Supporting information

Practical Synthesis of Optically Active α,α -Disubstituted Malonamic Acids through Asymmetric Hydrolysis of Malonamide Derivatives with *Rhodococcus* sp. CGMCC 0497

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Materials and Methods

The commercially available reagents were used without further purification. Polarimetry was carried out using an optical activity Perkin Elmer 241ML polarimeter and the measurements were made at the sodium D-line with a 10cm pathlength cell. Concentrations(c) are given in g/100ml. Enantiomeric excesses: Chiral HPLC was conducted with a PE NELSON NCI900 using Chiralpak AS or Chiralcel OJ column at a flow rate of 0.7ml/min with 2-propanol/hexane as the mobile phase.

Microorganism and Cultivation

The strain *Rhodococcus* sp. CGMCC 0497 is available in CGMCC (China General Microbiological Culture Collection Center). *Rhodococcus* sp. CGMCC 0497 was subcultured at 30°C for 24 hours in a 100ml shaking flask containing 20ml of a medium consisting of 0.5g of polypepton, 0.5g of beef extract and 1g of glucose per 100ml of tap water, pH 7.0. Then the subculture was inoculated into a 5l shaking flask containing 1l of the rich medium consisting of 1g of glucose, 0.5g of beef extract, 0.25g of methacrylamide, 100mg of K₂HPO₄·3H₂O, 75mg of KH₂PO₄, 10 mg of NaCl, 0.1ml of mineral medium per 100ml of tap water with methacrylamide added 24 hours later. The pH of each medium was adjusted to around 7.0-7.2 by addition of 2N NaOH or 3N HCl. After incubation at 30°C with reciprocal shaking for 48 hr. The organism was harvested by centrifugation using an HIMAC centrifuge CR20B2 (Hitachi, Japan) with a RPR9-2 rotor (6800g, 30min 10°C). Cells were washed with 100mM potassium phosphate buffer (pH=7.0) and centrifuged.

2-benzyl-2-methyl-malonitrile 1. To a suspension of NaH (60%) 400mg (10mmol) in 40ml THF and 4ml DMF, was added drop by drop a solution of malonitrile (1.32g, 20mmol) in 5ml THF at room temperature. After 2h, benzyl bromide or chloride (10mmol) in THF (10ml) was added within 2 h. Stirring was continued at room temperature for 10 h. The reaction was quenched by aqueous NH₄Cl solution, extracted with ethyl acetate, dried on MgSO₄ and purified by flash chromatograph (74%). The product was dissolved in acetone (50ml). Methyl iodide (20mmol) and solid K₂CO₃ (25mmol) were added. The mixture was stirred overnight at room temperature. After filtration and concentration, the residue was purified by flash chromatograph to yield α,α -disubstituted malonitriles (98%). white solid, m.p. 94.3-95.3°C, Lit.¹ 94.5-95.5°C; ¹H NMR (300 MHz, CDCl₃): δ 7.35-

7.45(m, 5H, Ar-H), 3.22(s, 2H, CH₂), 1.81(s, 3H, CH₃); IR (KBr): 2251(CN), 765, 703; MS *m/z* (%): 170(M⁺, 1), 91(100).

Diamide Synthesis

To a suspension of NaH (60%) 400mg (10mmol) in 40ml THF and 4ml DMF, was added drop by drop a solution of malonic acid diester (1.32g, 20mmol) in 5ml THF at room temperature. After 2h, benzyl bromide or chloride (10mmol) in THF (10ml) was added within 2 h. Stirring was continued at room temperature or at gentle reflux for 3-10 h. The reaction was quenched by aqueous NH₄Cl solution, extracted with ethyl acetate, dried on MgSO₄ and purified by flash chromatograph. The product was dissolved in acetone (50ml). Methyl iodide (20mmol) and solid K₂CO₃ or KOH (25mmol) were added. The mixture was stirred overnight at room temperature. After filtration and concentration, the residue was purified by flash chromatograph to yield α,α -disubstituted malonic acid diesters.

To a solution of α,α -disubstituted malonic acid diester(4.5mmol) in ethanol(15ml) was added 2N KOH 15ml at room temperature. The reaction was continued at 50°C for 10-30 hours and quenched by 3N HCl, extracted with ethyl acetate, dried on MgSO₄ and purified by flash chromatograph. The product was dissolved in SOCl₂(3ml) and heated to gentle reflux. After 6 hours, the mixture was added slowly to ice-cold stronger ammonia water and the stirring was continued overnight. After filtration and recrystallization, give a white solid of α,α -disubstituted malonamide.

