Four Acid-Catalysed Dehydrations Proceed without Interference

Rio Carlo Lirag and Ognjen Š. Miljanić*

Department of Chemistry, University of Houston, 112 Fleming Building, Houston, Texas 77204-5003, United StatesEmail: miljanic@uh.eduPhone: +1.832.842.8827Web: www.miljanicgroup.com

Supporting Information

General Methods	S2
Structures of Possible Dehydration Products	
Parallel Dehydration Reactions	S5
Reaction #1	S5
Reaction #2	
Reaction #3	
Reaction #4	
Reaction #5	
Reaction #6	
Reaction #7	
Reaction #8	
Reaction #9	
Reaction #10	
Reaction #11	
Reaction #12	
Reaction #13	
Reaction #14	
Reaction #15	
Reaction #16	
Reaction #17	
Synthesis and Spectroscopic Characterization Data for New Compounds	\$39
NMR Spectral Data for New Compounds	S43
References	\$58

General Methods

All reactions were performed under nitrogen atmosphere in oven-dried glassware. Reagents were purchased from commercial suppliers and used without further purification. Solvents were dried by adding activated 4 Å molecular sieves. Microwave-assisted reactions were performed in a Biotage Initiator 2.0 microwave reactor, producing monochromatic microwave radiation with the frequency of 2.45 GHz. Mass spectral measurements were performed by the Mass Spectrometry Facilities of the Department of Chemistry, University of Houston and the Department of Chemistry at the University of Texas at Austin. NMR spectra were obtained on JEOL ECA-500 MHz spectrometer, with working frequency (for ¹H nuclei) of 500 MHz. All ¹³C-NMR spectra were recorded with simultaneous decoupling of ¹H nuclei. ¹H NMR chemical shifts are reported in ppm units relative to the residual signal of the solvent (CDCl₃: 7.25 ppm) and were recorded at 25 °C. NMR yields were calculated by adding approx. 1.0 equivalent of 1,3,5-trimethoxybenzene (Alfa Aesar, 99%) as the internal standard to the crude reaction mixture. Infrared spectra were recorded on a Nicolet iS10 FT-IR spectrometer equipped with a Thermo Scientific iTR for multi-purpose ATR sampling. Melting points were measured in open capillary tubes using Mel-Temp Thermo Scientific apparatus, and are uncorrected.

Short column chromatography for purification was performed using basic alumina Act 1 (Sorbent Technologies), 50–200 μm. Analytical TLC was performed on JT Baker alumina oxide IB-F plates.

Structures of Possible Dehydration Products



Figure S1. Possible imine products and their signature ¹H NMR signals.



Figure S2. Possible alkene and boronate ester products and their signature ¹H NMR signals.



Figure S3. Possible acetal products and their signature ¹H NMR signals.



Figure S4. Possible ester/diester products and their signature ¹H NMR signals.

Parallel Dehydration Reactions

Reaction #1



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), phenylboronic acid (**5a**, 39.0 mg, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 2,2-dimethyl-1,3propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2-phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (12.2 mg, 0.064 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR spectroscopy with an internal standard.

7**A**: ¹H NMR (500 MHz, CDCl₃): δ 9.03 (s, 1H), 8.90 (d, *J*=2.3 Hz, 1H), 8.61 (d, *J*=8.6 Hz, 1H), 8.51 (dd, *J*=8.9, 2.3 Hz, 1H), 7.38 (d, *J*=8.6 Hz, 2H), 6.97 (d, *J*=9.2 Hz, 2H), 3.86 (s, 9H) ppm. Spectral data agree with a previous literature report.¹

7**B**: ¹H NMR (500 MHz, CDCl₃): δ 7.80 (d, *J*=6.9 Hz, 2H), 7.43 (t, *J*=7.5 Hz, 1H), 7.35 (t, *J*=7.4 Hz, 2H), 3.77 (s, 4H), 1.03 (s, 6H) ppm. Spectral data agree with a previous literature report.²

7**C**: ¹H NMR (500 MHz, CDCl₃): δ 7.14–7.33 (m, 10H), 4.31 (t, *J*=7.1 Hz, 2H), 3.60 (s, 2H), 2.92 (t, *J*=7.1 Hz, 2H) ppm. Spectral data agree with a previous literature report.³

7**D**: ¹H NMR (500 MHz, CDCl₃): δ 7.31–7.34 (m, 10H), 5.46 (s, 2H) ppm. Spectral data agree with a previous literature report.⁴



Figure S5. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #1. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), pentafluorophenylboronic acid (**5b**, 67.8 mg, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 2,2dimethyl-1,3-propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (12.2 mg, 0.064 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 days, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR spectroscopy with an internal standard.

8B: IR (neat): 2962, 1386, 1325, 1255, 1205, 1143, 1122, 666 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 3.81 (s, 3H), 1.06 (s, 6H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 149.53, 147.58, 143.25, 141.20, 138.22, 136.16, 72.92, 32.00, 21.85 ppm. ¹⁹F NMR (470 MHz, CDCl₃): -131.78 to -131.85 (m, 2F), -151.72 to -151.82 (m, 1F), -162.03 to -162.14 (m, 2F) ppm. HRMS (CI): Calcd for C₁₁H₁₁BF₅O₂⁺: 281.0772. Found: 281.0760.



Figure S6. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #2. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), 2,4-dimethoxybenzaldehyde (**1c**, 53.2 mg, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 2,2-dimethyl-1,3propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2-phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR spectroscopy with an internal standard.

9B: IR (neat): 2953, 2829, 1397, 1350, 1284, 1095, 1031, 824 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.56 (d, *J*=8.4 Hz, 1H), 6.51 (dd, *J*=8.6, 2.4 Hz, 1H), 6.42 (d, *J*=2.3 Hz, 1H), 5.69 (s, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.73 (d, *J*=11.0 Hz, 2H), 3.65 (d, *J*=11.0 Hz, 2H), 1.31 (s, 3H), 0.76 (s, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 161.37, 157.69, 128.13, 119.78, 104.69, 98.40, 96.99, 77.98, 55.66, 55.49, 30.32, 23.18, 21.99 ppm. LRMS (ESI): Calcd for C₁₄H₂₁O₄⁺: 253.14. Found: 252.98.

