**Other Training Examples for SynthesisGPT**

**Training Example 1: Labeled by Shen Yuan**

[Input]

Reaction 20141222-US08902305B2-0231 description:

To a N,N-dimethylformamide (10 mL) suspension of sodium hydride (97%, 0.784 g, 32.7 mmol) was added methyl 2-oxoindoline-5-carboxylate (2.34 g, 12.3 mmol). The formed mixture was stirred for 10 min at room temperature followed by the addition of 4-[(6-chloro-1-oxidopyridin-3-yl)methyl]morpholine (1.87 g, 8.2 mmol). The resulting reaction mixture was set under N2 atmosphere and stirred for 1 h at 135° C. The N,N-dimethylformamide solution was diluted with saturated aqueous sodium hydrogen carbonate (30 mL) and extracted with chloroform, and ethyl acetate (containing 5% methanol). The combined organic phases were concentrated in vacuo. The remaining N,N-dimethylformamide was removed by co-evaporation with toluene. The residue was dissolved in ethyl acetate/chloroform, (150 mL, 2:1), and phosphorus trichloride (4.5 g, 33 mmol) was added. The reaction mixture was stirred for 1 h at 60° C., and then cooled to room temperature. The mixture was poured into a saturated aqueous sodium hydrogen carbonate solution followed by extraction of the aqueous phase with chloroform (4×). The combined organic extracts were concentrated in vacuo, and the residue was purified on a silica gel column using chloroform/methanol, (10:1), as the eluent to afford 1.05 g (35% yield) of the title compound as a yellow-brown solid: 1H NMR (DMSO-d6, 400 MHz) δ 10.83 (br s, 1H), 8.11 (s, 1H), 8.04 (s, 1H), 7.91 (d, J=8.0 Hz, 1H), 7.63 (t, J=8.0 Hz, 2H), 7.00 (d, J=8.0 Hz, 1H), 3.87 (s, 3H), 3.62 (br s, 4H), 3.41 (s, 2H), 2.42 (br s, 4H); MS (EI) m/z 368 (M++1).

Reactant:

R1:sodium hydride,49;

R2:methyl 2-oxoindoline-5-carboxylate,100;

R3:4-[(6-chloro-1-oxidopyridin-3-yl)methyl]morpholine,246;

R4:phosphorus trichloride,796;

Product:

P1:title compound,1280;

Solvent:

S1:N,N-dimethylformamide,5;

S2:N,N-dimethylformamide,411;

S3:sodium hydrogen carbonate,477;

S4:N,N-dimethylformamide,656;

S5:sodium hydrogen carbonate,984;

Catalyst:

None

Time:

T1:10 min,191;

T2:1 h,392;

T3:1 h,884;

Temperature:

E1:room temperature,201;

E2:135° C,399;

E3:60° C.,891;

E4:room temperature,918;

Yield:

Y1:35% yield,1262;

[Output]:

R1.R2>S1.E1.T1>M1

M1.R3>E2.T2>M2

M2.R4>E3.T3>P1

**Training Example 2**

[Input]

Reaction 20040708-US20040132720A1-0125 description:

Finely powdered D3 (9.7 g, 34 mmole) under argon was heated with gentle stirring up to its melting point (>250° C.) at which point the dark brown oil was observed to undergo decarboxylation. Heating was maintained until gas evolution ceased (0.25 h), then the mixture was allowed to cool. The residue was treated with 1M NaOH solution (120 ml) and Et2O (100 ml) and stirred well for 0.5 h. The aqueous layer was isolated, filtered, then acidified with conc. HCl acid and extracted with EtOAc. The extract was dried (Na2SO4) and concentrated under vacuum to afford the title compound as a pale yellow solid (5.9 g, 72%).

REACTANTs:

R1: NaOH,321;

R2: D3,16;

PRODUCTs:

P1: title compound,568;

SOLVENTs:

S1: Et2O,348;

CATALYSTs:

None

TIMEs:

T1: 0.25 h,242;

T2: 0.5 h,383;

TEMPERATUREs:

E1: >250° C.,106;

YIELD:

Y1: 72%,614;

[Output]

R2>E1.T1>M1

M1.R1>T2>P1

**Training Example 3**

[Input]

Reaction 20141202-US08901305B2-0220 description:

(S)-tert-butyl (4-methyl-1-((5-oxo-5,6-dihydrobenzo[c][2,7]naphthyridin-8-yl)oxy)pentan-2-yl)carbamate (10 mg, 0.024 mmol) in dichloromethane (1 mL) was cooled to 0° C. To the solution was added hydrogen chloride (0.886 mg, 0.012 mL, 0.024 mmol, 2M in diethyl ether) dropwise. The temperature of the reaction mixture was maintained at 0° C. for 30 min and then the reaction mixture was allowed to warm to room temperature and stirred for 2 h. The reaction mixture was then concentrated under reduced pressure to afford (S)-8-((2-amino-4-methylpentyl)oxy)benzo[c][2,7]naphthyridin-5(6H)-one (4 mg, 0.012 mmol, 49% yield) as a pale yellow solid. LC/MS (ESI) m/e 312.2 [(M+H)+, calcd for C18H22N3O2 312.2]; LC/MS retention time (method A): tR=1.1 min; HPLC retention time (method A): tR=6.85 min; HPLC retention time (method B): tR=7.51 min 1H NMR (400 MHz, D2O) δ ppm 9.30 (br. s., 1H), 8.77 (br. s., 1H), 8.36 (br. s., 1H), 8.07 (br. s., 1H), 6.95 (br. s., 1H), 6.72 (br. s., 1H), 4.41 (d, J=9.03 Hz, 1H), 4.26 (br. s., 1H), 3.89 (br. s., 1H), 3.38 (s, 1H), 1.72-1.88 (m, 2H), 1.05 (d, J=2.51 Hz, 6H).

