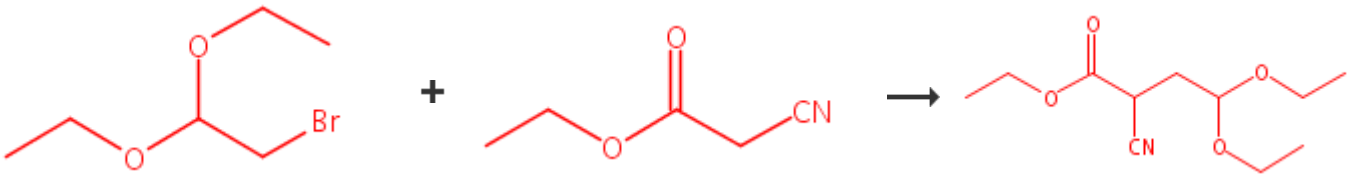
1. Single Step



78%

Overview

Steps/Stages

1.1 R:K_2CO_3, C:NaI, 4 h, 145°C

Notes

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

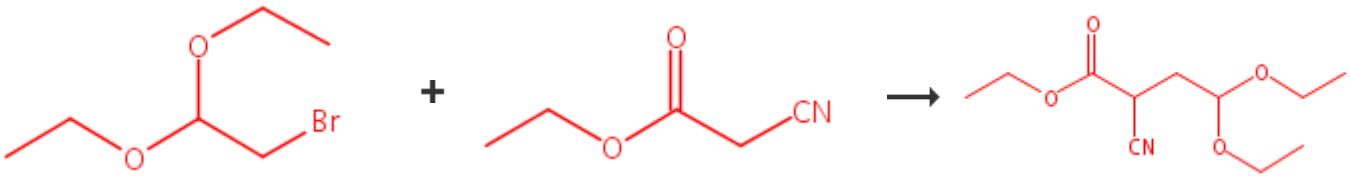
References

Preparation of quinazolines and related compounds for modulating STEP (striatal-enriched protein tyrosine phosphatase) activity

By Suzuki, Masaki et al

From Jpn. Kokai Tokkyo Koho, 2013032343, 14 Feb 2013

2. Single Step



78%

Overview

Steps/Stages

1.1 R:K_2CO_3, C:NaI, 4 h, 145°C

Notes

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

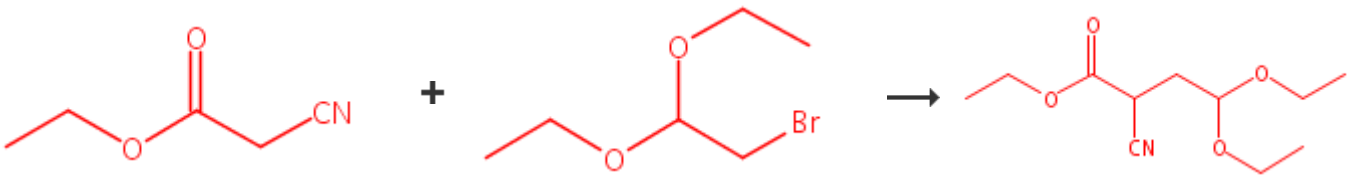
References

Quinazoline derivatives as striatal-enriched tyrosine phosphatase modulators and their preparation and use as as therapeutic compounds

By Suzuki, Masaki et al

From PCT Int. Appl., 2011082337, 07 Jul 2011

3. Single Step



72%

Overview

Steps/Stages

1.1 R:DBU, S:DMF, 0°C; 30 min, 0°C
1.2 S:DMF, 0°C; 30 min, 0°C; 3 h, 80°C
1.3 S:H_2O

Notes

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

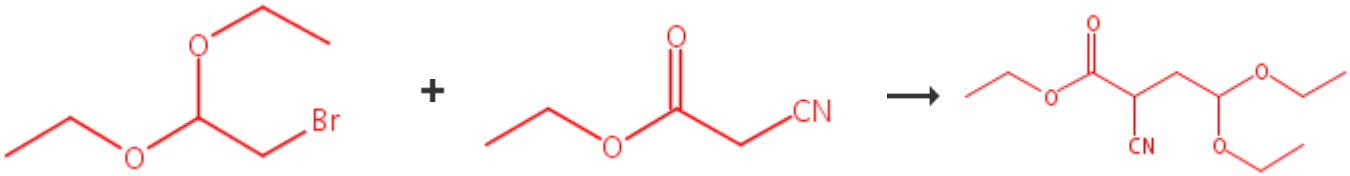
References

One-Pot Synthesis of 3-Substituted 2-Arylpyrrole in Aqueous Media via Addition-Annulation of Arylboronic Acid and Substituted Aliphatic Nitriles

