

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: $\text{TUNNEL_COEF} * \text{FGI_COEF} * \text{STEP} * 20 + 1000000 * (\text{CONFLICT} + \text{NON_SELECTIVITY} + \text{FILTERS} + \text{PROTECT})$

Chemical scoring formula: $\text{SMALLER}^3, \text{SMALLER}^{1.5}$

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: 76.25

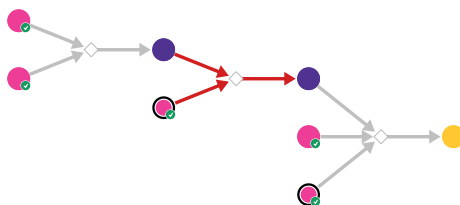
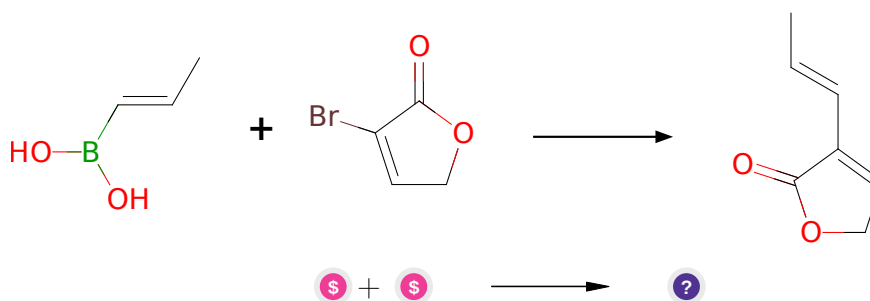


Figure 1: Outline of path 1

2.1.1 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

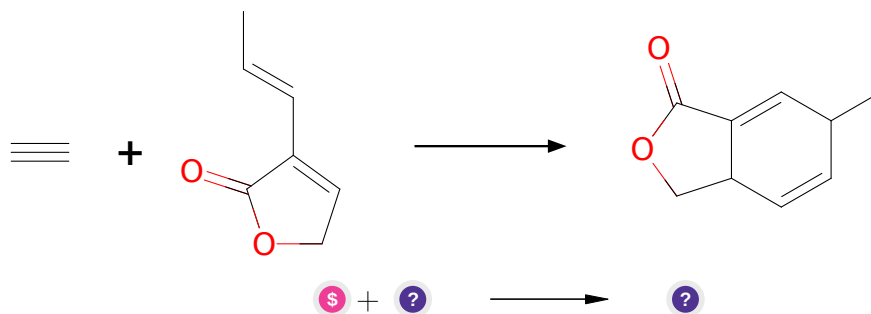
Typical conditions: Pd catalyst.base.solvent

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

2.1.2 Diels-Alder



Substrates:

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

Products:

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

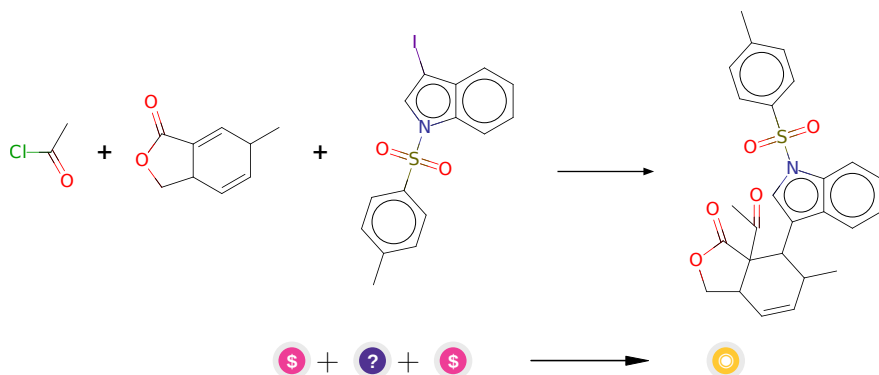
Typical conditions: H₂O.MeOH.EtOH.isooctane

