Supporting Information for:

Catalytic Carbonylation of α -Lactones to Succinic Anhydrides

Yutan D. Y. L. Getzler, Vinod Kundnani, Emil B. Lobkovsky, and Geoffrey W. Coates*

Department of Chemistry and Chemical Biology, Baker Laboratory, Cornell University

Ithaca, New York 14853-1301

gc39@cornell.edu

General Considerations

All manipulations of air- and/or water-sensitive compounds were carried out under dry nitrogen using a Braun Unilab drybox or standard Schlenk line techniques. NMR spectra were recorded on Varian Gemini or Inova spectrometers (300 MHz, 400 MHz and 500 MHz) and referenced versus residual non-deuterated or monoprotonated solvent shifts. IR data was collected by a Mattson RS-10500 Research Series FTIR. Enantiomeric excess of (*S*)-methylsuccinic anhydride was measured on an HP 6890 Series GC equipped with a Supelco 2-4318 α -DEX 225 column (0.25mm x 30m). X-ray crystallographic data were collected using a SMART CCD Area Detector System (Mo K α , λ = 0.71073 Å), and frames were integrated with the Siemens SAINT program. Anhydrides were identified by comparison of their NMR shift data to literature values where available. High-resolution mass spectra were obtained in the Mass Spectrometry Laboratory, School of Chemical Sciences, University of Illinois, on a 70-VSE mass spectrometer purchases, in part, with a grant from the Division of Research Resources, National Institutes of Health (RR 04648).

Materials

Toluene was degassed by purging with nitrogen and then dried and further degassed over columns of alumina and reduced copper. Lactones were distilled from CaH₂ or activated

3 Å sieves under nitrogen and degassed by repetitive freeze-pump-thaw cycles. Research grade carbon monoxide was purchased from Matheson. γ -Butyrolactone was purchased from Aldrich and purified as noted above. The following compounds were prepared according to literature procedure: catalyst **2**,^{1a} γ -lactone starting materials,¹ (S)-methylsuccinic anhydride **5**.² All other materials were commercially available and used as received.

Optimization of catalyst loading was performed in a custom designed and fabricated six-chamber stainless-steel high-pressure reactor (Scheme S1). The reactor design allowed for incorporation of 8 mL glass vials.

High Pressure Reactor 2.0 - 8ml vial

Scheme S1. Six-chamber stainless-steel high-pressure reactor.

- (1) (a) Getzler, Y. D. Y. L.; Mahadevan, V.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 1174-1175. (b) Mahadevan, V.; Getzler, Y. D. Y. L.; Coates, G. W. *Angew. Chem., Int. Ed.* **2002**, *41*, 2781-2784. (c) Schmidt, J. A. R.; Mahadevan, V.; Getzler, Y. D. Y. L.; Coates, G. W. *Org. Lett.* **2004**, *6*, 373-376.
- (2) Polonski, T. *J. Chem. Soc., Perkin Trans. I* **1988**, *3*, 629-637.

The following compounds were identified by comparison to authentic material: succinic anhydride (Table 1, Entry 10), methylsuccinic anhydride (Table 1, Entry 1), γ -butyrolactone (**7**). Ethylsuccinic anhydride (Table 1, Entry 5) was previously prepared,³ however, the ¹H- and ¹³C- NMR spectra are in DMSO-*d*₆; presented here are spectra in CDCl₃. Also previously prepared was *trans*-2,3-dimethylsuccinic anhydride (**4**; Table 1, Entry 4).⁴

Synthetic Procedures

General procedure for the carbonylation of heterocycles:

A six-chamber stainless-steel high-pressure reactor was equipped with magnetic stir bars and dried overnight under vacuum at 100°. In a nitrogen glove box, each chamber was charged with the appropriate mass of catalyst **2** followed by the appropriate volume of dry, degassed toluene to make the solution 1.8 M in substrate. Finally, 0.1 ml of lactone was added (density was assumed to be 1 g/ml), the reactor was sealed, brought out of the glove box, pressured to 200 psi with carbon monoxide and heated to the indicated temperature. After 24 hours the reactor was placed on dry ice for a minimum of 15 minutes and vented slowly. The crude reaction mixture was analyzed by NMR and, where appropriate, by chiral GC. Prior to characterization, product anhydrides were purified by sublimation or distillation, as appropriate.

