Supplemental Material

A Streamlined Synthesis for 2,3-Dihydroxyterephthalamides

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Synthesis of New Compounds

General. All reagents and solvents were purchased from Aldrich Chemical Company or Fisher Scientific and used as purchased. All solvents were dried over activated alumina and stored over 4Å molecular sieves. All reactions were carried out under Ar. Thionyl chloride was purified by distillation from triphenyl phosphite. Water was distilled and further purified by a Millipore cartridge system (resisitivity 18 x 10^6). All melting points were obtained using a Mel-Temp melting point apparatus (Laboratory Devices). Thin layer chromatography (TLC) was performed using alumina-backed silica plates and visualized with a 254 nm UV lamp. All organic extracts were dried over $MgSO_4$ and solvents were removed with a rotary evaporator. ^1H and ^{13}C NMR spectra were obtained on a Bruker DRX500 (500 MHz) or Bruker AMX400 spectrometer (400 MHz) as noted. All NMR samples were taken in $CDCl_3$, d_6-DMSO, d_8THF, or d_6-acetone as noted. All Microanalyses were performed by the Microanalytical Services Laboratory in the College of Chemistry, University of California, Berkeley. Compounds **2-5** and **8** were previously synthesized by published methods. [8,9]

2,3-Dihydroxy terephthaloyl chloride (12)
Compound **2** (0.207 g, 1.05 mmol), suspended in 15 mL of 1,4-dioxane, dissolved upon addition of thionyl chloride (0.4 mL, 5.4 mmol) and the solution turned pale yellow. The solution was stirred for 12 h. at 45 ^oC under Ar. The liquids were removed and the yellow solid was coevaporated 3 times with dry $CHCl_3$. Crystals suitable for X-ray diffraction were grown by sublimation (45-65 ^oC, 0.1 torr). ^1H NMR ($CDCl_3$): δ 7.66 (s, 2H, 2 CH), 9.74 (s, 2H, 2 OH).

***N,N'*-Cyclohexyl-2,3-Dihydroxyterephthalamide (7)**
Compound **2** (0.2g, 1.0 mmol) was suspended in $CHCl_3$ and ca. 1.5 mL of $SOCl_2$ was added. The solution was heated at reflux overnight under Ar then evaporated to a yellow oil. This acid chloride (**13**) was dissolved in CH_2Cl_2 and added slowly to a CH_2Cl_2 solution of cyclohexylamine cooled in an ice water bath and allowed to warm to RT under Ar while stirring overnight. The solution was extracted with 3 X 1M HCl to

remove the excess cyclohexylamine. Evaporation of the CH_2Cl_2 yielded a white solid (0.25 g, 60 % yield). MP 250 ^oC, NMR in $CDCl_3$: 7.05 (s, 2H, arom. CH), 6.69 (d, 1H, NH), 3.96 (m, 1H, CH), 1.23-2.03 (m, 1H, CH_2). ^{13}C NMR (CDCl3): δ 168.0, 150.5, 117.8, 116.3, 48.8, 48.7, 32.5, 31.1, 25.6, 25.3. Anal. Calcd (found) for $C_{20}H_{28}O_4N_2$: C 66.64 (66.94); H 7.83 (7.97); N 7.77 (7.79).

2,3-Dihydroxy methyl benzoate 4-carboxylic acid (14)

Compound **3** (0.506 g, 2.2 mmol) was suspended in 150 mL of distilled, deionized water and $NaHCO_3$ (0.125 g, 1.49 mmol) was added. The suspension was heated at 40 ^oC and all solids dissolved. After 12 h. the reaction was cooled to rt; the unreacted starting material precipitated and was filtered (0.162 g, 100% recovery). The supernatant was acidified with HCl and the resulting white precipitate was filtered and dried in a vacuum oven (0.203 g, 0.96 mmol, 65% yield). mp 223-226 ^oC. ^1H NMR (D_6-DMSO): δ 3.85 (s, 3H, CH_3), 7.15 (dd, 1H, CH), 7.22 (dd, 1H, CH), 10.4 (br s, 1H, OH). ^{13}C NMR (D_6-DMSO): δ 53.1, 116.9, 117.4, 118.6, 119.0, 119.3, 149.9, 150.0, 151.4, 169.1, 169.2, 172.0. Anal. Calcd (found) for $C_9H_8O_6$: C 50.95 (50.70); H 3.80 (3.97).

2,3-Dihydroxy methyl benzoate 4-carbonyl chloride (20)

Compound **14** (0.537 g, 2.5 mmol) was dissolved in 25 mL of 1,4-dioxane with the addition of $SOCl_2$ (1.3 mL, 17.8 mmol) and the reaction turned pale yellow. The solution was heated at 45-50 ^oC for 12 h. under Ar. The liquids were removed and the yellow solid was coevaporated 3 times with dry $CHCl_3$ and sublimed (45-65 ^oC, 0.1 torr). mp 88-96 ^oC. ^1H NMR ($CDCl_3$): δ 3.40 (s, 3H, CH_3), 7.40 (dd, 1H, CH), 7.53 (dd, 1H, CH), 9.62 (s, 1H, OH), 11.02 (s, 1H, OH). ^{13}C NMR ($CDCl_3$): δ 53.1, 117.2, 119.1, 120, 121.6, 151.2, 151.5, 169.7. Anal. Calcd (found) for $C_9H_7O_5Cl$: C 46.88 (46.5); H 3.06 (2.97).

