Paths of analysis*

L10_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

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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: `84.06`

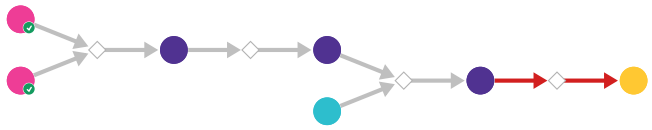
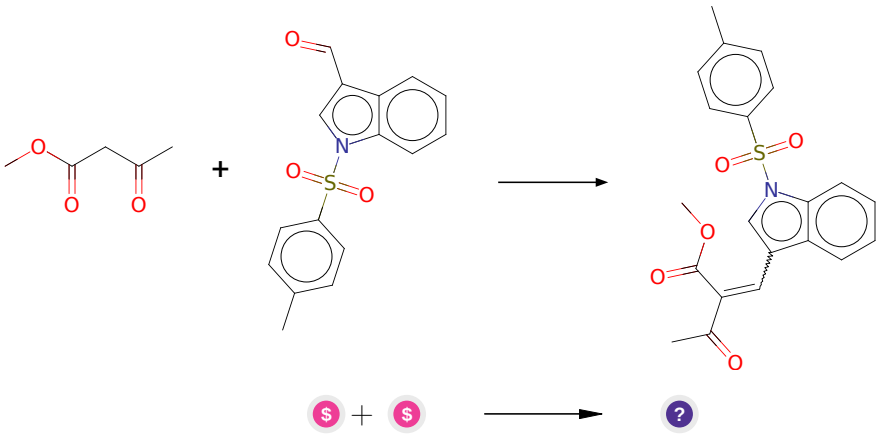


Figure 1: Outline of path 1

2.1.1 Knoevenagel Condensation



Substrates:

1. Methyl acetoacetate - *available at Sigma-Aldrich*
2. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

Products:

1. COC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

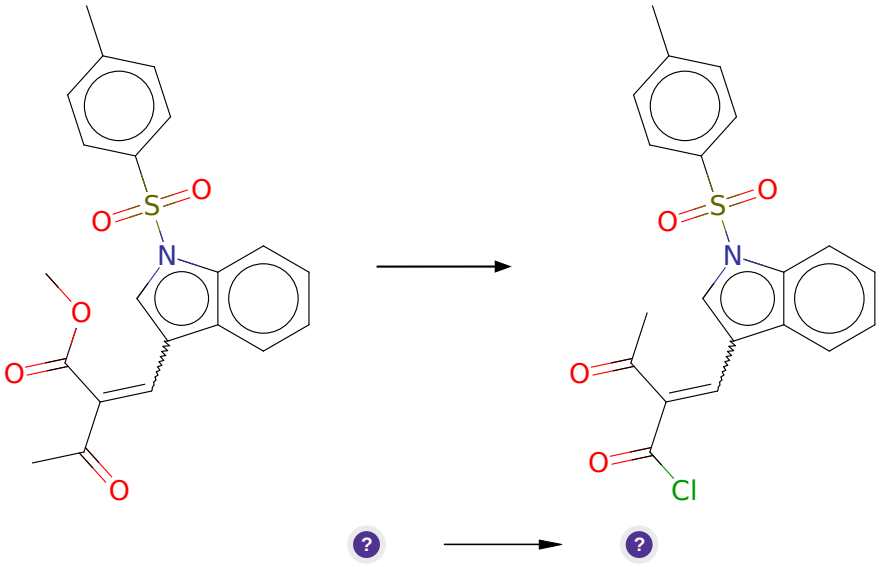
Typical conditions: base e.g.piperidine. solvent

Protections: none

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

Retrosynthesis ID: 252

2.1.2 Synthesis of acid chlorides from esters



Substrates:

1. COC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

Products:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)Cl

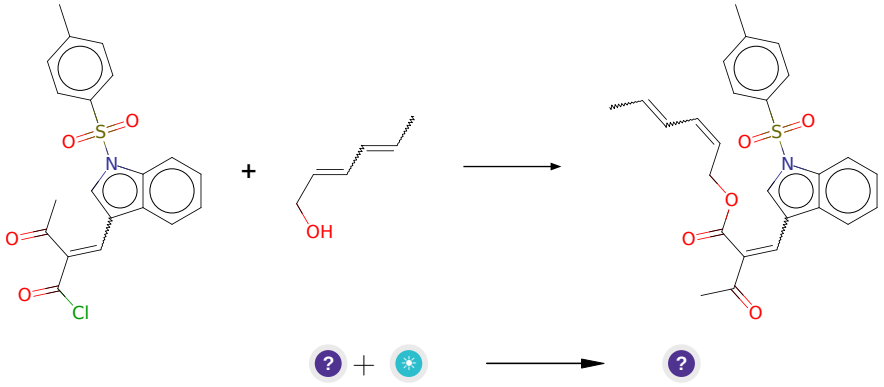
Typical conditions: 1. LiOH.H2O.THF.2. evaporate.3.SOCl2.or.oxalyl.chloride

Protections: none

Reference: *10.1021/ja073476s* and *10.1016/j.tet.2007.04.043* and *10.1002/adsc.200303011* and *10.3390/50500714*

Retrosynthesis ID: 24406

2.1.3 Reaction of acyl chlorides with alcohols and phenols



Substrates:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)Cl
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