REACTANTs:

R1: (S)-tert-butyl (4-methyl-1-((5-oxo-5,6-dihydrobenzo[c][2,7]naphthyridin-8-yl)oxy)pentan-2-yl)carbamate,0;

R2: hydrogen chloride,195;

PRODUCTs:

P1: (S)-8-((2-amino-4-methylpentyl)oxy)benzo[c][2,7]naphthyridin-5(6H)-one,519;

SOLVENTs:

S1: dichloromethane,126;

CATALYSTs:

None

TIMEs:

T1: 30 min,345;

T2: 2 h,438;

TEMPERATUREs:

E1: 0° C,163;

E2: 0° C,335;

E3: room temperature,405;

YIELD:

Y1: 49% yield,609;

[Output]

R1.R2>S1.E1.E2.T1>M1

M1>E3.T2>P1

**Training Example 4**

[Input]

Reaction 20100427-US07705028B2-0287 description:

A solution of [3-[2-(2,6-dichlorophenyl)ethyl]-5-(1-methylethyl)-4-isoxazolyl]methanol (0.085 g, 0.27 mmol), methyl 6-(4-hydroxyphenyl)-2-naphthalenecarboxylate (0.075 g, 0.27 mmol), triphenyl phosphine (0.071 g, 0.27 mmol) and diisopropyl azodicarboxylate (0.049 mL, 0.27 mmol) in toluene (2.7 mL) was placed in microwave reaction tube and heated to 80° C. for 1000 seconds. The solution was concentrated and the residue dissolved in a solution of ethyl acetate and methanol, filtered and concentrated. The filtrate was purified by chromatography (silica gel, hexane to 3:7 ethyl acetate:hexanes) to provide the title compound (0.038 g, 24.5%). 1H NMR (DMSO-d6): δ 8.62 (s, 1H), 8.25 (s, 1H), 8.18 (d, J=9 Hz, 1H), 8.06 (d, J=9 Hz, 1H), 7.97 (dd, J=1, 9 Hz, 1H), 7.92 (dd, J=2, 9 Hz, 1H), 7.81 (d, J=9 Hz, 2H), 7.42 (d, J=8 Hz, 2H), 7.25 (t, J=8 Hz, 1H), 7.14 (d, J=9 Hz, 2H), 4.99 (s, 2H), 3.90 (s, 3H), 3.35 (septet, J=7 Hz, overlapping H2O 1H), 3.24-3.20 (m, 2H), 2.89-2.85 (m, 2H), 1.25 (d, J=7 Hz, 6H). ESI-LCMS m/z 574 (M+H)+.

REACTANTs:

R1: [3-[2-(2,6-dichlorophenyl)ethyl]-5-(1-methylethyl)-4-isoxazolyl]methanol,14;

R2: methyl 6-(4-hydroxyphenyl)-2-naphthalenecarboxylate,109;

R3: diisopropyl azodicarboxylate,228;

R4: triphenyl phosphine,183;

PRODUCTs:

P1: title compound,613;

SOLVENTs:

S1: toluene,282;

CATALYSTs:

None

TIMEs:

T1: 1000 seconds,362;

TEMPERATUREs:

E1: 80° C.,351;

YIELD:

24.5%,638;

[Output]

R1.R2.R3.R4>S1.E1.T1>P1

**Training Example 5**

[Input]

Reaction 20000118-US06015825-0014 description:

A mixture of 2-(2,4-difluorophenyl)-1-(4-fluorophenyl)-1-ethanone (5.0 g, 20 mmol-see EP-A-0069442), sodium 1,2,4-triazole (2.18 g, 24 mmol) and N,N-dimethylacetamide (100 ml) was stirred at 100° C. for 18 hours. The mixture was diluted with xylene (300 ml) and concentrated under reduced pressure. The residue was dissolved in ethyl acetate (500 ml) and washed with water (3×50 ml). The organic solution was dried (MgSO4) and concentrated under reduced pressure. Purification by flash chromatography (eluting with ethyl acetate:dichloromethane 1:1) gave a white solid (1.05 g, 18%), which was characterised by 1H-N.M.R. spectroscopy.

REACTANTs:

R1: 2-(2,4-difluorophenyl)-1-(4-fluorophenyl)-1-ethanone,13;

R2: sodium 1,2,4-triazole,101;

R3: N,N-dimethylacetamide,145;

PRODUCTs:

P1: solid,563;

SOLVENTs:

S1: xylene,242;

CATALYSTs:

None

TIMEs:

T1: 18 hours,203;

TEMPERATUREs:

E1: 100° C.,191;

YIELD:

Y1: 18%,578;

[Output]

R1.R2.R3>S1.E1.T1>P1