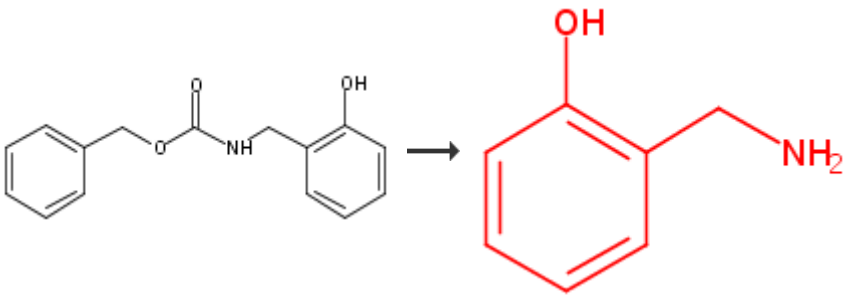
1. Single Step



95%

Overview

Steps/Stages

1.1 R:H_2, C:Pd, S:AcOEt, 18 h, rt

Notes

Reactants: 1, Reagents: 1, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Concise Copper-Catalyzed Synthesis of Tricyclic Biaryl Ether-Linked Aza-Heterocyclic Ring Systems

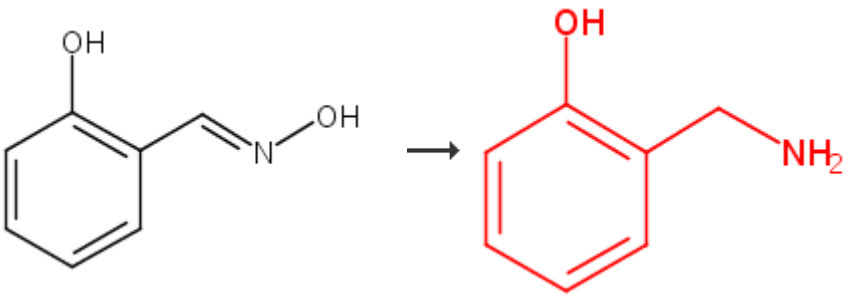
By Mestichelli, Paola et al

From Organic Letters, 15(21), 5448-5451; 2013

Experimental Procedure

To a solution of the protected intermediate (1.83 g) in EtOAc (10 mL) was added 10% Pd/C 10% (40 mg). This suspension was stirred under an atmosphere of hydrogen gas (balloon) for 18 hours. The reaction mixture was filtered through Celite® and the solvent removed under reduced pressure. The title compound as a white solid (Yield: 95 %) which was used without characterization or purification **2-hydroxy-benzylamine**

2. Single Step



96%

Overview

Steps/Stages

Notes

1.1 R:Zn, R:AcOH, 0.5 h, rt

ultrasound, Reactants: 1, Reagents: 2, Steps: 1, Stages: 1, Most stages in any one step: 1

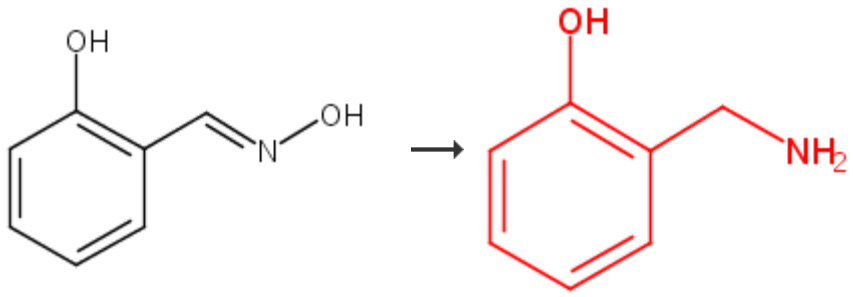
References

The efficient reduction of oximes to amines with Zn and acetic acid under ultrasonic irradiation

By Cao, Yu-Qing et al

From Organic Chemistry: An Indian Journal, 5(4), 412-415; 2009

3. Single Step

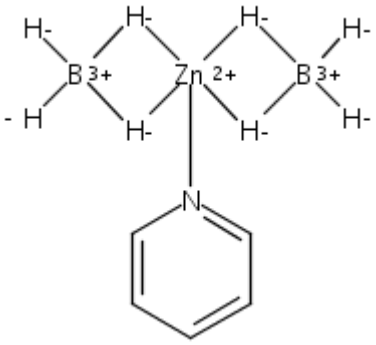


96%

Overview

Steps/Stages

1.1 R:



S:THF, 0.5 h, reflux

Notes

Reactants: 1, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

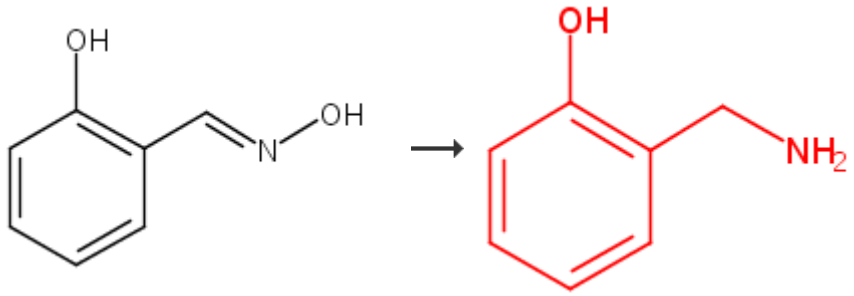
References

First report for the efficient reduction of oximes to amines with zinc borohydride in the form of (pyridine)(tetrahydroborato)zinc complex

By Zeynizadeh, Behzad and Zahmatkesh, Karam

From Journal of the Chinese Chemical Society (Taipei, Taiwan), 52(1), 109-112; 2005

4. Single Step



93%

Overview

Steps/Stages

1.1 R:$ZrCl_4$, R:Al_2O_3
1.2 > 1 min, rt

1.3 R:$NaBH_4$, 2 min, rt

Notes

mechanochemical, green chemistry-solvent, no solvent, Reactants: 1, Reagents: 3, Steps: 1, Stages: 3, Most stages in any one step: 3

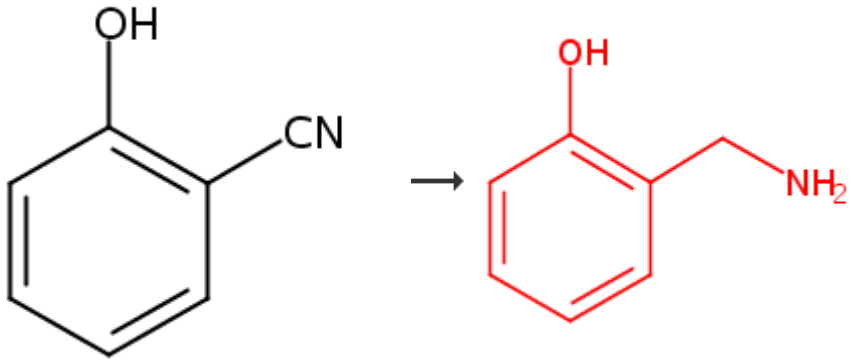
References

A rapid and practical protocol for solvent-free reduction of oximes to amines with NaBH4/ZrCl4/Al2O3 system

By Zeynizadeh, Behzad and Kouhkan, Mehri

From Bulletin of the Korean Chemical Society, 32(9), 3448-3452; 2011

5. Single Step



90%

Overview

Steps/Stages

1.1 R:H_3PO_4, R:SmI_2, S:THF

Notes

4 eq. SmI2, THF, H3PO4 (85%), r.t./30 sec., Reduction, Reactants: 1, Reagents: 2, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

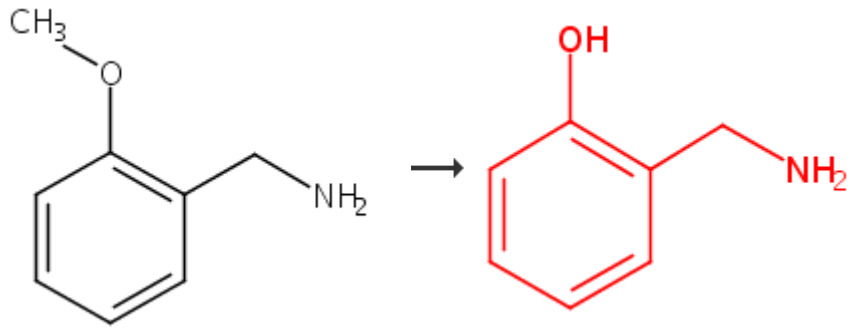
References

Reductions with samarium(II) iodide

By Molander, Gary A.