By Yousuf, Md. and Adhikari, Susanta

From Organic Letters, 19(8), 2042-2045; 2017

4. Single Step



70%

Overview

Steps/Stages

1.1 R:NaOMe, S:DMF, 4 h, 90°C

Notes

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

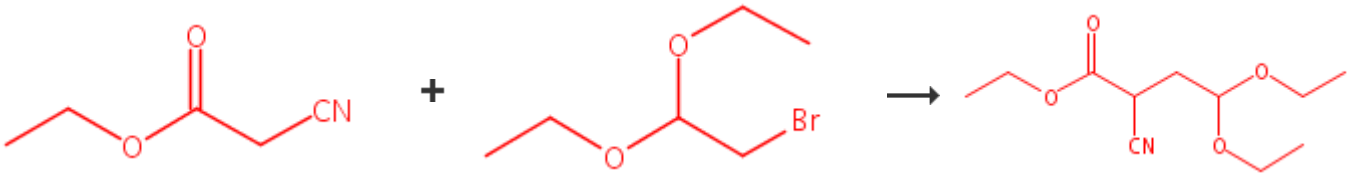
References

Preparation of substituted pyrimidine and pyrimidoindole compounds as anti-tubulin, antimitotic, antitumor, anti-opportunistic agents, dihydrofolate reductase inhibitors

By Gangjee, Aleem

From PCT Int. Appl., 2016022890, 11 Feb 2016

5. Single Step



74%

Overview

Steps/Stages

1.1 R:K_2CO_3, R:NaI, rt; rt → 145°C; 4.5 h, 145°C

Notes

no solvent, Reactants: 2, Reagents: 2, Steps: 1, Stages: 1, Most stages in any one step: 1

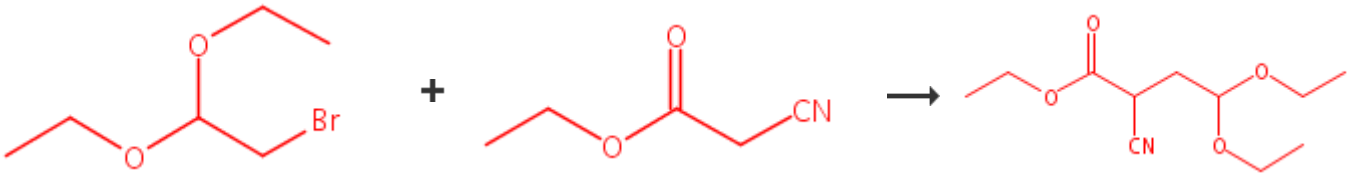
References

Pre-steady state kinetic analysis of cyclobutyl derivatives of 2'-deoxyadenosine 5'-triphosphate as inhibitors of HIV-1 reverse transcriptase