Thermal racemization of (*S*)-methylsuccinic anhydride by catalyst **2**:

As above, the reactor was equipped with magnetic stir bars and dried overnight under vacuum at 100°. In a nitrogen glove box, one chamber was charged with 2.6 mg (0.0033 mmol, 1 equivalent) of catalyst **2**, 68.8 mg (0.60 mmol, 180 equivalent) of (*S*)-methylsuccinic anhydride **5** and 0.34 ml of dry, degassed toluene. The reactor was sealed, brought out of the glove box, pressured to 200 psi with carbon monoxide and heated to 80°. After 24 hours, the reactor was placed on dry ice and vented slowly. The crude reaction mixture was analyzed by NMR and chiral GC. GC program as follows: inlet (T = 150 °C, 15 psi, 52.9 ml/min, 50:1 split, split flow 49.9 ml/min); detector (250 °C, 35

(3) Bergmeir, S. C.; Ismail, K. A. *Synthesis*, **2000**, 10, 1369-1370.

(4) Ozegowski, R.; Kunath, A.; Schick, H. *Tetrahedron: Asymmetry*, **1995**, 6, 1191-1194.

ml/min H₂ flow, 400 ml/min air flow, 20 ml/min makeup He); column (13.0 psi, 1.0 ml/min); oven (70 °C hold for 4.60 min; 30 °C/min to 180 °C, hold for 4.00 min; 30 °C to 220 °C, hold for 6.40 min). The anhydrides come at 12.50 and 12.61 minutes; the later peak is the *S* enantiomer.

Indexed Spectral Data for Previously Unidentified Compounds

(graphical data follows as figures S1-S10)

Ethylsuccinic anhydride (3-ethyl-dihydro-furan-2,5-dione; Table 1, entry 5)

¹H NMR (CDCl₃, 400 MHz, Figure S1) δ 1.04 (3H, t, *J*=7.6 Hz), 1.70-1.82 (1H, m), 1.92-2.03 (1H, m), 2.68 (1H, m), 3.12 (2H, m). ¹³C NMR (CDCl₃, 75 MHz, Figure S2) δ 11.12, 24.33, 33.75, 42.09, 170.43, 173.79. IR (thin film from CDCl₃ on KBr plate, cm⁻¹) ν_{CO} = 1862 (w, sh), 1782 (s, sh); HRMS (EI) *m/z* calcd (C₆H₈O₃ + H⁺) 129.0546, found 129.0552.

Decylsuccinic anhydride (3-decyl-dihydro-furan-2,5-dione; Table 1, entry 6)

¹H NMR (CDCl₃, 300 MHz, Figure S3) δ 0.889 (3H, m), 1.20-1.45 (16H, br m), 1.66 (1H, m), 1.94 (1H, m), 2.67 (1H, m), 3.11 (1H, m). ¹³C NMR (CDCl₃, 126 MHz, Figure S4) δ 14.32, 22.89, 26.92, 29.30, 29.49 (broad, likely two peaks), 29.69, 29.74, 31.23, 32.09, 34.31, 40.89, 170.29, 173.85. IR (KBr pellet, cm⁻¹) ν_{CO} = 1861 (w, sh), 1779 (s, sh); HRMS (EI) *m/z* calcd (C₁₄H₂₄O₃ + H⁺) 241.1798, found 241.1802.

n-Butoxymethylsuccinic anhydride (3-butoxymethyl-dihydro-furan-2,5-dione; Table 1, entry 7)

¹H NMR (CDCl₃, 400 MHz, Figure S5) δ 0.89 (3H, t, *J*=7.4 Hz), 1.31 (2H, m), 1.50 (2H, m), 3.01 (1H, d, *J*=0.8 Hz), 3.03 (1H, d, *J*=2.2 Hz), 3.26 (1H, m), 3.45 (2H, m), 3.60 (1H, dd, *J*^a=3.1 Hz, *J*^b=9.2 Hz), 3.87 (1H, dd, *J*^a=3.3 Hz, *J*^b=9.2 Hz). ¹³C NMR (CDCl₃, 75 MHz, Figure S6) δ 13.98, 19.35, 31.52, 31.69, 42.41, 68.34, 71.70, 170.45, 172.95. IR (thin film from CDCl₃ on KBr plate, cm⁻¹) ν_{CO} = 1860 (m, sh), 1784 (s, sh); HRMS (EI) *m/z* calcd (C₉H₁₄O₄) 186.0892, found 186.0889.