From Organic Reactions (Hoboken, NJ, United States), 46, No pp. given; 1994

6. Single Step



84%

Overview

Steps/Stages

1.1 R:HBr, S:H_2O, 3 h, reflux

1.2 R:NaOH, S:H_2O, 0°C, neutralized

Notes

Reactants: 1, Reagents: 2, Solvents: 1, Steps: 1, Stages: 2, Most stages in any one step: 2

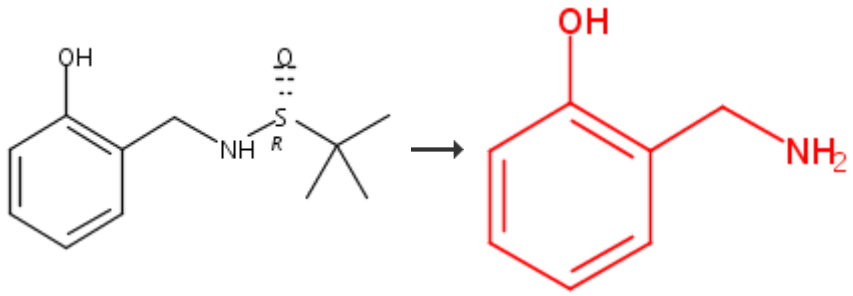
References

Synthesis, SAR studies, and evaluation of 1,4-benzoxazepine derivatives as selective 5-HT1A receptor agonists with neuroprotective effect: Discovery of Piclozotan

By Kamei, Katsuhide et al

From Bioorganic & Medicinal Chemistry, 14(6), 1978-1992; 2006

7. Single Step



78%

Overview

Steps/Stages

Notes

1.1 R:O_2, C:I_2, S:H_2O, S:THF, 50°C

0.5 mmol scale used, Reactants: 1, Reagents: 1, Catalysts: 1, Solvents: 2, Steps: 1, Stages: 1, Most stages in any one step: 1

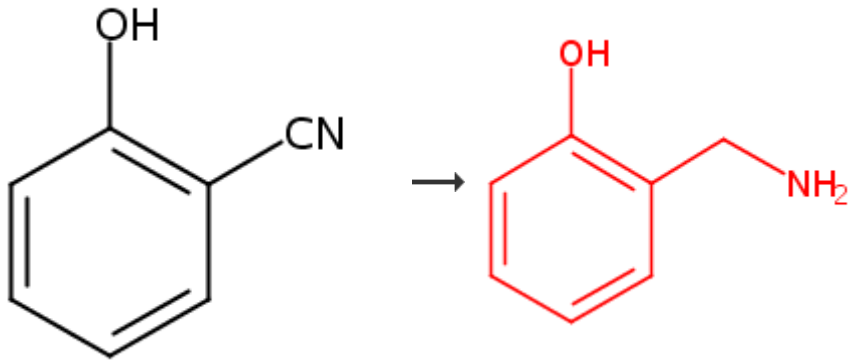
References

Iodine mediated deprotection of N-tert-butanesulfinyl amines: a functional group compatible method

By Chen, Wen et al

From Chemical Communications (Cambridge, United Kingdom), 50(47), 6259-6262; 2014

8. Single Step



88%

Overview

Steps/Stages

1.1 R:KOH, R:SmI_2, S:THF

Notes

8 eq. SmI2, THF, KOH (50%), r.t./9 min., Reduction, Reactants: 1, Reagents: 2, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

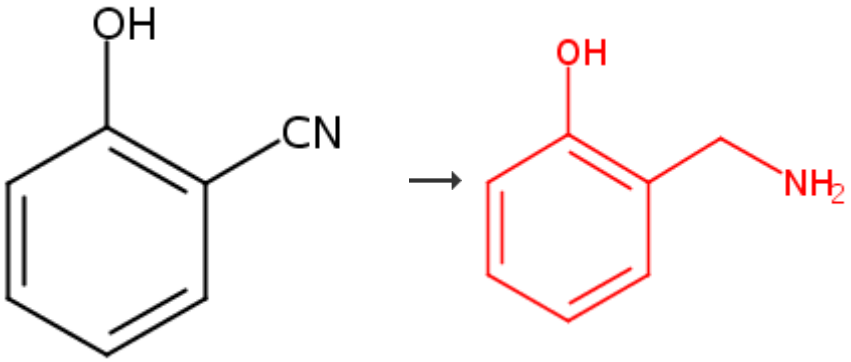
References

Reductions with samarium(II) iodide

By Molander, Gary A.

From Organic Reactions (Hoboken, NJ, United States), 46, No pp. given; 1994

9. Single Step



75%

Overview

Steps/Stages

1.1 R:$LiAlH_4$, S:Et_2O, S:THF, 0°C; 30 min, rt; 24 h, 40°C

1.2 R:NH_4Cl, S:H_2O

Notes

Reactants: 1, Reagents: 2, Solvents: 3, Steps: 1, Stages: 2, Most stages in any one step: 2

References

Pyruvate kinase activators for use for increasing lifetime of the red blood cells and treating anemia

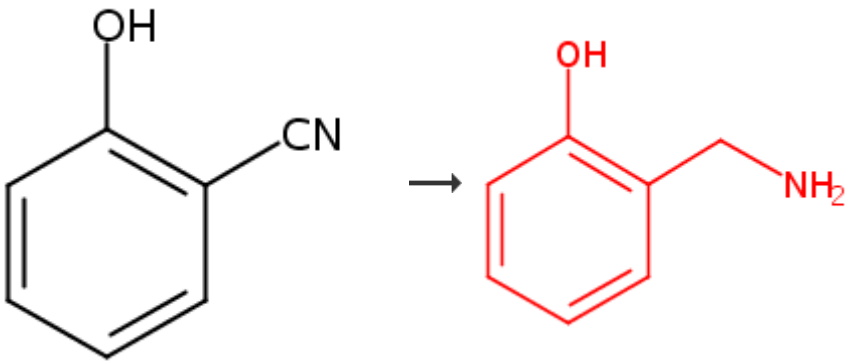
By Su, Shin-San Michael

From PCT Int. Appl., 2012151440, 08 Nov 2012

Experimental Procedure

General procedure for compound 11: To a solution of 2-cyano phenol **10** (0.2 gm, 0.075 mmoles) in a dry solvent mixture of THF and ether, $LiAlH_4$ (0.13 gm, 0.018 mmoles) was added at 0°C portion wise. The resulting mixture was allowed to stir at room temperature for 30 min followed by stirring at 40°C for 24 hrs. After completion of reaction, the mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate and water. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to obtain product **11**. Solid, yield (0.2 gm), 75%

10. Single Step



75%

Overview

Steps/Stages

Notes

1.1 R:$LiAlH_4$, S:Et_2O, S:THF, 0°C; 30 min, rt; 24 h, 40°C

1.2 R:NH_4Cl, S:H_2O

Reactants: 1, Reagents: 2, Solvents: 3, Steps: 1, Stages: 2, Most stages in any one step: 2

References

Preparation of oxobenzoxazinearylsulfonamide derivatives for use as PKM2 activators

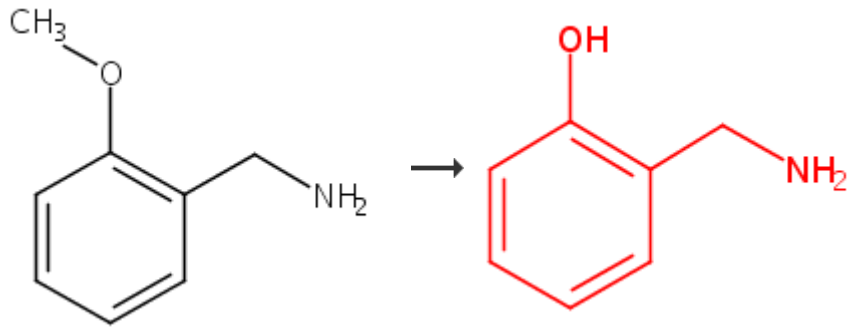
By Salituro, Francesco G. and Saunders, Jeffrey O.

From PCT Int. Appl., 2012088314, 28 Jun 2012

Experimental Procedure

General procedure for compound 11: To a solution of 2-cyano phenol **10** (0.2 gm, 0.075 mmoles) in a dry solvent mixture of THF and ether, $LiAlH_4$ (0.13 gm, 0.018 mmoles) was added at 0°C portion wise. The resulting mixture was allowed to stir at room temperature for 30 min followed by stirring at 40°C for 24 hrs. After completion of reaction, the mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate and water. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to obtain product **11.** Solid, yield 75% (0.2 gm).