2,3-Dihydroxy methyl benzoate 4-octylamide (15)

Compound **14** (0.250g, 1.2 mmol) was dissolved in 15 mL of dry THF with the addition of 1 mL of $SOCl_2$ and stirred for 12 h. under Ar. The solvent was evaporated and the yellow oil was dissolved in 15 mL of dry CH_2Cl_2, cooled with a dry ice/acetone bath and added slowly to octylamine (1 mL, 6 mmol) dissolved in 5 mL of CH_2Cl_2 under Ar and cooled in a dry ice/acetone bath. The reaction was allowed to warm to rt for 2 h. while stirring, then extracted with 1M HCl (2 x 30 mL), dried, and evaporated to a white solid. The solid was boiled in 25 mL of water and filtered while hot to afford **15** as a white solid (0.273 g, 0.85 mmol, 72% yield). MP 130-134 ^oC. ^1H NMR ($CDCl_3$): δ 0.84 (t, 3H), 1.2 (m, 10H), 1.5 (m, 2H), 3.28 (m, 2H), 3.88 (s, 3H), 7.21 (d, 1H), 7.35 (d, 1H), 8.95 (t, 1H, NH), 10.3 (bs, 1H, OH), 13.0 (bs, 1H, OH)., ^{13}CMR ($CDCl_3$): δ 14.1, 22.6, 27.0, 29.2, 29.3, 29.4, 31.8, 40.0, 52.7, 114.5, 115.5, 118.3, 150.0, 151.7, 168.3, 170.1, FAB-MS(+), m/z : 324. Anal. Calcd (found) for $C_{17}H_{25}O_5N$: C 63.14 (62.81), H 7.79 (7.79), N 4.33 (4.13).

2,3-Dihydroxybenzoic acid 4-octylamide (17)

Compound **15** (0.485 g, 1.5 mmol) was suspended in 5 mL distilled, deionized water and upon addition of 15 mL of 1M KOH the solid dissolved. N_2 was bubbled through the

solution for 10 min. then it was stirred for 2 h. under Ar. Addition of HCl precipitated **17** as a white solid (0.345 g, 1.1 mmol, 74% yield). MP 197-200 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 0.82 (t, 3H), 1.2 (m, 10H), 1.5 (m, 2H), 3.27 (m, 2H), 7.22 (d, 1H), 7.33 (d, 1H), 8.92 (t, 1H, NH), 12.83 (bs, 1H, OH). ^{13}CMR ($CDCl_3$): δ 14.3, 22.5, 26.8, 29.0, 29.1, 31.6, 115, 116.5, 118, 119, 150.3, 151.7, 168.9, 172.1, FAB-MS(+) m/z: 310, Anal. Calcd (found) for $C_{16}H_{23}O_5N$: C 62.12 (62.05), H 7.49 (7.64), N 4.53 (4.84).

***N*-octyl, *N'*-ethylpiperidine-2,3-Dihydroxyterephthalamide (19)**
Compound **17** (0.100 g, 0.32 mmol) was dissolved in 10 mL of dry dioxane with 1mL of $SOCl_2$ and heated at reflux for 5 h. under Ar. Evaporation afforded a yellow-brown oil which was dissolved in 10 mL of $CHCl_3$, cooled in an ice water bath, and added slowly to 1-(2-aminoethyl)piperidine (0.06 mL, 0.42 mmol) dissolved in 10 mL of $CHCl_3$ under Ar cooled in an ice water bath. The reaction was stirred for 3 h. in an ice water bath, then 3 h. at rt and extracted with $NH_4CH_3CO_2$ (pH 9, 0.1M, 2x 20 mL) and HCl (1M, 20 mL). Evaporation yielded a tan oil which upon trituration with EtOAc (3 mL) afforded **20** as a white solid. ^{1}H NMR ($CDCl_3$): δ 0.87 (t, 3H), 1.26-1.67 (m, 20H), 2.62-2.74 (m, 5H), 3.43 (q, 2H), 3.62 (t, 2H), 6.98 (d, 1H), 7.04 (d, 1H), 7.06 (bs, 1H, NH), 8.35 (bs, 1H, NH). Anal. Calcd (found) for $C_{23}H_{38}O_4N_3Cl$: C 60.58 (60.28), H 8.4 (8.54), N 9.21 (8.86).

X-Ray Crystallography Details

Empirical Formula	$Cl_2C_8O_4H_4$
Formula Weight	235.02
Crystal Color, Habit	yellow, tablet
Crystal Dimensions	0.50 x 0.14 x 0.05 mm
Crystal System	orthorhombic
Lattice Type	Primitive
No. of Reflections Used for Unit	
Cell Determination (2θ range)	933 (3.5 - 45.0^{o})
Lattice Parameters	a = 13.781(3) Å
	b = 4.835(1) Å
	c = 13.241(3) Å

	V = 882.3(8) Å3
Space Group	Pccn (#56)
Z value	4
Dcalc	1.769 g/cm^3
F000	472.00
μ(MoKα)	7.15 cm^{-1}

B. Intensity Measurements

Diffractometer	SMART
Radiation	MoKα (λ = 0.71069 Å) graphite monochromated
Temperature	-109.0^{o}C
Scan Type	ω (0.3^o per frame)
2θmax	49.4^o
No. of Reflections Measured	Total: 3949 Unique: 899 (Rint = 0.050)
Corrections	Lorentz-polarization Absorption (Tmax = 1.00, Tmin = 1.00)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares

Function Minimized	Σ w (|Fo| - |Fc|)^2
Least Squares Weights	$1/\sigma^2(Fo) = 4Fo^2/\sigma^2(Fo^2)$
p-factor	0.030
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>3.00σ(I))	402
No. Variables	64
Reflection/Parameter Ratio	6.28
Residuals: R; Rw; Rall	0.050; 0.061; 0.000
Goodness of Fit Indicator	1.81
Max Shift/Error in Final Cycle	0.56
Maximum peak in Final Diff. Map	0.36 e-/Å^3
Minimum peak in Final Diff. Map	-0.28 e-/Å^3