9E: IR (neat): 2962, 2825, 1531, 1381, 1348, 1312, 1029, 719 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.66 (d, *J*=2.3 Hz, 1H), 8.44 (dd, *J*=8.6, 2.3 Hz, 1H), 8.14 (d, *J*=8.6 Hz, 1H), 6.00 (s, 1H), 3.76 (d, *J*=11.4 Hz, 2H), 3.68 (d, *J*=11.4 Hz, 2H), 1.21 (s, 3H), 0.80 (s, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 148.57, 147.92, 138.44, 129.65, 126.92, 119.59, 96.28, 77.98, 30.39, 23.14, 21.76 ppm. LRMS (APCI): Calcd for C₁₂H₁₃N₂O₆⁻: 281.08. Found: 281.98.

9F: ¹H NMR (500 MHz, CDCl₃): δ 8.82 (s, 1H), 8.08 (d, *J*=8.6 Hz, 1H), 7.20 (d, *J*=9.1 Hz, 2H), 6.90 (d, *J*=9.1 Hz, 2H), 6.57 (dd, *J*=8.8, 2.3 Hz, 1H), 6.46 (d, *J*=2.5 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.82 (s, 3H) ppm. Spectral data agree with a previous literature report.⁵



Figure S7. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #3. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), benzaldehyde (**1e**, 32.5 μ L, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 2,2-dimethyl-1,3-propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2-phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 days, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR spectroscopy with an internal standard.

10B: ¹H NMR (500 MHz, CDCl₃): δ 7.51 (d, *J*=7.0 Hz, 2H), 7.33–7.39 (m, 3H), 5.40 (s, 1H), 3.78 (d, *J*=11.1 Hz, 2H), 3.66 (d, *J*=11.1 Hz, 2H), 1.31 (s, 3H), 0.80 (s, 3H) ppm. Spectral data agree with a previous literature report.⁶

10F: ¹H NMR (500 MHz, CDCl₃): δ 8.48 (s, 1H), 7.89 (dd, *J*=7.5, 2.7 Hz, 2H), 7.46 (t, *J*=3.1 Hz, 3H), 7.24 (d, *J*=9.1 Hz, 2H), 6.93 (d, *J*=9.1 Hz, 2H), 3.83 (s, 3H) ppm. Spectral data agree with a previous literature report.⁷



Figure S8. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #4. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 4nitrobenzaldehyde (**1b**, 48.4 mg, 0.32 mmol), *p*-anisaldehyde (**1d**, 38.9 μ L, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 2,2-dimethyl-1,3-propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2-phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux with. After 2 days, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

11A: ¹H NMR (500 MHz, CDCl₃): δ 8.58 (s, 1H), 8.31 (d, *J*=8.7 Hz, 2H), 8.06 (d, *J*=8.6 Hz, 2H), 7.31 (d, *J*=8.6 Hz, 2H), 6.96 (d, *J*=8.6 Hz, 2H), 3.85 (s, 3H) ppm. Spectral data agree with a previous literature report.⁸

11B: ¹H NMR (500 MHz, CDCl₃): δ 7.43 (d, *J*=8.6 Hz, 2H), 6.89 (d, *J*=8.6 Hz, 2H), 5.35 (s, 1H), 3.79 (s, 3H), 3.75 (d, *J*=11.0 Hz, 2H), 3.63 (d, *J*=11.0 Hz, 2H), 1.29 (s, 3H), 0.79 (s, 3H) ppm. Spectral data agree with a previous literature report.⁶

11F: ¹H NMR (500 MHz, CDCl₃): δ 8.40 (s, 1H), 7.83 (d, *J*=8.6 Hz, 2H), 7.20 (d, *J*=8.6 Hz, 2H), 6.97 (d, *J*=8.6 Hz, 2H), 6.92 (d, *J*=9.0 Hz, 2H), 3.86 (s, 3H), 3.82 (s, 3H) ppm. Spectral data agree with a previous literature report.⁷



Figure S9. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #5. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 4nitrobenzaldehyde (**1b**, 48.4 mg, 0.32 mmol), 4-chlorobenzaldehyde (**1f**, 45.0 mg, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 2,2-dimethyl-1,3propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2-phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

12B: ¹H NMR (500 MHz, CDCl₃): δ 7.44 (d, *J*=8.5 Hz, 2H), 7.33 (d, *J*=8.5 Hz, 2H), 5.36 (s, 1H), 3.76 (d, *J*=11.1 Hz, 2H), 3.63 (d, *J*=11.1 Hz, 2H), 1.27 (s, 3H), 0.79 (s, 3H) ppm. Spectral data agree with a previous literature report.⁹

12E: ¹H NMR (500 MHz, CDCl₃): δ 8.22 (d, *J*=8.7 Hz, 2H), 7.68 (d, *J*=8.7 Hz, 2H), 5.46 (s, 1H), 3.79 (d, *J*=11.3 Hz, 2H), 3.67 (d, *J*=11.3 Hz, 2H), 1.27 (s, 3H), 0.82 (s, 3H) ppm. Spectral data agree with a previous literature report.⁶

12F: ¹H NMR (500 MHz, CDCl₃): δ 8.43 (s, 1H), 7.82 (d, *J*=8.3 Hz, 2H), 7.43 (d, *J*=8.4 Hz, 2H), 7.23 (d, *J*=8.7 Hz, 2H), 6.93 (d, *J*=8.7 Hz, 2H), 3.83 (s, 3H) ppm. Spectral data agree with a previous literature report.¹⁰



Figure S10. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #6. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), 2,4-dimethoxybenzaldehyde (**1c**, 53.2 mg, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), aniline (**2b**, 29.2 μ L, 0.32 mmol), 2,2-dimethyl-1,3propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2-phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

13A: ¹H NMR (500 MHz, CDCl₃): δ 9.01 (s, 1H), 8.92 (d, *J*=2.2 Hz, 1H), 8.60 (d, *J*=8.7 Hz, 1H), 8.55 (dd, *J*=8.6, 2.0 Hz, 1H), 7.46 (t, *J*=7.8 Hz, 2H), 7.32–7.36 (m, 3H) ppm. Spectral data agree with a previous literature report.¹