By Kim, Jiae et al

From Bioorganic & Medicinal Chemistry Letters, 22(12), 4064-4067; 2012

6. Single Step



70%

Overview

Steps/Stages

1.1 R:K_2CO_3, C:NaI, S:DMF, rt → reflux; overnight, reflux

Notes

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

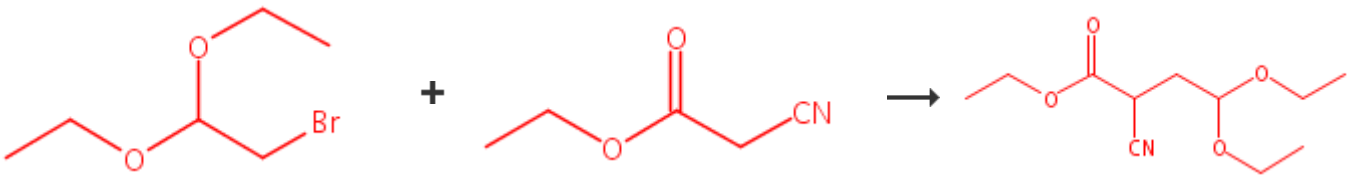
References

Preparation of nucleoside compounds for treating enterovirus 71 infection

By Shang, Luqing et al

From Faming Zhuanli Shenqing, 102526087, 04 Jul 2012

7. Single Step



66%

Overview

Steps/Stages

1.1 R:NaH, S:DMF, rt → 80°C; 15 min, 80°C
1.2 80°C; 2 h, reflux

Notes

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

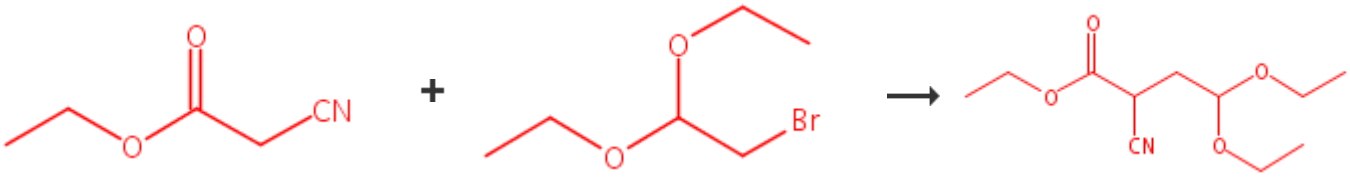
References

Study on synthesis of 4-chloropyrrolo[2,3-d]pyrimidine

By Wei, Ben-mei et al

From Huaxue Shiji, 29(5), 301-302; 2007

8. Single Step



63%

Overview

Steps/Stages

1.1 R:K_2CO_3, S:DMF, rt → 80°C; 0.5 h, 80°C; 80°C → 95°C

1.2 R:NaI, 2.5 h, 95°C; 4 h, reflux; reflux → rt

Notes

optimization study, optimized on solvent and base, Reactants: 2, Reagents: 2, Solvents: 1, Steps: 1, Stages: 2, Most stages in any one step: 2

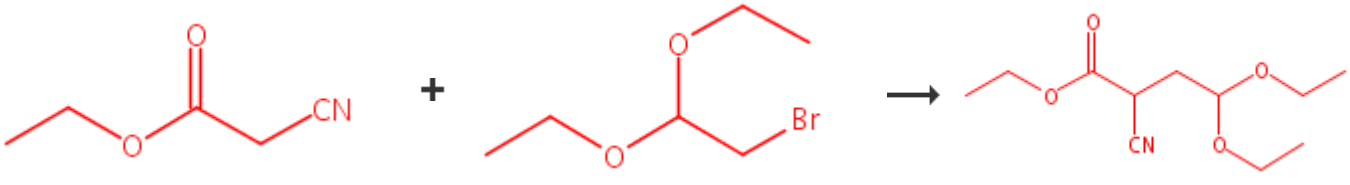
References

Synthesis of fused ring nitrogen containing pharmaceutical intermediate 2-amino-pyrrolo[2,3-d]pyrimidin-4-one

By Li, Zhen-qi et al

From Changzhou Daxue Xuebao, Ziran Kexueban, 22(1), 48-51; 2010

9. Single Step



60%

Overview

Steps/Stages

1.1 R:NaH, S:Benzene, S:DMF, -10°C; 1 h, rt
1.2 2 h, 100°C

Notes

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

References

Preparation of aryl and heteroaryl sulfonamides as CCR2 antagonists

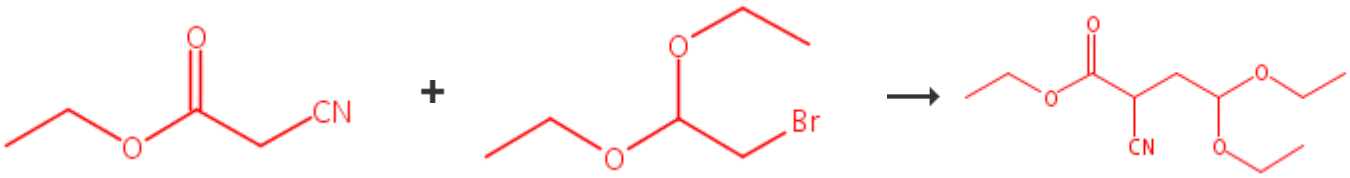
By Ungashe, Solomon et al

From U.S. Pat. Appl. Publ., 20110118248, 19 May 2011

Experimental Procedure

To a suspension of NaH (60% dispersion in mineral oil, 1.62 g, 40.5 mmol) in DMF (35 mL) and benzene (12 mL) was added ethyl cyanoacetate (4.7 mL, 44.2 mmol) dropwise at 10° C. After stirring for 1 hour at room temperature, 2-bromo-1,1-diethoxyethane (5.6 mL, 0.82 equiv.) was added and the reaction mixture was heated at 100° C. for 2 hours. The reaction mixture was then cooled to room temperature and filtered. The filtrate was condensed, and water was added. The mixture was extracted with ether. The extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel (20% EtOAc/hexanes). The desired product was obtained as colorless oil (5 g, 60%). MS: (M+Na)/z=252.

