Paths of analysis*

BMK1

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

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

2.1 Path 1

Score: `195.90`

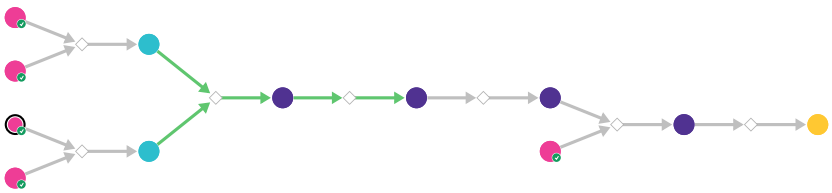
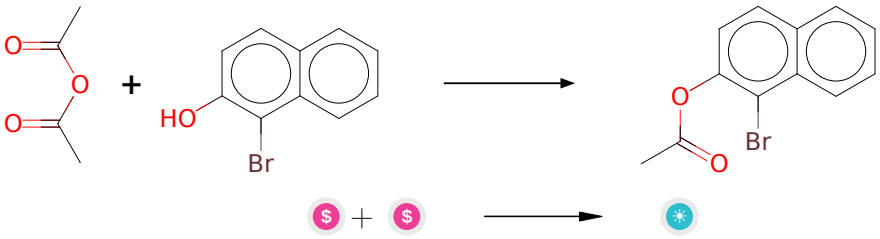


Figure 1: Outline of path 1

2.1.1 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)

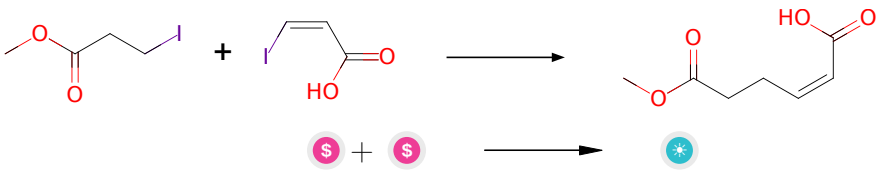
Typical conditions: Cu(II).triflate.DCM.RT

Protections: none

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

Retrosynthesis ID: 11601

2.1.2 Palladium catalysed alkylation of vinyl iodides



Substrates:

1. cis-3-Iodoacrylic acid - *available at Sigma-Aldrich*
2. Methyl 3-iodopropanoate - *available at Sigma-Aldrich*

Products:

1. (z)-hex-2-enedioic acid 6-methyl ester

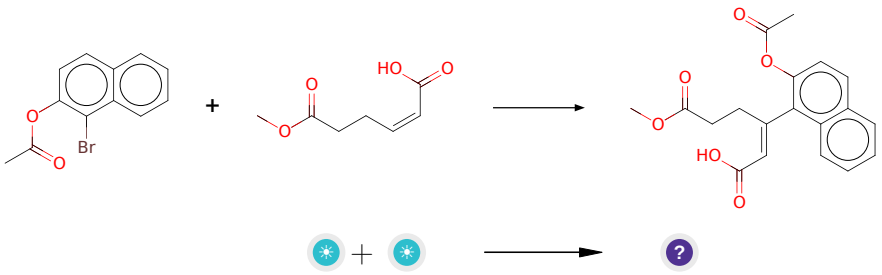
Typical conditions: [Pd].catalyst

Protections: none

Reference: *10.1016/j.bmcl.2005.12.066* and *10.1021/ol052070m* and *10.1021/ol5023195* and *10.1002/anie.200703134* and *10.1016/j.bmcl.2005.09.084* and *10.1021/ol0344873*

Retrosynthesis ID: 25162

2.1.3 Heck Reaction



Substrates:

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

2. (z)-hex-2-enedioic acid 6-methyl ester

Products:

1. COC(=O)CC/C(=C\C(=O)O)c1c(OC(C)=O)ccc2ccccc12

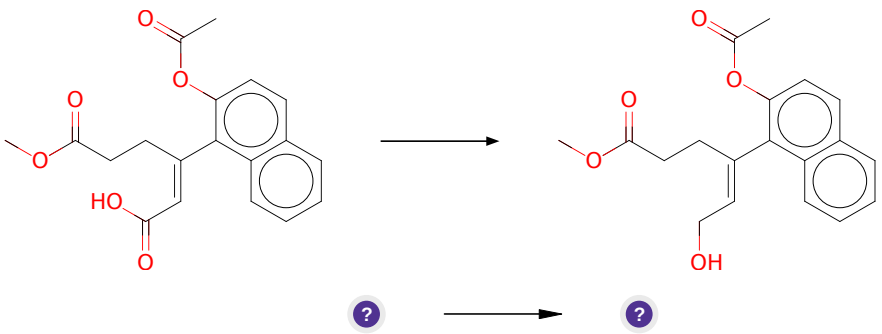
Typical conditions: Pd (cat). Ligand e.g. TXPTS. Base. Temp