Figure S11. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #7. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), 2,4-dimethoxybenzaldehyde (**1c**, 53.2 mg, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), cyclohexylamine (**2c**, 36.6 μ L, 0.32 mmol), 2,2-dimethyl-1,3-propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

14A: IR (neat): 3089, 2928, 1634, 1594, 1528, 1384, 1343, 904 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.84 (d, *J*=2.3 Hz, 1H), 8.75 (s, 1H), 8.45 (dd, *J*=8.7, 2.3 Hz, 1H), 8.32 (d, *J*=8.7 Hz, 1H), 3.39 (m, 1H), 1.81 (dt, *J*=13.5, 3.8 Hz, 2H), 1.78 (dd, *J*=13.2, 3.5 Hz, 2H), 1.69 (dt, *J*=12.7, 3.8 Hz, 1H), 1.59 (qd, *J*=12.2, 3.4 Hz, 2H), 1.39 (qt, *J*=12.1, 3.0 Hz, 2H), 1.28 (qt, *J*=12.3, 3.5 Hz, 1H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 152.79, 148.73, 148.30, 136.63, 131.67, 127.45, 120.08, 70.26, 34.05, 25.59, 24.49 ppm. HRMS (CI): Calcd for C₁₃H₁₆N₃O₄⁺: 278.1141. Found: 278.1135.



Figure S12. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #8. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), 2,4-dimethoxybenzaldehyde (**1c**, 53.2 mg, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), 4-chloroaniline (**2d**, 40.8 mg, 0.32 mmol), 2,2-dimethyl-1,3-propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

15A: IR (neat): 3107, 1594, 1522, 1395, 1337, 1090, 835 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.99 (s, 1H), 8.93 (s, 1H), 8.56 (d, *J*=8.3 Hz, 1H), 8.55 (dd, *J*=8.5, 2.3 Hz, 2H), 7.42 (d, *J*=8.7 Hz, 2H), 7.27 (d, *J*=8.7 Hz, 2H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 153.62, 149.18, 148.76, 148.53, 135.83, 133.95, 131.53, 129.73, 127.66, 122.90, 120.49 ppm. HRMS (CI): Calcd for C₁₃H₉ClN₃O₄⁺: 306.0282. Found: 306.0281.



Figure S13. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #9. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), *p*-anisaldehyde (**1d**, 38.9 μ L, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), *cis*-1,2-cyclopentanediol (**6b**, 32.7 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2-phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

16B (*major diastereomer*): ¹H NMR (500 MHz, CDCl₃): δ 7.43 (d, *J*=8.6 Hz, 2H), 6.89 (d, *J*=8.6 Hz, 2H), 5.58 (s, 1H), 4.65 (d, *J*=4.4 Hz, 2H), 3.80 (s, 3H), 2.05 (dd, *J*=13.9, 6.4 Hz, 2H), 1.90 (m, 1H), 1.64 (m, 1H), 1.48 (m, 2H) ppm. Spectral data agree with a previous literature report.¹¹

16B (*minor diastereomer*): ¹H NMR (500 MHz, CDCl₃): δ 7.37 (d, *J*=8.6 Hz, 2H), 6.88 (d, *J*=8.6 Hz, 2H), 6.00 (s, 1H), 4.67 (d, *J*=4.3 Hz, 2H), 3.80 (s, 3H), 1.96 (dd, *J*=13.0, 6.2 Hz, 2H), 1.80 (m, 1H), 1.64 (m, 1H), 1.45 (m, 2H) ppm. Spectral data agree with a previous literature report.¹¹



Figure S14. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #10. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), *p*-anisaldehyde (**1d**, 38.9 μ L, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 2-methylene-1,3-propanediol (**6c**, 26.1 μ L, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2-phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 3 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

17B: ¹H NMR (500 MHz, CDCl₃): δ 7.41 (d, *J*=8.8 Hz, 2H), 6.88 (d, *J*=8.8 Hz, 2H), 5.57 (s, 1H), 4.99 (s, 2H), 4.50 (d, *J*=4.8 Hz, 4H), 3.80 (s, 3H) ppm. Spectral data agree with a previous literature report.¹²



Figure S15. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #11. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).



In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), 2,4-dimethoxybenzaldehyde (**1c**, 53.2 mg, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 1,3-propanediol (**6d**, 23.0 μ L, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2-phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

18B: IR (neat): 2957, 2842, 1615, 1511, 1266, 1124, 1095, 1033, 982 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.52 (d, *J*=8.5 Hz, 1H), 6.50 (dd, *J*=8.5, 2.5 Hz, 1H), 6.42 (d, *J*=2.5 Hz, 1H), 5.79 (s, 1H), 4.23 (ddd, *J*=11.4, 5.3, 1.0 Hz, 2H), 3.98 (td, *J*=12.0, 2.5 Hz, 2H), 3.80 (s, 3H), 3.78 (s, 3H), 2.21 (m, 1H), 1.40 (dt, *J*=13.0, 1.0 Hz, 1H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 161.33, 157.55, 128.03, 120.05, 104.62, 98.34, 96.98, 67.73, 55.66, 55.47, 25.96 ppm. LRMS (ESI): Calcd for C₁₂H₁₇O₄⁺: 225.11. Found: 225.00.



Figure S16. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #12. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).

Reaction #13

In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), 2,4-dimethoxybenzaldehyde (**1c**, 53.2 mg, 0.32 mmol), hexanoic acid (**3b**, 40.1 μ L, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 2,2-dimethyl-1,3propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 1-hexanol (**4b**, 120.5 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

19C: ¹H NMR (500 MHz, CDCl₃): δ 4.04 (t, *J*=7.0 Hz, 2H), 2.27 (t, *J*=7.3 Hz, 2H), 1.57–1.63 (m, 4H), 1.29 (m, 10H), 0.86–0.89 (m, 6H) ppm. Spectral data agree with a previous literature report.¹³

Figure S17. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #13. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).

