A facile one-pot method for the synthesis of polysubstituted phthalides derivatives

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Supplementary Information

Section A: General Information

Section B: Experimental procedures and spectral analysis

Section C: ¹H, ¹³C NMR , IR Spectra and element analysis of compounds 1a-1j

GENERAL

^1H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz on JNM-ECA-400 instrument with tetramethylsilane as an internal standard in the DMSO. IR spectra were recorded in KBr disk using a Nicolet 6700 FT-IR spectrophotometer. ESI-MS (high resolution) mass spectra were obtained by using a Waters Xevo G2 Qtof (ESI) mass spectrometer. Melting points were determined using a RY-1 apparatus and were uncorrected.

Typical experimental procedure: Ethyl 4-chloroacetoacetate (2 mmol) and ethanal (1 mmol) were placed in a flask under an atmosphere of nitrogen. Piperidine (1 mmol), glacial acetic acid (1 mmol), indion (1 mmol) concentrated hydrochloric acid (0.01 ml) and ethanol (10 ml) was added. The resulting mixture was heated at 80 °C for 12 h. After cooling to room temperature, the solvent was removed by evaporation. The residue was poured into 50 ml of water and extracted with ether. The organic layer was separated and was washed with saturated sodium chloride solution. After dried over sodium sulfate, the solvent was removed and the residue was purified by column chromatography on silica gel to give the product 1a (0.15g, white powder) in 63% yield.

Selected spectral data of new compounds :

Compound 1a: mp: 138.3-139.1°C; ¹H NMR (DMSO-d₆, 400 MHz): δ, ppm, 11.12(s, 1H, OH), 6.91(s, 1H, Ph-H), 5.24(s, 2H, CH₂), 4.3(q, 2H, CH₂), 2.45(s, 3H, CH₃), 1.29(t, 3H, CH₃); ¹³C NMR (DMSO-d₆, 100 MHz) δ, ppm, 170.2, 166.7, 159.5, 150.9, 136.9, 124.2, 123.6, 113.3, 106.6, 68.3, 61.0, 14.0, 13.6; HRMS: cal. For C₁₂H₁₁O₅ 235.0612; found 235.0612.

Compound 1b: mp: 162.5-163.2°C; ¹H NMR (DMSO-d₆, 400 MHz): δ, ppm, 11.12(s, 1H, OH), 6.91(s, 1H, Ph-H), 5.24(s, 2H, CH₂), 4.3(q, 2H, CH₂), 2.81 (t, 2H, CH₂), 1.53 (m, 2H, CH₂), 1.29 (t, 3H, CH₃), 0.90(t, 3H, CH₃); ¹³C NMR (DMSO-d₆, 100 MHz) δ, ppm, 169.8, 166.7, 159.5, 151.2, 141.5, 123.9, 112.9, 106.6, 68.3, 60.9, 30.0, 42.0, 14.0, 14.0; MS (FAB), HRMS: cal. For C₁₄H₁₅O₅ 263.0925; found 263.0920.

Compound 1c: mp: 181.5-181.8°C; ^1H NMR (DMSO- d_6 , 400 MHz): δ , ppm, 11.43 (s, 1H, OH), 7.65 (d, 1H, Ph-H), 7.39 (m, 2H, Ph-H), 7.15 (m, 2H, Ph-H), 5.34(m, 2H, CH₂), 3.89 (q, 2H, CH₂), 0.79(t, 3H, CH₃); IR (KBr): ν 3343; 1750; 1675; 1588; 1434 cm^{-1} ; m/e 379.0(M + 1) ; Anal: cal. For C₁₇H₁₃BrO₅: C, 54.13; H, 3.47; Found: C, 54.13; H, 3.56.

Compound 1d: mp: 230.3-230.8°C; ^1H NMR (DMSO- d_6 , 400 MHz): δ , ppm, 11.38 (s, 1H, OH), 7.46 (d, 2H, Ph-H), 7.26 (d, 2H, Ph-H), 7.11 (s, 1H, Ph-H), 5.29(s, 2H, CH₂), 3.96(q, 2H, CH₂), 0.90(t, 3H, CH₃); IR (KBr): ν 3497; 1755; 1672; 1588; 1434 cm^{-1} ; m/e 333.1(M + 1); Anal: cal. For C₁₇H₁₃ClO₅: C, 61.36; H, 3.94; Found: C, 61.38; H, 3.98.

Compound 1e: mp: 172.1-172.5°C; ^1H NMR (DMSO- d_6 , 400 MHz): δ , ppm, 11.16(s, 1H, OH), 7.35 (m, 1H, Ph-H), 7.05(m, 2H, Ph-H), 6.98(m, 2H, Ph-H), 5.29(m, 2H, CH₂), 3.90(q, 2H, CH₂), 3.62 (s, 3H, CH₃), 0.90(t, 3H, CH₃); IR (KBr): ν 3497; 1756; 1663; 1597; 1498 cm^{-1} ; m/e 329.1(M + 1); Anal: cal. For C₁₈H₁₆O₆: C, 65.85; H, 4.91; Found: C, 65.55; H, 4.95.

Compound 1f: mp: 226.3-226.9°C; ^1H NMR (DMSO- d_6 , 400 MHz): δ , ppm, 11.32(s, 1H, OH), 10.48(s, 1H, OH), 7.33(s, 1H, Ph-H), 7.06(m, 2H, Ph-H), 6.96(m, 1H, Ph-H), 5.26(s, 2H, CH₂), 4.01(q, 2H, CH₂), 0.97(t, 3H, CH₃); IR (KBr): ν 3343; 1741; 1664; 1604; 1510 cm^{-1} ; m/e 392.9(M + 1); Anal: cal. For C₁₇H₁₃BrO₆: C, 51.93; H, 3.33; Found: C, 52.01; H, 3.38.