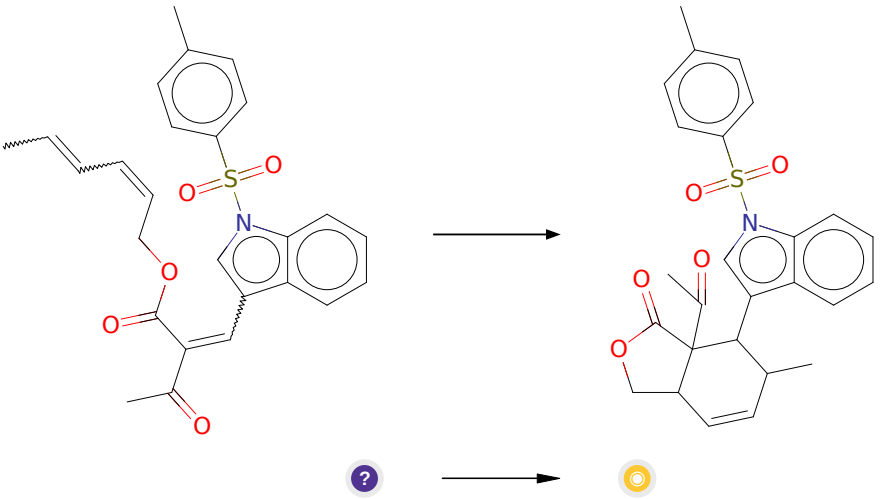
Typical conditions: base.DCM

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

2.1.4 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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: 93.83

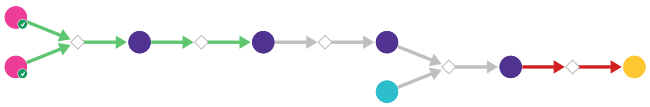
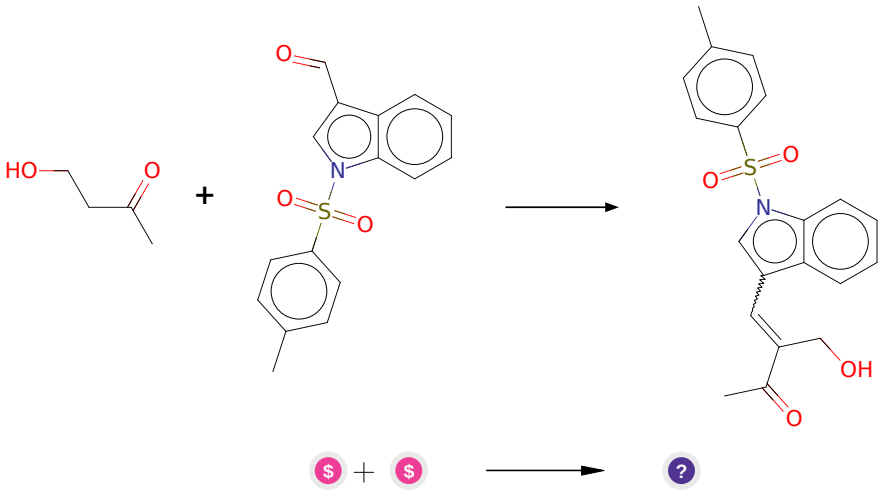


Figure 2: Outline of path 2

2.2.1 Aldol Condensation



Substrates:

1. 4-Hydroxy-2-butanone - *available at Sigma-Aldrich*
2. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

Products:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)CO

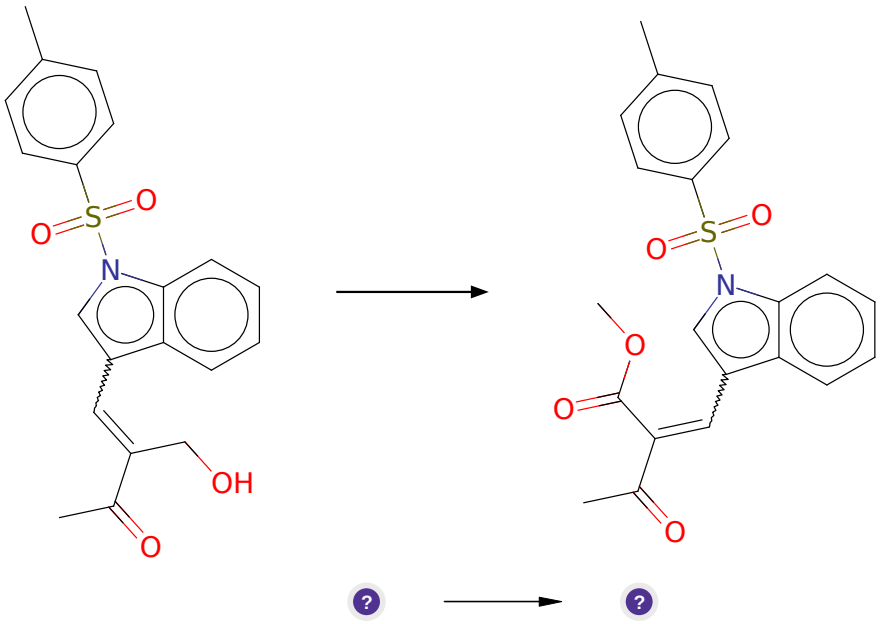
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.2.2 Tandem oxidation-esterification



Substrates:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)CO

Products:

1. COC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

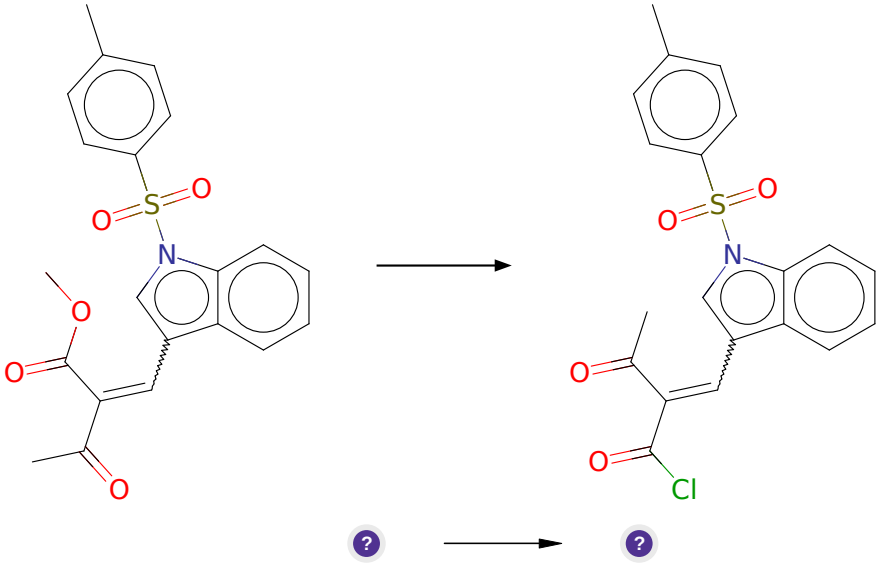
Typical conditions: Oxidant (eg. I2.K2CO3 or Ca(OCl)2).MeOH

Protections: none

Reference: *10.1016/S0040-4039(00)73550-7* and *10.1016/j.tet.2005.03.097* and *10.1021/ol062940f*

Retrosynthesis ID: 25234

2.2.3 Synthesis of acid chlorides from esters



Substrates:

1. COC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

Products:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)Cl

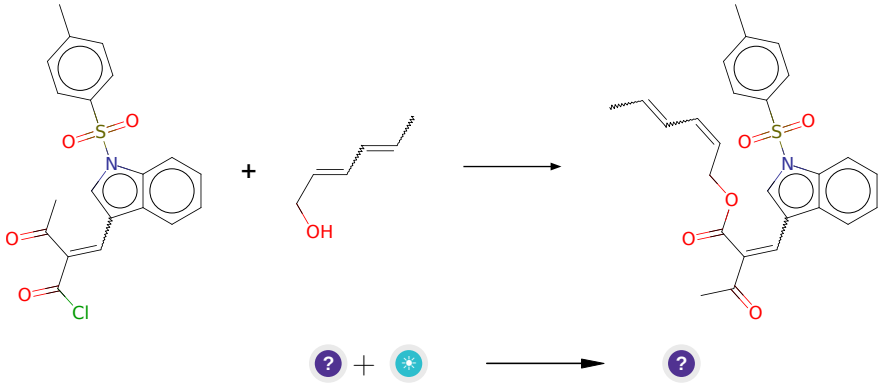
Typical conditions: 1. LiOH.H2O.THF.2. evaporate.3.SOCl2.or.oxalyl.chloride

Protections: none

Reference: *10.1021/ja073476s* and *10.1016/j.tet.2007.04.043* and *10.1002/adsc.200303011* and *10.3390/50500714*

Retrosynthesis ID: 24406

2.2.4 Reaction of acyl chlorides with alcohols and phenols



Substrates:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)Cl
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

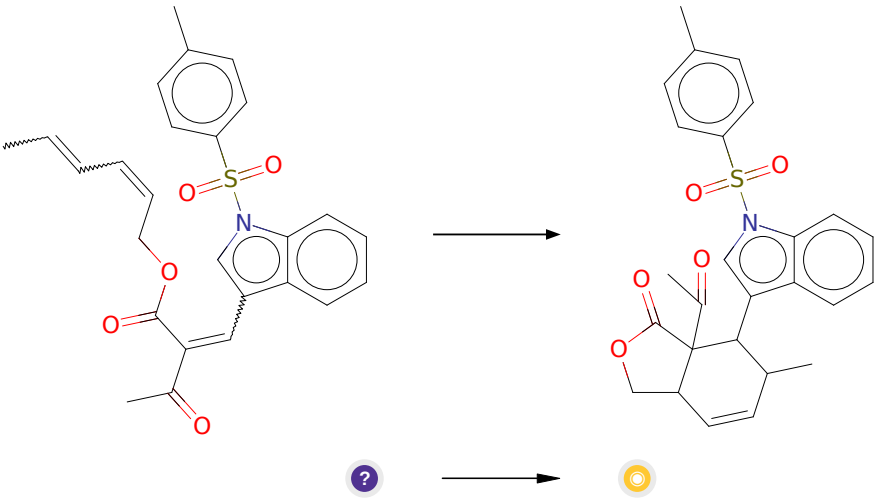
Typical conditions: base.DCM

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

2.2.5 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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