In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), 2,4-dimethoxybenzaldehyde (**1c**, 53.2 mg, 0.32 mmol), 3-bromopropionic acid (**3c**, 49.0 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 2,2-dimethyl-1,3-propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

20C: IR (neat): 2957, 1733, 1232, 1173, 1131, 748, 699 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.21– 7.32 (m, 5H), 4.35 (t, *J*=7.0 Hz, 2H), 3.54 (t, *J*=7.0 Hz, 2H), 2.96 (t, *J*=7.0 Hz, 2H), 2.90 (t, *J*=7.0 Hz, 2H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 170.60, 137.65, 128.99, 128.64, 126.75, 65.56, 37.80, 35.13, 25.86 ppm. HRMS (CI): Calcd for C₁₁H₁₄BrO₂⁺: 257.0177. Found: 257.0178.

Figure S18. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #14. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).

In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), 2,4-dimethoxybenzaldehyde (**1c**, 53.2 mg, 0.32 mmol), benzoic acid (**3d**, 39.1 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 2,2-dimethyl-1,3propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 2-phenylethanol (**4a**, 115 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 3 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

21C: ¹H NMR (500 MHz, CDCl₃): δ 8.10 (d, *J*=7.6 Hz, 2H), 7.59 (t, *J*=7.6 Hz, 1H), 7.47 (t, *J*=7.6 Hz, 2H), 7.26–7.38 (m, 5H), 4.59 (t, *J*=7.0 Hz, 2H), 3.13 (t, *J*=7.0 Hz, 2H) ppm. Spectral data agree with a previous literature report.¹⁴

Figure S19. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #15. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).

In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (**1a**, 62.8 mg, 0.32 mmol), benzaldehyde (**1e**, 32.5 μ L, 0.32 mmol), phenylacetic acid (**3a**, 43.6 mg, 0.32 mmol), *p*-anisidine (**2a**, 39.4 mg, 0.32 mmol), 2,2-dimethyl-1,3-propanediol (**6a**, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (**4c**, 63.4 mg, 0.32 mmol), 1,3-propanediol (**6d**, 69.4 μ L, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 2 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

22C: ¹H NMR (500 MHz, CDCl₃): δ 7.27–7.34 (m, 5H), 4.25 (t, *J*=6.0 Hz, 2H), 3.63 (s, 2H), 3.62 (q, *J*=5.9 Hz, 1H), 2.17 (s, 1H), 1.85 (quin, *J*=5.9 Hz, 2H), 1.67 (t, *J*=5.9 Hz, 1H) ppm. Spectral data agree with a previous literature report.¹⁵

22G: IR (neat): 3436, 2961, 2875, 1729, 1371, 1255, 1006, 696 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.25–7.34 (m, 5H), 3.94 (s, 1H), 3.65 (s, 1H), 3.19 (d, *J*=7.0 Hz, 1H), 0.85 (s, 6H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 172.37, 134.02, 129.33, 128.74, 127.33, 69.91, 68.32, 41.63, 36.57, 21.51 ppm. LRMS (ESI): Calcd for C₁₃H₁₉O₃⁺: 223.13. Found: 222.86.

22H: ¹H NMR (500 MHz, CDCl₃): δ 7.49 (dd, *J*=8.1, 1.4 Hz, 2H), 7.33–7.39 (m, 3H), 5.51 (s, 1H), 4.27 (ddd, *J*=11.5, 5.2, 1.2 Hz, 2H), 3.99 (td, *J*=12.6, 2.3 Hz, 2H), 2.19–2.27 (m, 1H), 1.44 (m, 1H) ppm. Spectral data agree with a previous literature report.¹⁶

Figure S20. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #16. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).

In a round-bottom flask fitted with a reflux condenser and a Dean-Stark adapter, compounds 2,4dinitrobenzaldehyde (1a, 62.8 mg, 0.32 mmol), 2,4-dimethoxybenzaldehyde (1c, 53.2 mg, 0.32 mmol), phenylacetic acid (3a, 43.6 mg, 0.32 mmol), *p*-anisidine (2a, 39.4 mg, 0.32 mmol), 2,2-dimethyl-1,3propanediol (6a, 33.3 mg, 0.32 mmol), 1,1-diphenylethanol (4c, 63.4 mg, 0.32 mmol), 1,6-hexanediol (6e, 113.4 mg, 0.96 mmol) and *p*-toluenesulfonic acid monohydrate (18.3 mg, 0.096 mmol) were dissolved in PhMe (60 mL). The solution was heated to reflux. After 3 d, a 1.0 mL aliquot was taken (temperature of the solution: 85 °C), dried in vacuo and analyzed using ¹H NMR with an internal standard.

23C (*monoester*): ¹H NMR (500 MHz, CDCl₃): δ 7.27–7.33 (m, 5H), 4.08 (t, J=6.8 Hz, 2H), 3.62 (t, J=6.8 Hz, 2H), 3.61 (s, 2H), 1.59–1.65 (m, 2H), 1.51–1.57 (m, 2H), 1.33–1.34 (m, 4H), 1.22 (t, J=5.4 Hz, 1H) ppm. Spectral data agree with a previous literature report.¹⁷

23C (*diester*): ¹H NMR (500 MHz, CDCl₃): δ 7.24–7.33 (m, 10H), 4.06 (t, *J*=6.8 Hz, 4H), 3.61 (s, 4H), 1.55–1.61 (m, 4H), 1.27–1.30 (m, 4H) ppm. Spectral data agree with a previous literature report.¹⁷

Figure S21. ¹H NMR spectra of the individual dehydration products and crude reaction mixture #17. For clarity, only the integration of the signature peaks of the observed products is shown in the ¹H NMR spectrum of the crude mixture (top).

Synthesis and Spectroscopic Characterization Data for New Compounds

Phenethyl-3-bromopropanoate (20C): Compounds 3-bromopropionic acid (153 mg, 1.0 mmol), 2-phenylethanol (122 mg, 120 μ L, 1.0 mmol) and *p*-toluenesulfonic acid monohydrate (10 mg) were dissolved in PhMe (10 mL), and heated at reflux under nitrogen with Dean-Stark trap for 24 h. The solution was dried in vacuo to give the crude product as pale yellow oil (154 mg, 60%). This compound readily loses HBr upon work-up and thus was analyzed as crude. IR (neat): 2957, 1733, 1232, 1173, 1131, 748, 699 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.21–7.32 (m, 5H), 4.35 (t, *J*=7.0 Hz, 2H), 3.54 (t, *J*=7.0 Hz, 2H), 2.96 (t, *J*=7.0 Hz, 2H), 2.90 (t, *J*=7.0 Hz, 2H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 170.60, 137.65, 128.99, 128.64, 126.75, 65.56, 37.80, 35.13, 25.86 ppm. HRMS (CI): Calcd for C₁₁H₁₄BrO₂⁺: 257.0177. Found: 257.0178.