Protections: none

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

Retrosynthesis ID: 10557

2.1.3 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

2.2 Path 2

Score: 76.25

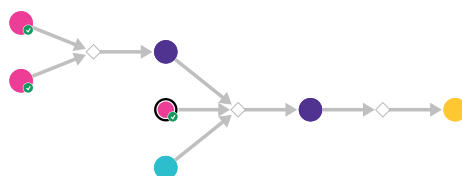
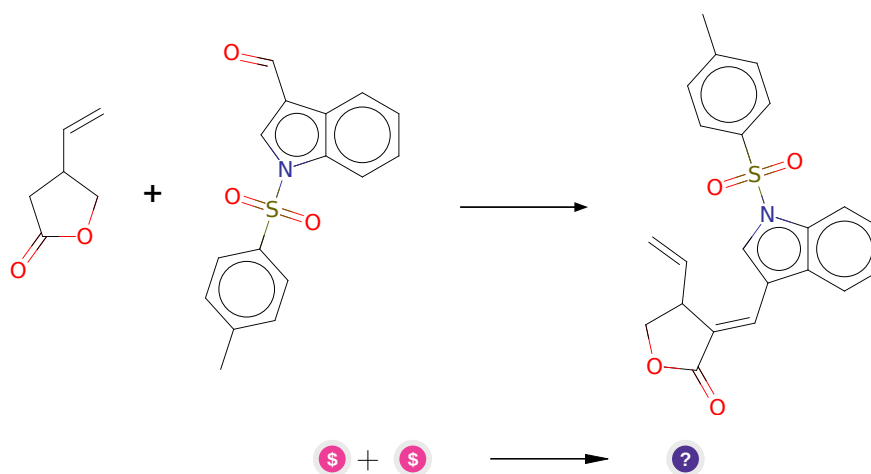


Figure 2: Outline of path 2

2.2.1 Condensation of esters with aldehydes



Substrates:

1. 4-ethenyloxolan-2-one - *available at Sigma-Aldrich*
2. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

Products:

1. C=CC1COC(=O)/C1=C/c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

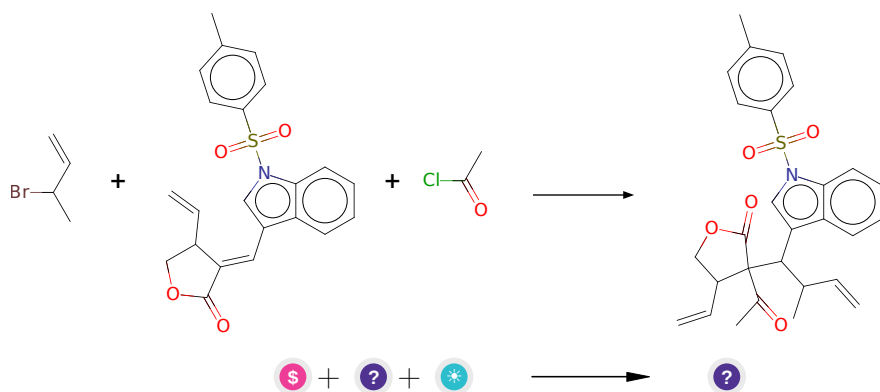
Typical conditions: 1.LDA.2RCHO

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/c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12
3. 3-brom-but-1-en

Products:

1. C=CC(C)C(c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C1(C(C)=O)C(=O)OCC1C=C

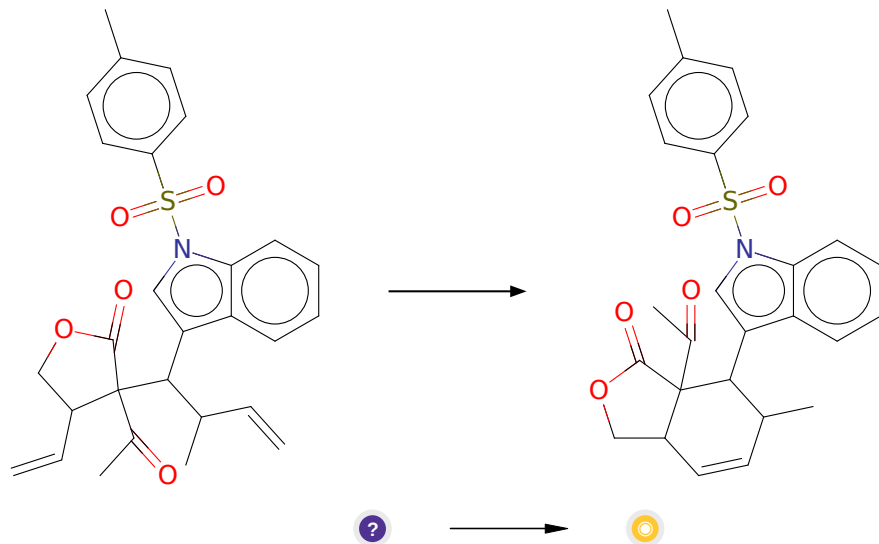
Typical conditions: 1.RCuLi.2.AcCl.HMPA

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(c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C1(C(C)=O)C(=O)OCC1C=C

Products:

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

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

Protections: none

Reference: DOI: [10.1002/anie.200800693](https://doi.org/10.1002/anie.200800693) and [10.1021/acs.orglett.8b04003](https://doi.org/10.1021/acs.orglett.8b04003) and [10.1021/jo0264729](https://doi.org/10.1021/jo0264729) and [10.1021/ja072334v](https://doi.org/10.1021/ja072334v) and [10.1002/ejoc.201001102](https://doi.org/10.1002/ejoc.201001102)

Retrosynthesis ID: 31014187

2.3 Path 3

Score: 76.25

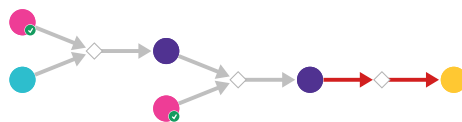
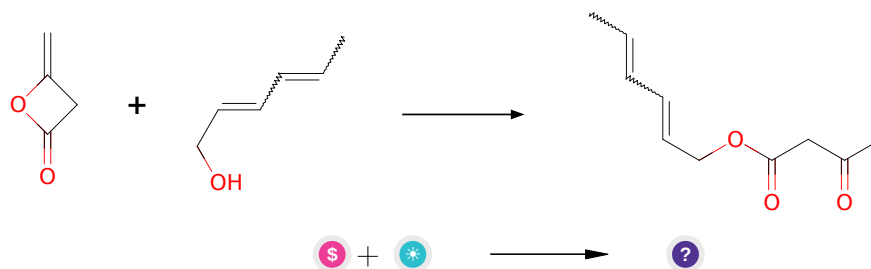


Figure 3: Outline of path 3

2.3.1 Reaction of alcohols with diketene



Substrates:

1. diketene - *available at Sigma-Aldrich*
2. sorbic alcohol

Products:

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

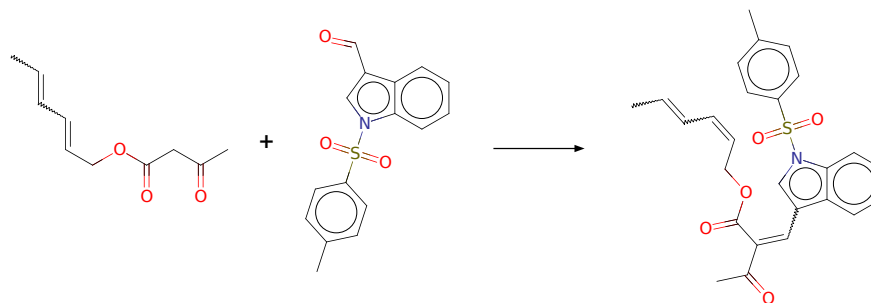
Typical conditions: DCM.heat

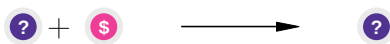
Protections: none

Reference: WO2012/31028 A2 (p.39) AND [10.1021/ol051945u](#) AND [10.1021/ol0069756](#) AND [10.1002/adsc.200800532](#)