Protections: none

Reference: *10.1016/j.tetlet.2013.01.077* or *10.1016/j.tetlet.2013.10.076* 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: 9173

2.1.4 Reduction of carboxylic acids to alcohols



Substrates:

1. COC(=O)CC/C(=C\C(=O)O)c1c(OC(C)=O)ccc2ccccc12

Products:

1. COC(=O)CC/C(=C\CO)c1c(OC(C)=O)ccc2ccccc12

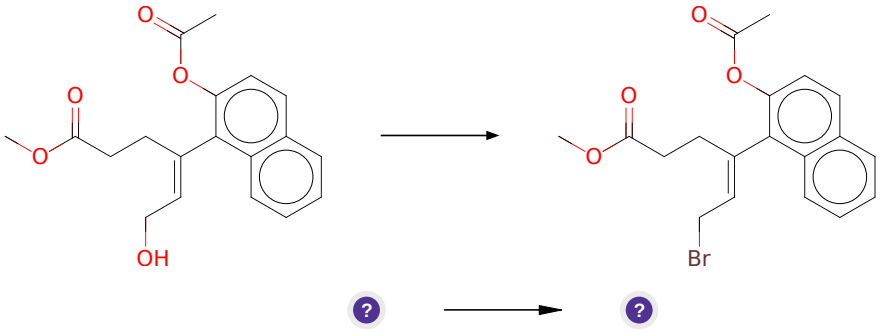
Typical conditions: BH3xTHF.or.ClCOOEt.Et3N.then.NaBH4

Protections: none

Reference: *10.1021/jo00956a011* and *10.1248/cpb.16.492* and *10.1016/S0040-4039(98)01781-X* and *10.1021/ja508846g* and *10.1016/j.bmc.2011.07.054*

Retrosynthesis ID: 9142

2.1.5 Appel Reaction



Substrates:

1. COC(=O)CC/C(=C\CO)c1c(OC(C)=O)ccc2ccccc12

Products:

1. COC(=O)CC/C(=C\CBr)c1c(OC(C)=O)ccc2ccccc12

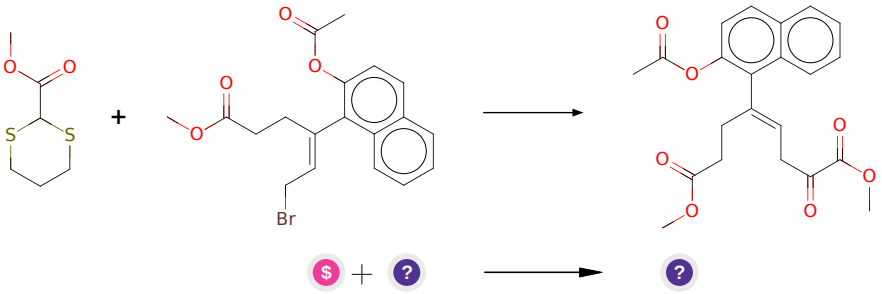
Typical conditions: PPh3.CBr4

Protections: none

Reference: *10.1021/ja800574m* and *10.1016/j.tet.2012.05.010* and *10.1016/j.tet.2004.09.021* (experimantal)

Retrosynthesis ID: 9990037

2.1.6 Corey-Seebach



Substrates:

1. methyl 1,3-dithiane-2-carboxylate - *available at Sigma-Aldrich*
2. COC(=O)CC/C(=C\CBr)c1c(OC(C)=O)ccc2ccccc12

Products:

1. COC(=O)CC/C(=C\CC(=O)C(=O)OC)c1c(OC(C)=O)ccc2ccccc12

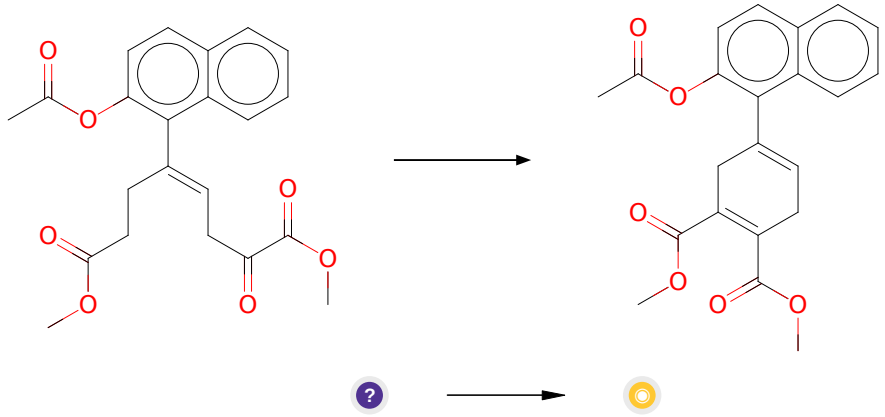
Typical conditions: 1.BuLi.TMEDA.2.TCCA

Protections: none

Reference: *10.1039/P19860000183* AND *10.1016/S0040-4020(01)85646-5* AND *10.1039/c5ob00638d* deprotection: *10.1016/j.tetlet.2006.06.131*