Propane-1,3-diyl bis(2-phenylacetate). Phenylacetic acid (463 mg, 3.4 mmol), 1,3-propanediol (129.5 mg, 123 μ L, 1.7 mmol) and *p*-toluenesulfonic acid monohydrate (65 mg) were dissolved in PhMe (25mL) and heated at reflux under nitrogen with Dean-Stark trap for 24 h. The solution was cooled to room temperature, washed twice with 25mL of saturated aqueous solution of NaHCO₃, followed by brine and dried over anhydrous MgSO₄. The solution was dried in vacuo and passed through a short basic alumina column (eluted by hexane then 10% ethyl acetate in hexane) to give the title compound as a clear oil (258 mg, 49%). IR (neat): 2964, 1730, 1455, 1244, 1135, 1042, 695 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.25–7.33 (m, 10H), 4.13 (t, *J*=6.3 Hz, 4H), 3.61 (s, 4H), 1.94 (quin, *J*=6.4 Hz, 2H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 170.56, 137.59, 128.99, 128.64, 126.75, 65.46, 37.79, 35.11, 25.83 ppm. LRMS (ESI): Calcd for C₁₉H₂₁O₄⁺: 313.14. Found: 312.84.

3-Hydroxy-2,2-dimethylpropyl-2-phenylacetate (22G): Phenylacetic acid (136 mg, 1.0 mmol), 2,2-dimethyl-1,3-propanediol (417 mg, 4.0 mmol) and *p*-toluenesulfonic acid monohydrate (10 mg) were mixed in PhMe (10mL), and added into a thick-walled microwave pressure vial. A batch of 4 Å molecular sieves was added the vial was sealed and exposed to microwave irradiation for 1 h at 170 °C. After cooling, the solution was washed twice with 15 mL of saturated aqueous solution of NaHCO₃, followed by brine and dried over anhydrous MgSO₄. The solution was dried in vacuo and passed through a short basic alumina column (eluted by hexane, followed by 10% ethyl acetate in hexane) to give the title compound as a clear oil (120 mg, 54%). IR (neat): 3436, 2961, 2875, 1729, 1371, 1255, 1006, 696 cm⁻¹.¹H NMR (500 MHz, CDCl₃): δ 7.25–7.34 (m, SH), 3.94 (s, 1H), 3.65 (s, 1H), 3.19 (d, *J*=7.0 Hz, 1H), 0.85 (s, 6H) ppm.¹³C NMR (125 MHz, CDCl₃): δ 172.37, 134.02, 129.33, 128.74, 127.33, 69.91, 68.32, 41.63, 36.57, 21.51 ppm. LRMS (ESI): Calcd for C₁₃H₁₉O₃+: 223.13. Found: 222.86.

2,2-Dimethylpropane-1,3-diyl bis(2-phenylacetate). Phenylacetic acid (545 mg, 4.0 mmol), 2,2-dimethyl-1,3-propanediol (104 mg, 1.0 mmol) and *p*-toluenesulfonic acid monohydrate (10 mg) were mixed in PhMe (10 mL) and placed into a thick-walled microwave pressure vial. A batch of 4 Å molecular sieves was added, the vial was sealed and exposed to microwave irradiation for 1 h at 170 °C. After cooling, the solution was washed twice with 15 mL of saturated aqueous solution of NaHCO₃,

followed by brine and dried over anhydrous MgSO₄. The solution was dried in vacuo and passed through a short basic alumina column (eluted by hexane, followed by 10% ethyl acetate in hexane) to give the title compound as a clear oil (102 mg, 30%). IR (neat): 2966, 1731, 1372, 1248, 1135, 1005, 695 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.23–7.32 (m, 10H), 3.81 (s, 4H), 3.60 (s, 4H), 0.83 (s, 6H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 171.46, 134.06, 129.35, 128.67, 127.21, 69.40, 41.53, 34.80, 21.70 ppm. LRMS (ESI): Calcd for C₂₁H₂₅O₄⁺: 341.17. Found: 340.92.

2-(2,4-Dimethoxyphenyl)-1,3-dioxane (18B): Compounds 2,4-dimethoxybenzaldehyde (166 mg, 1.00 mmol), 1,3-propanediol (91.3 mg, 86.7 μL, 1.20 mmol) and *p*-toluenesulfonic acid monohydrate (10 mg) were dissolved in PhMe (10 mL). Anhydrous MgSO₄ was added to the solution, which was then stirred under nitrogen for 12 h at 80 °C. The solution was cooled to room temperature, washed twice with 15 mL of saturated aqueous solution of NaHCO₃, followed by brine and dried over anhydrous MgSO₄. The solution was dried in vacuo and passed through a short basic alumina column (eluted by hexane, followed by 10% ethyl acetate in hexane) to give the tile compound as a clear oil (95 mg, 42%). IR (neat): 2957, 2842, 1615, 1511, 1266, 1124, 1095, 1033, 982 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.52 (d, *J*=8.5 Hz, 1H), 6.50 (dd, *J*=8.5, 2.5 Hz, 1H), 6.42 (d, *J*=2.5 Hz, 1H), 5.79 (s, 1H), 4.23 (ddd, *J*=11.4, 5.3, 1.0 Hz, 2H), 3.98 (td, *J*=12.0, 2.5 Hz, 2H), 3.80 (s, 3H), 3.78 (s, 3H), 2.21 (m, 1H), 1.40 (dt, *J*=13.0, 1.0 Hz, 1H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 161.33, 157.55, 128.03, 120.05, 104.62, 98.34, 96.98, 67.73, 55.66, 55.47, 25.96 ppm. LRMS (ESI): Calcd for C₁₂H₁₇O₄⁺: 225.11. Found: 225.00.

