Supporting Information

Using *N*-nitrosodichloroacetamides to conveniently convert
linear primary amines into alcohols

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1. Additional Data from the Rearrangement and Nitrosylation Reactions

Table S1: Thermal rearrangements of some *N*-nitrosoamides.

Nitrosoamide	Entry	Conditions	Temperature	Time	Conversion	Product Distribution (Ester / Alkene)
S1	1	standard	85 °C	5 h	93%	5.0 : 1
	2	standard	70 °C	24 h	89%	4.8 : 1
S2	3	standard	50 °C	24 h	full	7.0 : 1
	4	standard	50 °C	5 h	47%	6.8 : 1
S3	5	standard	50 °C	24 h	full	7.7 : 1
	6	standard	50 °C	5 h	72%	8.7 : 1
3	7	standard	40 °C	24 h	full	6.9 : 1
	8	standard	40 °C	5 h	75%	6.0 : 1
	9	standard (solvent = toluene)	50 °C	24 h	full	5.4 : 1
	10	solvent = EtOAc	50 °C	24 h	full	6.4 : 1
	11	solvent = CCl ₄	50 °C	24 h	91%	5.8 : 1
	12	solvent = hexane	50 °C	24 h	84%	5.6 : 1

Conditions: 0.1 M in toluene or the indicated solvent, warmed for the indicated time and temperature, solvent removed, conversion and product distribution measured by ¹H NMR of the crude product.

Table S2: *N*-nitrosoamide rearrangements that produce additional byproducts.

Nitrosoamide	Entry	Conditions	Temperature	Time	Conversion	Product Distribution
 S3	1	toluene (standard)	50 °C	24 h	full	88 (D) : 12 (E)
	2	toluene + 1 equiv TEA	50 °C	24 h	full	89 (D) : 11 (E)
	3	toluene + 1 equiv AcOH	50 °C	24 h	full	53 (D) : 36 (A) : 11 (E)
	4	toluene + 1 equiv AcOH and TEA	50 °C	24 h	full	53 (D) : 36 (A) : 11 (E)
 S4	5	5:1 Ac ₂ O / AcOH	0 °C during nitrosylation	full	53 (A) : 22 (E) : 10 (R) : 15 (D)	
	6	5:1 Ac ₂ O / DCA	0 °C during nitrosylation	full	36 (C) : 23 (A) : 22 (E) : 7 (R) : 12 (D)	
	7	5:1 Ac ₂ O / TFA	0 °C during nitrosylation	full	64 (D) : 15 (A) : 17 (E) : 4 (R)	
	8	5:1 TFAA / TFA	0 °C during nitrosylation	full	messy: approx. 50 (D) : 50 (other)	

Conditions: For entries 1–4: 0.1 M in the indicated solvent, warmed for the indicated time and temperature, solvent removed, crude product analyzed. For entries 5–8: crude product from the nitrosylation reaction analyzed. Conversion and product distribution measured by ¹H NMR. Abbreviations: DCA = dichloroacetic acid, TFA = trifluoroacetic acid, TFAA = trifluoroacetic anhydride.

Table S3: *N*-Nitrosylation of some amides.

Amide	Entry	Solvent	Conversion	Spontaneous Rearrangement
S5	1	standard	full	none
S6	2	standard	full	none
27	3	0.1 M (for solubility)	full	none
2	4	standard	77%	8%
	5	5:1 Ac ₂ O / DCA	full	8%
S7	6	standard	55%	full
	7	5:1 Ac ₂ O / DCA	84%	full
	8	5:1 Ac ₂ O / TFA	full	full

Conditions: 0.3 M in 5:1 acetic anhydride / acetic acid or indicated solvent mixture, dry, 0 °C, 2 equiv NaNO₂, 2 h, additional 2 equiv NaNO₂, additional 4 h, conversion and product distribution measured by ¹H NMR of the crude product. Abbreviations: DCA = dichloroacetic acid, TFA = trifluoroacetic acid.

