Paths of analysis*

Y7A

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

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

2.1 Path 1

Score: `1000146.56`

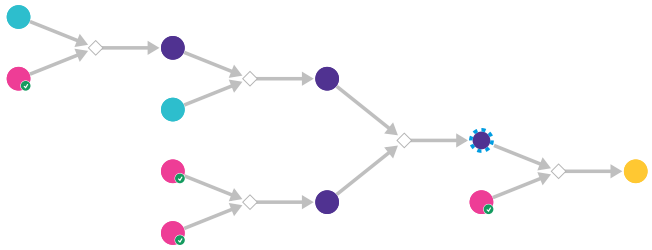
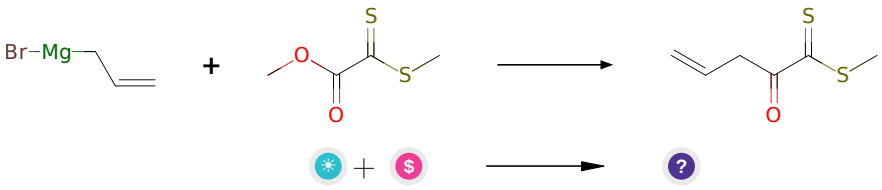


Figure 1: Outline of path 1

2.1.1 Synthesis of ketones from esters via Grignard addition



Substrates:

1. dimethyl-1,1-dithiooxalat
2. Allylmagnesium bromide solution - *available at Sigma-Aldrich*

Products:

1. C=CCC(=O)C(=S)SC

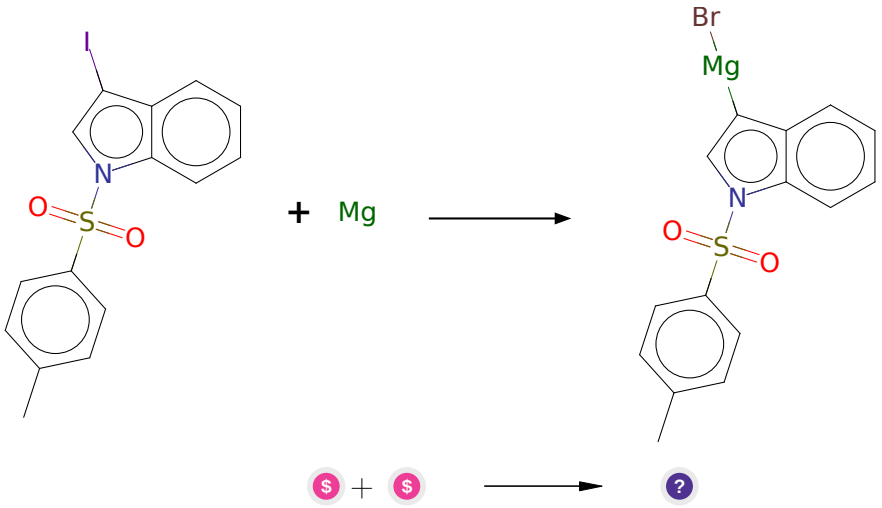
Typical conditions: THF. Low temp

Protections: none

Reference: *10.1021/jm800136b* and *10.1021/ol402802g*

Retrosynthesis ID: 10011836

2.1.2 Synthesis of aryl Grignard reagents



Substrates:

1. 3-Iodo-1-tosyl-1H-indole - *available at Sigma-Aldrich*
2. Magnesium - *available at Sigma-Aldrich*

Products:

1. Cc1ccc(S(=O)(=O)n2cc([Mg]Br)c3ccccc32)cc1

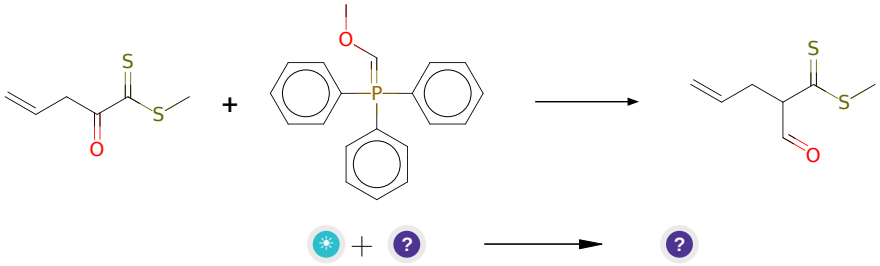
Typical conditions: iPrMgCl.LiCl.THF or other conditions Mg.THF or tBuLi.MgBr2

Protections: none

Reference: DOI: *10.1016/S0040-4039(99)01404-5* and *10.1021/jo0000574* and WO2014123793 p.137 and *10.1021/jm400491x* and *10.3762/bjoc.12.36*

Retrosynthesis ID: 10011460

2.1.3 Olefination of ketones followed by hydrolysis



Substrates:

1. triphenylphosphonium methoxymethylide
2. C=CCC(=O)C(=S)SC

Products:

1. C=CCC(C=O)C(=S)SC

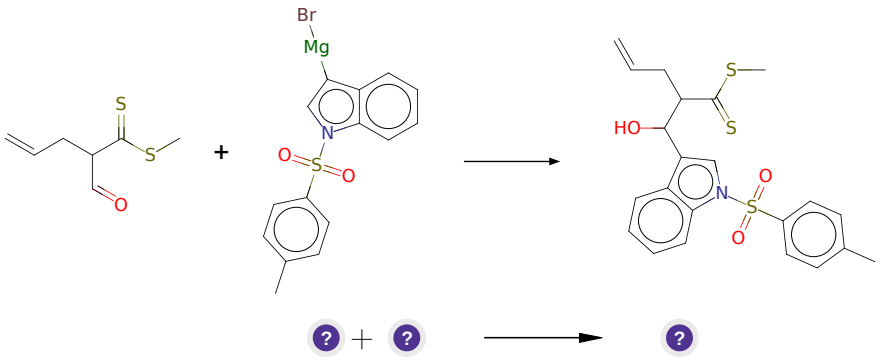
Typical conditions: KHMDS.THF hydrolysis: pTsOH.water.acetone

Protections: none

Reference: *10.1002/anie.201811403* and *10.1002/anie.201809130* and *10.1002/anie.201705809* and *10.1002/anie.201409038* and *10.1021/ol3028994* (SI)

Retrosynthesis ID: 31014861

2.1.4 Grignard-Type Reaction



Substrates:

1. C=CCC(C=O)C(=S)SC
2. Cc1ccc(S(=O)(=O)n2cc([Mg]Br)c3ccccc32)cc1

Products:

1. C=CCC(C(=S)SC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

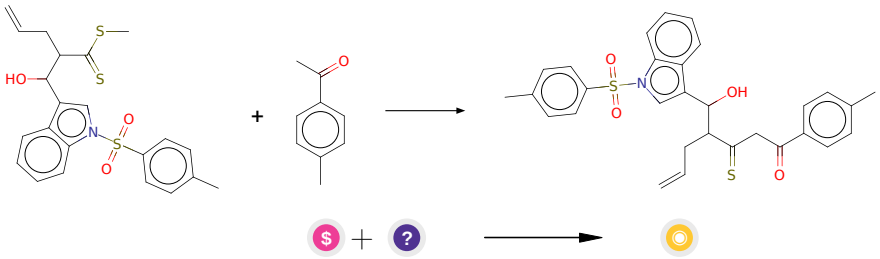
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1055/s-0030-1260809* or *10.1021/jm061429p* or *10.1021/jo0621423* or *10.1021/ja00373a036* or *10.1016/S0040-4020(01)00457-4*

Retrosynthesis ID: 25123

2.1.5 Condensation of ketones with dithioesters



Substrates:

1. Methyl p-tolyl ketone - *available at Sigma-Aldrich*
2. C=CCC(C(=S)SC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=S)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Typical conditions: NaH.DMF

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6][CH]([#6])[OH]	alcohols	Methoxymethyl Ether (MOM) 2-Methoxyethoxymethyl Ether (MEM) Tetrahydropyranyl Ether (THP) Benzyl Ether (PMB) t-Butyldimethylsilyl Ether (TBDMS) Methyl Ether

Reference: *10.1021/jo400599e* and *10.1002/ejoc.201301667*

Retrosynthesis ID: 9996413

2.2 Path 2

Score: `1000195.39`

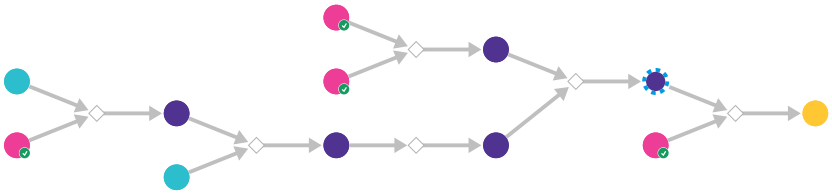
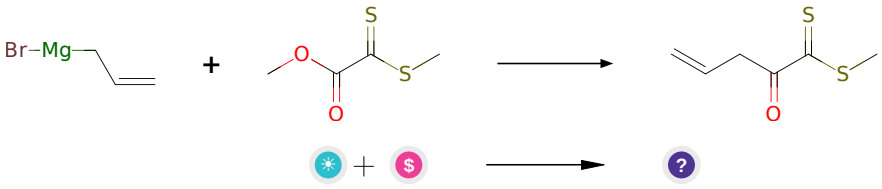


Figure 2: Outline of path 2

2.2.1 Synthesis of ketones from esters via Grignard addition



Substrates:

1. dimethyl-1,1-dithiooxalat

2. Allylmagnesium bromide solution - *available at Sigma-Aldrich*

Products:

1. C=CCC(=O)C(=S)SC

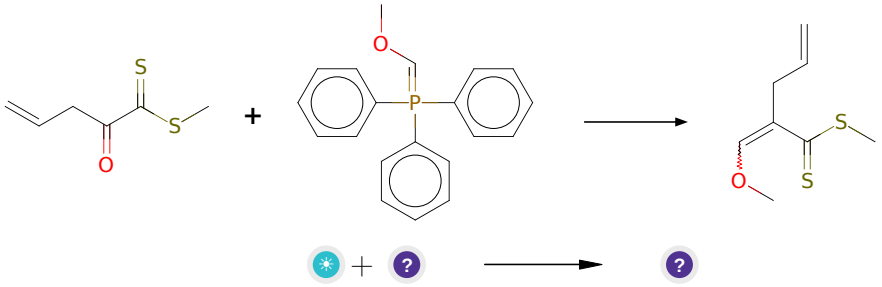
Typical conditions: THF. Low temp

Protections: none

Reference: *10.1021/jm800136b* and *10.1021/ol402802g*

Retrosynthesis ID: 10011836

2.2.2 Olefination of ketones



Substrates:

1. triphenylphosphonium methoxymethylide
2. C=CCC(=O)C(=S)SC

Products:

1. C=CCC(=COC)C(=S)SC

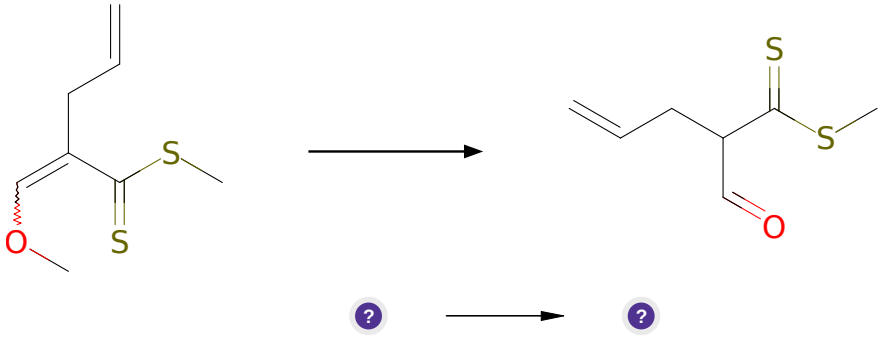
Typical conditions: KHMDS.THF

Protections: none

Reference: *10.1002/anie.201811403* and *10.1002/anie.201809130* and *10.1002/anie.201705809* and *10.1002/anie.201409038* and *10.1021/ol3028994* (SI)

Retrosynthesis ID: 31014859

2.2.3 Synthesis of ketones and aldehydes from enol ethers



Substrates:

1. C=CCC(=COC)C(=S)SC

Products:

1. C=CCC(C=O)C(=S)SC

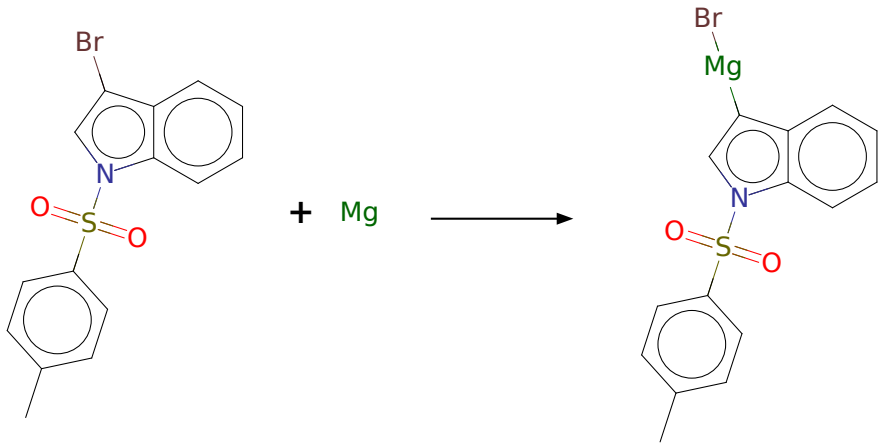
Typical conditions: [H+].THF

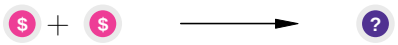
Protections: none

Reference: *10.1081/SCC-120023437* AND *10.1016/j.bmcl.2007.11.020* AND *10.1016/j.tet.2011.03.084* AND *10.1021/ja00270a023* AND *10.1055/s-1994-25424* AND

Retrosynthesis ID: 14842

2.2.4 Synthesis of aryl Grignard reagents





Substrates:

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

Products:

1. Cc1ccc(S(=O)(=O)n2cc([Mg]Br)c3ccccc32)cc1

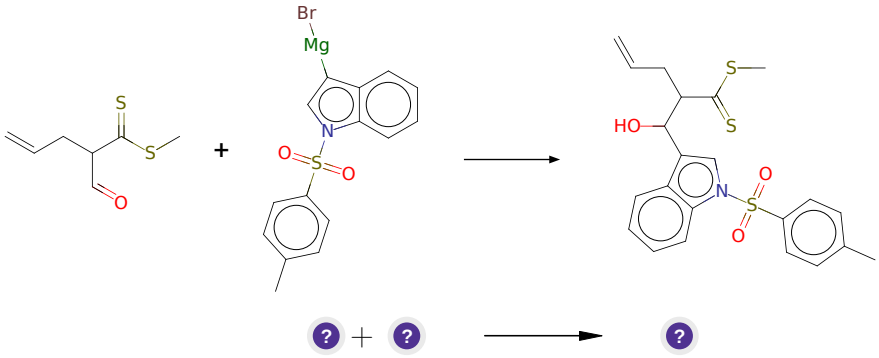
Typical conditions: iPrMgCl.THF or other conditions like BuLi.MgBr2 or Mg.THF

Protections: none

Reference: DOI: *10.1016/S0040-4039(99)01404-5* and *10.1021/jo0000574* and *10.1002/anie.200454084* and *10.1021/ol400150z*

Retrosynthesis ID: 10011461

2.2.5 Grignard-Type Reaction



Substrates:

1. C=CCC(C=O)C(=S)SC
2. Cc1ccc(S(=O)(=O)n2cc([Mg]Br)c3ccccc32)cc1

Products:

1. C=CCC(C(=S)SC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

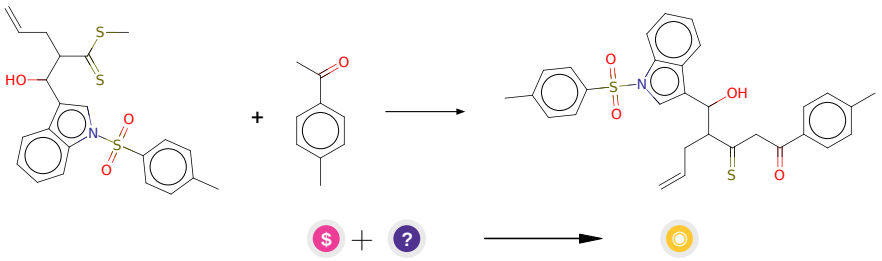
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1055/s-0030-1260809* or *10.1021/jm061429p* or *10.1021/jo0621423* or *10.1021/ja00373a036* or *10.1016/S0040-4020(01)00457-4*

Retrosynthesis ID: 25123

2.2.6 Condensation of ketones with dithioesters



Substrates:

1. Methyl p-tolyl ketone - *available at Sigma-Aldrich*
2. C=CCC(C(=S)SC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=S)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Typical conditions: NaH.DMF

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6][CH]([#6])[OH]	alcohols	Methoxymethyl Ether (MOM) 2-Methoxyethoxymethyl Ether (MEM) Tetrahydropyranyl Ether (THP) Benzyl Ether (PMB) t-Butyldimethylsilyl Ether (TBDMS) Methyl Ether

Reference: *10.1021/jo400599e* and *10.1002/ejoc.201301667*

Retrosynthesis ID: 9996413

2.3 Path 3

Score: 1000195.39

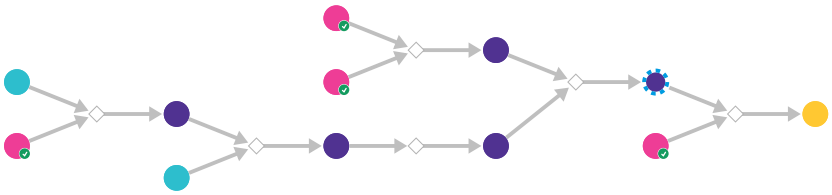
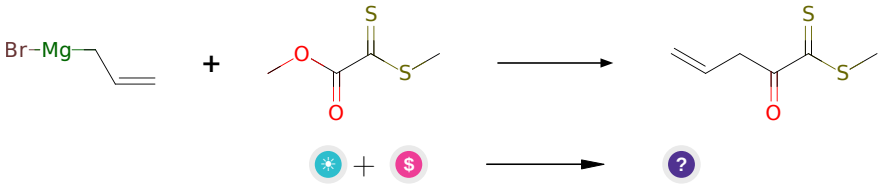


Figure 3: Outline of path 3

2.3.1 Synthesis of ketones from esters via Grignard addition



Substrates:

1. dimethyl-1,1-dithiooxalat
2. Allylmagnesium bromide solution - *available at Sigma-Aldrich*

Products:

1. C=CCC(=O)C(=S)SC

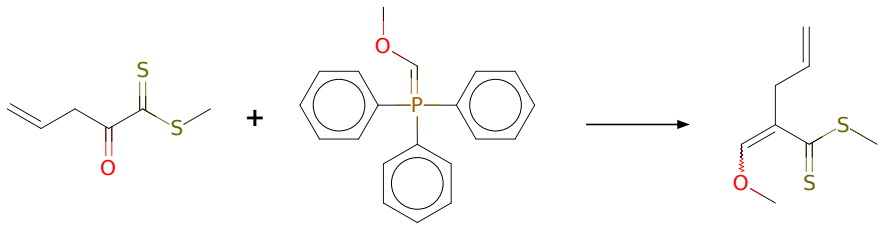
Typical conditions: THF. Low temp

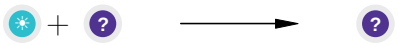
Protections: none

Reference: *10.1021/jm800136b* and *10.1021/ol402802g*

Retrosynthesis ID: 10011836

2.3.2 Olefination of ketones





Substrates:

1. triphenylphosphonium methoxymethylide
2. C=CCC(=O)C(=S)SC

Products:

1. C=CCC(=COC)C(=S)SC

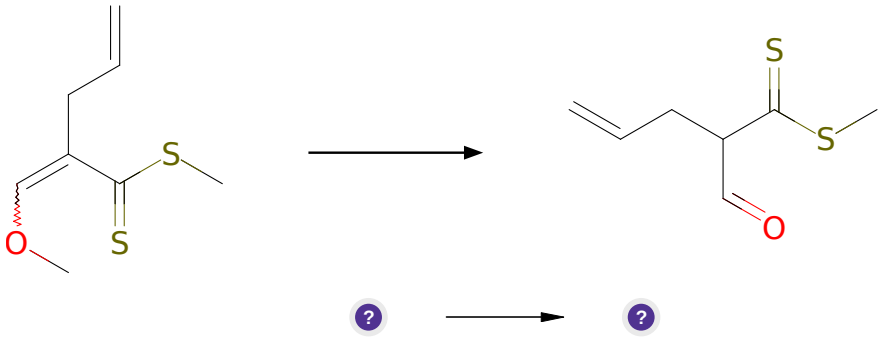
Typical conditions: KHMDS.THF

Protections: none

Reference: *10.1002/anie.201811403* and *10.1002/anie.201809130* and *10.1002/anie.201705809* and *10.1002/anie.201409038* and *10.1021/ol3028994* (SI)

Retrosynthesis ID: 31014859

2.3.3 Synthesis of ketones and aldehydes from enol ethers



Substrates:

1. C=CCC(=COC)C(=S)SC

Products:

1. C=CCC(C=O)C(=S)SC

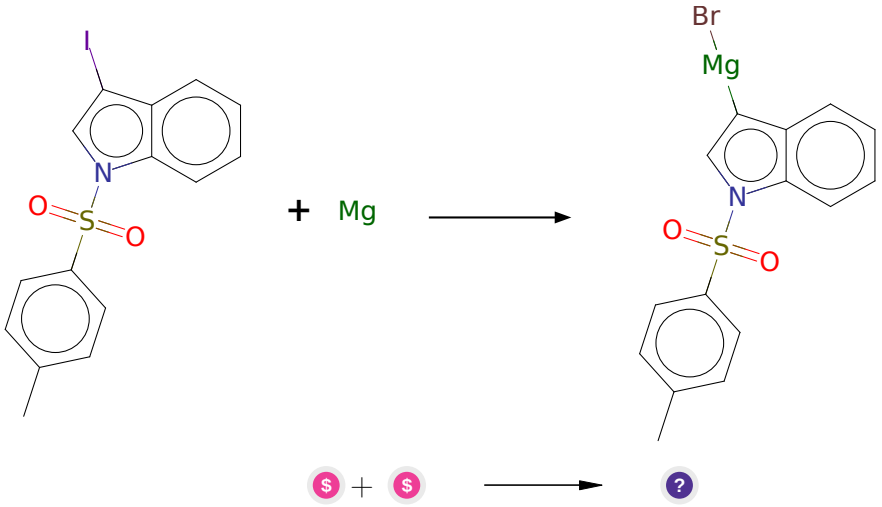
Typical conditions: [H+].THF

Protections: none

Reference: *10.1081/SCC-120023437* AND *10.1016/j.bmcl.2007.11.020* AND *10.1016/j.tet.2011.03.084* AND *10.1021/ja00270a023* AND *10.1055/s-1994-25424* AND

Retrosynthesis ID: 14842

2.3.4 Synthesis of aryl Grignard reagents



Substrates:

1. 3-Iodo-1-tosyl-1H-indole - *available at Sigma-Aldrich*
2. Magnesium - *available at Sigma-Aldrich*

Products:

1. Cc1ccc(S(=O)(=O)n2cc([Mg]Br)c3ccccc32)cc1

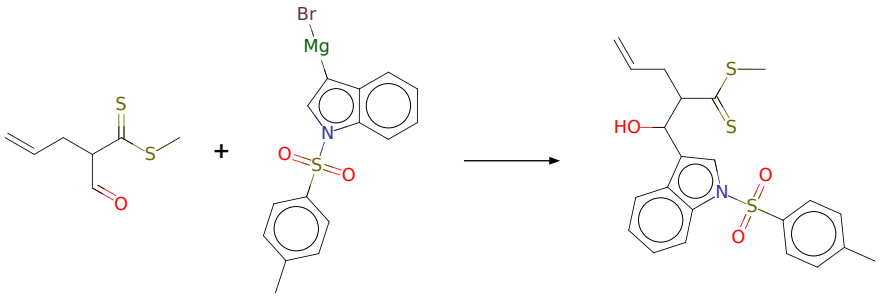
Typical conditions: iPrMgCl.LiCl.THF or other conditions Mg.THF or tBuLi.MgBr2