2-(2,4-Dimethoxyphenyl)-5,5-dimethyl-1,3-dioxane **(9B)**: Compounds 2,4-dimethoxybenzaldehyde (166 mg, 1.00 mmol), 2,2-dimethyl-1,3-propanediol (104 mg, 1.0 mmol) and ptoluenesulfonic acid monohydrate (10 mg) were dissolved in PhMe (10 mL). Anhydrous MgSO4 was added to the solution, which was then stirred under nitrogen for 12 h at 80 °C. The solution was cooled to room temperature, washed twice with 15 mL of saturated aqueous solution of NaHCO₃, followed by brine and dried over anhydrous MgSO4. The solution was dried in vacuo and passed through a short basic alumina column (eluted with hexane, followed by 5% ethyl acetate in hexane, followed by 10% ethyl acetate in hexane) to give the title compound as a white crystalline solid (145 mg, 57%). Melting point: 71.5-72.5 °C. IR (neat): 2953, 2829, 1397, 1350, 1284, 1095, 1031, 824 cm⁻¹.¹H NMR (500 MHz, CDCl₃): δ 7.56 (d, J=8.4 Hz, 1H), 6.51 (dd, J=8.6, 2.4 Hz, 1H), 6.42 (d, J=2.3 Hz, 1H), 5.69 (s, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.73 (d, J=11.0 Hz, 2H), 3.65 (d, J=11.0 Hz, 2H), 1.31 (s, 3H), 0.76 (s, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 161.37, 157.69, 128.13, 119.78, 104.69, 98.40, 96.99, 77.98, 55.66, 55.49, 30.32, 23.18, 21.99 ppm. LRMS (ESI): Calcd for C₁₄H₂₁O₄+: 253.14. Found: 252.98.

2-(2,4-Dinitrophenyl)-1,3-dioxane: Compounds 2,4-dinitrobenzaldehyde (196 mg, 1.00 mmol), 1,3-propanediol (91.3 mg, 86.7 μ L, 1.20 mmol) and *p*-toluenesulfonic acid monohydrate (10 mg) were dissolved in PhMe (10 mL). The solution was stirred under nitrogen for 12 h at 80 °C. The solution was cooled to room temperature, washed twice with 15 mL of saturated aqueous solution of NaHCO₃, followed by brine and dried over anhydrous MgSO₄. The solution was dried in vacuo and passed through a short basic alumina column (eluted by hexane, followed by 10% ethyl acetate in hexane) to

give the title compounds as a white solid (214 mg, 84%). Melting point: 78–81 °C. IR (neat): 2870, 1533, 1349, 1094, 1023, 741, 717 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.66 (d, *J*=2.3 Hz, 1H), 8.43 (dd, *J*=8.6, 2.3 Hz, 1H), 8.10 (d, *J*=8.6 Hz, 1H), 6.11 (s, 1H), 4.25 (ddd, *J*=11.4, 5.1, 1.1 Hz, 2H), 4.02 (td, *J*=12.6, 2.7 Hz, 2H), 2.19 (m, 1H), 1.48 (d, *J*=13.7 Hz, 1H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 148.49, 147.88, 138.59, 129.59, 126.82, 119.67, 96.25, 67.83, 25.52 ppm. LRMS (APCI): Calcd for C₁₀H₉N₂O₆: 253.05. Found: 253.95.

2-(2,4-Dinitrophenyl)-5,5-dimethyl-1,3-dioxane (9E): Compounds 2,4-dinitrobenzaldehyde (196 mg, 1.00 mmol), 2,2-dimethyl-1,3-propanediol (104 mg, 1.0 mmol) and *p*-toluenesulfonic acid monohydrate (10 mg) were dissolved in PhMe (10 mL). The solution was stirred under nitrogen for 12 h at 80 °C, and was thencooled to room temperature, washed twice with 15 mL of saturated aqueous solution of NaHCO₃, followed by brine and dried over anhydrous MgSO₄. The solution was dried in vacuo and passed through a short basic alumina column (eluted with hexane, followed by 10% ethyl acetate in hexane) to give the title compound as an off-white solid (180 mg, 64%). Melting point: 94–96 °C. IR (neat): 2962, 2825, 1531, 1381, 1348, 1312, 1029, 719 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.66 (d, *J*=2.3 Hz, 1H), 8.44 (dd, *J*=8.6, 2.3 Hz, 1H), 8.14 (d, *J*=8.6 Hz, 1H), 6.00 (s, 1H), 3.76 (d, *J*=11.4 Hz, 2H), 3.68 (d, *J*=11.4 Hz, 2H), 1.21 (s, 3H), 0.80 (s, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 148.57, 147.92, 138.44, 129.65, 126.92, 119.59, 96.28, 77.98, 30.39, 23.14, 21.76 ppm. LRMS (APCI): Calcd for C₁₂H₁₃N₂O₆: 281.08. Found: 281.98.

2-(2,4-Dinitrophenyl)tetrahydro-3H-cyclopenta[**1,3**]**dioxole**. Compounds 2,4-dinitrobenzaldehyde (196 mg, 1.00 mmol), *cis*-1,2-cyclopentanediol (102 mg, 1.00 mmol) and *p*-toluenesulfonic acid monohydrate (10 mg) were dissolved in PhMe (10 mL). The solution was stirred under nitrogen for 12 h at 80 °C, and was then cooled to room temperature, washed twice with 15 mL of saturated aqueous solution of NaHCO₃, followed by brine and dried over anhydrous MgSO₄. The solution was dried in vacuo and passed through a short basic alumina column (eluted with hexane, followed first by 5% ethyl acetate in hexane, then 10% ethyl acetate in hexane) to give the title compound as a light-yellow solid (107 mg, 38%). Melting point: 89–91 °C. IR (neat): 2962, 1530, 1381, 1347, 1328, 1019, 726, 704 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.73 (d, *J*=2.3 Hz, 1H), 8.46 (dd, *J*=8.6, 2.3 Hz, 1H), 8.17 (d, *J*=8.6 Hz, 1H), 6.19 (s, 1H), 4.74 (dd, *J*=3.4, 1.2 Hz, 2H) 1.98 (dt, *J*=15.5, 2.8 Hz, 2H), 1.60 (m, 2H), 1.50 (m, 2H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 148.90, 148.13, 138.10, 129.84, 127.30, 119.82, 97.55, 82.67, 33.08, 22.54 ppm. LRMS (APCI): Calcd for C₁₂H₁₁N₂O₆: 279.06. Found: 279.97.