10. Single Step



60%

Overview

Steps/Stages

1.1 R:NaH, S:Benzene, S:DMF, -10°C; 1 h, rt
1.2 2 h, 100°C; 100°C → rt

Notes

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

References

Fused heteroaryl pyridyl and phenyl benzenesulfonamides as CCR2 modulators for the treatment of inflammation

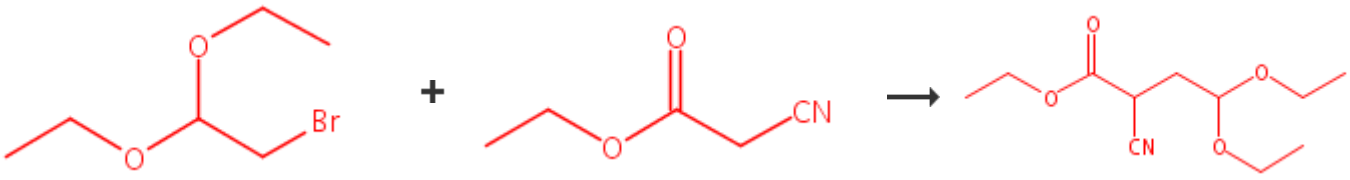
By Krasinski, Antoni et al

From PCT Int. Appl., 2009009740, 15 Jan 2009

Experimental Procedure

[00330] Example 8: Preparation of 4-Chloro-N-(5-methyl-2-(2-methyl-7H-pyrrolo[2,3-d]pyrimidine-4-carbonyl)pyridin-3-yl)-3-(trifluoromethyl)benzenesulfonamide **[00331]** Step 1: To a suspension of NaH (60% dispersion in mineral oil, 1.62 g, 40.5 mmol) in DMF (35 mL) and benzene (12 mL) was added ethyl cyanoacetate (4.7 mL, 44.2 mmol) dropwise at 10° C. After stirring for 1 hour at room temperature, 2-bromo-1,1-diethoxyethane (5.6 mL, 0.82 equiv.) was added and the reaction mixture was heated at 100° C for 2 hours. The reaction mixture was then cooled to room temperature and filtered. The filtrate was condensed, and water was added. The mixture was extracted with ether. The extracts were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel (20% EtOAc/hexanes). The desired product was obtained as colorless oil (5 g, 60%). MS: (M+Na)/z=252.

11. Single Step



63%

Overview

Steps/Stages

1.1 R:K_2CO_3, C:NaI, S:EtO_2CCH_2CN, 10 h, reflux; reflux → rt

Notes

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

References

Novel cyclobutyl compounds as kinase inhibitors for cancer treatment

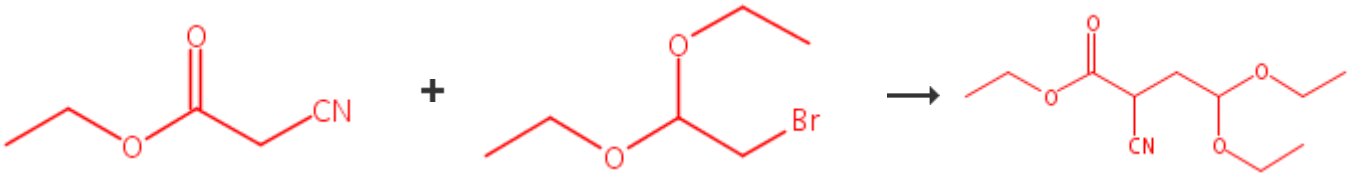
By Heinrich, Timo et al

From Ger. Offen., 102006016426, 11 Oct 2007

Experimental Procedure

(a) 130 ml (860 mmol) of bromoacetaldehyde diethyl acetal was heated to reflux with ethyl cyanoacetate (430 ml, 4.04 mol), sodium iodide (8.1 g; 54.04 mmol) and potassium carbonate (115.9 g; 839 mmol) for 10 h. After cooling to room temperature (RT), the reaction mixture was stirred with 800 ml of water, the aqueous phase was extracted with diethyl ether, then the combined organic phases were dried and concentrated. 124.99 g (63%) of a colorless liquid ethyl 2-cyano-4,4-diethoxybutyrate was obtained by Chromatography.

12. Single Step



57%

Overview

Steps/Stages

1.1 R:K_2CO_3, C:NaI, rt → 150°C

Notes

Dean Stark trap used, Reactants: 2, Reagents: 1, Catalysts: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Processes for preparing JAKs inhibitors and related intermediate compounds