2. Synthetic Procedures

2.1 Abbreviations

DCM = dichloromethane	HOBT hydrate = hydroxybenzotriazole hydrate
DMF = <i>N,N</i> -dimethylformamide	MeOH = methanol
DMSO = dimethylsulfoxide	Quant = quantitative conversion
EDC hydrochloride = <i>N</i> -(3-dimethylaminopropyl)- N'-ethylcarbodiimide hydrochloride	TEA = triethylamine
Ether = diethyl ether	TFA = trifluoroacetic acid
EtOAc = ethyl acetate	THF = tetrahydrofuran
	y = yield

2.2 General Procedures

Column chromatography was performed with 60 Å 40–63 µm silica-P flash silica gel.

Solvents for reactions (DMF, DCM, THF, and toluene) were dried using a LC Technology Solutions purification system. Other solvents were used as received unless noted otherwise.

Chemicals were purchased from Fisher, VWR, or Sigma-Aldrich and used as received unless noted otherwise.

NMR Spectra were measured in CDCl₃ at ambient temperature unless otherwise noted.

¹H NMR spectra were recorded on either a 600 or 200 MHz Varian spectrometer. Chemical shifts are reported in ppm (δ) relative to tetramethylsilane using the solvent as a reference (CDCl₃ = 7.26 ppm, DMSO-*d*₆ = 2.49 ppm, D₂O = 4.80 ppm, CD₃OD = 3.30). The following is an example data point: chemical shift (multiplicity [s = singlet, d = doublet, t = triplet, q = quartet, pent = pentet, sext = sextet, sept = septet, oct = octet, m = multiplet, br = broad, and combinations thereof], coupling constants [Hz], integration, assignment [if any]).

¹³C NMR spectra were recorded on a 600 or 200 MHz (150 or 50 MHz) Varian spectrometer with complete proton decoupling. Chemical shifts are reported in ppm (δ) relative to tetramethylsilane using the solvent or MeOH as a reference (CDCl₃ = 77.0 ppm, DMSO-*d*₆ = 39.5 ppm, CD₃OD = 49.0 ppm, MeOH = 49.5).

IR spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR spectrometer with Perkin Elmer Spectrum software. Spectra are partially reported (ν_{max} , cm⁻¹).

HRMS were obtained at The University of Illinois Urbana-Champaign.

TLC was performed on 60 Å F₂₅₄ pre-coated silica gel plates. Samples were visualized by either ultraviolet irradiation, potassium permanganate staining, or cerium ammonium molybdenate staining.

Yield refers to isolated material.

Quantitative recovery means that mostly pure material was recovered in approximately the expected mass, and the material was used directly for the next step without purification.

2.3 Standard Amine-to-Alcohol Conversion Procedure

Standard dichloroacetylation procedure Into a flask were added the starting free amine (1 equiv), distilled EtOAc (1 M), and methyl dichloroacetate (1.5 equiv). The mixture was stirred at ambient temperature overnight. Volatiles were removed under reduced pressure to yield the dichloroacetamide, which was used directly for the subsequent reaction.

Standard nitrosylation procedure The crude dichloroacetamide was dissolved in the required solvent mixture (typically 0.3 M in 1:1 acetic anhydride / dichloroacetic acid). The flask was capped with a rubber septum and stirred in an ice bath (0 °C, 30 min). To the mixture was added solid sodium nitrite (2 equiv, creating a blue solution and slowly evolving brown gas). The flask was capped with a rubber septum and vented with a syringe packed with anhydrous calcium sulfate, and stirred (2 h). To the mixture was added additional sodium nitrite (2 equiv). The mixture was stirred (additional 4 h), diluted with EtOAc (0.1 M), washed with cold water (equal volume) and then cold sodium carbonate (10% aqueous, 3 x equal volume), diluted with cold sodium carbonate (10% aqueous, equal volume), and stirred rapidly (30 min, to quench any remaining anhydride). The organic phase was isolated, washed with potassium phosphate monobasic (1 M aqueous, pH 5, equal volume), dried with sodium sulfate, and used directly for the subsequent transformation without removing the solvent.

Standard rearrangement procedure The solution of the crude *N*-nitrosoamide was warmed in an oil bath (40 °C, 24 h). Volatiles were removed under reduced pressure to yield the crude dichloroacetate ester, which was used directly for the subsequent transformation.