11. Single Step



68%

Overview

Steps/Stages

1.1 R:BBr_3, S:CH_2Cl_2, -78°C; 30 min, rt; 45 min, 40°C; 6 h, rt

1.2 R:NaOH, S:H_2O, -20°C, pH 13

Notes

Reactants: 1, Reagents: 2, Solvents: 2, Steps: 1, Stages: 2, Most stages in any one step: 2

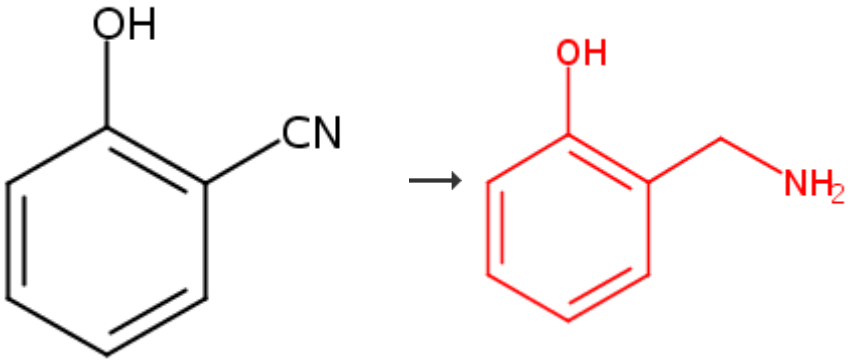
References

Process for preparation of α-amino acid esters

By Shi, Yian et al

From Faming Zhuanli Shenqing, 102675135, 19 Sep 2012

12. Single Step



73%

Overview

Steps/Stages

1.1 R:H_2, R:NH_3, C:Ni, S:MeOH, 1.5 h, 100°C, 90 bar

Notes

Raney nickel used, high pressure, Reactants: 1, Reagents: 2, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Synthesis of Methyl Carbamates from Primary Aliphatic Amines and Dimethyl Carbonate in Supercritical CO2: Effects of Pressure and Cosolvents and Chemoselectivity

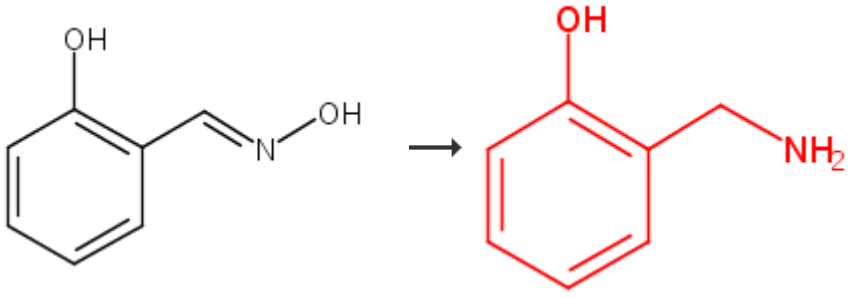
By Selva, Maurizio et al

From Journal of Organic Chemistry, 70(7), 2771-2777; 2005

Experimental Procedure

o-and *p*-Hydroxybenzylamines (2h and 2i) were prepared through the catalytic hydrogenation of the corresponding nitriles. [i] Accordingly, the nitrile (1 g, 8.4 mmol), Raney-Ni (~0.3 g wet of MeOH), and a 2M solution of NH_3 in MeOH (20 mL) were made to react at 100 °C and for 1.5 h, in a stainless steel autoclave pressurized with H_2 at 90 bar. Amines 2h and 2i were purified by flash chromatography (FCC) and they were isolated in 73 and 35% yields, respectively.

13. Single Step



65%

Overview

Steps/Stages

Notes

1.1 R:Zn, S:MeOH, rt

1.2 R:NH_4
$^{+}$ •HCO_2
$^{-}$, S:MeOH, overnight, rt; rt, pH 3

1.3 R:NH_4OH, S:H_2O, rt, neutralized

Reactants: 1, Reagents: 3, Solvents: 2, Steps: 1, Stages: 3, Most stages in any one step: 3

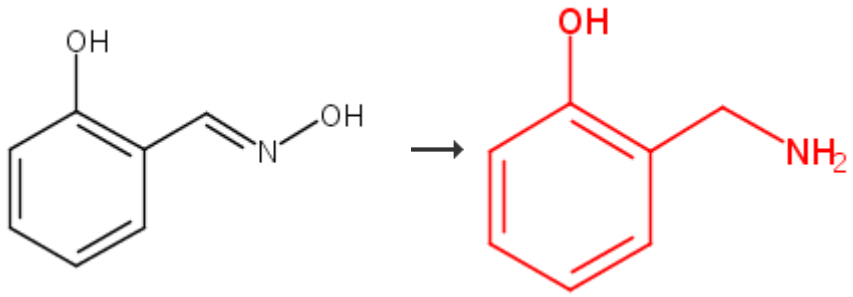
References

Preparation of N-benzylamide derivatives as herbicides

By Lu, Long et al

From Faming Zhuanli Shenqing, 101367769, 18 Feb 2009

14. Single Step



68%

Overview

Steps/Stages

1.1 R:Na amalgam, S:EtOH, S:H_2O, < 55°C, neutralized

1.2 R:HCl, < 55°C, neutralized

1.3 R:NH_4OH, S:Et_2O, rt

Notes

Reactants: 1, Reagents: 3, Solvents: 3, Steps: 1, Stages: 3, Most stages in any one step: 3

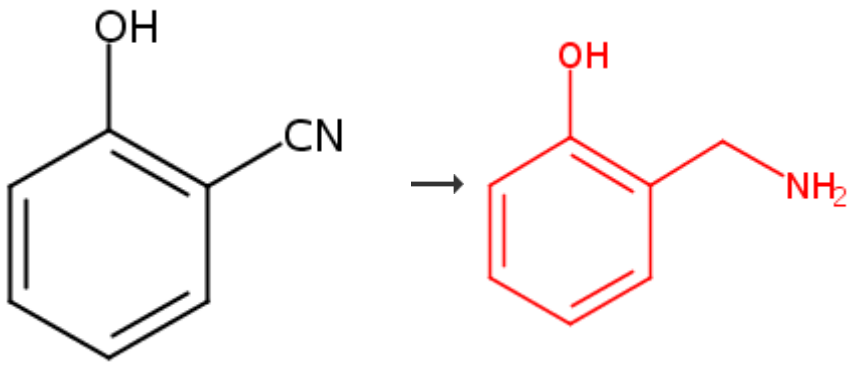
References

Metal chelates of cerium(III), thorium(IV), and dioxouranium(VI); complexes with some derivatives of aryl schiff bases

By Moustafa, M. E.

From Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry, 33(3), 453-468; 2003

15. Single Step



59%

Overview

Steps/Stages

1.1 R:NaOH, R:H_2, C:Ni, S:H_2O, S:EtOH, 4 h, rt, 40 bar

Notes

Raney nickel used, Reactants: 1, Reagents: 2, Catalysts: 1, Solvents: 2, Steps: 1, Stages: 1, Most stages in any one step: 1

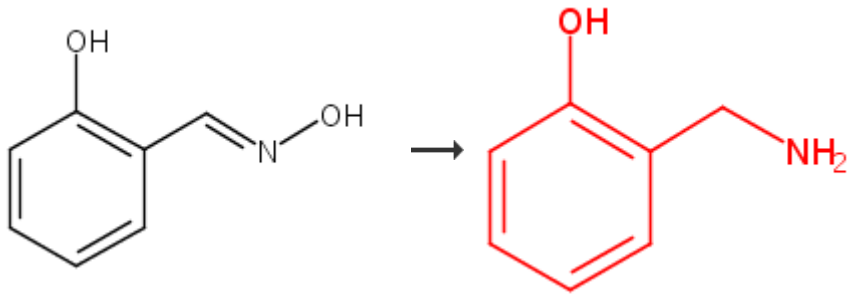
References

Series of Mn complexes based on N-centered ligands and superoxide - reactivity in an anhydrous medium and SOD-like activity in an aqueous medium correlated to MnII/MnIII redox potentials. Part II

By Durot, Stephanie et al

From European Journal of Inorganic Chemistry, (17), 3513-3523; 2005

16. Single Step



69%

Overview

Steps/Stages

1.1 R:HCl, R:H_2, C:Carbon, C:Pd, S:MeOH, S:H_2O

Notes

Reactants: 1, Reagents: 2, Catalysts: 2, Solvents: 2, Steps: 1, Stages: 1, Most stages in any one step: 1