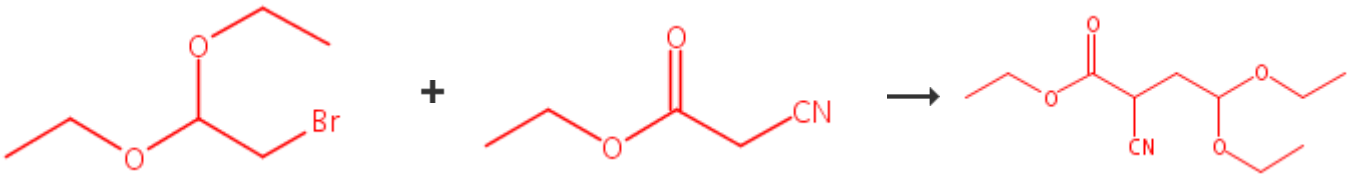
By Zhou, Jiacheng et al

From PCT Int. Appl., 2010083283, 22 Jul 2010

Experimental Procedure

2-Cyano-4,4-diethoxy-butyric acid ethyl ester (4). Bromoacetaldehyde diethylacetal **(3**, 541 g, 2.75 mol) was added to a suspension of powdered potassium carbonate (379.6 g, 2.75 mol, 1.0 equiv) and sodium iodide (33 g, 0.22 mol, 0.08 equiv) in ethyl cyanoacetate**(2**, 1.55 Kg, 13.75mol, 5.0 equiv). Upon addition of the aldehyde to the reaction mixture, the resulting solution turned yellow. The reaction mixture was slowly heated to 140-150 °C collecting the volatile material in a Dean Stark trap. This material was discarded. Fairly vigorous gas evolution was observed to begin at 140 °C. The reaction was monitored by G. C. and was observed to be near completion at 90 minutes. Heating was continued for an additional 45 minutes when gas evolution was observed to have ceased. The reaction mixture was then cooled to room temperature and partitioned between 4 L water and 2 L methyl *tert*-butyl ether (MTBE). The layers were separated and the aqueous layer was extracted with an additional 2 L of MTBE. The aqueous layer was checked for product by G. C. then discarded. The organic layers were dried over sodium sulfate, filtered and concentrated in vacuum. The crude product was purified by fractional distillation (91-105 °C @ 0.53-0.65mm/Hg) to afford 2-cyano-4,4-diethoxy-butyric acid ethyl ester **(4**, 359.4 g, 630.5 g theoretical, 57%) as a oil. ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm 4.60 (t, 1H, J = 5.6 Hz), 4.15 (m, 3H), 3.59 (m, 2H), 3.45 (m,1H), 2.11 (t, 2H, J = 6.2 Hz), 1.22 (t, 3H, J = 6.9 Hz), 1.10 (dt, 6H, J =7.1, 6.9 Hz).

13. Single Step



55%

Overview

Steps/Stages

1.1 R:K_2CO_3, C:Bu_4N^+ •Br^-, S:DMF, 90°C

Notes

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

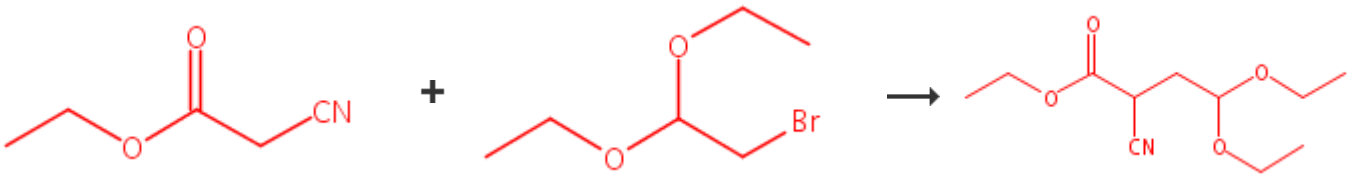
References

Targeting conserved water molecules: Design of 4-aryl-5-cyanopyrrolo[2,3-d]pyrimidine Hsp90 inhibitors using fragment-based screening and structure-based optimization

By Davies, Nicholas G. M. et al

From Bioorganic & Medicinal Chemistry, 20(22), 6770-6789; 2012

14. Single Step



Overview

Steps/Stages

Notes

1.1 R:NaH, S:DMF, 5°C; 1 h, 25°C
1.2 4 h, 95°C

industrial, optimization study, optimized on time, Reactants: 2, Reagents: 1, Solvents: 1, Steps: 1, Stages: 2, Most stages in any one step: 2

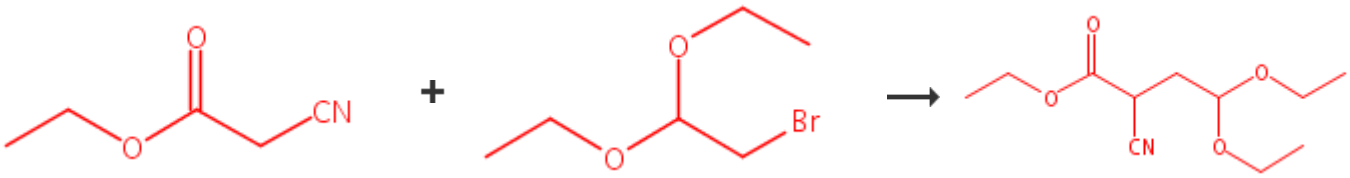
References

Method for preparing 4-chloropyrrolo[2,3-d]pyrimidine

By Pan, Yuan et al

From Faming Zhuanli Shenqing, 104860950, 26 Aug 2015

15. Single Step



51%

Overview

Steps/Stages

1.1 R:K_2CO_3, R:NaI, 24 h, reflux; reflux → rt

Notes

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

References

Preparation of piperidine derivatives as immunosuppressant for the treatment of diseases associated with pathologic JAK3 activation