2-benzyl-2-methyl-malonamide 4a. white solid, m.p. 195.4-196.4°C, Lit.²202-203°C; ¹H NMR (300 MHz, DMSO): δ 7.22-7.12(m, 9H, ArH, 2NH₂), 3.06(s, 2H, CH₂), 1.10(s, 3H, CH₃); IR(KBr): ν 3389, 3205(NH), 1692, 1663(C=O); MS *m/z* (%): 206(M⁺, 7), 189(10), 162(M⁺-CONH₂, 100), 160(41).

2-(2'-chlorobenzyl)-2-methyl-malonamide 4b. white solid, m.p. 227.0-228.0 °C; ¹H NMR (300 MHz, DMSO): δ 7.41-7.20(m, 8H, Ar-H, 2NH₂), 3.27(s, 2H, CH₂), 1.11(s, 3H, CH₃); IR(KBr): ν 3433, 3381, 3216(NH), 1647(C=O); MS *m/z* (%): 205(M⁺-Cl, 100), 198(13), 196(M⁺-CONH₂, 37); Anal. Calcd. for C₁₁H₁₃N₂O₂Cl: C, 54.89; H, 5.44; N, 11.64; Cl, 14.73. Found: C, 54.90; H, 5.43; N, 11.66; Cl, 14.54.

2-(3'-chlorobenzyl)-2-methyl-malonamide 4c. white solid, m.p. 195.4-196.4°C; ¹H NMR (300 MHz, DMSO): δ 7.26-7.13(m, 8H, ArH, 2NH₂), 3.06(s, 2H, CH₂), 1.11(s, 3H, CH₃); IR(KBr): ν 3379, 3213(NH), 1689, 1671 (C=O); MS *m/z* (%): 242(M⁺+2, 4), 240(M⁺, 11), 198(33), 196(M⁺-CONH₂, 100); Anal. Calcd. for C₁₁H₁₃N₂O₂Cl: C, 54.89; H, 5.44; N, 11.64; Cl, 14.73. Found: C, 54.62; H, 5.17; N, 11.51; Cl, 14.64.

2-(4'-chlorobenzyl)-2-methyl-malonamide 4d. white solid, m.p. 244.6-245.6°C; ¹H NMR (300 MHz, DMSO): δ 7.29(d, 2H, J=8.7Hz, Ar-H), 7.19-7.16(m, 6H, ArH, 2NH₂), 3.04(s, 2H, CH₂), 1.10(s, 3H, CH₃); IR(KBr): ν 3387, 3202(NH), 1648(C=O); MS *m/z* (%): 242(M⁺+2, 8), 240(M⁺, 23), 198(31), 196(100); Anal. Calcd. for C₁₁H₁₃N₂O₂Cl: C, 54.89; H, 5.44; N, 11.64; Cl, 14.73. Found: C, 54.76; H, 5.23; N, 11.55; Cl, 14.70.

2-(4'-methylbenzyl)-2-methyl-malonamide 4e. white solid, m.p. 246.9-247.9°C; ¹H NMR (300 MHz, DMSO): δ 7.19(s, 2H, NH₂), 7.12(s, 2H, NH₂), 7.03(s, 4H, ArH), 3.00(s,

2H, CH₂), 1.08(s, 3H, CH₃); IR(KBr): ν 3387, 3206(NH), 1689, 1647(C=O); MS m/z (%): 220(M⁺, 39), 176(100), 159(49), 105(94); Anal. Calcd. for C₁₂H₁₆N₂O₂: C, 65.43; H, 7.32; N, 12.72. Found: C, 65.32; H, 7.50; N, 12.72.

2-(4'-methoxybenzyl)-2-methyl-malonamide 4f. white solid, m.p. 239.3-240.3°C; ¹H NMR (300 MHz, DMSO): δ 7.17(s, 2H, NH₂), 7.10(s, 2H, NH₂), 7.05, 6.77(AB, 4H, J=8.7Hz, ArH), 3.86(s, 3H, OMe), 2.97(s, 2H, CH₂), 1.07(s, 3H, CH₃); IR(KBr): ν 3358, 3203(NH), 1649(C=O); MS m/z (%): 236(M⁺, 16), 192(17), 121(100); HRMS: Calcd. for (C₁₂H₁₆N₂O₃)⁺ 236.11609, Found: 236.11829.