2.3 Path 3

Score: 93.83

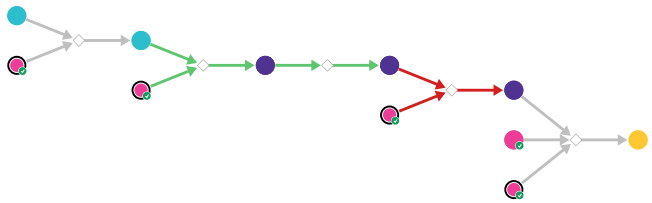
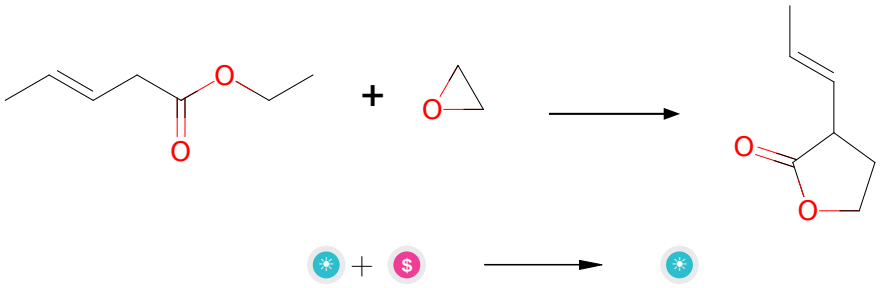


Figure 3: Outline of path 3

2.3.1 Synthesis of lactones from epoxides



Substrates:

1. pent-3t()-enoic acid ethyl ester
2. Oxirane - *available at Sigma-Aldrich*

Products:

1. 3-(1-propenyl)-tetrahydro-2-furanone

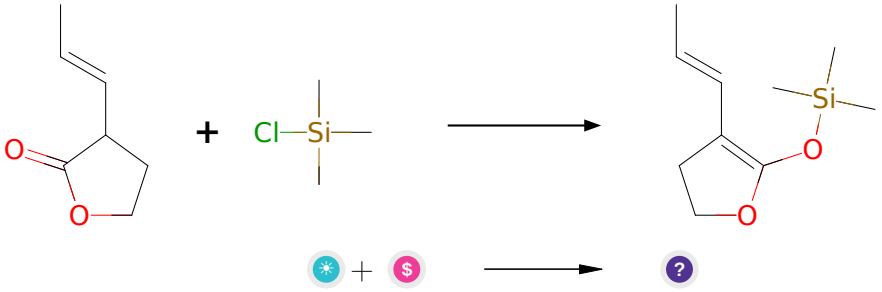
Typical conditions: EtONa.EtOH.rt

Protections: none

Reference: *10.1021/ja9049959* and *10.1016/j.tetlet.2014.12.024* and *10.1021/jo00077a012* and *10.1016/0040-4039(96)00494-7* and *10.1002/chem.201403294*

Retrosynthesis ID: 21258

2.3.2 Enol esters and ethers synthesis



Substrates:

1. 3-(1-propenyl)-tetrahydro-2-furanone
2. TMSCl - *available at Sigma-Aldrich*

Products:

1. C/C=C/C1=C(O[Si](C)(C)C)OCC1

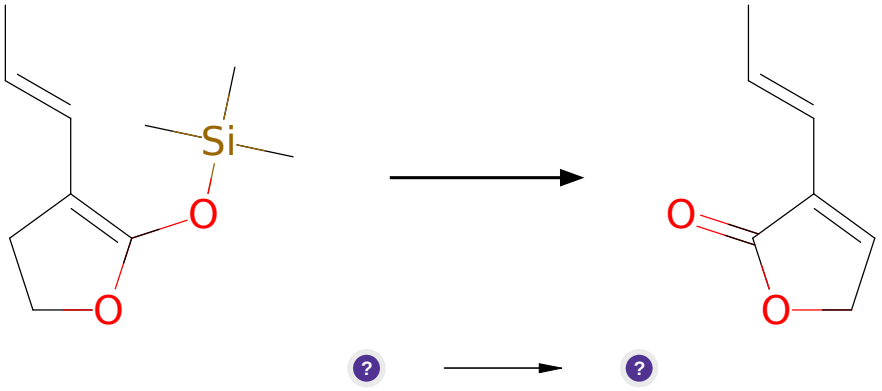
Typical conditions: 1. Et3N.Electrophile

Protections: none

Reference: *10.1016/S0040-4020(03)00977-3* AND *10.1021/ja00056a002*

Retrosynthesis ID: 7799

2.3.3 Dehydrogenation of silyl enol ethers



Substrates:

1. C/C=C/C1=C(O[Si](C)(C)C)OCC1

Products:

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

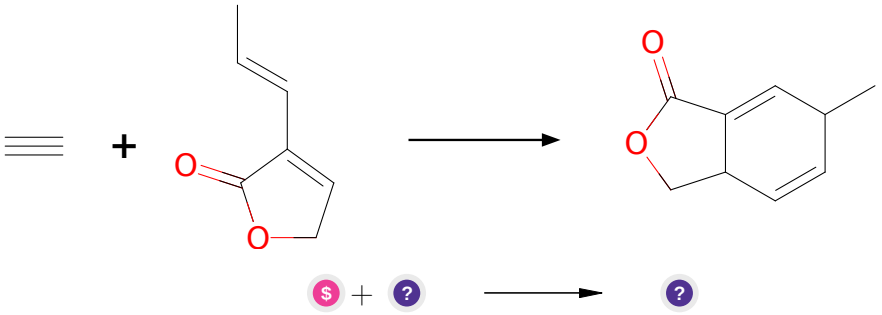
Typical conditions: Pd(OAc)2.Cu(OAc)2.O2.MeCN