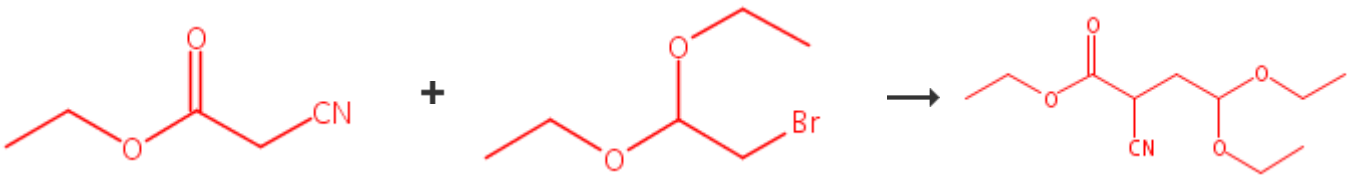
By Babu, Yarlagadda S. et al

From PCT Int. Appl., 2010014930, 04 Feb 2010

Experimental Procedure

a. A mixture of ethyl cyanoacetate **81** (227.97 g, 2015.52 mmol), bromo acetaldehyde diethyl ether (**80**) (80 g, 405.94 mmol), potassium carbonate (55.99 g, 405.13 mmol) and sodium iodide (4 g, 26.67 mmol) was refluxed for 20 h (CO_2 evolution was observed during the reaction). The reaction mixture was stirred at reflux for additional 4 h after the evolution of CO_2 has ceased. The reaction was cooled to room temperature, diluted with water (400 mL) and diethyl ether (400 mL). The organic layer was separated and the aqueous layer was extracted with diethyl ether (250 mL). The ether layers were combined washed with water (2 x 100 mL), brine (200 mL), dried, filtered and concentrated in vacuum. The product obtained was distilled under vacuum to furnish ethyl-2-cyano-4,4-diethoxybutanoate (**82**) (47.5 g, 51.0 %) as a colorless oil. B.P: 103 °C/1 mm Hg. ^{1}H NMR (300 MHz, DMSO) δ 4.61 (t, *J* = 5.7, 1H), 4.24 - 4.08 (m, 3H), 3.67 - 3.54 (m, 2H), 3.53 - 3.40 (m, 2H), 2.12 (t, *J* = 6.0, 2H), 1.23 (t, *J* = 7.1, 3H), 1.11 (td, *J* = 4.9, 7.0, 6H); IR (neat): 3482, 2980, 2901, 2361, 2252, 1749, 1446, 1374, 1262, 1218, 1128, 1062 and 857 cm^{-1}; MS (ES$^+$): 263.6 (M + 35); Analysis: CaIc for $C_{11}H_{19}NO_4$.0.25 H_2O: C, 56.51; H, 8.40; N, 5.99; Found: C, 56.71; H, 8.16; N, 5.96.

16. Single Step



Overview

Steps/Stages

1.1 R:NaOMe, S:DMF, 30 min, rt
1.2 rt; 4 h, 90°C

Notes

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

References

Synthesis and Discovery of Water-Soluble Microtubule Targeting Agents that Bind to the Colchicine Site on Tubulin and Circumvent Pgp Mediated Resistance

By Gangjee, Aleem et al

From Journal of Medicinal Chemistry, 53(22), 8116-8128; 2010

Experimental Procedure

The synthesis of **10** utilized a reported method.[35] To a solution of ethyl 2-cyanoacetate **8** (10 mmol, 1.13 g) in anhydrous dimethylformamide (DMF, 20 mL) was added sodium methoxide (10 mmol, 0.54 g). After stirring for 30 min, 2-bromo-1,1-diethoxyethane (10 mmol, 1.97 g)was added, and the reaction was heated at 90 °C for 4 h. After cooling to room temperature, the reaction solution was extracted with diethyl ether (2 x 20 mL). The ether layer was collected, dried over sodium sulfate, and evaporated to give a pale yellow liquid.

Reaction Protocol

Procedure

1. Add sodium methoxide (10 mmol, 0.54 g) to a solution of ethyl 2-cyanoacetate (10 mmol) in anhydrous dimethylformamide (DMF, 20 mL).
2. After stirring for 30 minutes, Add 2-bromo-1,1-diethoxyethane (10 mmol) to the mixture.

View more...