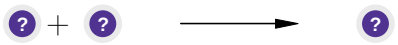
Protections: none

Reference: DOI: *10.1016/S0040-4039(99)01404-5* and *10.1021/jo0000574* and WO2014123793 p.137 and *10.1021/jm400491x* and *10.3762/bjoc.12.36*

Retrosynthesis ID: 10011460

2.3.5 Grignard-Type Reaction





Substrates:

1. C=CCC(C=O)C(=S)SC
2. Cc1ccc(S(=O)(=O)n2cc([Mg]Br)c3ccccc32)cc1

Products:

1. C=CCC(C(=S)SC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

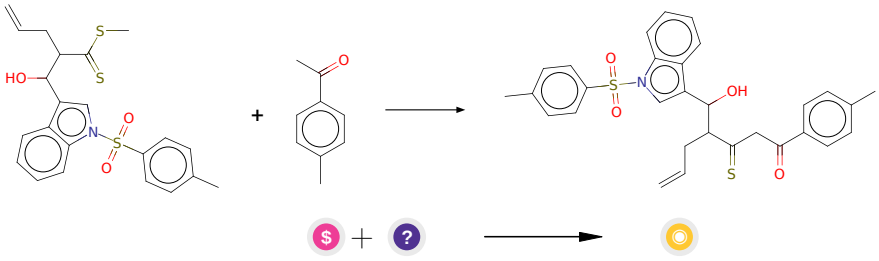
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1055/s-0030-1260809* or *10.1021/jm061429p* or *10.1021/jo0621423* or *10.1021/ja00373a036* or *10.1016/S0040-4020(01)00457-4*

Retrosynthesis ID: 25123

2.3.6 Condensation of ketones with dithioesters



Substrates:

1. Methyl p-tolyl ketone - *available at Sigma-Aldrich*
2. C=CCC(C(=S)SC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=S)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Typical conditions: NaH.DMF

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6][CH]([#6])[OH]	alcohols	Methoxymethyl Ether (MOM) 2-Methoxyethoxymethyl Ether (MEM) Tetrahydropyranyl Ether (THP) Benzyl Ether (PMB) t-Butyldimethylsilyl Ether (TBDMS) Methyl Ether

Reference: *10.1021/jo400599e* and *10.1002/ejoc.201301667*

Retrosynthesis ID: 9996413

2.4 Path 4

Score: `1000212.97`

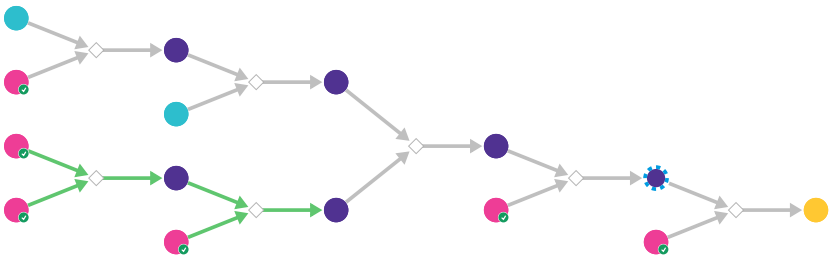
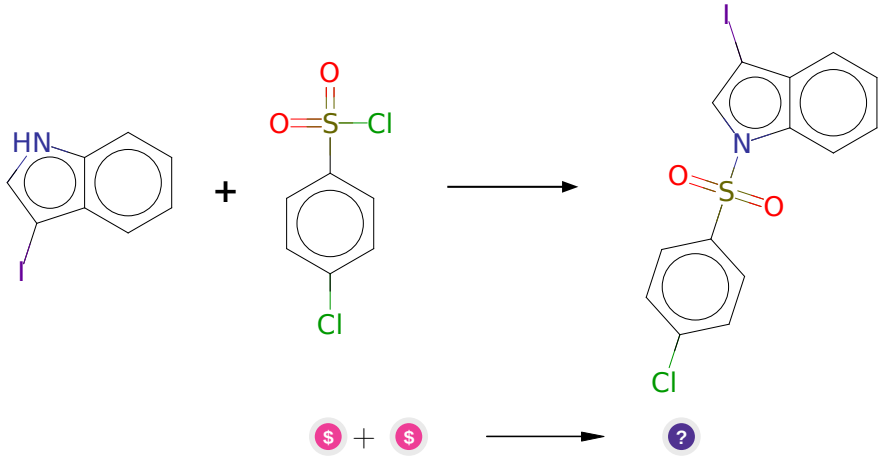


Figure 4: Outline of path 4

2.4.1 Sulfonylation of N-Heterocycles



Substrates:

1. 3-jod-indol - *available at Sigma-Aldrich*
2. 4-Chlorobenzenesulfonyl chloride - *available at Sigma-Aldrich*

Products:

1. O=S(=O)(c1ccc(Cl)cc1)n1cc(I)c2ccccc21

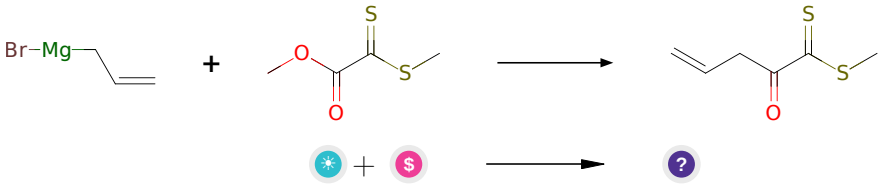
Typical conditions: NaH.DMF

Protections: none

Reference: *10.1021/ol0478133* (SI) AND *10.1002/anie.200352634* AND *10.1021/ja973656+*

Retrosynthesis ID: 14719

2.4.2 Synthesis of ketones from esters via Grignard addition



Substrates:

1. dimethyl-1,1-dithiooxalat
2. Allylmagnesium bromide solution - *available at Sigma-Aldrich*

Products:

1. C=CCC(=O)C(=S)SC

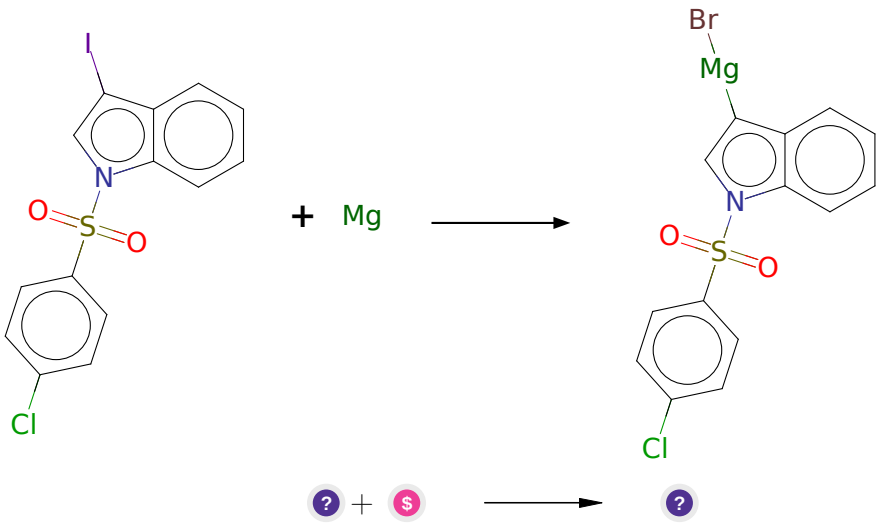
Typical conditions: THF. Low temp

Protections: none

Reference: *10.1021/jm800136b* and *10.1021/ol402802g*

Retrosynthesis ID: 10011836

2.4.3 Synthesis of aryl Grignard reagents



Substrates:

1. O=S(=O)(c1ccc(Cl)cc1)n1cc(I)c2ccccc21
2. Magnesium - *available at Sigma-Aldrich*

Products:

1. O=S(=O)(c1ccc(Cl)cc1)n1cc([Mg]Br)c2ccccc21

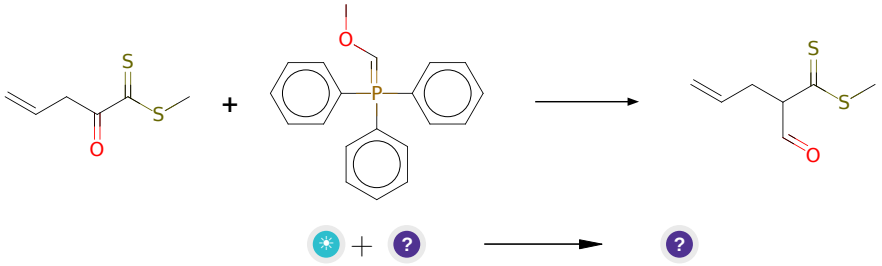
Typical conditions: iPrMgCl.LiCl.THF or other conditions Mg.THF or tBuLi.MgBr2

Protections: none

Reference: DOI: *10.1016/S0040-4039(99)01404-5* and *10.1021/jo0000574* and WO2014123793 p.137 and *10.1021/jm400491x* and *10.3762/bjoc.12.36*

Retrosynthesis ID: 10011460

2.4.4 Olefination of ketones followed by hydrolysis



Substrates:

1. triphenylphosphonium methoxymethylide
2. C=CCC(=O)C(=S)SC

Products:

1. C=CCC(C=O)C(=S)SC

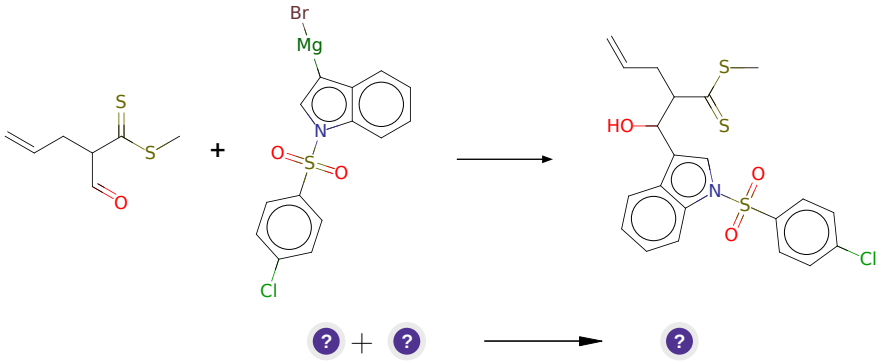
Typical conditions: KHMDS.THF hydrolysis: pTsOH.water.acetone

Protections: none

Reference: *10.1002/anie.201811403* and *10.1002/anie.201809130* and *10.1002/anie.201705809* and *10.1002/anie.201409038* and *10.1021/ol3028994* (SI)

Retrosynthesis ID: 31014861

2.4.5 Grignard-Type Reaction



Substrates:

1. O=S(=O)(c1ccc(Cl)cc1)n1cc([Mg]Br)c2ccccc21
2. C=CCC(C=O)C(=S)SC

Products:

1. C=CCC(C(=S)SC)C(O)c1cn(S(=O)(=O)c2ccc(Cl)cc2)c2ccccc12

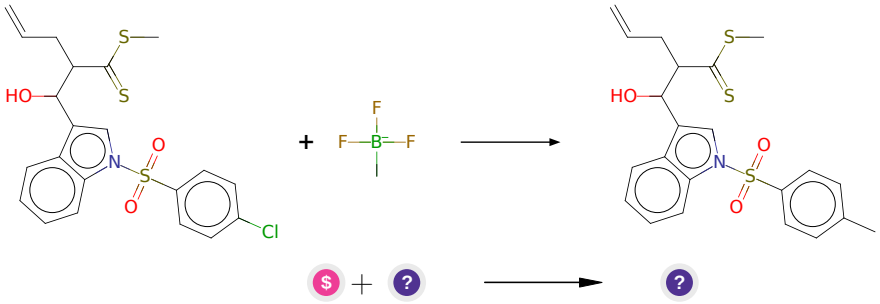
Typical conditions: Mg or Li.ether

Protections: none

Reference: *10.1055/s-0030-1260809* or *10.1021/jm061429p* or *10.1021/jo0621423* or *10.1021/ja00373a036* or *10.1016/S0040-4020(01)00457-4*

Retrosynthesis ID: 25123

2.4.6 Suzuki Coupling of arylchlorides and methyltrifluoroborates



Substrates:

1. Potassium methyltrifluoroborate - *available at Sigma-Aldrich*
2. C=CCC(C(=S)SC)C(O)c1cn(S(=O)(=O)c2ccc(Cl)cc2)c2ccccc12

Products:

1. C=CCC(C(=S)SC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

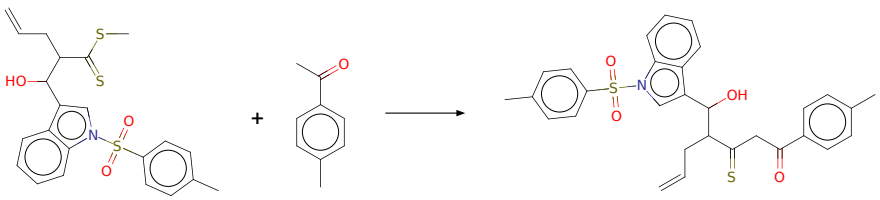
Typical conditions: Pd(dppf)2Cl2.Cs2CO3.THF/H2O.110C

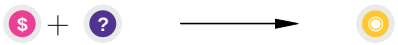
Protections: none

Reference: *10.1021/jo900152n* and *10.1016/j.tetlet.2014.10.078*

Retrosynthesis ID: 10033513

2.4.7 Condensation of ketones with dithioesters





Substrates:

1. Methyl p-tolyl ketone - *available at Sigma-Aldrich*
2. C=CCC(C(=S)SC)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Products:

1. C=CCC(C(=S)CC(=O)c1ccc(C)cc1)C(O)c1cn(S(=O)(=O)c2ccc(C)cc2)c2ccccc12

Typical conditions: NaH.DMF

Protections:

Functional group SMARTS	Classification	Protecting groups
[#6][CH]([#6])[OH]	alcohols	Methoxymethyl Ether (MOM) 2-Methoxyethoxymethyl Ether (MEM) Tetrahydropyranyl Ether (THP) Benzyl Ether (PMB) t-Butyldimethylsilyl Ether (TB-DMS) Methyl Ether

Reference: *10.1021/jo400599e* and *10.1002/ejoc.201301667*

Retrosynthesis ID: 9996413