Retrosynthesis ID: 15272

2.1.7 Addition of enolate anion to 1,2-dicarbonyl compounds followed by dehydration



Substrates:

1. COC(=O)CC/C(=C\CC(=O)C(=O)OC)c1c(OC(C)=O)ccc2ccccc12

Products:

1. COC(=O)C1=C(C(=O)OC)CC(c2c(OC(C)=O)ccc3ccccc23)=CC1

Typical conditions: TiCl4.NEt3.

Protections: none

Reference: *10.1016/j.tet.2014.12.099* AND *10.1021/ol403461b* AND *10.1016/0040-4039(96)01843-6* AND *10.1016/S0968-0896(99)00312-0*

Retrosynthesis ID: 14990

2.2 Path 2

Score: 234.96

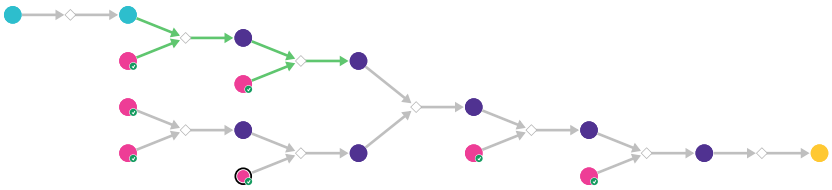
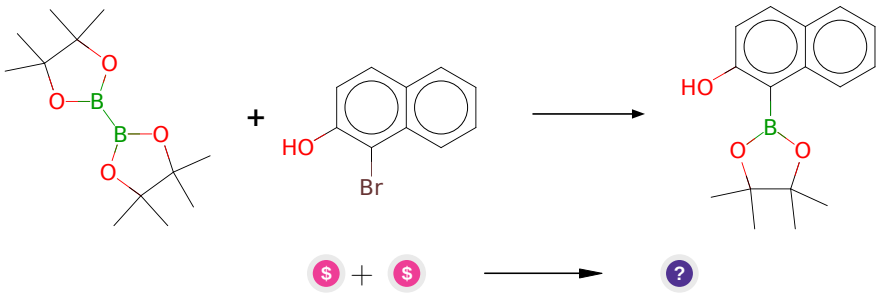


Figure 2: Outline of path 2

2.2.1 Miyaura Borylation



Substrates:

1. Bis(pinacolato)diboron - *available at Sigma-Aldrich*
2. 1-Bromo-2-naphthol - *available at Sigma-Aldrich*

Products:

1. CC1(C)OB(c2c(O)ccc3ccccc23)OC1(C)C

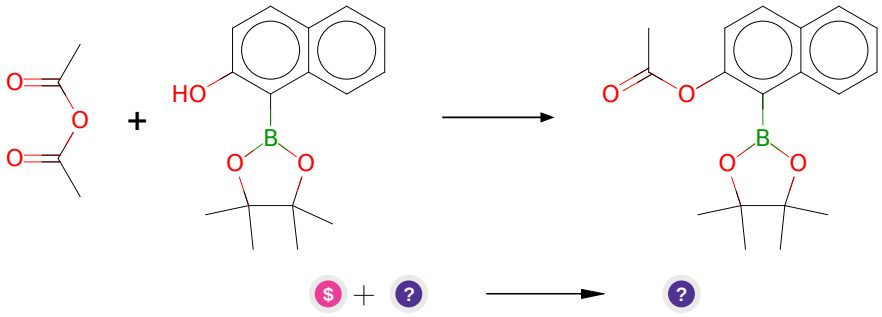
Typical conditions: PdCl2(dppf)2.KOAc.Dioxane or DMSO.80oC

Protections: none

Reference: DOI: *10.1021/ja509198w* and *10.1021/jm800832q* and *10.1021/jm401499g* and *10.1039/C1CC12020D* (SI, page S4) and *10.1055/s-0035-1561355* (SI, page 12) and *10.1021/ol2000556* and *10.1021/jo102070e* and WO2010/75270 A1, 2010 (page 37)

Retrosynthesis ID: 1209

2.2.2 Cu(OTf)2 catalyzed acylation of phenols



Substrates:

1. Acetic anhydride - *available at Sigma-Aldrich*
2. CC1(C)OB(c2c(O)ccc3ccccc23)OC1(C)C

Products:

1. CC(=O)Oc1ccc2ccccc2c1B1OC(C)(C)C(C)(C)O1

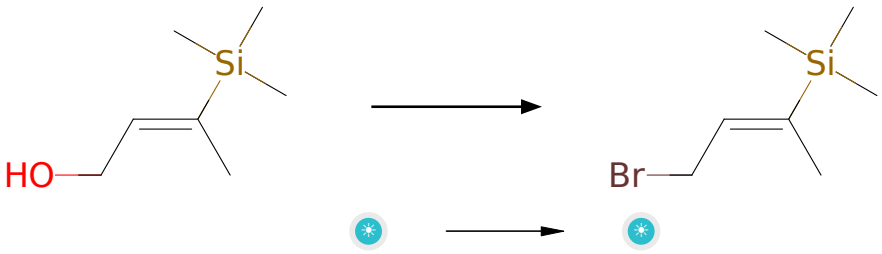
Typical conditions: Cu(II).triflate.DCM.RT

Protections: none

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

Retrosynthesis ID: 11601

2.2.3 Appel Reaction



Substrates:

1. 3-trimethylsilanyl-but-2-en-1-ol

Products:

1. C7H15BrSi

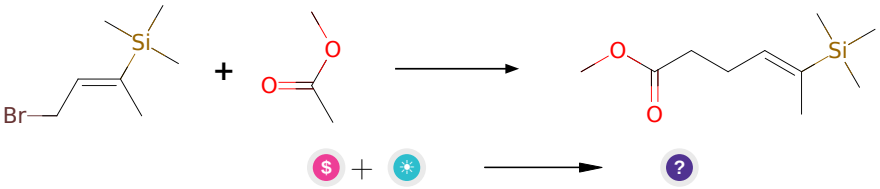
Typical conditions: PPh3.CBr4

Protections: none

Reference: *10.1021/ja800574m* and *10.1016/j.tet.2012.05.010* and *10.1016/j.tet.2004.09.021* (experimantal)

Retrosynthesis ID: 9990037

2.2.4 Alkylation of Esters



Substrates:

1. Methyl acetate - *available at Sigma-Aldrich*
2. C7H15BrSi

Products:

1. COC(=O)CC/C=C(\C)[Si](C)(C)C

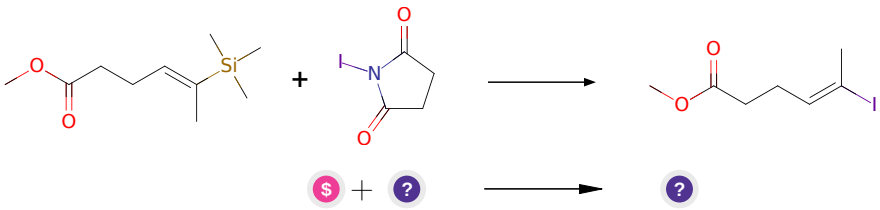
Typical conditions: base e.g. BuLi.THF

Protections: none

Reference: *10.1021/ja065404r* and *10.1016/S0040-4020(01)88337-X* and *10.1021/ja058303m* and *10.1021/acs.orglett.9b03078* and *10.1016/S0040-4020(01)80336-7*

Retrosynthesis ID: 31017104

2.2.5 Iodination of Silyl Derivatives



Substrates:

1. N-Iodosuccinimide - *available at Sigma-Aldrich*

2. COC(=O)CC/C=C(\C)[Si](C)(C)C

Products:

1. COC(=O)CC/C=C(\C)I

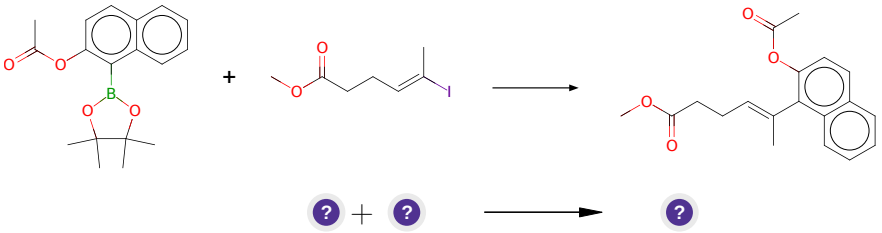
Typical conditions: NIS. 50C. MeCN

Protections: none

Reference: DOI:*10.1016/j.tetlet.2011.02.057* or DOI: *10.1016/S0040-4039(96)02000-X* or DOI: *10.1016/S0040-4020(02)00334-4*

Retrosynthesis ID: 9211

2.2.6 Suzuki coupling of arylboronic pinacol esters with vinyl iodides



Substrates:

1. CC(=O)Oc1ccc2ccccc2c1B1OC(C)(C)C(C)(C)O1
2. COC(=O)CC/C=C(\C)I

Products:

1. COC(=O)CC/C=C(\C)c1c(OC(C)=O)ccc2ccccc12

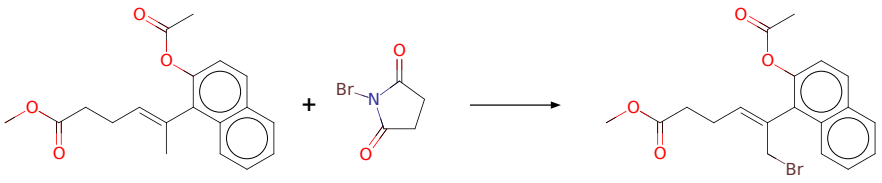
Typical conditions: Pd catalyst.base.solvent

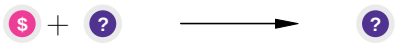
Protections: none

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: 10176

2.2.7 Wohl-Ziegler Bromination





Substrates:

1. N-Bromosuccinimide - *available at Sigma-Aldrich*
2. COC(=O)CC/C=C(\C)c1c(OC(C)=O)ccc2ccccc12

Products:

1. COC(=O)CC/C=C(\CBr)c1c(OC(C)=O)ccc2ccccc12

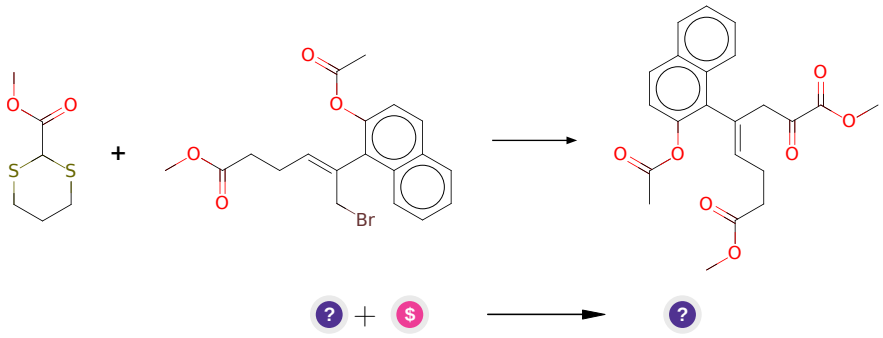
Typical conditions: NBS.AIBN or (BzO)2 or heat

Protections: none

Reference: *10.1016/j.steroids.2018.10.005* (Scheme 1) and *10.1016/j.bmc.2010.06.075* (Scheme 2) and *10.1021/acs.orglett.9b03865* (p. SI 6)

Retrosynthesis ID: 245554

2.2.8 Corey-Seebach



Substrates:

1. COC(=O)CC/C=C(\CBr)c1c(OC(C)=O)ccc2ccccc12
2. methyl 1,3-dithiane-2-carboxylate - *available at Sigma-Aldrich*

Products:

1. COC(=O)CC/C=C(\CC(=O)C(=O)OC)c1c(OC(C)=O)ccc2ccccc12

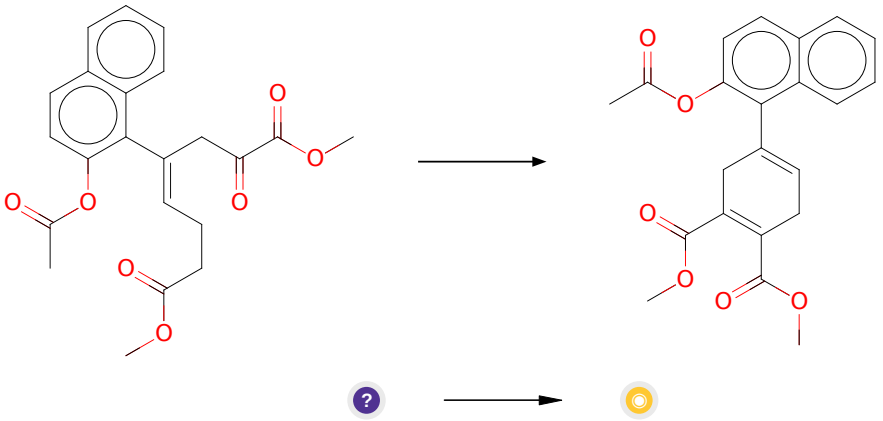
Typical conditions: 1.BuLi.TMEDA.2.TCCA

Protections: none

Reference: *10.1039/P19860000183* AND *10.1016/S0040-4020(01)85646-5* AND *10.1039/c5ob00638d* deprotection: *10.1016/j.tetlet.2006.06.131*

Retrosynthesis ID: 15272

2.2.9 Addition of enolate anion to 1,2-dicarbonyl compounds followed by dehydration



Substrates:

1. COC(=O)CC/C=C(\CC(=O)C(=O)OC)c1c(OC(C)=O)ccc2ccccc12

Products:

1. COC(=O)C1=C(C(=O)OC)CC(c2c(OC(C)=O)ccc3ccccc23)=CC1

Typical conditions: TiCl4.NEt3.