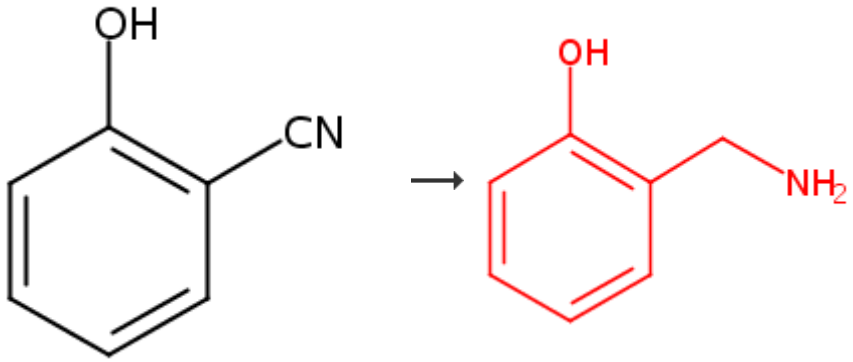
References

The action of thiophenols on (N,N'-disalicylidene-1-cyclohexene-1,2-diaminato)cobalt(II)

By Sakata, Kazunori et al

From Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry, 20(7), 901-8; 1990

17. Single Step



Overview

Steps/Stages

1.1 R:H_2, C:Pd

Notes

prophetic reaction, Reactants: 1, Reagents: 1, Catalysts: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

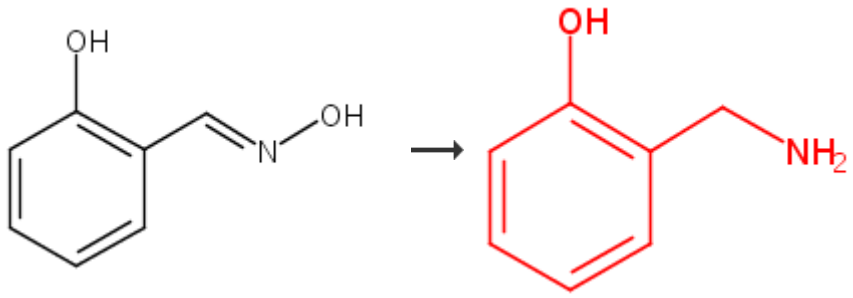
References

Optimized real time nucleic acid detection processes

By Rabbani, Elazar et al

From U.S. Pat. Appl. Publ., 20120252007, 04 Oct 2012

18. Single Step



Overview

Steps/Stages

1.1 R:Na amalgam, S:H_2O, S:EtOH, < 55°C

1.2 R:HCl, S:H_2O, neutralized

1.3 R:NH_4OH, S:H_2O, S:Et_2O, > 1 min, rt

Notes

N2, Reactants: 1, Reagents: 3, Solvents: 3, Steps: 1, Stages: 3, Most stages in any one step: 3

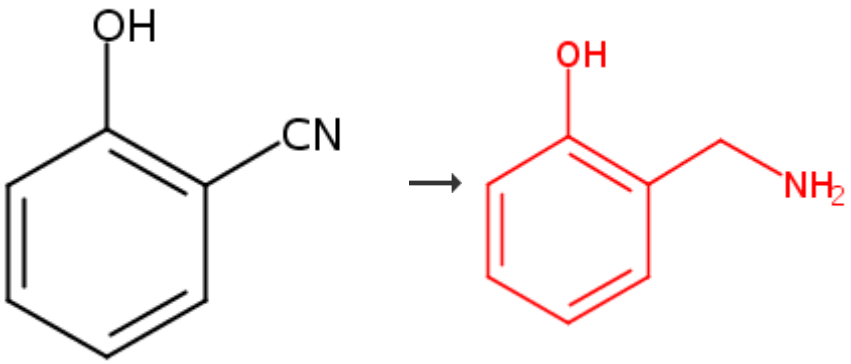
References

A trinuclear nickel(II) complex with dissimilar bridges: Synthesis, crystal structure, spectroscopy and magnetism

By Wang, Qing-Lun et al

From Journal of Molecular Structure, 892(1-3), 88-92; 2008

19. Single Step



Overview

Steps/Stages

1.1 R:$LiAlH_4$

Notes

prophetic reaction, literature preparation, Reactants: 1, Reagents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Preparation of amino acid amides as HIV protease inhibitors

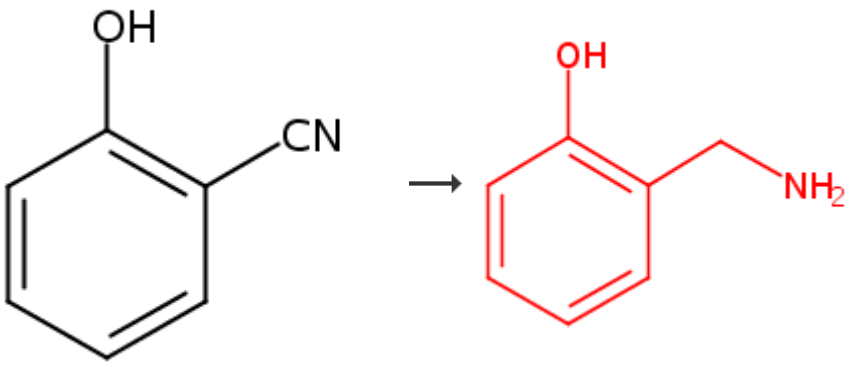
By Kucera, David John and Scott, Robert William

From U.S. Pat. Appl. Publ., 20040204591, 14 Oct 2004

Experimental Procedure

Amine was generated by $LiAlH_4$ reduction of 2-cyanophenol (Ludeman, S. M., et. al. J . *Med. Chem.* 1975,18, 1252-3).

20. Single Step



Overview

Steps/Stages

Notes

1.1 R:$LiAlH_4$

literature preparation, Reactants: 1, Reagents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

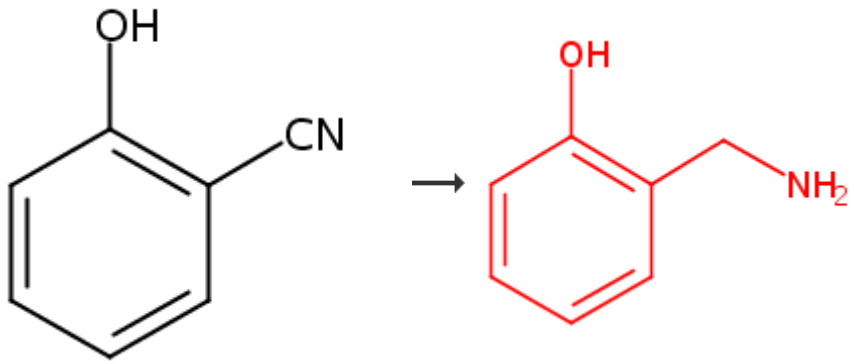
References

Preparation of amino acid amides as HIV protease inhibitors

By Canon-Koch, Stacie S. et al

From PCT Int. Appl., 2002100844, 19 Dec 2002

21. Single Step



Overview

Steps/Stages

1.1 R:$LiAlH_4$

Notes

literature preparation, prophetic reaction, Reactants: 1, Reagents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Preparation of amino acid amides as HIV protease inhibitors

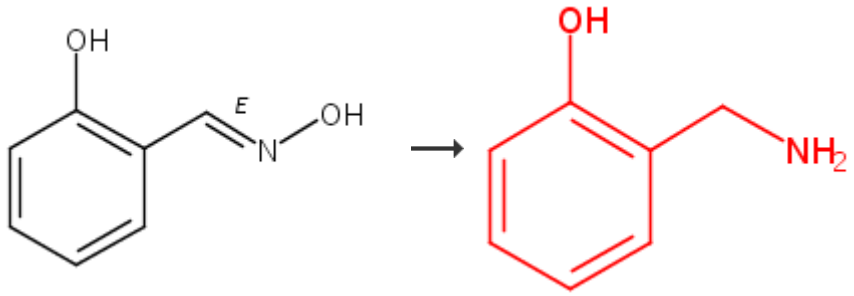
By Canon-Koch, Stacie S. et al

From PCT Int. Appl., 2002100845, 19 Dec 2002

Experimental Procedure

Example A44 Amine was generated by $LiAlH_4$ reduction of 2-cyanophenol (Ludeman, S.M., et. al. J. *Med. Chem.* **1975,***18,* 1252-3.).