Retrosynthesis ID: 14881

2.3.2 Knoevenagel Condensation





Substrates:

1. CC=CC=CCOC(=O)CC(C)=O
2. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

Products:

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

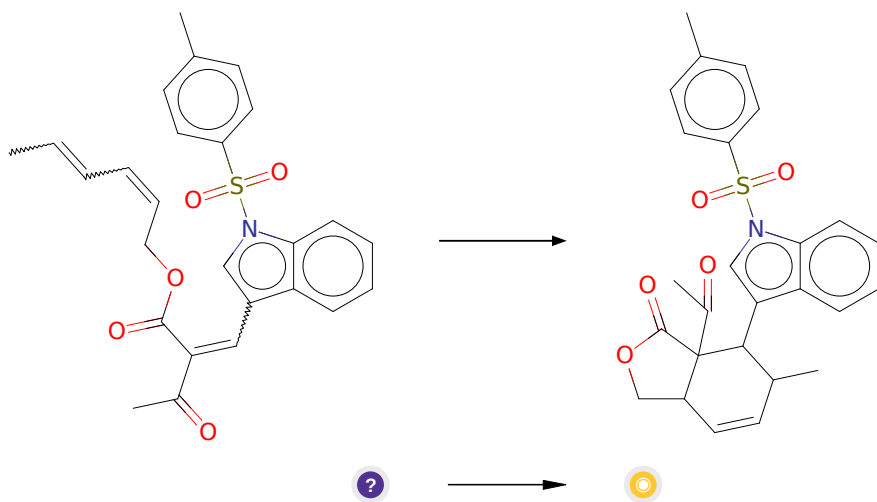
Typical conditions: base e.g.piperidine. solvent

Protections: none

Reference: [10.1002/0471264180.or015.02](#) and [10.13005/ojc/350154](#)

Retrosynthesis ID: 252

2.3.3 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](https://doi.org/10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z) AND [10.1021/ja062508t](https://doi.org/10.1021/ja062508t)

Retrosynthesis ID: 18116

2.4 Path 4

Score: 76.25

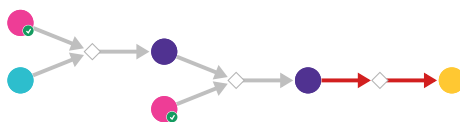
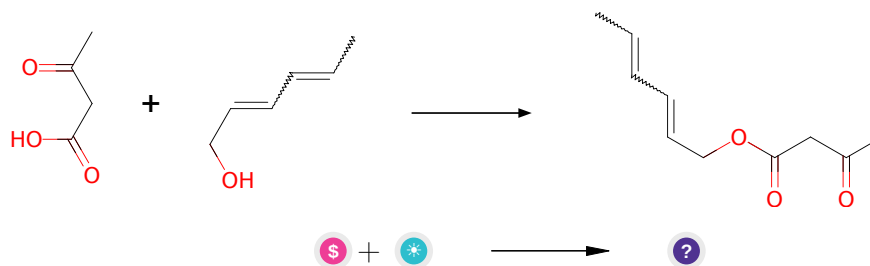


Figure 4: Outline of path 4

2.4.1 Steglich Esterification



Substrates:

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

Products:

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

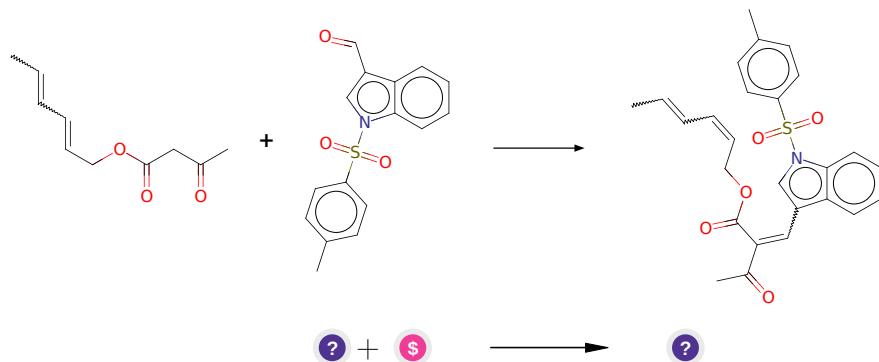
Typical conditions: alcohol.DCC.DMAP.DCM or thiol.DCC.DMAP.DCM

Protections: none

Reference: [10.1002/anie.197805221](https://doi.org/10.1002/anie.197805221)

Retrosynthesis ID: 10171

2.4.2 Knoevenagel Condensation



Substrates:

1. CC=CC=CCOC(=O)CC(C)=O
2. 1-Tosyl-1H-indole-3-carbaldehyde - *available at Sigma-Aldrich*

Products:

1. CC=CC=CCOC(=O)C(=C)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(C)=O

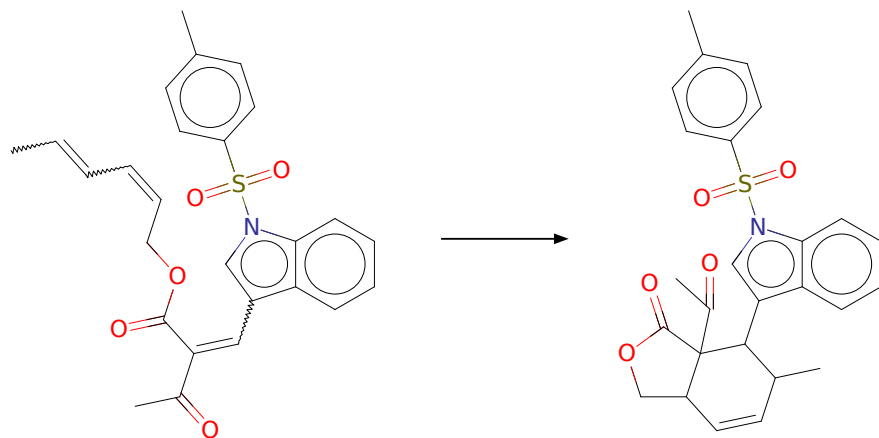
Typical conditions: base e.g. piperidine. solvent

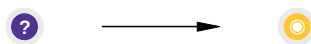
Protections: none

Reference: [10.1002/0471264180.or015.02](#) and [10.13005/ojc/350154](#)

Retrosynthesis ID: 252

2.4.3 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](https://doi.org/10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z) AND [10.1021/ja062508t](https://doi.org/10.1021/ja062508t)