Compound 1g: mp: 210.2-210.6°C; ^1H NMR (DMSO- d_6 , 400 MHz): δ , ppm, 11.22(s, 1H, OH), 9.17(s, 1H, OH), 7.03(s, 1H, Ph-H), 6.81(m, 2H, Ph-H), 6.75(m, 1H, Ph-H), 5.26(s, 2H, CH₂), 4.01(q, 2H, CH₂), 3.71 (s, 3H, CH₃), 0.94(t, 3H, CH₃); IR (KBr): ν 3448; 1755; 1658; 1597; 1518 cm^{-1} ; m/e 345.2(M + 1); Anal: cal. For C₁₈H₁₆O₇: C, 62.79; H, 4.68; Found: C, 62.42; H, 4.71.

Compound 1h: mp: 215.6-216.6°C; ^1H NMR (DMSO- d_6 , 400 MHz): δ , ppm, 11.33(s, 1H, OH), 9.70 (s, 1H, OH), 7.07(s, 1H, Ph-H), 6.93(s, 1H, Ph-H), 6.88(s, 1H, Ph-H), 5.26(s, 2H, CH₂), 4.05(q, 2H, CH₂), 3.78 (s, 3H, CH₃), 0.99(t, 3H, CH₃); IR (KBr): ν 3461; 1758; 1654; 1590; 1505 cm^{-1} ; m/e 424.9(M + 1); Anal: cal. For C₁₇H₁₅BrO₇: C, 51.08; H, 3.57; Found: C, 51.16; H, 3.62.

Compound 1i: mp: 170.4-171.2°C; ^1H NMR (DMSO- d_6 , 400 MHz): δ , ppm, 11.47 (s, 1H, OH), 7.55 (m, 1H, Ph-H), 7.26 (m, 1H, Ph-H), 7.24 (m, 1H, Ph-H), 7.16 (s, 1H, Ph-H), 5.34 (s, 2H, CH₂), 3.95 (q, J = 7 Hz, 2H, CH₂), 0.86 (t, J = 7 Hz, 3H, CH₃); IR (KBr): ν 3344; 1755; 1676; 1604; 1498 cm^{-1} ; MS (FAB), m/e 351.2 (M + 1); HRMS: cal. For C₁₇H₁₃ClFO₅ 351.0430; found 351.0409.

Compound 1j: mp: 216.9-217.3°C; ^1H NMR (DMSO- d_6 , 400 MHz): δ , ppm, 11.52 (s, 1H, OH), 8.31 (d, 1H, Ph-H), 8.11 (s, 1H, Ph-H), 7.75 (m, 2H, Ph-H), 7.18 (s, 1H, Ph-H), 5.32(s, 2H, CH₂), 3.97 (q, 2H, CH₂), 0.88 (t, 3H, CH₃); IR (KBr): ν 3496; 1766; 1662; 1530; 1429 cm^{-1} ; m/e 343.1 (M + 1); Anal: cal. For C₁₇H₁₃NO₇: C, 59.48; H, 3.82; Found: C, 59.56; H, 3.92.

Compound 1a:

^1H NMR

^{13}C NMR

HRMS

Mass Spectrum Molecular Formula Report

Compound 1b

¹H NMR

¹³C NMR

HRMS

Compound 1c

¹H NMR

IR

Sample: XXQ-05-10

Background Scans = 12 Sensitivity = 1

Resolution = 4 Scans = 12

File Name: 04002135

Tuesday, April 07, 2009 10:25:27

Operator :Song

Song

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MS

Compound 1d

^1H NMR

$\mathbb{R}$

Sample: XXQ-05-14

Background Scans = 12 Sensitivity = 1

Resolution = 4 Scans = 12

File Name: 04002130

Friday, April 03, 2009 09:11:15

Operator :Song

Song

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MS

¹H NMR

IR

Sample: XXQ-05-12

Background Scans = 12 Sensitivity = 1

Resolution = 4

Scans = 12

File Name: 04002136

Tuesday, April 07, 2009 10:47:23

Operator :Song

Song

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MS

Compound 1f

^1H NMR

IR

MS

Compound 1g

^1H NMR

IR

MS

Compound 1h

^1H NMR

IR

Sample: XXQ-05-38

Background Scans = 12 Sensitivity = 1

Resolution = 4 Scans = 12

File Name: 04002134

Friday, April 03, 2009 11:30:45

Operator : Song

long

Page1

MS

Compound 1i

^1H NMR

^{13}C NMR

File : D:\XXQ\B5B\XXQ-05-36-01.D
Operator : [B5B1]XF
Acquired : 18 Dec 2008 14:55 using AcqMethod WXX.M
Instrument : GCMS
Sample Name : XXQ-05-36
Misc Info :
Vial Number: 1

Element analysis (1c,1d,1e,1f,1g,1h,1j)

北京人学分析测试中心
微量有机元素分析报告

送样人: 徐晓倩

仪器型号 **Elementar Vario MICRO CUBR (Germany)**

样品编号	百分含量 (%)				
	N	C	H	S	O
1c		54.13	3.56		
1c		54.08	3.53		
1d		61.38	3.98		
1d		61.35	3.99		
1e		65.55	4.95		
1f		52.01	3.38		
1f		51.95	3.37		
1g		62.42	4.71		
1g		62.41	4.76		
1h		51.16	3.62		
1h		51.23	3.63		
1j	4.12	59.56	3.92		
1j	4.08	59.51	3.87		

分析人: wang

日期: April 07, 2011