22. Single Step



68%

Overview

Steps/Stages

1.1 R:H_2O, S:EtOH

Notes

Classification: N-Deoxygenation; Reduction; # Conditions: Na-Hg EtOH H2O; pH 8-9 <50 deg, Reactants: 1, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

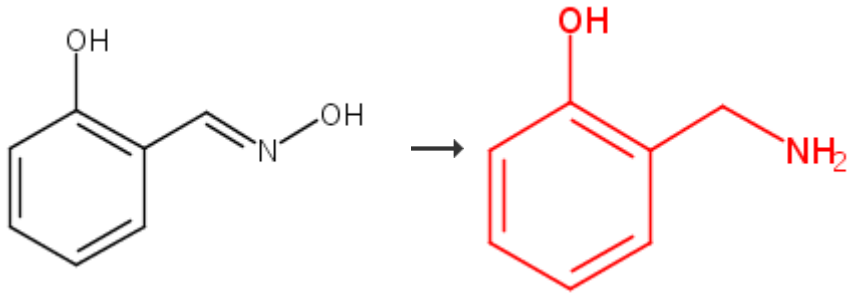
References

Studies on Schiff bases in connection with the mechanism of transamination

By Witkop, Bernhard and Beiler, Theodore W.

From Journal of the American Chemical Society, 76, 5589-97; 1954

23. Single Step



35%

Overview

Steps/Stages

1.1 R:H_2, C:Pd, S:MeOH, 4 h, rt, 13 psi

Notes

Reactants: 1, Reagents: 1, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Hydroxy-1-aminoindans and Derivatives: Preparation, Stability, and Reactivity

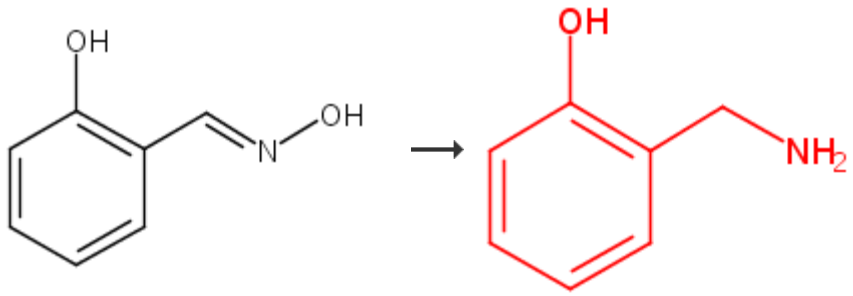
By Herzig, Yaacov et al

From Journal of Organic Chemistry, 71(11), 4130-4140; 2006

Experimental Procedure

2-Aminomethyl Phenol. A mixture of salicyloxime (3 g, 22 mmol) and 5% Pd/C (0.5 g) in MeOH (50 mL) was hydrogenated at room temperature under 13 psi pressure, with vigorous stirring, for 4 h. The catalyst was filtered through Celite, and the filtrate was further purified by column chromatography (hexane/EtOAc, 1:1) to provide 2-aminomethyl Phenol, yield 35% as a colorless solid ^{1}H NMR (DMSO-*d*$_6$) δ 7.05 (m, 2H), 6.70 (m, 2H), 3.85 (s, 2H). ^{13}C NMR (DMSO-*d*$_6$) δ 157.0, 127.7, 127.3, 126.6, 118.0, 115.0, 43.0. MS (ES$^+$) *m*/*z* 230 ([C_7H_7O]$_2$NH, 100), 214 (MH^+, 10). HRMS (DCI/CH_4) *m*/*z* calcd for C_7H_9NO (M^+), 123.068414; found, 123.06642.

24. Single Step



Overview

Steps/Stages

1.1

Notes

Na amalgam, Reactants: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

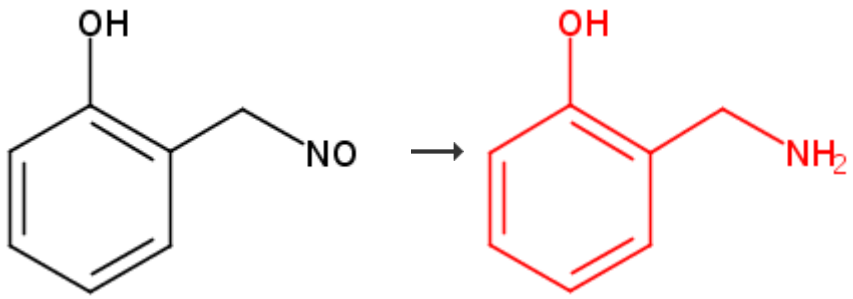
References

Pyridoxal-mediated dephosphonylation of 1-amino phosphonic acids

By Calvo, Kim C.

From Journal of Organic Chemistry, 52(16), 3654-8; 1987

25. Single Step



Overview

Steps/Stages

Notes

1.1 R:AcOH, R:Zn, S:AcOH

Reactants: 1, Reagents: 2, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

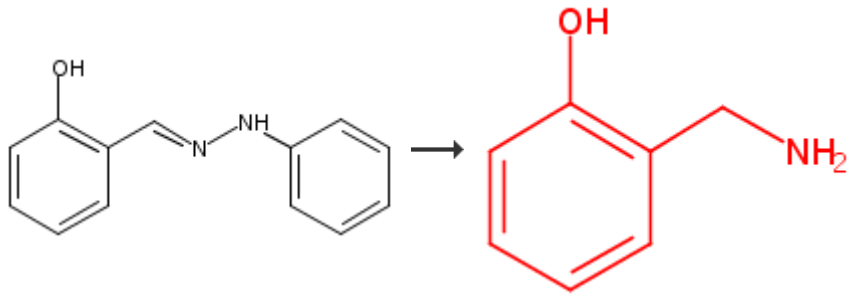
References

Synthesis and antiviral activity of gossypol derivatives

By Auelbekov, S. A. et al

From Khimiko-Farmatsevticheskii Zhurnal, 19(7), 829-32; 1985

26. Single Step



Overview

Steps/Stages

Notes

1.1 R:NH_3, S:EtOH

Reactants: 1, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

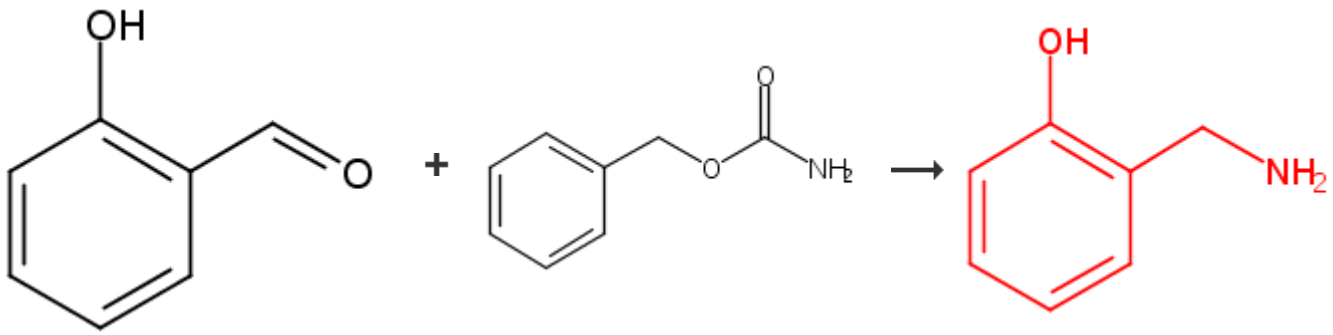
References

A convenient synthesis of amines

By Siddiqui, Amin A. et al

From Synthetic Communications, 7(1), 71-8; 1977

27. 2 Steps



Overview

Steps/Stages

Notes

1.1 R:F_3CCO_2H, R:Et_3SiH, S:MeCN, 18 h, rt

2.1 R:H_2, C:Pd, S:AcOEt, 18 h, rt

Reactants: 2, Reagents: 3, Catalysts: 1, Solvents: 2, Steps: 2, Stages: 2, Most stages in any one step: 1

References

Concise Copper-Catalyzed Synthesis of Tricyclic Biaryl Ether-Linked Aza-Heterocyclic Ring Systems

By Mestichelli, Paola et al

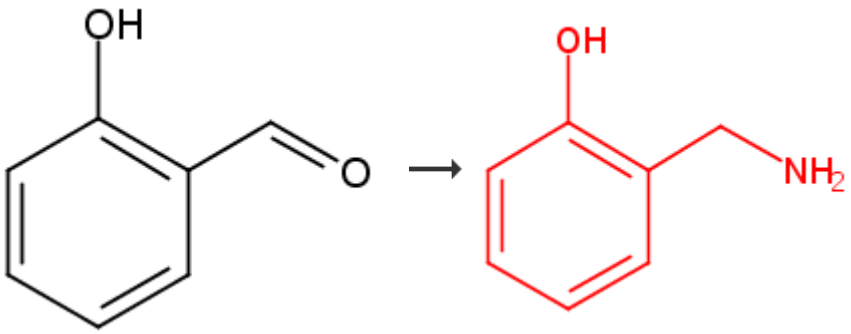
From Organic Letters, 15(21), 5448-5451; 2013