Protections: none

Reference: *10.1271/bbb.60.405* and *10.1039/C3CC46778C* and US2015284405 p.40 and *10.1016/S0040-4039(01)81518-5* and US2010204477 p. 15-16 and *10.1016/0040-4039(95)00694-8* and *10.1021/jo00089a034* and *10.1016/S0040-4020(01)90587-3* and *10.1080/00397919008052802* and *10.1021/ja00218a060*

Retrosynthesis ID: 9999877

2.3.4 Diels-Alder



Substrates:

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

Products:

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

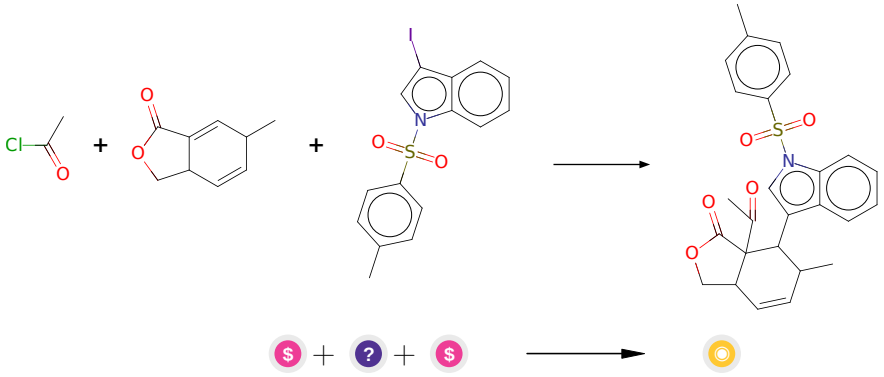
Typical conditions: H2O.MeOH.EtOH.isooctane

Protections: none

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

Retrosynthesis ID: 10557

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



Substrates:

1. 3-Iodo-1-tosyl-1H-indole - *available at Sigma-Aldrich*
2. CC1C=CC2COC(=O)C2=C1
3. Acetyl chloride - *available at Sigma-Aldrich*

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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: 93.83

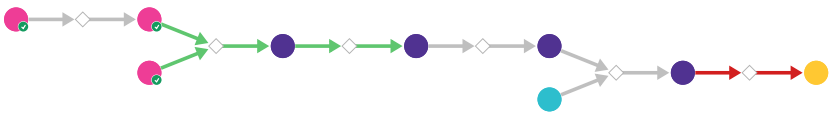
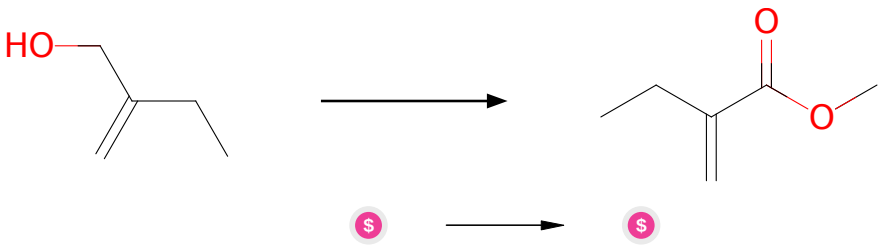


Figure 4: Outline of path 4

2.4.1 Tandem oxidation-esterification



Substrates:

1. 2-methylidenebutan-1-ol - *available at Sigma-Aldrich*

Products:

1. methyl 2-methylidenebutanoate - *available at Sigma-Aldrich*

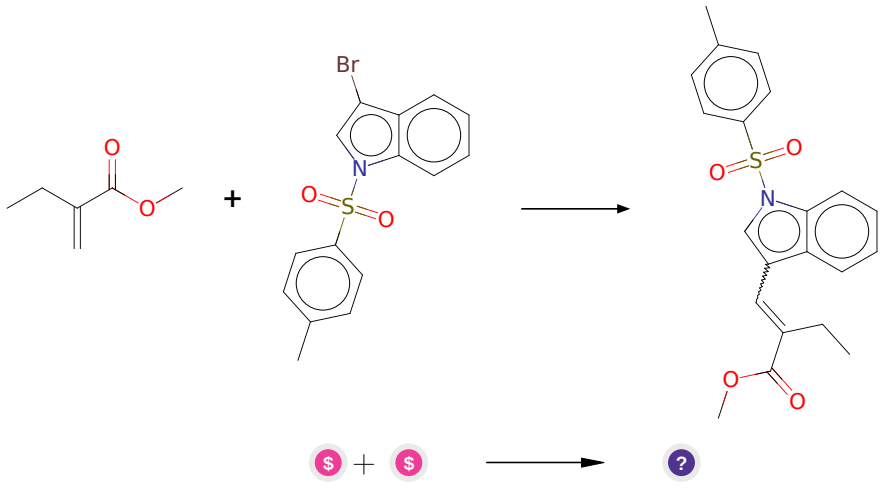
Typical conditions: Oxidant (eg. I2.K2CO3 or Ca(OCl)2).MeOH

Protections: none

Reference: *10.1016/S0040-4039(00)73550-7* and *10.1016/j.tet.2005.03.097* and *10.1021/ol062940f*

Retrosynthesis ID: 25234

2.4.2 Heck Reaction



Substrates:

1. methyl 2-methylidenebutanoate - *available at Sigma-Aldrich*
2. 3-Bromo-1-(p-toluenesulfonyl)indole - *available at Sigma-Aldrich*