2-(4'-florobenzyl)-2-methyl-malonamide 4g. white solid, m.p. 206.1-207.1°C; ¹H NMR (300 MHz, DMSO): δ 7.21-7.03(m, 8H, ArH, 2NH₂), 3.04(s, 2H, CH₂), 1.09(s, 3H, CH₃); IR(KBr): ν 3392, 3203(NH), 1694, 1649(C=O); MS m/z (%): 224(M⁺, 10), 207(3), 180(49), 109(100); Anal. Calcd. for C₁₁H₁₃N₂O₂F: C, 58.92; H, 5.84; N, 12.49; F, 8.47. Found: C, 58.75; H, 5.72; N, 12.54; F, 8.05.

2-(4'-bromobenzyl)-2-methyl-malonamide 4h. white solid, m.p. 251.5-252.5°C; ¹H NMR (300 MHz, DMSO): δ 7.42, 7.11(AB, 4H, J=8.4Hz, ArH), 7.21(s, 2H, NH₂), 7.16(s, 2H, NH₂), 3.03(s, 2H, CH₂), 1.10(s, 3H, CH₃); IR(KBr): ν 3391, 3201(NH), 1689(C=O), 1647; MS m/z (%): 286(M⁺+2, 11), 284(M⁺, 11), 242(80), 240(100); Anal. Calcd. for C₁₁H₁₃N₂O₂Br: C, 46.34; H, 4.60; N, 9.82; Br, 28.02. Found: C, 46.40; H, 4.62; N, 9.77; Br, 27.98.

2-phenylethyl-2-methyl-malonamide 4i. white solid, m.p. 169.3-170.3°C; ¹H NMR (300 MHz, DMSO): δ 7.30-7.11(m, 9H, ArH, 2NH₂), 2.47-2.41(m, 2H, CH₂), 2.02-1.96(m, 2H, CH₂), 1.32(s, 3H, CH₃); IR(KBr): ν 3417, 3371, 3250, 3214(NH), 1652(C=O); MS m/z (%): 220(M⁺, 0.1), 219(1), 116(100), 99(30), 91(33); Anal. Calcd. for C₁₂H₁₆N₂O₂: C, 65.43; H, 7.32; N, 12.72. Found: C, 65.18; H, 7.09; N, 12.62.

2-butyl-2-methyl-malonamide 4j.³ white solid, m.p. 176.0-177.0°C; ¹H NMR (300 MHz, DMSO): δ 7.15(s, 2H, NH₂), 7.02(s, 2H, NH₂), 1.70-1.64(m, 2H, CH₂), 1.26-1.19(m, 5H, CH₂, CH₃), 1.14-1.06(m, 2H, CH₂), 0.83(t, 3H, J=7.2Hz, CH₃); IR(KBr): ν 3387, 3232(NH), 1693(C=O), 1641(C=O); MS m/z (%): 155(M⁺-17, 1), 129(M⁺+1-CONH₂, 29), 116(M⁺-Bu, 33), 86(100).

2-benzyl-2-ethyl-malonamide 4k. white solid, m.p. 173.4-174.4°C, Lit.⁴ 190-194°C; ¹H NMR (300 MHz, DMSO): δ 7.31(br s, 2H, NH₂), 7.27-7.12(m, 7H, ArH, NH₂), 3.09(s, 2H, CH₂), 1.73(q, 2H, J=7.4Hz, CH₂), 0.78(t, 3H, J=7.4Hz, CH₃); IR (KBr): ν 3382, 3210(NH), 1692(C=O); MS m/z (%): 220(M⁺, 5), 203(5), 177(16), 148(100), 131(50), 91(92.4), 65(15.0), 44(14.5).

2-butyl-2-ethyl-malonamide 4l. white solid, m.p. 180.9-181.9°C, Lit.⁴ 185°C; ¹H NMR (300 MHz, DMSO): δ 7.70(s, 2H, NH₂), 7.13(s, 2H, NH₂), 1.77-1.67(m, 4H, 2CH₂), 1.25-1.18(m, 2H, CH₂), 1.88-1.01(m, 2H, CH₂), 0.82(t, 3H, J=7.2Hz, CH₃), 0.68(t, 3H, J=7.2Hz, CH₃); IR (KBr): ν 3387, 3213(NH), 1693(C=O), 1641(C=O); MS m/z (%): 169(M⁺-17, 2), 143(M⁺+1-CONH₂, 35), 130(M⁺-Bu, 22), 100(100).