Experimental Procedure

Step 1
Synthesis of protected intermediate based by the method of Dube *et al.*[3] A solution of salicylhaldehyde (**9**, 1 equivalent, 8.188 mmol), benzylcarbamate (3 equivalents, 24.564 mmol), triethylsilane (3 equivalents, 24.564 mmol), and TFA (2 equivalents, 16.376 mmol) in CH_3CN (40 mL) was stirred at room temperature for 18 hours. The mixture was diluted with Et_2O, washed with saturated $NaHCO_3$ solution and brine. The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure. The residue was purified by column chromatography (SiO_2, Petroleum Ether : Et_2O, 70:30). The protected intermediate as a colourless oil (90%). **IR:** υ_{max} (neat)/cm^{-1} 3325 m (aromatic C-H), 1666 st (C=O), 1538 m (aromatic C=C), 1489 m (aromatic C=C), 1446 m (aromatic C=C). **^{1}H NMR**: δ_H (500 MHz, $CDCl_3$) = 8.50 (1H, br, OH or NH), 7.36-7.29 (5H, m, aryl CH), 7.22 (1H, t, *J* = 7.3 Hz, aryl CH), 7.08 (1H, dd, *J* = 7.5, 1.5 Hz, aryl CH), 6.93 (1H, d, *J* = 8.0 Hz, aryl CH), 6.85- 6.82 (1H, td, *J* = 7.5, 1.0 Hz, aryl CH), 5.57 (1H, br s, OH or NH), 5.10 (2H, s, OCH_2), 4.28 (2H, d, *J* = 6.5 Hz, CH_2N) ppm. **^{13}C NMR**: δ_C (125 MHz, $CDCl_3$) = 158.6 (C), 155.3 (C), 135.8 (C), 130.6 (CH), 129.9 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 124.6 (C), 120.2 (CH), 117.6 (CH), 67.7 (CH_2), 41.4 (CH_2) ppm.

Step 2
To a solution of the protected intermediate (1.83 g) in EtOAc (10 mL) was added 10% Pd/C 10% (40 mg). This suspension was stirred under an atmosphere of hydrogen gas (balloon) for 18 hours. The reaction mixture was filtered through Celite® and the solvent removed under reduced pressure. The title compound as a white solid (Yield: 95 %) which was used without characterization or purification **2-hydroxy-benzylamine**

28. 2 Steps



Overview

Steps/Stages **Notes**

1.1 R:$NaHCO_3$, R:H_2NOH-HCl, S:H_2O, S:AcOEt, overnight, rt

2.1 R:Zn, S:MeOH, rt

2.2 R:NH_4

$^{+}$ •HCO_2

$^{-}$, S:MeOH, overnight, rt; rt, pH 3

2.3 R:NH_4OH, S:H_2O, rt, neutralized

Reactants: 1, Reagents: 5, Solvents: 3, Steps: 2, Stages: 4, Most stages in any one step: 3

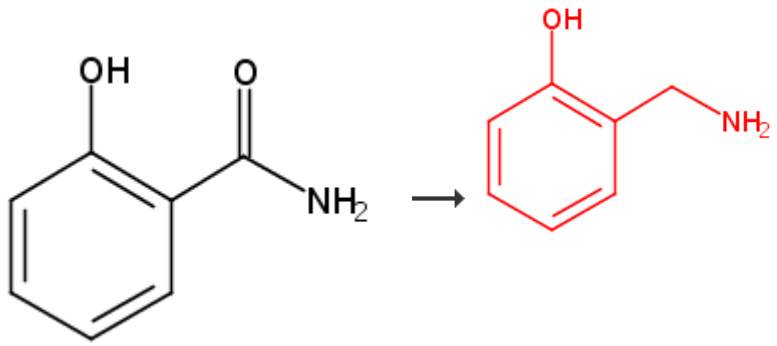
References

Preparation of N-benzylamide derivatives as herbicides

By Lu, Long et al

From Faming Zhuanli Shenqing, 101367769, 18 Feb 2009

29. Single Step



100%

Overview

Steps/Stages

1.1 R:BH_3-THF, S:THF, rt; 48 h, reflux

1.2 R:MeOH

1.3 R:HCl, S:H_2O, rt; 18 h, reflux

Notes

Reactants: 1, Reagents: 3, Solvents: 2, Steps: 1, Stages: 3, Most stages in any one step: 3

References

Synthesis and Luminescence Studies of Aryl Substituted Tetraamide Complexes of Europium(III): A New Approach to pH Responsive Luminescent Europium Probes

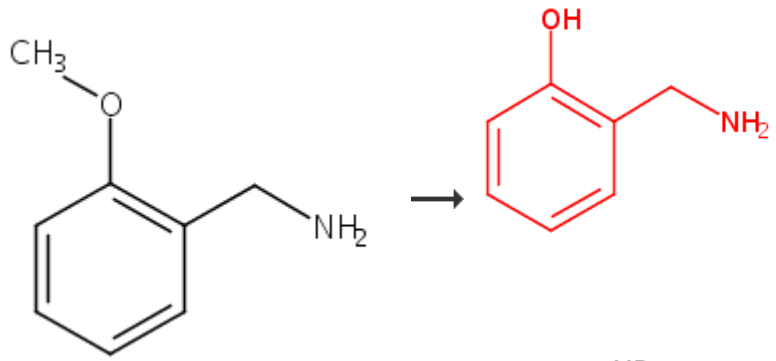
By Woods, Mark and Sherry, A. Dean

From Inorganic Chemistry, 42(14), 4401-4408; 2003

Experimental Procedure

General/Typical Procedure: 2-Hydroxybenzylamine Hydrochloride (9a). Amide 8a (5.35 g, 39 mmol) was dissolved into BH_3·THF (1 M, 200 mL) under argon. This solution was maintained at reflux with stirring for 48 h. Remaining borane was then quenched by dropwise addition of methanol. The solvents were then removed in vacuo and methanol (2 × 50 mL) added and removed under reduced pressure. The residue was dissolved in HCl (2 M, 30 mL) and heated under reflux for 18 h. The solvents were removed under reduced pressure. 2-Hydroxybenzylamine Hydrochloride (9a) as sticky gum (6.30 g, quantitative yield). Mp = 147-149.5 °C. ^{1}H NMR (270 MHz, D_2O): δ) 7.28 (2H, m, Ar), 6.92 (2H, m, Ar), 4.11 (2H, s, $ArCH_2NH_2$). ^{13}C NMR (67.5 MHz, D_2O): δ = 39.7 ($ArCH_2NH_2$), 115.7 (4-Ph), 119.3 (1-Ph), 120.7 (6-Ph), 131.1 (5-Ph), 131.2 (3-Ph), 154.9 (2-Ph). ν_{max}/cm^{-1} : 3044 br (NH), 2987, 1599, 1505, 1459, 1380, 1246, 1185, 1123, 755. m/z (EI+): 123 (84% $[M]^+$), 106 (50% $[M\text{-}OH]^+$), 78 (100% $[M\text{-}O\text{-}CH_2NH_2]^+$).