Protections: none

Reference: *10.1016/j.tet.2014.12.099* AND *10.1021/ol403461b* AND *10.1016/0040-4039(96)01843-6* AND *10.1016/S0968-0896(99)00312-0*

Retrosynthesis ID: 14990

2.3 Path 3

Score: 246.70

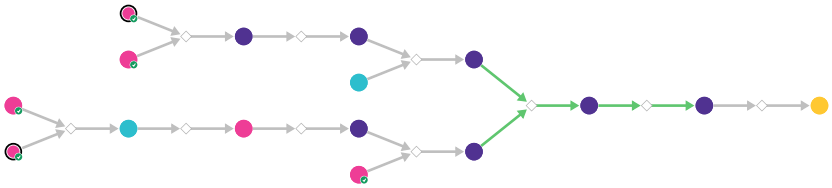
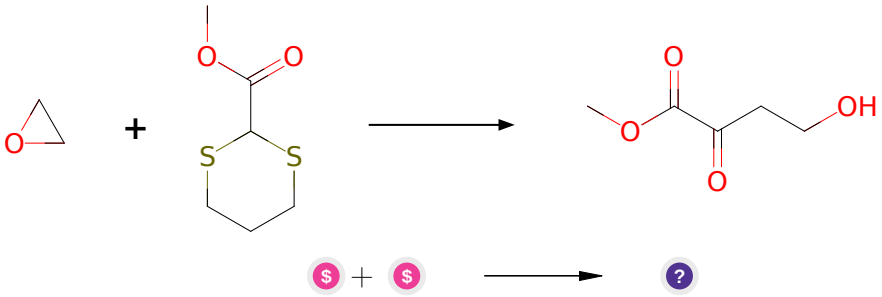


Figure 3: Outline of path 3

2.3.1 Corey-Seebach



Substrates:

1. Oxirane - *available at Sigma-Aldrich*
2. methyl 1,3-dithiane-2-carboxylate - *available at Sigma-Aldrich*

Products:

1. COC(=O)C(=O)CCO

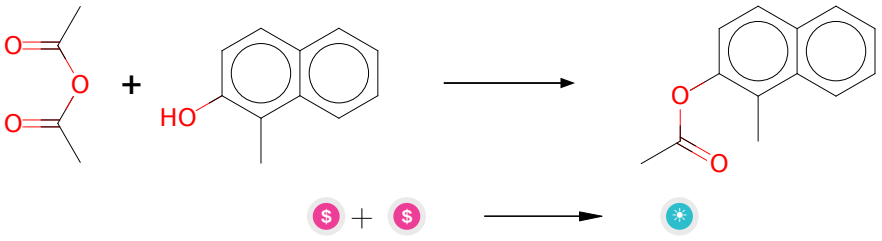
Typical conditions: BuLi.THF.-30C.HgO.H2O.THF

Protections: none

Reference: *10.1055/s-1977-24412*

Retrosynthesis ID: 11198

2.3.2 Cu(OTf)2 catalyzed acylation of phenols



Substrates:

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

Products:

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

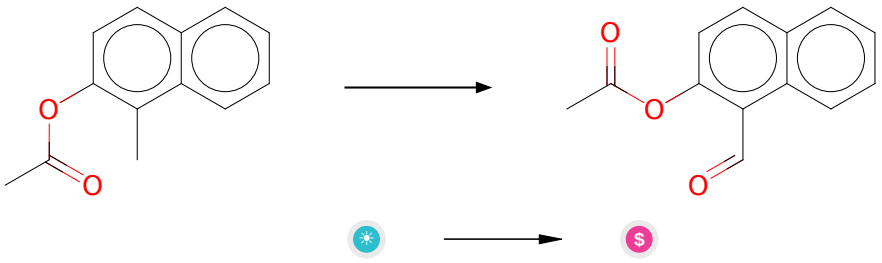
Typical conditions: Cu(II).triflate.DCM.RT

Protections: none

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

Retrosynthesis ID: 11601

2.3.3 Benzylic oxidation



Substrates:

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

Products:

1. 1-formyl-2-naphthyl acetate - *ChemBridgeCorporation*

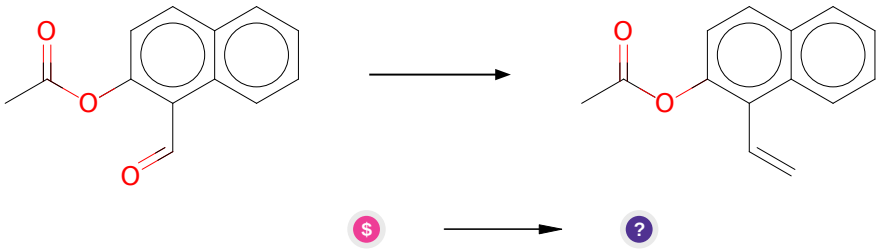
Typical conditions: DDQ.toluene.heat or CrO3.AcOH or PhP(O)HOAlkyl.O2 or CAN.THF.AcOH.H2O