Available Experimental Data

State

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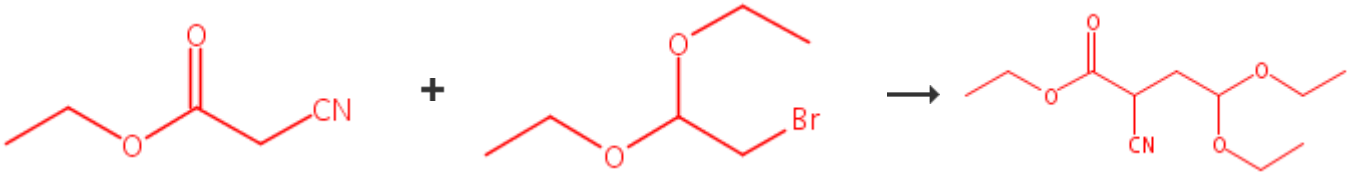
17. Single Step



Overview

Steps/Stages

1.1 R:K_2CO_3, R:NaI, rt

Notes

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

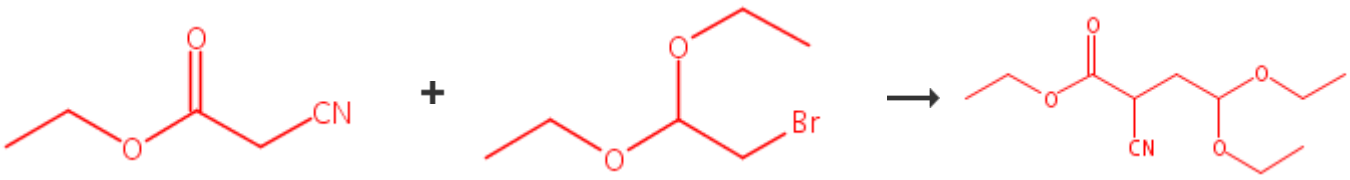
References

Preparation of pyrrolopyrimidines as protein kinase inhibitors

By Cox, Paul Joseph et al

From PCT Int. Appl., 2003000695, 03 Jan 2003

18. Single Step



29%

Overview

Steps/Stages

1.1 R:K_2CO_3, C:KI, 12 h, rt → reflux

Notes

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

References

Preparation of pyrrolopyrimidine and purine derivatives for the treatment of abnormal cell growth

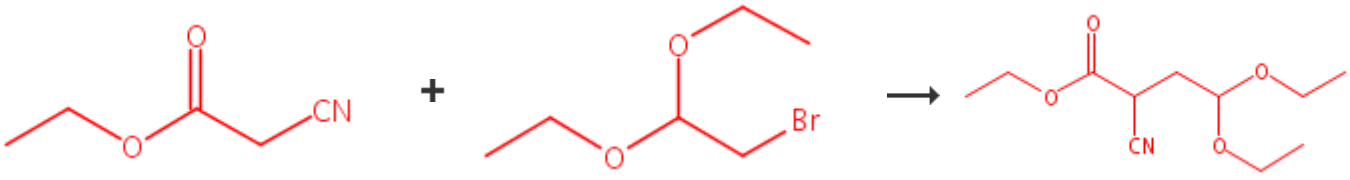
By Cheng, Hengmiao et al

From PCT Int. Appl., 2013042006, 28 Mar 2013

Experimental Procedure

Step 5: Preparation of thyl 2-cyano-4,4-diethoxybutanoate. A mixture of ethyl 2-cyanoacetate (1000 g, 8.84 mol), 2-bromo-1 ,1- diethoxyethane (400 g, 2.03 mol), KI (33.4 g, 0.201 mol) and K_2CO_3 (280 g, 2.03 mol) was heated to reflux for 12 hrs. The reaction mixture was diluted with CH_2Cl_2 (1000 mL) and the resulting precipitate was filtered off and the filtrate was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue distilled to give the title compound that was used as is in the next step. (136 g, 29.2 % yield) as a light yellow oil.