***tert*-Butyl-dimethyl-silyloxymethylsuccinic anhydride (3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-dihydro-furan-2,5-dione; Table 1, entry 8)**

¹H NMR (CDCl₃, 300 MHz, Figure S7) δ 0.06 (3H, s), 0.07 (3H, s), 0.86 (9H, s), 3.00 (1H, d, *J*=1.5 Hz), 3.02 (1H, d, *J*=3.2 Hz), 3.21 (1H, m), 3.76 (1H, dd, *J*^a=2.8 Hz, *J*^b=9.9 Hz), 4.15 (1H, dd, *J*^a=2.5 Hz, *J*^b=9.9 Hz). ¹³C NMR (CDCl₃, 75 MHz, Figure S8) δ -5.55, -5.44, 18.31, 25.83, 31.48, 44.15, 61.96, 170.60, 173.29. IR (thin film from CDCl₃ on KBr plate, cm⁻¹) ν_{CO} = 1859 (m, sh), 1786 (s, sh).

But-3-enylsuccinic anhydride (3-but-3-enyl-dihydro-furan-2,5-dione; Table 1, entry 9)

¹H NMR (CDCl₃, 300 MHz, Figure S9) δ 1.71-1.82 (1H, m), 2.03-2.33 (3H, m), 2.60-2.75 (1H, m), 3.05-3.20 (3H, m), 5.05-5.15 (2H, m), 5.70-5.85 (1H, m). ¹³C NMR (CDCl₃, 75 MHz, Figure S10) δ 30.20, 31.06, 34.36, 40.04, 117.19, 136.18, 170.20, 173.90. IR (thin film from CDCl₃ on KBr plate, cm⁻¹) ν_{CO} = 1863 (w, sh), 1783 (s, sh); HRMS (EI) *m/z* calcd (C₈H₁₀O₃) 154.0630, found 154.0628.

Figure S1. ^1H NMR of ethylsuccinic anhydride (3-ethyl-dihydro-furan-2,5-dione), CDCl_3 , 400 MHz.

Figure S2. ^{13}C NMR of ethylsuccinic anhydride (3-ethyl-dihydro-furan-2,5-dione), CDCl_3 , 75 MHz.

Figure S3. ^1H NMR of Decylsuccinic anhydride (3-decyl-dihydro-furan-2,5-dione), CDCl_3 , 300 MHz.

Figure S4. ^{13}C NMR of Decylsuccinic anhydride (3-decyl-dihydro-furan-2,5-dione), CDCl_3 , 126 MHz.

Figure S5. ^1H NMR of *n*-butoxymethylsuccinic anhydride (3-butoxymethyl-dihydro-furan-2,5-dione), CDCl_3 , 400 MHz.

Figure S6. ^{13}C NMR of *n*-butoxymethylsuccinic anhydride (3-butoxymethyl-dihydro-furan-2,5-dione), CDCl_3 , 75 MHz.

Figure S7. ^1H NMR of *tert*-butyl-dimethyl-silyloxymethylsuccinic anhydride (3-(*tert*-Butyldimethyl-silanyloxymethyl)-dihydro-furan-2,5-dione), CDCl_3 , 300 MHz.

Figure S8. ^{13}C NMR of *tert*-butyl-dimethyl-silyloxymethylsuccinic anhydride (3-(*tert*-Butyl-dimethyl-silanyloxymethyl)-dihydro-furan-2,5-dione), CDCl_3 , 75 MHz.

Figure S9. ^1H NMR of butenylsuccinic anhydride (3-but-3-enyl-dihydro-furan-2,5-dione), CDCl_3 , 300 MHz.

Crystallographic Data for *trans*-2,3-Dimethylsuccinic Anhydride (**4**)

Figure S11. X-ray crystal structure of **4**.

Table S1. Crystal data and structure refinement for **4**.