2-allyl-2-benzyl-malonamide 4m. white solid, ^1H NMR (300 MHz, DMSO): δ 7.60(br s, 2H, NH_2), 7.25-7.15(m, 7H, ArH, NH_2), 5.74-5.60(m, 1H, $=\text{CH}$), 5.09-5.04(m, 2H, $=\text{CH}_2$), 3.10(s, 2H, CH_2), 2.49-2.46(m, 2H, CH_2); IR (KBr): ν 3379, 3223(NH), 1691, 1641; MS m/z (%): 232(M^+ , 1), 191(100), 188(28), 174(80), 91(75).

Hydrolysis Products of α,α -Disubstituted Malonamides

(R)-2-(2'-chlorobenzyl)-2-methyl-malonamic acid 5b. white solid, m.p. 104.6-105.6°C; $[\alpha]_{\text{D}}^{25}$ -16.93 (c 1.14, MeOH), 97%ee; ^1H NMR (300 MHz, $[\text{D}_6]$ acetone): δ 12.0 (br s, 1H, OH), 7.42-7.18(m, 5H, ArH, NH), 6.85(br s, 1H, NH), 3.47(s, 2H, CH_2), 1.41(s, 3H, CH_3); IR (KBr): ν 3475, 3325 (NH), 3000-2850 (br OH), 1698($\text{C}=\text{O}$); MS m/z (%): 206 (M^+ -Cl, 73), 162(100); Anal. Calcd. for $\text{C}_{11}\text{H}_{12}\text{NO}_3\text{Cl}$: C, 54.67; H, 5.00; N, 5.80; Cl, 14.67. Found: C, 54.71; H, 5.11; N, 5.74; Cl, 14.59.

(R)-2-(3'-chlorobenzyl)-2-methyl-malonamic acid 5c. white solid, m.p. 111.1-112.1°C; $[\alpha]_{\text{D}}^{25}$ -9.63(c 1.25, MeOH), 95%ee; ^1H NMR (300 MHz, $[\text{D}_6]$ acetone): δ 12.2(br s, 1H, OH), 7.32-7.18(m, 5H, ArH, NH), 6.90(br s, 1H, NH), 3.24(s, 2H, CH_2), 1.42(s, 3H, CH_3); IR(KBr): ν 3454, 3331(NH), 3084(br, OH), 1749, 1670($\text{C}=\text{O}$); MS m/z (%): 243(M^+ +2, 3), 241(M^+ , 11), 44(100); Anal. Calcd. for $\text{C}_{11}\text{H}_{12}\text{NO}_3\text{Cl}$: C, 54.67; H, 5.00; N, 5.80; Cl, 14.67. Found: C, 54.95; H, 5.07; N, 5.71; Cl, 14.76.

(R)-2-(4'-chlorobenzyl)-2-methyl-malonamic acid 5d. white solid, m.p. 114.8-115.8°C; $[\alpha]_{\text{D}}^{21}$ -12.99 (c 0.83, MeOH), >99%ee; ^1H NMR (300 MHz, $[\text{D}_6]$ acetone): δ 12.1(br s, 1H, OH), 7.31-7.23(m, 5H, ArH, NH), 6.91(br s, 1H, NH), 3.25(d, 1H, $J=13.8\text{Hz}$, CH), 3.20(d, 1H, $J=13.2\text{Hz}$, CH), 1.41(s, 3H, CH_3); IR(KBr): ν 3403, 3227(NH), 2800-3300(br OH), 1727, 1688($\text{C}=\text{O}$); MS m/z (%): 243(M^+ +2, 1), 241(M^+ , 1), 197(M^+ -CONH₂, 25), 127(33), 125(100); Anal. Calcd. for $\text{C}_{11}\text{H}_{12}\text{NO}_3\text{Cl}$: C, 54.67; H, 5.00; N, 5.80; Cl, 14.67. Found: C, 54.72; H, 5.22; N, 5.61; Cl, 14.86.

(R)-2-(4'-methylbenzyl)-2-methyl-malonamic acid 5e. white solid, m.p. 182.6-183.6°C; $[\alpha]_{\text{D}}^{21}$ -11.18 (c 0.96, MeOH), >99%ee; ^1H NMR (300 MHz, $[\text{D}_6]$ acetone): δ 12.4(br s, 1H, OH), 7.27(brs, 1H, NH), 7.11, 7.05(AB, 4H, $J=8.1\text{Hz}$, ArH), 6.91(brs, 1H, NH), 3.19(s, 2H, CH_2), 2.27(s, 3H, CH_3), 1.41(s, 3H, CH_3); IR(KBr): ν 3451, 3329(NH), 2850-3350(br, OH), 1745, 1670($\text{C}=\text{O}$); MS m/z (%): 221(M^+ , 3), 105(100); Anal. Calcd. for $\text{C}_{12}\text{H}_{15}\text{NO}_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.11; H, 6.92; N, 6.20.