30. Single Step



- HBr

Overview

Steps/Stages

1.1 R:Br_2, S:AcOH, rt

Notes

Reactants: 1, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

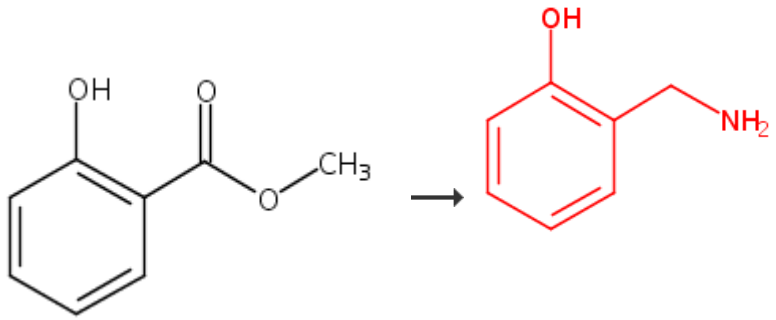
References

Preparation of substituted pyrazines as protein kinase modulators

By Buhr, Chris A. et al

From PCT Int. Appl., 2003093297, 13 Nov 2003

31. 2 Steps



- HCl

Overview

Steps/Stages

Notes

1.1 R:NH_3, S:H_2O, rt; 2 d, 50°C

2.1 R:BH_3-THF, S:THF, rt; 48 h, reflux

2.2 R:MeOH

2.3 R:HCl, S:H_2O, rt; 18 h, reflux

Reactants: 1, Reagents: 4, Solvents: 2, Steps: 2, Stages: 4, Most stages in any one step: 3

References

Synthesis and Luminescence Studies of Aryl Substituted Tetraamide Complexes of Europium(III): A New Approach to pH Responsive Luminescent Europium Probes

By Woods, Mark and Sherry, A. Dean

From Inorganic Chemistry, 42(14), 4401-4408; 2003

Experimental Procedure

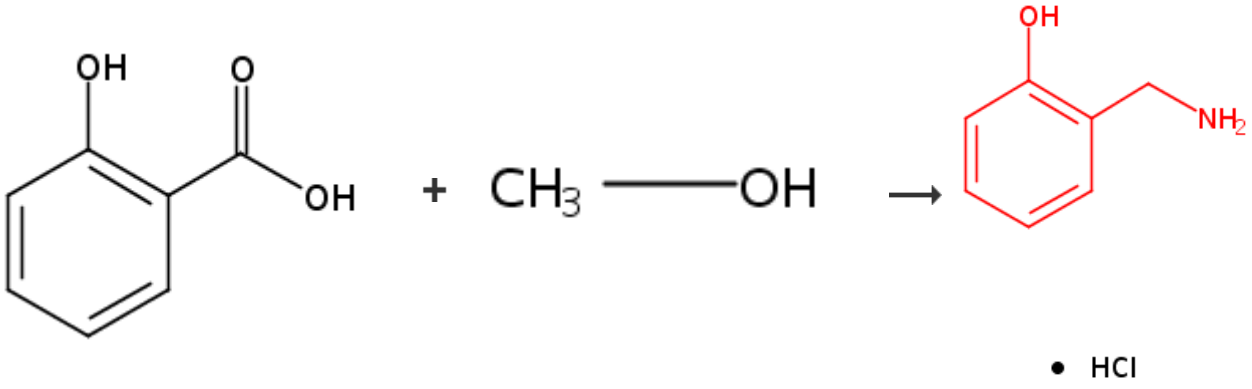
Step 1

General/Typical Procedure: 2-Hydroxybenzoylamide (8a). Methyl salicylate, 7a (8.10 g, 53 mmol), was dissolved in aqueous ammonia (150 mL), and the solution was stirred at 50 °C for 2 days. After removal of the solvent in vacuo, the residue was dissolved in water (30 mL) and extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were dried (Na_2SO_4) and the solvent removed in vacuo. 2-Hydroxybenzoylamide (8a) as a colorless solid (7.68 g, 96%). Mp = 134.5-135.5 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ = 12.1 (1H, s, OH), 7.46 (1H, ddd overlapping, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 2 Hz, 6-Ph), 7.40 (1H, dd, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 2 Hz, 5-Ph), 7.02 (1H, dd, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 1 Hz, 4-Ph), 6.89 (1H, ddd overlapping, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 1 Hz, 3-Ph) 6.17 (2H, s br, NH_2). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 113.3 (1-Ph), 118.8 (5-Ph), 118.9 (4-Ph), 126.5 (6-Ph), 135.1 (3-Ph), 162.1 (2-Ph), 172.8 (C.dblunds.O). ν_{max}/cm^{-1} : 3424 (NH), 3192, 1667 (C.dblunds.O), 1629, 1589, 1491, 1448, 1425, 1361, 1254. m/z (EI+): 137 (29% $[M]^+$), 120 (37% $[M\text{-}OH]^+$), 92 (100% $[M\text{-}CONH_2]^+$).

Step 2

General/Typical Procedure: 2-Hydroxybenzylamine Hydrochloride (9a). Amide 8a (5.35 g, 39 mmol) was dissolved into BH_3·THF (1 M, 200 mL) under argon. This solution was maintained at reflux with stirring for 48 h. Remaining borane was then quenched by dropwise addition of methanol. The solvents were then removed in vacuo and methanol (2 × 50 mL) added and removed under reduced pressure. The residue was dissolved in HCl (2 M, 30 mL) and heated under reflux for 18 h. The solvents were removed under reduced pressure. 2-Hydroxybenzylamine Hydrochloride (9a) as sticky gum (6.30 g, quantitative yield). Mp = 147-149.5 °C. ^{1}H NMR (270 MHz, D_2O): δ) 7.28 (2H, m, Ar), 6.92 (2H, m, Ar), 4.11 (2H, s, $ArCH_2NH_2$). ^{13}C NMR (67.5 MHz, D_2O): δ = 39.7 ($ArCH_2NH_2$), 115.7 (4-Ph), 119.3 (1-Ph), 120.7 (6-Ph), 131.1 (5-Ph), 131.2 (3-Ph), 154.9 (2-Ph). ν_{max}/cm^{-1} : 3044 br (NH), 2987, 1599, 1505, 1459, 1380, 1246, 1185, 1123, 755. m/z (EI+): 123 (84% $[M]^+$), 106 (50% $[M\text{-}OH]^+$), 78 (100% $[M\text{-}O\text{-}CH_2NH_2]^+$).

32. 3 Steps



Overview

Steps/Stages **Notes**

1.1 C:H_2SO_4, S:H_2O, S:MeOH, rt; 48 h, reflux

1.2 R:K_2CO_3

2.1 R:NH_3, S:H_2O, rt; 2 d, 50°C

3.1 R:BH_3-THF, S:THF, rt; 48 h, reflux

3.2 R:MeOH

3.3 R:HCl, S:H_2O, rt; 18 h, reflux

Reactants: 2, Reagents: 5, Catalysts: 1, Solvents: 3, Steps: 3, Stages: 6, Most stages in any one step: 3

References

Synthesis and Luminescence Studies of Aryl Substituted Tetraamide Complexes of Europium(III): A New Approach to pH Responsive Luminescent Europium Probes

By Woods, Mark and Sherry, A. Dean

From Inorganic Chemistry, 42(14), 4401-4408; 2003

Experimental Procedure

Step 1

General/Typical Procedure: Methyl Salicylate (7a). Salicylic acid (10.30 g, 75 mmol) was dissolved in methanol (150 mL), and after adding concentrated H_2SO_4 (3 mL), the solution was heated under reflux with stirring for 48 h. The solvents were then removed in vacuo, and K_2CO_3 was added until no further effervescence was observed. The residue was taken up into water (30 mL) and extracted with CH_2Cl_2 (2 × 200 mL). The organic extracts were combined and dried (Na_2SO_4) and the solvents removed in vacuo. Methyl Salicylate (7a) as a colorless oil (10.62 g, 93%). ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.84 (1H dd, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 2 Hz, 3-Ph), 7.46 (1H, ddd overlapping, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 2 Hz, 4-Ph), 6.99 (1H, dd, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 1 Hz, 6-Ph), 6.89 (1H, ddd overlapping, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 1 Hz, 5-Ph), 3.96 (3H, s, CH_3). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ) 52.3 (CH_3), 112.4 (1-Ph), 117.6 (5-Ph), 119.2 (4-Ph), 130.0 (3-Ph), 135.8 (6-Ph), 161.6 (2-Ph), 170.6 (C.dblunds.O). ν_{max}/cm^{-1} : 3189 (OH), 2956, 1681 (C.dblunds.O), 1615, 1586, 1486, 1441, 1305, 1253, 1216, 1158, 1090, 1033, 757, 701. m/z (EI+): 152 (7% $[M]^+$), 138 (12% $[M-CH_2]^+$), 120 (42% $[M-MeOH]^+$), 92 (100% $[M-HCO_2Me]^+$).