Products:

1. CCC(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)OC

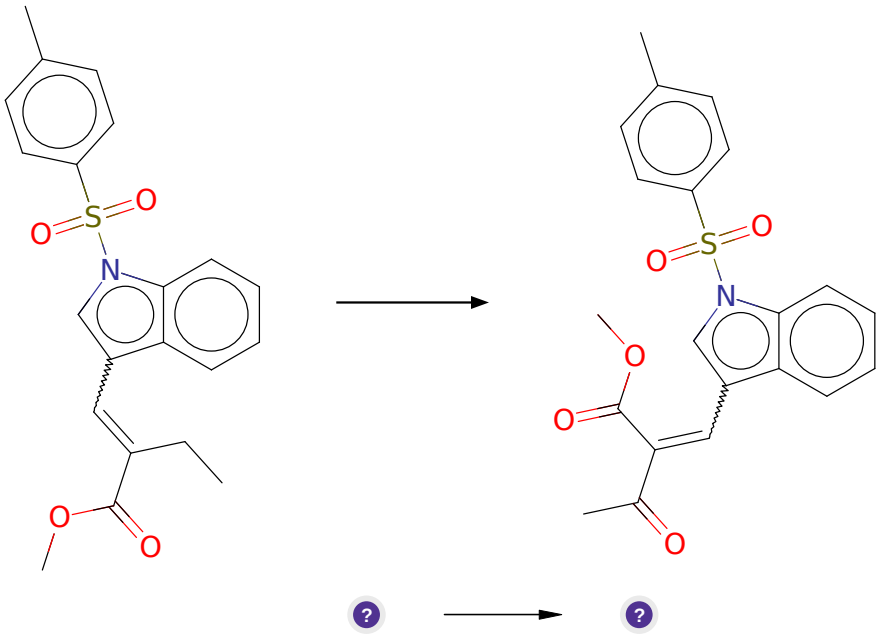
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

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

2.4.3 Allylic oxidation to ketone



Substrates:

1. CCC(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)OC

Products:

1. COC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

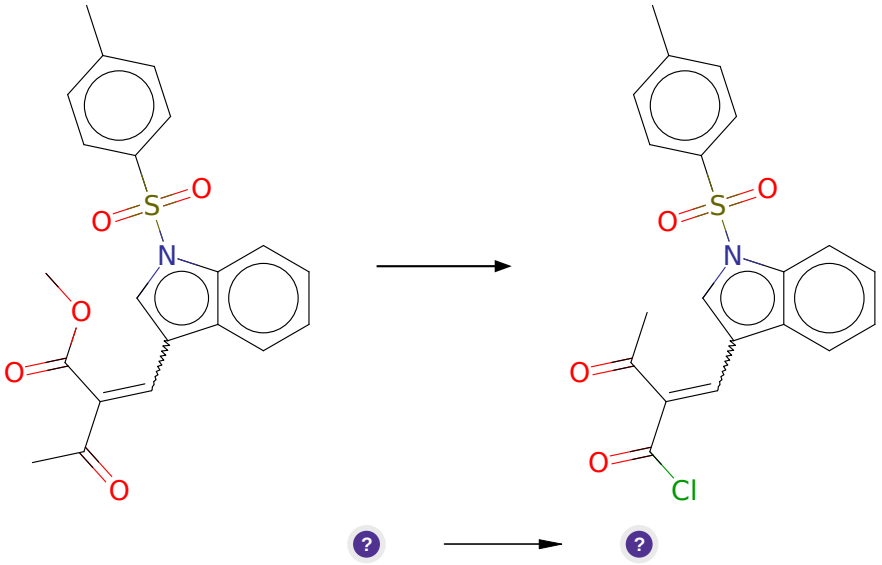
Typical conditions: tBuOOH.Mn(III).or.CrO3.py

Protections: none

Reference: *10.1021/ol0612298* AND *10.1021/jo01263a079* AND *10.1016/j.tetlet.2011.08.166* AND *10.1021/ja0340735*

Retrosynthesis ID: 7200

2.4.4 Synthesis of acid chlorides from esters



Substrates:

1. COC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

Products:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)Cl

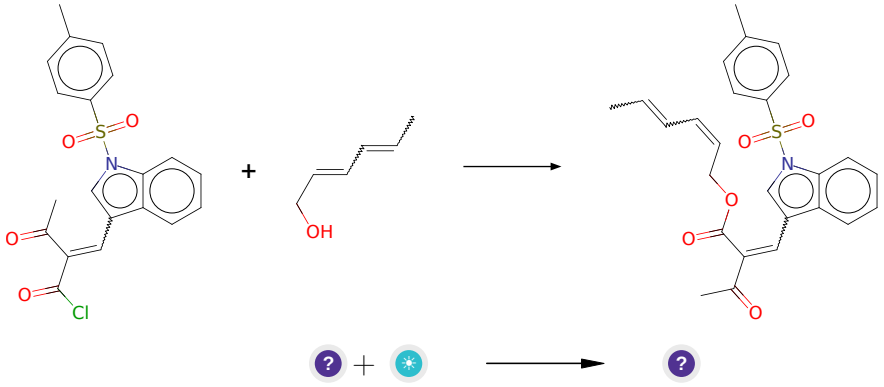
Typical conditions: 1. LiOH.H2O.THF.2. evaporate.3.SOCl2.or.oxalyl.chloride