Protections: none

Reference: *10.3987/COM-10-S(E)11* and *10.1038/s41467-019-10414-7* and *10.1002/ejoc.201402486* and *10.1021/acssuschemeng.9b00002*

Retrosynthesis ID: 31008183

2.3.4 Tebbe Olefination



Substrates:

1. 1-formyl-2-naphthyl acetate - *ChemBridgeCorporation*

Products:

1. C=Cc1c(OC(C)=O)ccc2ccccc12

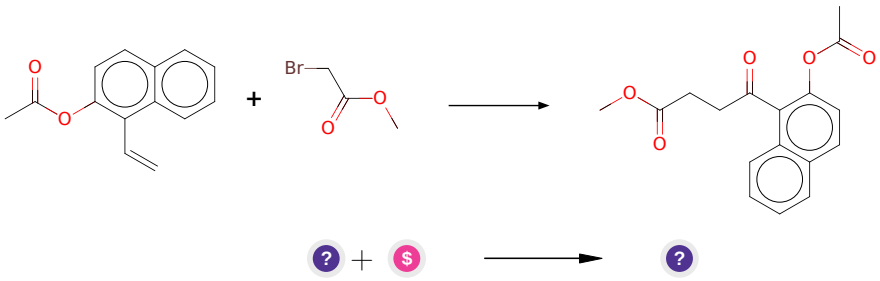
Typical conditions: Cp2TiCl2.AlMe3.toluene

Protections: none

Reference: *10.1016/j.tet.2007.03.015* and *10.1002/9780470638859.conrr617*

Retrosynthesis ID: 11714

2.3.5 Synthesis of 1,4-dicarbonyls



Substrates:

1. C=Cc1c(OC(C)=O)ccc2ccccc12
2. Methyl bromoacetate - *available at Sigma-Aldrich*

Products:

1. COC(=O)CCC(=O)c1c(OC(C)=O)ccc2ccccc12

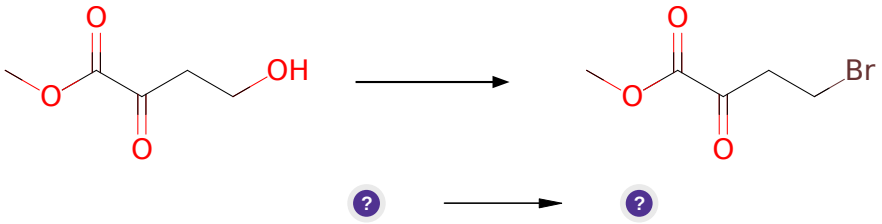
Typical conditions: TBHP.Co(acac)2

Protections: none

Reference: *10.1021/ol5004687*

Retrosynthesis ID: 7202

2.3.6 Appel Reaction



Substrates:

1. COC(=O)C(=O)CCO

Products:

1. COC(=O)C(=O)CCBr

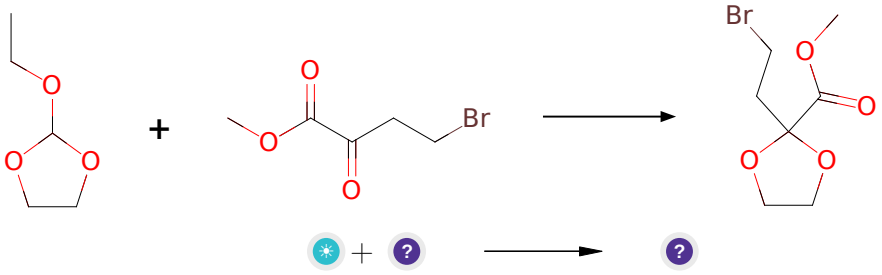
Typical conditions: PPh3.CBr4

Protections: none

Reference: *10.1021/ja800574m* and *10.1016/j.tet.2012.05.010* and *10.1016/j.tet.2004.09.021* (experimantal)

Retrosynthesis ID: 9990037

2.3.7 Acetalization of Carbonyl Compounds Catalyzed by Indium Triflate



Substrates:

1. 2-ethoxy-[1,3]dioxolane
2. COC(=O)C(=O)CCBr

Products:

1. COC(=O)C1(CCBr)OCCO1

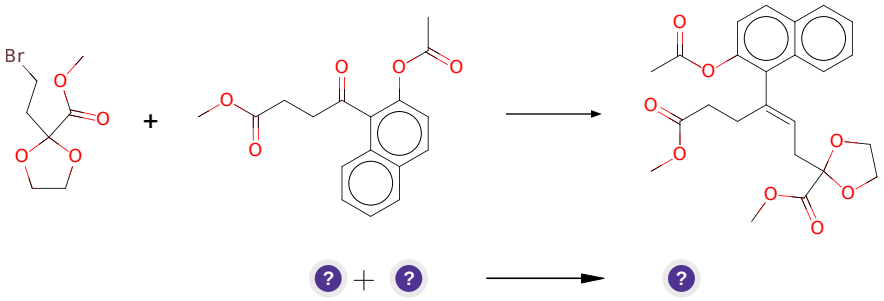
Typical conditions: indium triflate. MeOH. CH2Cl2. 20C