Empirical formula	C ₆ H ₈ O ₃	
Formula weight	128.12	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 10.989(3) Å	α = 90°
	b = 8.841(2) Å	β = 90°
	c = 13.026(4) Å	γ = 90°
Volume	1265.5(6) Å ³	
Z	8	
Density (calculated)	1.345 Mg/m ³	
Absorption coefficient	0.108 mm ⁻¹	
F(000)	544	
Crystal size	0.50 x 0.15 x 0.02 mm ³	
Theta range for data collection	3.13 to 23.27°.	
Index ranges	-12 ≤ h ≤ 11, -7 ≤ k ≤ 9, -14 ≤ l ≤ 14	
Reflections collected	4221	
Independent reflections	901 [R(int) = 0.0417]	
Completeness to theta = 23.27°	99.0 %	
Absorption correction	SADABS	
Max. and min. transmission	0.9978 and 0.9478	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	901 / 0 / 114	
Goodness-of-fit on F ²	1.096	
Final R indices [I > 2σ(I)]	R1 = 0.0433, wR2 = 0.0934	
R indices (all data)	R1 = 0.0672, wR2 = 0.1029	
Largest diff. peak and hole	0.115 and -0.149 e/Å ⁻³	

Table S2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **4**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	4747(2)	2904(2)	6795(1)	59(1)
O(2)	6418(2)	1465(2)	6943(1)	44(1)
O(3)	7929(2)	33(2)	7553(1)	56(1)
C(1)	5414(2)	2218(3)	7347(2)	40(1)
C(2)	5358(2)	1945(3)	8480(2)	36(1)
C(3)	6655(2)	1487(3)	8738(2)	36(1)
C(4)	7109(2)	878(3)	7741(2)	40(1)
C(5)	4783(3)	3220(4)	9075(2)	54(1)
C(6)	6835(3)	462(4)	9655(2)	46(1)

Table S3. Bond lengths [Å] and angles [°] for **4**.

O(1)-C(1)	1.192(3)
O(2)-C(4)	1.388(3)
O(2)-C(1)	1.392(3)
O(3)-C(4)	1.195(3)
C(1)-C(2)	1.498(3)
C(2)-C(5)	1.507(4)
C(2)-C(3)	1.519(3)
C(3)-C(4)	1.492(3)
C(3)-C(6)	1.513(4)
C(4)-O(2)-C(1)	109.2(2)
O(1)-C(1)-O(2)	120.2(2)
O(1)-C(1)-C(2)	130.6(2)
O(2)-C(1)-C(2)	109.2(2)
C(1)-C(2)-C(5)	113.8(2)
C(1)-C(2)-C(3)	102.8(2)
C(5)-C(2)-C(3)	118.6(2)
C(4)-C(3)-C(6)	115.3(2)
C(4)-C(3)-C(2)	102.5(2)
C(6)-C(3)-C(2)	117.2(2)
O(3)-C(4)-O(2)	119.5(2)
O(3)-C(4)-C(3)	131.0(2)
O(2)-C(4)-C(3)	109.5(2)

Table S4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **4**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	60(1)	66(1)	50(1)	14(1)	-15(1)	6(1)
O(2)	54(1)	44(1)	35(1)	-2(1)	6(1)	1(1)
O(3)	50(1)	53(1)	67(1)	-6(1)	15(1)	10(1)
C(1)	41(2)	36(2)	43(1)	2(1)	-3(1)	-5(2)
C(2)	33(1)	39(2)	37(1)	2(1)	1(1)	4(1)
C(3)	36(2)	33(2)	38(1)	-3(1)	-1(1)	0(1)
C(4)	38(2)	33(2)	48(2)	-2(1)	5(1)	-9(1)
C(5)	57(2)	57(2)	49(2)	3(1)	7(2)	22(2)
C(6)	45(2)	51(2)	42(2)	-2(1)	-8(1)	7(2)

Table S5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **4**.

	x	y	z	U(eq)
H(2)	4860(20)	980(30)	8558(17)	56(8)
H(3)	7100(20)	2430(30)	8831(16)	50(8)
H(5C)	4770(20)	2970(30)	9810(20)	59(8)
H(5B)	5240(30)	4160(30)	8970(20)	80(11)
H(5A)	3960(30)	3360(30)	8860(20)	73(9)
H(6C)	7700(30)	230(30)	9742(18)	58(8)
H(6B)	6560(20)	940(30)	10280(20)	56(8)
H(6A)	6360(30)	-520(40)	9540(20)	76(10)