Protections: none

Reference: *10.1021/ja073476s* and *10.1016/j.tet.2007.04.043* and *10.1002/adsc.200303011* and *10.3390/50500714*

Retrosynthesis ID: 24406

2.4.5 Reaction of acyl chlorides with alcohols and phenols



Substrates:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)Cl
2. sorbic alcohol

Products:

1. CC=CC=CCOC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

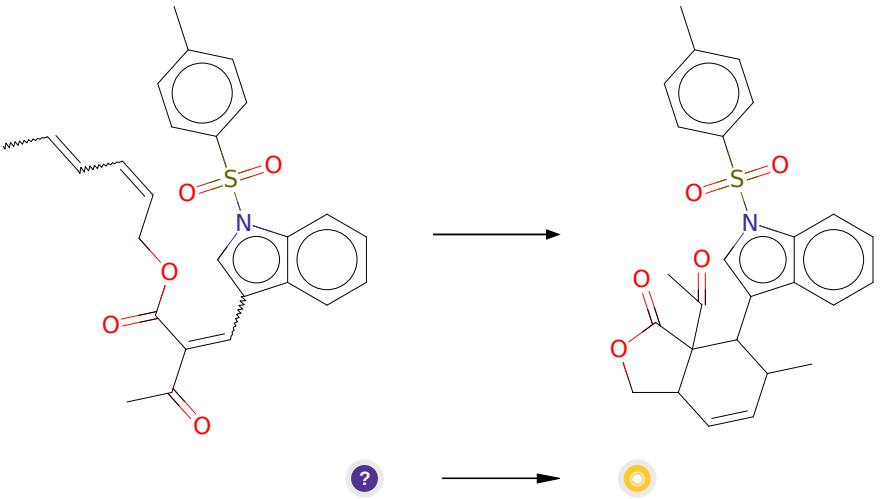
Typical conditions: base.DCM

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

2.4.6 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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: 93.83

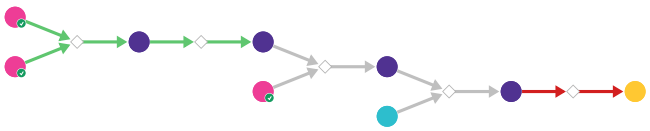
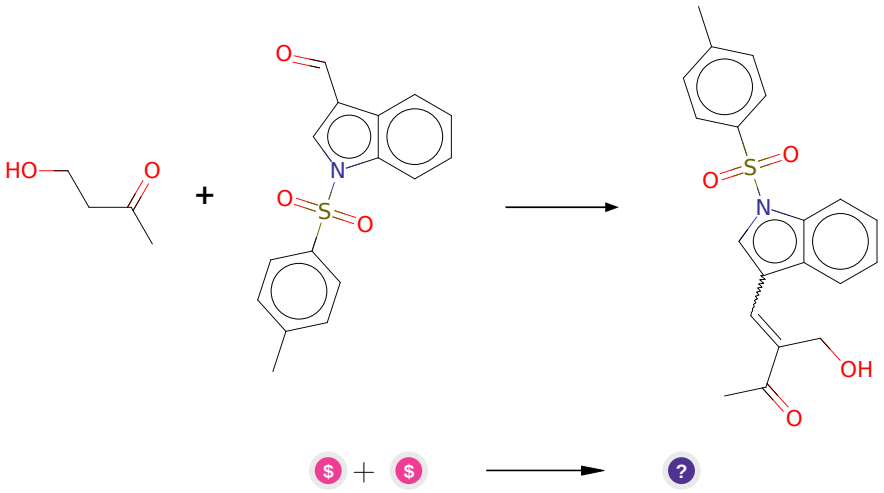


Figure 5: Outline of path 5

2.5.1 Aldol Condensation



Substrates:

1. 4-Hydroxy-2-butanone - *available at Sigma-Aldrich*
2. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