(R)-2-(4'-methoxybenzyl)-2-methyl-malonamic acid 5f. white solid, m.p. 105.5-106.5°C; $[\alpha]_{\text{D}}^{22}$ -10.75 (c 1.06, MeOH), >99%ee; ^1H NMR (300 MHz, $[\text{D}_6]$ acetone): δ 12.5(br s, 1H, OH), 7.29(brs, 1H, NH), 7.14, 6.81(AB, 4H, $J=8.7\text{Hz}$, ArH), 6.93(brs, 1H, NH), 3.75(s, 3H, OMe), 3.17(s, 2H, CH_2), 1.41(s, 3H, CH_3); IR(KBr): ν 3428, 3358(NH), 2850-3250(br, OH), 1717, 1652($\text{C}=\text{O}$); MS m/z (%): 237(M^+ , 2), 121(100). HRMS Calcd. for $\text{C}_{12}\text{H}_{15}\text{NO}_4$: 237.100109. Found: 237.09736.

(R)-2-(4'-florobenzyl)-2-methyl-malonamic acid 5g. white solid, m.p. 116.9-117.9°C; $[\alpha]_{\text{D}}^{21}$ -9.46(c 1.46, MeOH); >99%ee; ^1H NMR (300 MHz, $[\text{D}_6]$ acetone): δ 7.29-7.24(m, 3H, ArH, NH), 7.05-6.99(m, 2H, ArH), 6.90(br s, 1H, NH), 3.23(s, 2H, CH_2), 1.42(s, 3H, CH_3); IR(KBr): ν 3445, 3421(NH), 3202(br, OH), 1656($\text{C}=\text{O}$); MS m/z (%): 226(M^+ +1, 5),

225(M⁺, 4), 109(100); Anal. Calcd. for C₁₁H₁₂NO₃F: C, 58.66; H, 5.37; N, 6.22; F, 8.44. Found: C, 58.78; H, 5.52; N, 5.88; F, 8.44.

(R)-2-(4'-bromoenzyl)-2-methyl-malonamic acid 5h. white solid, m.p. 119.5-120.5°C; [α]_D²⁰ -11.41 (c 1.17, MeOH), >99%ee; ¹H NMR (300 MHz, [D₆]acetone): δ 12.0(br s, 1H, OH), 7.43, 7.19(AB, 4H, J=8.1Hz, ArH), 7.26(br s, 1H, NH), 6.93(br s, 1H, NH), 3.21(s, 2H, CH₂), 1.41(s, 3H, CH₃); IR(KBr): ν 3407, 3227(NH), 2800-3200(br OH), 1725, 1685(C=O); MS *m/z* (%): 287(M⁺+2, 9), 285(M⁺, 10), 43(100); Anal. Calcd. for C₁₁H₁₂NO₃Br: C, 46.18; H, 4.23; N, 4.90; Br, 27.93. Found: C, 46.09; H, 4.20; N, 4.72; Br, 27.64.

(R)-2-phenylethyl-2-methyl-malonamic acid 5i. white solid, m.p. 104.5-105.5°C; [α]_D¹⁵ -4.72(c 0.924, CHCl₃), >99%ee; ¹H NMR (300 MHz, [D₆]acetone): δ 12.5(br s, 1H, OH), 7.39(br s, 1H, NH), 7.30-7.15(m, 5H, ArH), 7.05(br s, 1H, NH), 2.62-2.56(m, 2H, CH₂), 2.21-2.17(m, 2H, CH₂), 1.53(s, 3H, CH₃); IR(KBr): ν 3449, 3313, 3250(NH), 2500-3250(br OH), 1710, 1650(C=O); MS *m/z* (%): 222(M⁺+1, 11), 178(M⁺-CONH₂, 32), 73(100); Anal. Calcd. for C₁₂H₁₅NO₃: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.16; H, 6.83; N, 6.16.