Protections: none

Reference: DOI: *10.1016/j.tetlet.2006.10.111* or DOI: *10.1002/cber.19620950803*

Retrosynthesis ID: 9318

2.3.8 HWE/Wittig Olefination



Substrates:

1. COC(=O)CCC(=O)c1c(OC(C)=O)ccc2ccccc12
2. COC(=O)C1(CCBr)OCCO1

Products:

1. COC(=O)CC/C(=C\CC1(C(=O)OC)OCCO1)c1c(OC(C)=O)ccc2ccccc12

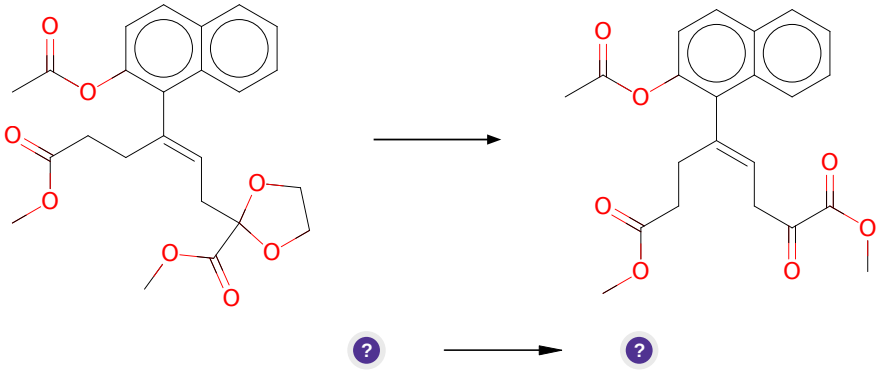
Typical conditions: 1.PPh3 or trialkylphosphite.2.base.aldehyde

Protections: none

Reference: *10.1002/anie.200705005* and *10.1021/ol052106a* and *10.1021/jo00075a064* and *10.1021/ol3027297* and *10.1080/00397910008087436*

Retrosynthesis ID: 9554

2.3.9 Hydrolysis of ketals



Substrates:

1. COC(=O)CC/C(=C\CC1(C(=O)OC)OCCO1)c1c(OC(C)=O)ccc2ccccc12

Products:

1. COC(=O)CC/C(=C\CC(=O)C(=O)OC)c1c(OC(C)=O)ccc2ccccc12

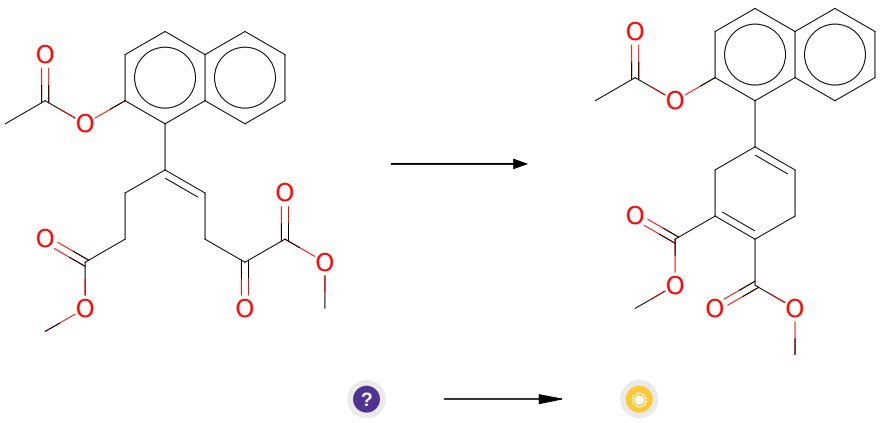
Typical conditions: H2O.HCl

Protections: none

Reference: *10.1021/jo0159035* and *10.1021/jo00194a003* and

Retrosynthesis ID: 31013139

2.3.10 Addition of enolate anion to 1,2-dicarbonyl compounds followed by dehydration



Substrates:

1. COC(=O)CC/C(=C\CC(=O)C(=O)OC)c1c(OC(C)=O)ccc2ccccc12

Products:

1. COC(=O)C1=C(C(=O)OC)CC(c2c(OC(C)=O)ccc3ccccc23)=CC1

Typical conditions: TiCl4.NEt3.

Protections: none

Reference: *10.1016/j.tet.2014.12.099* AND *10.1021/ol403461b* AND *10.1016/0040-4039(96)01843-6* AND *10.1016/S0968-0896(99)00312-0*

Retrosynthesis ID: 14990