Products:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)CO

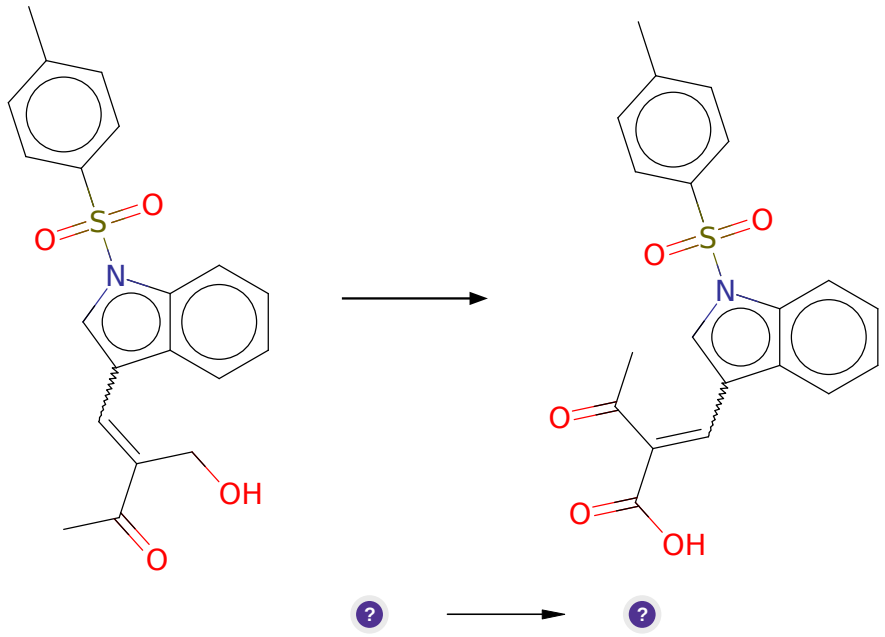
Typical conditions: NaOEt.base

Protections: none

Reference: *10.1080/00397911.2016.1206938*

Retrosynthesis ID: 10049

2.5.2 Jones Oxidation



Substrates:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)CO

Products:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)O

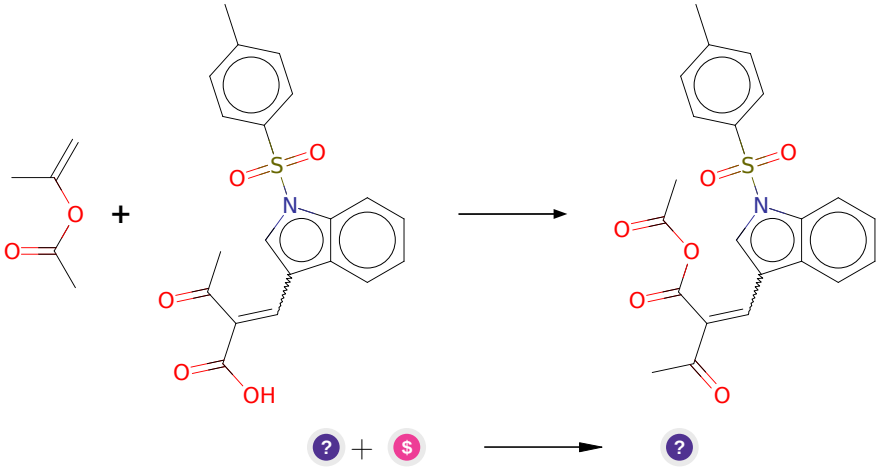
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

Reference: *10.1002/9780470638859.conrr349* and *10.1021/jm00270a004*

Retrosynthesis ID: 11160

2.5.3 Synthesis of Anhydrides from Carboxylic Acids and Vinyl Esters



Substrates:

1. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)O
2. Isopropenyl acetate - *available at Sigma-Aldrich*

Products:

1. CC(=O)OC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

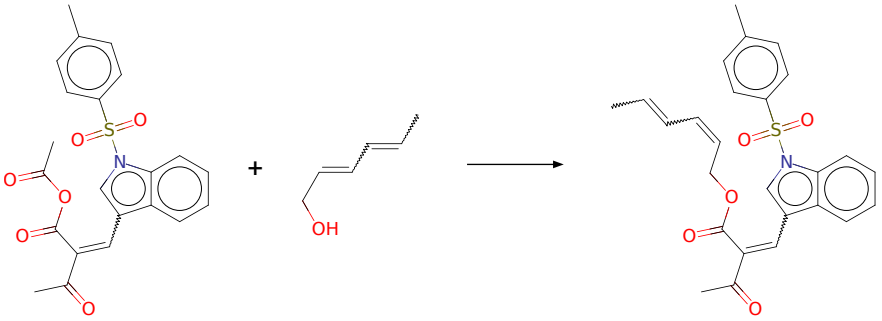
Typical conditions: DCM

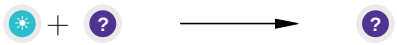
Protections: none

Reference: very common chemistry, see basic textbooks

Retrosynthesis ID: 11428

2.5.4 Cu(OTf)2 catalyzed acylation of primary alcohols and sulfides





Substrates:

1. sorbic alcohol
2. CC(=O)OC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

Products:

1. CC=CC=CCOC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

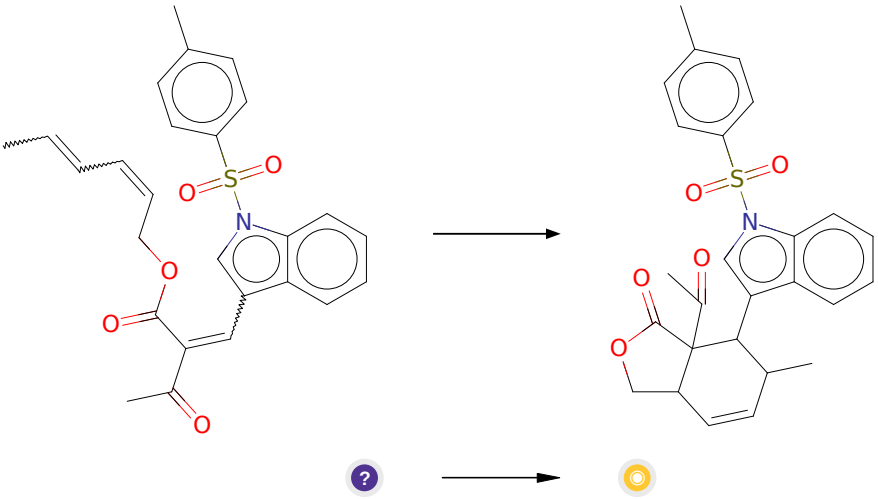
Typical conditions: Cu(II).triflate.DCM.RT

Protections: none

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

Retrosynthesis ID: 10493

2.5.5 Diels-Alder



Substrates:

1. CC=CC=CCOC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

Products:

1. CC(=O)C12C(=O)OCC1C=CC(C)C2c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

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