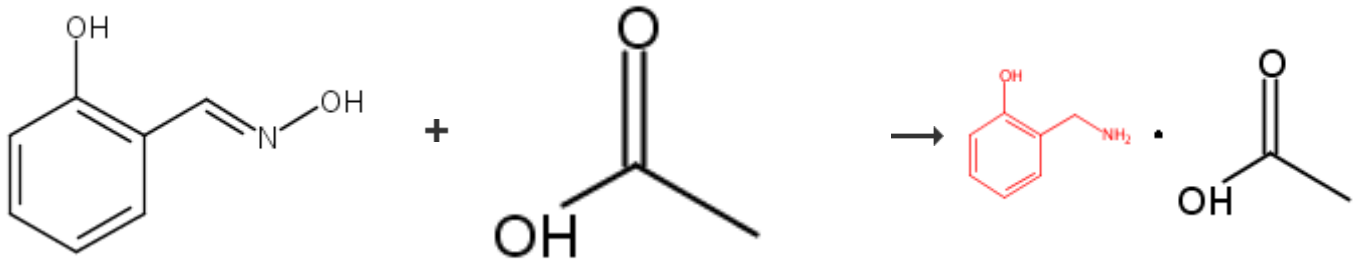
Step 2

General/Typical Procedure: 2-Hydroxybenzoylamide (8a). Methyl salicylate, 7a (8.10 g, 53 mmol), was dissolved in aqueous ammonia (150 mL), and the solution was stirred at 50 °C for 2 days. After removal of the solvent in vacuo, the residue was dissolved in water (30 mL) and extracted with CH_2Cl_2 (3 × 150 mL). The combined organic extracts were dried (Na_2SO_4) and the solvent removed in vacuo. 2-Hydroxybenzoylamide (8a) as a colorless solid (7.68 g, 96%). Mp = 134.5-135.5 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ = 12.1 (1H, s, OH), 7.46 (1H, ddd overlapping, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 2 Hz, 6-Ph), 7.40 (1H, dd, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 2 Hz, 5-Ph), 7.02 (1H, dd, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 1 Hz, 4-Ph), 6.89 (1H, ddd overlapping, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 8 Hz, $^3J_{H-H}$ = 1 Hz, 3-Ph) 6.17 (2H, s br, NH_2). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ = 113.3 (1-Ph), 118.8 (5-Ph), 118.9 (4-Ph), 126.5 (6-Ph), 135.1 (3-Ph), 162.1 (2-Ph), 172.8 (C.dblunds.O). ν_{max}/cm^{-1} : 3424 (NH), 3192, 1667 (C.dblunds.O), 1629, 1589, 1491, 1448, 1425, 1361, 1254. m/z (EI+): 137 (29% $[M]^+$), 120 (37% $[M-OH]^+$), 92 (100% $[M-CONH_2]^+$).

Step 3

General/Typical Procedure: 2-Hydroxybenzylamine Hydrochloride (9a). Amide 8a (5.35 g, 39 mmol) was dissolved into BH_3·THF (1 M, 200 mL) under argon. This solution was maintained at reflux with stirring for 48 h. Remaining borane was then quenched by dropwise addition of methanol. The solvents were then removed in vacuo and methanol (2 × 50 mL) added and removed under reduced pressure. The residue was dissolved in HCl (2 M, 30 mL) and heated under reflux for 18 h. The solvents were removed under reduced pressure. 2-Hydroxybenzylamine Hydrochloride (9a) as sticky gum (6.30 g, quantitative yield). Mp = 147-149.5 °C. ^{1}H NMR (270 MHz, D_2O): δ) 7.28 (2H, m, Ar), 6.92 (2H, m, Ar), 4.11 (2H, s, $ArCH_2NH_2$). ^{13}C NMR (67.5 MHz, D_2O): δ = 39.7 ($ArCH_2NH_2$), 115.7 (4-Ph), 119.3 (1-Ph), 120.7 (6-Ph), 131.1 (5-Ph), 131.2 (3-Ph), 154.9 (2-Ph). ν_{max}/cm^{-1} : 3044 br (NH), 2987, 1599, 1505, 1459, 1380, 1246, 1185, 1123, 755. m/z (EI+): 123 (84% $[M]^+$), 106 (50% $[M-OH]^+$), 78 (100% $[M-O-CH_2NH_2]^+$).

33. Single Step



71%

Overview

Steps/Stages

1.1 R:Zn, S:AcOH, heated; 6 h, rt

Notes

exothermic, Reactants: 2, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

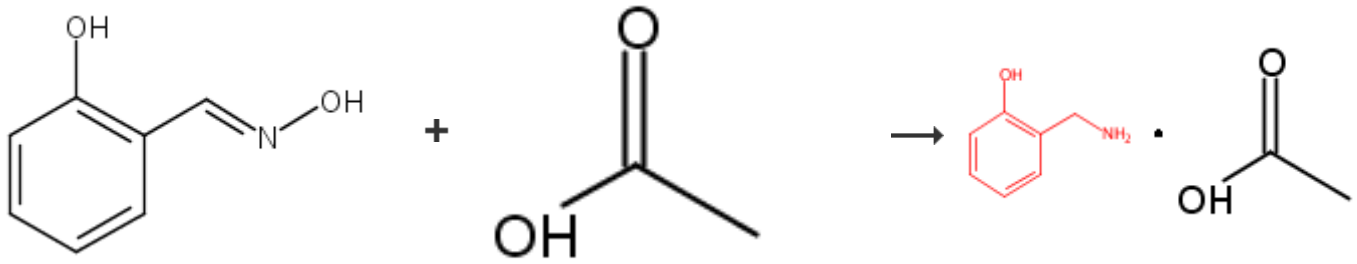
References

Synthesis and characterisation of aluminium(III) imine bis(phenolate) complexes with application for the polymerisation of rac-LA

By Forder, Thomas R. and Jones, Matthew D.

From New Journal of Chemistry, 39(3), 1974-1978; 2015

34. Single Step



74%

Overview

Steps/Stages

1.1 R:Zn, S:AcOH, rt → 10°C; 1 h, 10-15°C; 2 h, 20°C

Notes

Reactants: 2, Reagents: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Characterization of Scavengers of γ-Ketoaldehydes that do not Inhibit Prostaglandin Biosynthesis

By Zagol-Ikapitte, Irene et al

From Chemical Research in Toxicology, 23(1), 240-250; 2010

Experimental Procedure

Synthesis of Salicylamine (1) and Its Analogues. The reduction of appropriately substituted 2-hydroxybenzaldehyde oxime to the amine, using zinc in acetic acid, was the final step for preparing salicylamine (SA, **1**) and its analogues. In the case of salicylaldoxime (Acros, 2.9 g, 20 mmol), it was dissolved in acetic acid (20 mL), cooled in an ice-water bath (10 °C), followed by the addition of zinc dust (5 g) with stirring. The stirring was continued at 10-15 °C for 1 h and at 20 °C for 2 h. The reaction mixture was filtered, and the filtrate was evaporated. The solid was crystallized from ethanol. Salicylamine acetic acid salt (SA.AcOH, **2**); 2.7 g (74%). mp 187-188 °C. ^{1}H NMR δ 7.04 (dt, 2H, *J* = 1.44 and 5.68 Hz, 2,4-H), 6.69 (dt, 2H, *J* = 1.92 and 6.85 Hz, 4-H), 3.87 (s, 1H, CH_2), 1.62 (s, 3H, acetyl). MS of SA.AcOH (**2**) *m/z* 165 (M - H_2O), 124 (165 - acetyl), 107 (124 - NH_2), 77 (C_6H_5). SA·AcOH (**2**) has been dissolved in deuterium oxide. Hydrogen bonding between the solvent and the molecule decreases the electron density around the proton and may undergo rapid intermediate or slow exchange. This explains why we do not see the peaks from NH_2 and OH in the spectrum.

Reaction Protocol

Procedure

1. Dissolve salicylaldoxime (Acros, 20 mmol) in acetic acid (20 mL).
2. Cool the reaction mixture in an ice-water bath (10 °C).

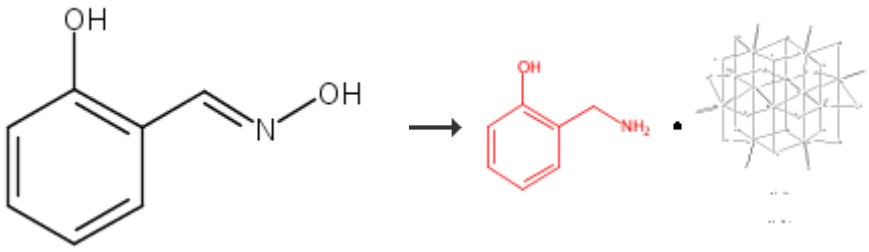
View more...

Available Experimental Data

^{1}H NMR, Mass Spec, MP

View with MethodsNow

35. Single Step



42%

Overview

Steps/Stages

1.1 R:VCl_3, R:NaOH, S:H_2O, S:EtOH, rt, pH 2.5

Notes

Reactants: 1, Reagents: 2, Solvents: 2, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Novel aspects of the reactivity of the salicylaldoxime vis-a-vis of tetra-, tri- and divalent ions of vanadium

By Boutamine, S. et al

From Reviews in Inorganic Chemistry, 28(3), 217-236; 2008