Retrosynthesis ID: 18116

2.5 Path 5

Score: 84.06

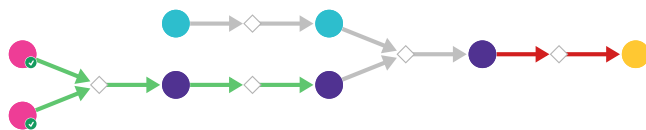
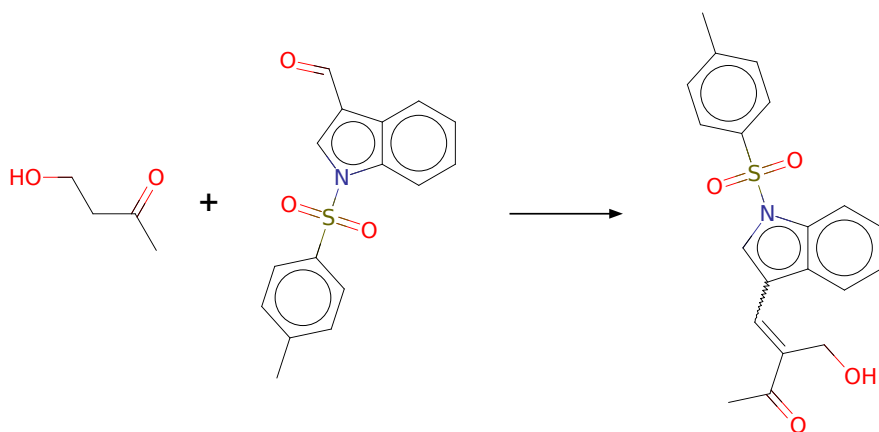
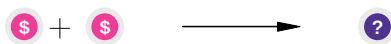


Figure 5: Outline of path 5

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

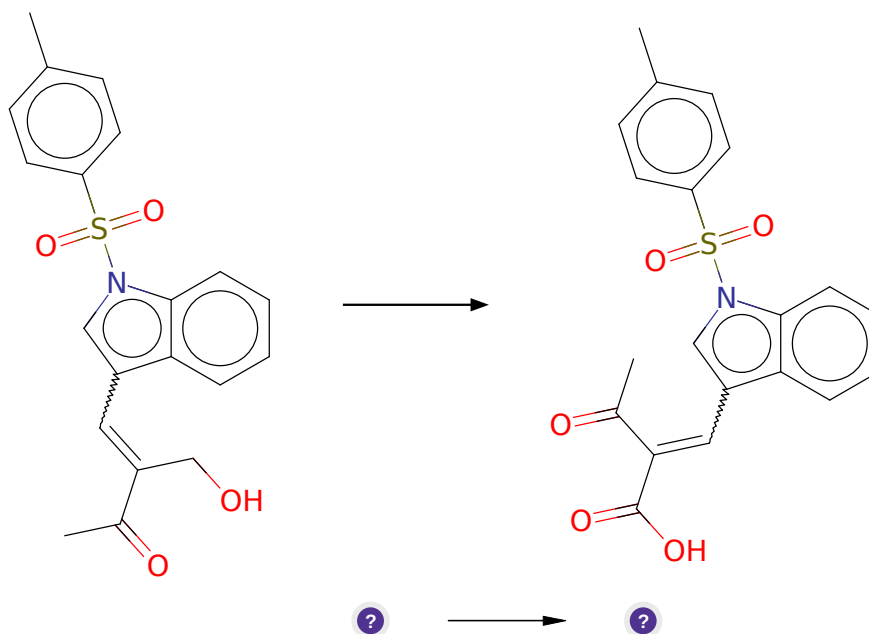
Typical conditions: NaOEt.base

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

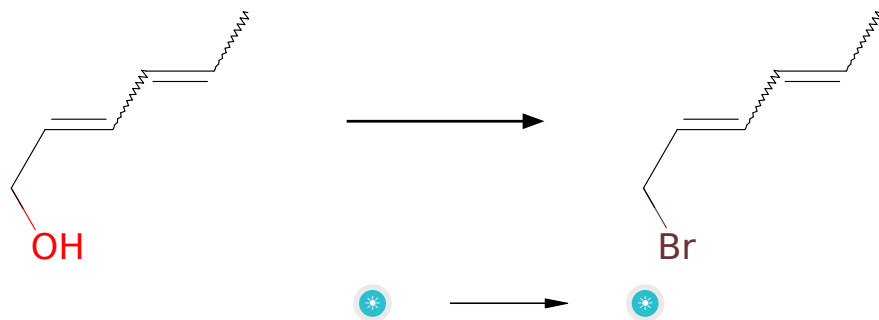
Typical conditions: cromate.sulfate.H2O.acetone