2-(2,4-Dinitrophenyl)-5-methylene-1,3-dioxane. Compounds 2,4-dinitrobenzaldehyde (196 mg, 1.00 mmol), 2-methylene-1,3-propanediol (88.1 mg, 81.5 μ L, 1.00 mmol) and *p*-toluenesulfonic acid monohydrate (10 mg) were dissolved in PhMe (10 mL). The solution was stirred under nitrogen for 24 h at 80 °C, and was then cooled to room temperature, washed twice with 15 mL of saturated aqueous solution of NaHCO₃, followed by brine and dried over anhydrous MgSO₄. The solution was dried in vacuo and passed through a short basic alumina column (eluted first with hexane, then 10% ethyl acetate in hexane) to give the title compound as a yellow solid (81 mg, 30%). Melting point: 84–86

°C. IR (neat): 2922, 2852, 1533, 1450, 1387, 1345, 1020, 828, 726 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.69 (d, *J*=2.3 Hz, 1H), 8.44 (dd, *J*=8.6, 2.3 Hz, 1H), 8.11 (d, *J*=8.6 Hz, 1H), 6.24 (s, 1H), 5.03 (s, 2H), 4.56 (d, *J*=13.0 Hz, 2H) 4.50 (d, *J*=13.0 Hz, 2H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 148.46, 148.00, 138.05, 137.26, 129.65, 126.92, 119.79, 112.08, 95.80, 71.56 ppm. LRMS (APCI): Calcd for C₁₁H₉N₂O₆⁻: 265.05. Found: 265.96.

N-(2,4-Dinitrobenzylidene)cyclohexanamine (14A): Compounds 2,4-dinitrobenzaldehyde (196 mg, 1.00 mmol) and cyclohexylamine (99.2 mg, 114 μL, 1.00 mmol) were dissolved in PhMe (10 mL). The solution was stirred under nitrogen for 12 h at 80 °C. The solvent was removed in vacuo to give the title imine as yellow-orange solid in quantitative yield. Melting point: 75–76 °C. IR (neat): 3089, 2928, 1634, 1594, 1528, 1384, 1343, 904 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.84 (d, *J*=2.3 Hz, 1H), 8.75 (s, 1H), 8.45 (dd, *J*=8.7, 2.3 Hz, 1H), 8.32 (d, *J*=8.7 Hz, 1H), 3.39 (m, 1H), 1.81 (dt, *J*=13.5, 3.8 Hz, 2H), 1.78 (dd, *J*=13.2, 3.5 Hz, 2H), 1.69 (dt, *J*=12.7, 3.8 Hz, 1H), 1.59 (qd, *J*=12.2, 3.4 Hz, 2H), 1.39 (qt, *J*=12.1, 3.0 Hz, 2H), 1.28 (qt, *J*=12.3, 3.5 Hz, 1H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 152.79, 148.73, 148.30, 136.63, 131.67, 127.45, 120.08, 70.26, 34.05, 25.59, 24.49 ppm. HRMS (CI): Calcd for C₁₃H₁₆N₃O₄⁺: 278.1141. Found: 278.1135.

4-Chloro-*N***-**(**2**,**4**-dinitrobenzylidene)**aniline** (**15A**): Compounds 2,4-dinitrobenzaldehyde (196 mg, 1.0 mmol) and 4-chloroaniline (127.6mg, 1.0 mmol) were dissolved in PhMe (10 mL). The solution was stirred under nitrogen for 12 h at 80 °C. The solvent was removed in vacuo to give the title imine as a red-orange solid in quantitative yield. Melting point: 161–163 °C. IR (neat): 3107, 1594, 1522, 1395, 1337, 1090, 835 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.99 (s, 1H), 8.93 (d, *J*=2.3 Hz, 1H), 8.58 (d, *J*=8.3 Hz, 1H), 8.55 (dd, *J*=8.5, 2.3 Hz, 1H), 7.42 (d, *J*=8.7 Hz, 1H), 7.27 (d, *J*=8.7 Hz, 1H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 153.62, 149.18, 148.76, 148.53, 135.83, 133.95, 131.53, 129.73, 127.66, 122.90, 120.49 ppm. HRMS (CI): Calcd for C₁₃H₂ClN₃O₄⁺: 306.0282. Found: 306.0281.

4-Chloro-*N***-**(**2**,**4-dimethoxybenzylidene**)**aniline**. Compounds 2,4-methoxybenzaldehyde (166 mg, 1.00 mmol) and 4-chloroaniline (128 mg, 1.00 mmol) were dissolved in PhMe (10 mL). The solution was stirred under nitrogen for 12 h at 80 °C, and the solvent was then removed in vacuo to give the title imine as a white solid in quantitative yield. Melting point: 73.5–74.5 °C. IR (neat): 2947, 1608, 1583, 1291, 1275, 1159, 1029, 819 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.77 (s, 1H), 8.08 (d, *J*=8.6 Hz, 1H), 7.31 (d, *J*=8.7 Hz, 2H), 7.13, (d, *J*=8.6 Hz, 2H), 6.58 (dd, *J*=8.7, 2.3 Hz, 1H), 6.46 (d, *J*=2.2 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 164.04, 161.10, 156.39, 151.64, 130.76, 129.15, 129.05, 122.50, 118.01, 105.80, 98.08, 55.63 ppm. LRMS (ESI): Calcd for C₁₅H₁₅ClNO₂⁺: 276.08. Found: 276.17.