19. Single Step



42%

Overview

Steps/Stages

1.1 R:K_2CO_3, R:NaI, 4 h, 130°C

Notes

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

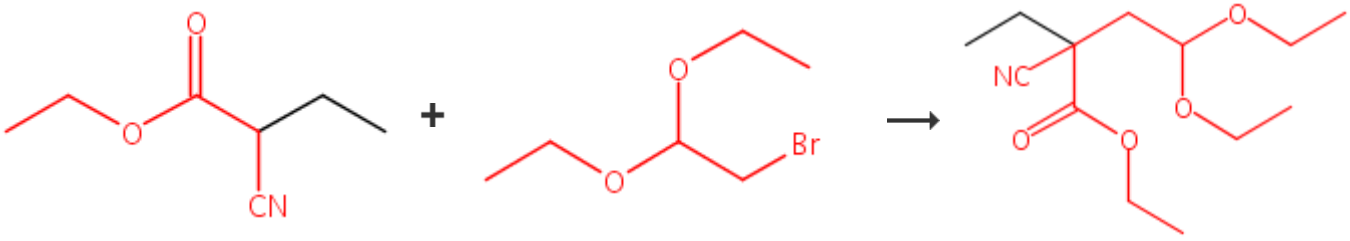
References

Preparation of nonclassical pyrrolo[2,3-d]pyrimidine antifolates

By Jordan, Christopher L. et al

From PCT Int. Appl., 9808382, 05 Mar 1998

20. Single Step



56%

Overview

Steps/Stages

1.1 R:K_2CO_3, S:DMF, 72 h, 70°C

Notes

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

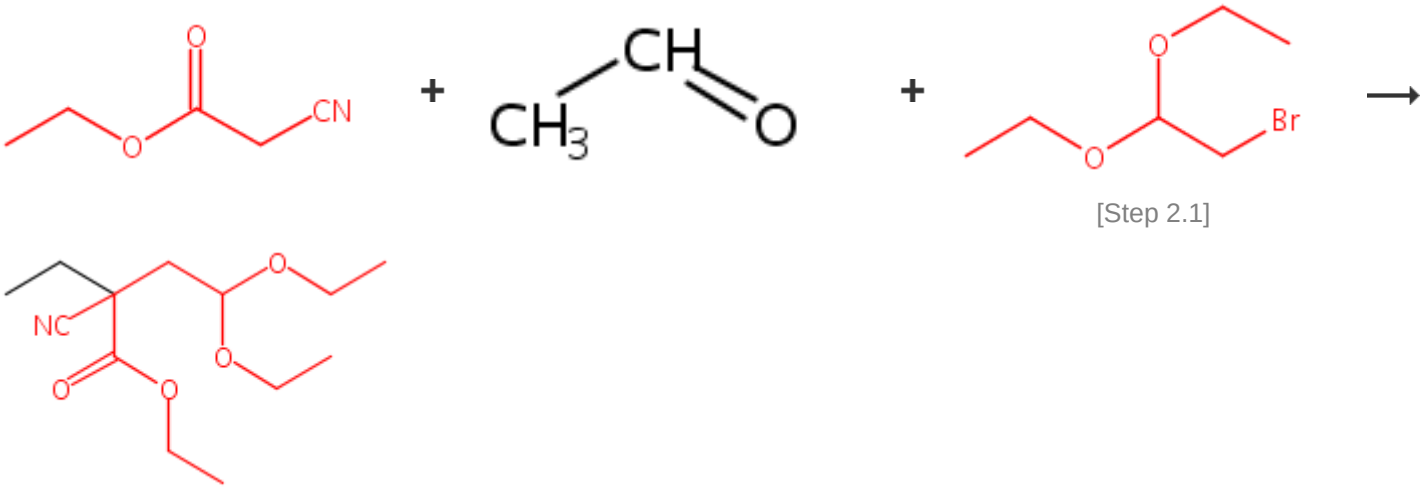
References

Preparation of pyrrolo[1,2-a]pyrazines as sPLA2 inhibitors

By Ohtani, Mitsuaki et al

From PCT Int. Appl., 9951605, 14 Oct 1999

21. 2 Steps



[Step 2.1]

Overview

Steps/Stages

1.1 R:Mg, C:Pd, S:AcOH, 3 h, rt, 1-2 atm

2.1 R:K_2CO_3, S:DMF, 72 h, 70°C

Notes

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

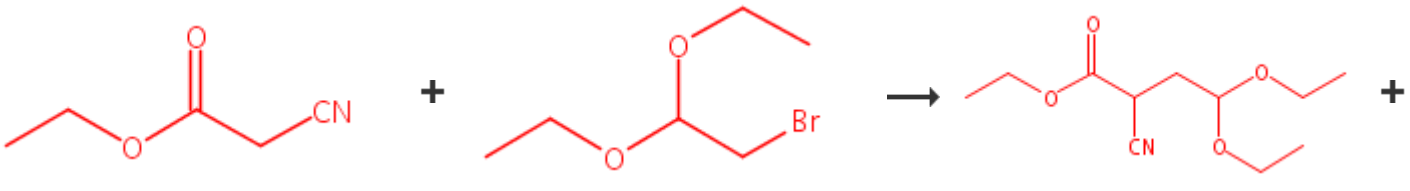
References

Preparation of pyrrolo[1,2-a]pyrazines as sPLA2 inhibitors

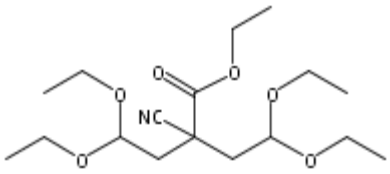
By Ohtani, Mitsuaki et al

From PCT Int. Appl., 9951605, 14 Oct 1999

22. Single Step



38%



30%

Overview

Steps/Stages

1.1 R:K_2CO_3, S:DMSO, 15 h, 70-80°C

Notes

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

References

Alkylation of methylene-active compounds with halo acetals and hydrolysis of the alkylation products

By Ismailov, V. M. et al

From Russian Journal of Organic Chemistry, 52(10), 1390-1393; 2016