(R)-2-butyl-2-methyl-malonamic acid 5j. white solid, m.p. 84.2-85.2°C, Lit.³ 90°C; [α]_D²⁵ -11.05(c 0.867, MeOH), 91%ee {Lit.³ [α]_D²⁶ -9.8(c 1.0, CHCl₃), 96%ee, R}; ¹H NMR (300 MHz, CDCl₃): δ 8.45(br s, 1H, OH), 7.21(br s, 1H, NH), 7.09(br s, 1H, NH), 1.95-1.85(m, 2H, CH₂), 1.49(s, 3H, CH₃), 1.40-1.25(m, 4H, 2CH₂), 0.90(t, 3H, J=6.8Hz, CH₃); IR(KBr): ν 3410, 3228(NH), 3200-3000(br OH), 1722(C=O), 1677(C=O); MS *m/z* (%): 156(M⁺-17, 1.8), 130(M⁺+1-CONH₂, 33.8), 129(8.9), 117(M⁺-Bu, 56.2), 99(28.5), 87(100), 86(50.6).

2-allyl-phenylpropionate 6.⁵ Oil, ¹H NMR (300 MHz, CDCl₃): δ 10.0(br s, 1H, OH), 7.32-7.17(m, 5H, ArH), 5.85-5.71(m, 1H =CH), 5.13-5.06(m, 2H, =CH₂), 3.03-2.94(m, 1H, CH), 2.82-2.72(m, 2H, CH₂), 2.44-2.25(m, 2H, CH₂); IR (film): ν 3200-2850(br OH), 1708(C=O); MS *m/z* (%): 190(M⁺, 4), 172(4), 148(19), 147(16), 144(22), 91(100).

Hydrolysis of 1 by Rhodococcus sp. CGMCC 0497

A suspension of 10g washed wet cells and 80ml 0.1mM potassium phosphate buffer (pH=7.0) was incubated at 30°C for 30mins with continuously magnetic stirring before the addition of the substrate, a solution of 100mg **1** dissolved in 100 μ l acetone. The reaction was quenched by centrifugation. The resulting supernatant was basified with 2N NaOH to pH=12, and extracted with diethyl ether. The organic solutions, after drying (MgSO₄) and concentration, gave the **2** and **4**. Separation was effected by column chromatography. The aqueous solution was then acidified using 3N HCl to pH=2 and extracted with diethyl ether. Acid **3** and **5** was obtained after removal of the solvent under reduced pressure and purification by flash chromatography on silica gel (elute: petroleum ether/EtOAc/AcOH 150:100:1). The enantiomeric excess of **2** was determined directly by Chiral HPLC. **3** was converted to the corresponding methyl or ethyl esters and then subjected to Chiral HPLC.

(S)-2-cyano-2-methyl-3-phenylpropanamide 2. white solid, m.p. 96.5-97.5°C; [α]_D¹⁹ +45.2 (c 0.80, CHCl₃), 93%ee; Enantiomeric excess was determined by HPLC on a Chiralcel OD column with hexane/2-propanol mixtures 8:2; ¹H NMR (300 MHz, CDCl₃): δ

7.40-7.20(m, 5H, Ar-H), 6.04(s, br, 1H, NH), 5.52(s, br, 1H, NH), 3.26(d, 1H, J=13.5Hz, CH), 2.96(d, 1H, J=13.5Hz, CH), 1.66(s, 3H, CH₃); IR(KBr): ν 3378, 3320(NH), 2244(CN), 1666(C=O); MS m/z (%): 189(M⁺+1, 3), 188(M⁺, 21), 173(M⁺-CH₃, 4), 144(M⁺-CONH₂, 19), 91(100); Anal. Calcd. for C₁₁H₁₂N₂O: C, 70.19; H, 6.43; N, 14.88. Found: C, 69.98; H, 6.51; N, 14.81.

(R)-2-cyano-2-methyl-3-phenylpropanoic acid 3. white solid, m.p. 94.6-95.6°C, Lit.⁶ 84°C; $[\alpha]_D^{25}$ -15.1 (c 0.53, CHCl₃), 52%ee, {Lit.³ $[\alpha]_D$ 27.2 (c 2, CHCl₃), S}; ¹H NMR (300 MHz, CDCl₃): δ 9.83(br s, 1H, OH), 7.37-7.28(m, 5H, Ar-H), 3.27(d, 1H, J=13.5Hz, CH), 3.07(d, 1H, J=13.8Hz), 1.65(s, 3H, CH₃); IR(KBr): ν 3074(br OH), 2263(CN), 1747(C=O); MS m/z (%): 189(M⁺, 2), 174(M⁺-CH₃, 3), 144(M⁺-COOH, 3), 91(100).

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