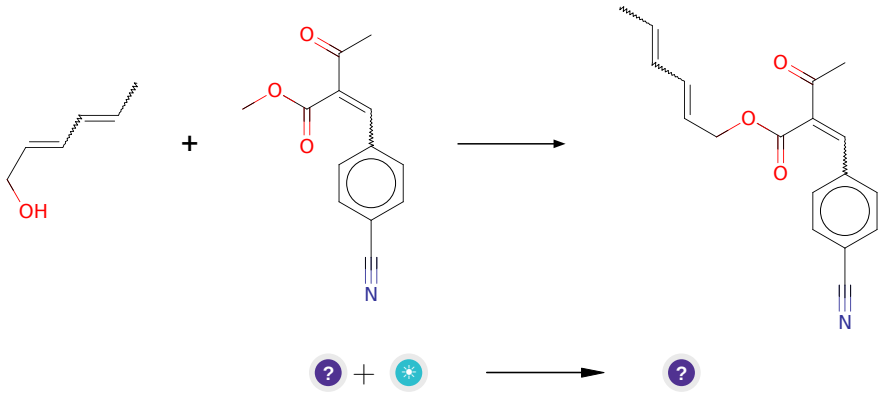
Typical conditions: tBuOOH.Pd(OH)2/C or PhI(OAc)2 or SeO2

Protections: none

Reference: *10.1021/ja0340735* and *10.1021/ol100603q* and *10.1016/j.tetlet.2016.05.063* (Scheme 2)

Retrosynthesis ID: 2583

2.5.3 Acid catalyzed transesterification



Substrates:

1. COC(=O)C(=Cc1ccc(C#N)cc1)C(C)=O
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)C(=Cc1ccc(C#N)cc1)C(C)=O

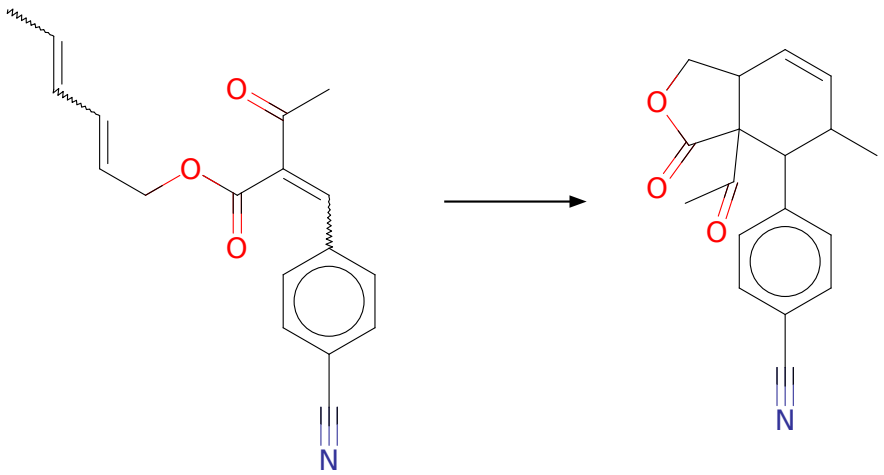
Typical conditions: H+

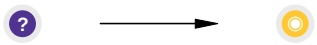
Protections: none

Reference: *10.1021/cr00020a004*

Retrosynthesis ID: 50438

2.5.4 Diels-Alder





Substrates:

1. CC=CC=CCOC(=O)C(=Cc1ccc(C#N)cc1)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1ccc(C#N)cc1

Typical conditions: Lewis acid or chiral Lewis acid. Solvent.

Protections: none

Reference: DOI: *10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z* AND *10.1021/ja062508t*

Retrosynthesis ID: 18116