Protections: none

Reference: [10.1002/9780470638859.conrr349](#) and [10.1021/jm00270a004](#)

Retrosynthesis ID: 11160

2.5.3 Appel Reaction



Substrates:

1. sorbic alcohol

Products:

1. 1-brom-hexa-2,4-dien

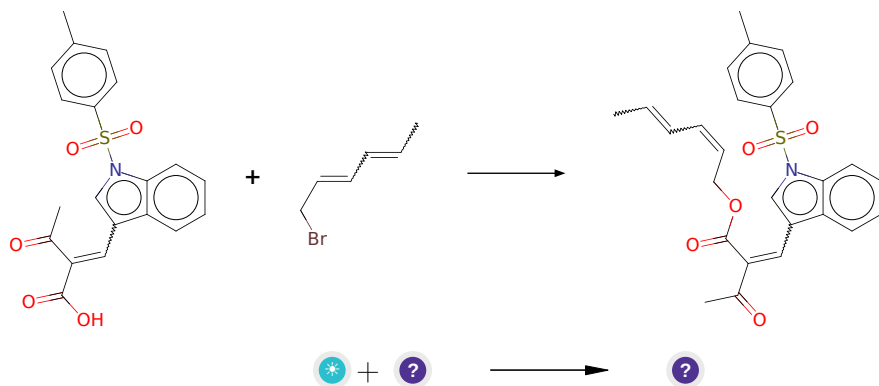
Typical conditions: PPh₃.CBr₄

Protections: none

Reference: [10.1021/ja800574m](#) and [10.1016/j.tet.2012.05.010](#) and [10.1016/j.tet.2004.09.021](#) (experimental)

Retrosynthesis ID: 9990037

2.5.4 Synthesis of esters from alkyl chlorides and carboxylic acids or thioacids



Substrates:

1. 1-brom-hexa-2,4-dien
2. CC(=O)C(=Cc1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12)C(=O)O

Products:

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

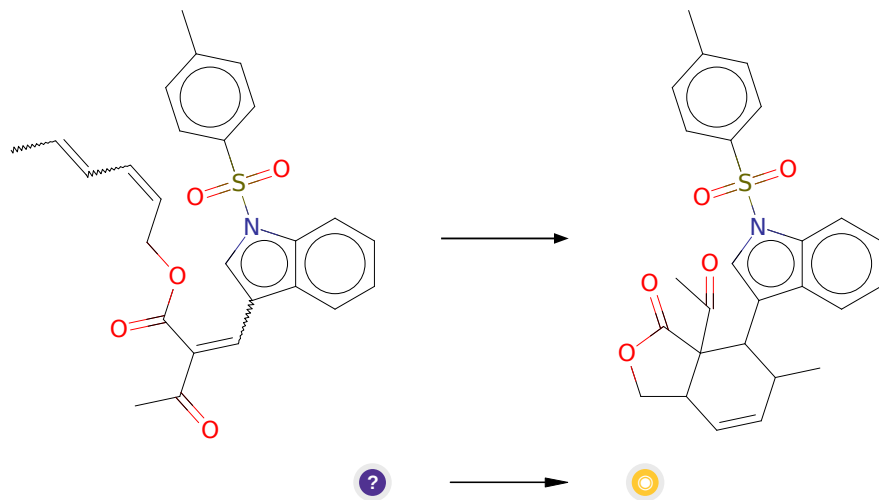
Typical conditions: K₂CO₃.DMF

Protections: none

Reference: [10.1016/j.bmcl.2005.08.026](#) AND [10.1021/ol034655r](#) (SI) AND [10.1039/C3RA41967C](#) AND [10.1016/j.bmcl.2012.03.093](#)

Retrosynthesis ID: 14685

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](https://doi.org/10.1002/1521-3773(20020517)41:10<1668::AID-ANIE1668>3.0.CO;2-Z) AND [10.1021/ja062508t](https://doi.org/10.1021/ja062508t)

Retrosynthesis ID: 18116