5,5-Dimethyl-2-(perfluorophenyl)-1,3,2-dioxaborinane (8B): Compounds pentafluorophenylboronic acid (212 mg, 1.00 mmol) and 2,2-dimethyl-1,3-propanediol (104 mg, 1.00 mmol) were dissolved in PhMe (10 mL). The solution was stirred under nitrogen for 12 h at 80 °C, and the solvent was then evaporated in vacuo to give the title compound as a white crystalline product in quantitative yield. Melting point: 73–75 °C. IR (neat): 2962, 1386, 1325, 1255, 1205, 1143, 1122, 666 cm^{-1. 1}H NMR (500 MHz, CDCl₃): δ 3.81 (s, 3H), 1.06 (s, 6H) ppm. ¹³C NMR (125 MHz, CDCl₃): δ 149.53, 147.58, 143.25, 141.20, 138.22, 136.16, 72.92, 32.00, 21.85 ppm. ^{19}F NMR (470 MHz, CDCl₃): –131.78 to –131.85 (m, 2F), –151.72 to –151.82 (m, 1F), –162.03 to –162.14 (m, 2F) ppm. HRMS (CI): Calcd for C₁₁H₁₁BF₅O₂+: 281.0772. Found: 281.0760.

NMR Spectral Data for New Compounds

¹³C NMR (CDCl₃, 125 MHz) Propane-1,3-diyl bis(2-phenylacetate)

¹³C NMR (CDCl₃, 125 MHz)3-Hydroxy-2,2-dimethylpropyl-2-phenylacetate (22G)

¹H NMR (CDCl₃, 500 MHz) 2-(2,4-dimethoxyphenyl)-1,3-dioxane (**18B**)

¹³C NMR (CDCl₃, 125 MHz) 2-(2,4-dimethoxyphenyl)-1,3-dioxane (**18B**)

¹H NMR (CDCl₃, 500 MHz) 2-(2,4-dimethoxyphenyl)-5,5-dimethyl-1,3-dioxane (**9B**)

¹³C NMR (CDCl₃, 125 MHz) 2-(2,4-dimethoxyphenyl)-5,5-dimethyl -1,3-dioxane (**9B**)

¹³C NMR (CDCl₃, 125 MHz)2-(2,4-dinitrophenyl)-1,3-dioxane

¹H NMR (CDCl₃, 500 MHz) 2-(2,4-dinitrophenyl)-5,5-dimethyl-1,3-dioxane (**9E**)

¹³C NMR (CDCl₃, 125 MHz)2-(2,4-dinitrophenyl)-5,5-dimethyl-1,3-dioxane (9E)

¹H NMR (CDCl₃, 500 MHz) 2-(2,4-dinitrophenyl)tetrahydro-3H-cyclopenta[1,3]dioxole

¹³C NMR (CDCl₃, 125 MHz)2-(2,4-dinitrophenyl)tetrahydro-3H-cyclopenta[1,3]dioxole

¹H NMR (CDCl₃, 500 MHz) 2-(2,4-dinitrophenyl)-5-methylene-1,3-dioxane

¹³C NMR (CDCl₃, 125 MHz)2-(2,4-dinitrophenyl)-5-methylene-1,3-dioxane

ŅO₂

`NO₂

`N

¹³C NMR (CDCl₃, 125 MHz) N-(2,4-dinitrobenzylidene)cyclohexanamine (**14A**)

¹³C NMR (CDCl₃, 125 MHz)
4-Chloro-N-(2,4-dinitrobenzylidene)aniline (15A)

¹³C NMR (CDCl₃, 125 MHz)4-Chloro-N-(2,4-dimethoxybenzylidene)aniline

¹H NMR (CDCl₃, 500 MHz) 5,5-Dimethyl-2-(perfluorophenyl)-1,3,2-dioxaborinane (**8B**)

¹³C NMR (CDCl₃, 125 MHz) 5,5-Dimethyl-2-(perfluorophenyl)-1,3,2-dioxaborinane (**8B**)

¹⁹F NMR (CDCl₃, 470 MHz) 5,5-Dimethyl-2-(perfluorophenyl)-1,3,2-dioxaborinane (**8B**)

References

- 1 Lirag, R. C.; Osowska, K.; Miljanić, O. Š. Org. Biomol. Chem. **2012**, *10*, 4847–4850.
- 2 Zhang, J.; Wu, H.-H.; Zhang, J. Eur. J. Org. Chem. 2013, 28, 6263–6266.
- 3 Andrus, M. B.; Harper, K. C.; Christiansen, M. A.; Binkley, M. A. *Tetrahedron Lett.* 2009, 50, 4541–4544.
- 4 Alberti, M. N.; Orfanopoulos, M. Org. Lett. **2008**, *10*, 2465–2468.
- 5 Vaccaro, W. D.; Sher, R.; Davis, Jr. H. R. Bioorg. Med. Chem. 1998, 6, 1429–1437.
- 6 Smith, B. M.; Kubczyk, T. M.; Graham, A. E. *Tetrahedron* **2012**, *68*, 7775–7781.
- 7 Kumar, A.; Samuelson, A. G. J. Organomet. Chem. 2010, 695, 338–345.
- 8 Bennett, J. S.; Charles, K. L.; Miner, M. R.; Heuberger, C. F.; Spina, E. J.; Bartels, M. F.; Foreman, T. *Green Chem.* **2009**, *11*, 166–168.
- 9 Sarkart, A.; Yemult, O. S.; Bandgar, B. P. Org. Prep. Proced. Int. 1996, 28, 613–617.
- 10 Osowska, K.; Miljanić, O. Š. Angew. Chem. Int. Ed. 2011, 50, 8345–8349.
- 11 Gladding, J. A.; Bacci, J. P.; Shaw, S. A.; Smith, III A. B. *Tetrahedron* **2011**, 67, 6697–6706.
- 12 Kim., E. J.; Ko, S. Y. Bioorgan. Med. Chem. 2005, 13, 4103–4112.
- 13 Yamamoto, N.; Obora, Y.; Ishii, Y. J. Org. Chem. 2011, 76, 2937–2941.
- 14 Kamijo, S.; Amaoka, Y.; Inoue, M. *Tetrahedron Lett.* **2011**, *52*, 4654–4657.
- 15 Kuhakarn, C.; Panchan, W.; Chiampanichayakul, S.; Samakkanad, N.; Pohmakotr, M.; Reutrakul, V.; Jaipetch, T. *Synthesis* **2009**, *6*, 929–934.
- 16 Myles, L.; Gathergood, N.; Connon, S. J. *Chem. Commun.* **2013**, *49*, 5316–5318.
- 17 Pfaff, D.; Nemecek, G.; Podlech, J. Beilstein J. Org. Chem. 2013, 9, 1572–1577.