Standard hydrolysis procedure The crude dichloroacetate ester was dissolved in MeOH (0.2 M), and TEA (2 equiv) was added. The mixture was stirred (2 h), diluted with potassium phosphate monobasic (1 M aqueous, pH 5, 0.5 M), stirred (10 min), further diluted with water, extracted with EtOAc, and dried with sodium sulfate. Volatiles were removed under reduced pressure to yield a crude alcohol, which was purified by silica gel chromatography.

2.4 Conversion of Amine 1 to Alcohol 5 (as an Example of the Standard Procedure)

Synthesis of dichloroacetamide 2 Into a flask were added ester **1** (1.10 g, 5.10 mmol, 1 equiv), EtOAc (distilled, 5 mL, 1 M), and methyl dichloroacetate (**2a**, 0.79 mL, 7.6 mmol, 1.5 equiv). The mixture was stirred at ambient temperature (21 h). Volatiles were removed under reduced pressure to yield crude amide **2** (1.64 g, full conversion, 99% mass recovery, white solid), which was used directly for the subsequent reaction. For analysis, an aliquot was purified by column chromatography (silica gel, 5:1 hexane/EtOAc) to yield pure amide **2**.

¹H NMR (CDCl₃, 200 MHz) δ 6.50 (brs, 1H, NH), 5.92 (s, 1H, Cl₂CH), 3.67 (s, 3H, OMe), 3.33 (q, J = 6.9 Hz, 2H, N-CH₂), 2.30 (t, J = 7.5 Hz, 2H, CH₂C=O), 1.70–1.47 (m, 4H, 2 x CH₂), 1.40–1.16 (m, 12H, (CH₂)₆).

¹³C NMR (CDCl₃, 50 MHz) δ 174.31, 163.98, 66.48, 51.44, 40.35, 34.06, 29.31, 29.23, 29.14, 29.08, 29.05, 26.62, 24.88.

IR (neat, cm⁻¹) 3267, 3090, 2919, 2851, 1720, 1662, 1559, 1166, 812, 655.

TLC (3:1) hexane/EtOAc, permanganate, R_f = 0.52.

HRMS calculated for [C₁₄H₂₅Cl₂NO₃H]⁺, requires m/z = 326.1290, found m/z = 326.1290 (ESI).

Synthesis of *N*-nitrosoamide 3 Into a flask were added crude amide **2** (5.04 mmol, 1 equiv) and a 1:1 mixture of dichloroacetic acid and acetic anhydride (16 mL, 0.3 M). The flask was capped with a rubber septum, sealed with tape, and cooled in an ice bath (0 °C, 30 min). To the mixture was added sodium nitrite (696 mg, 10.1 mmol, 2 equiv, producing a blue solution and slowly evolving some brown gas). The flask was capped with a rubber septum, sealed with tape, vented through a syringe packed with anhydrous calcium sulfate, and stirred in an ice bath (0 °C, 2 h). To the mixture was added additional sodium nitrite (696 mg, 10.1 mmol, 2 equiv). The mixture was stirred in an ice bath (0 °C, additional 4 h), diluted with EtOAc (40 mL), and washed with cold water (40 mL) and then cold sodium carbonate (10% aqueous, 50 + 2 x 40 mL). To quench any remaining anhydride, the organic phase was mixed with sodium carbonate (10% aqueous, 40 mL), maintained in an ice bath (0 °C), and stirred rapidly (30 min). The organic phase was isolated, washed with potassium phosphate monobasic (1 M aqueous, pH 5, 3 x 40 mL), and dried with sodium sulfate. The crude solution of *N*-nitrosoamide **3** was used directly for the subsequent transformation. An aliquot was removed for analysis. Volatiles were removed under reduced pressure from this aliquot, but since the product is not fully stable to silica gel or prolonged storage, analytical data was collected from the crude sample.

¹H NMR (CDCl₃, 200 MHz, major signals) δ 7.23 (s, 1H, CHCl₂), 3.79 (t, J = 7.3, 2H, N-CH₂), 3.67 (s, 3H, OMe), 2.30 (t, J = 7.5 Hz, 2H, O=C-CH₂), 1.72–1.48 (m, 2H, CH₂), 1.48–1.10 (m, 14H, (CH₂)₇).

¹³C NMR (CDCl₃, 50 MHz, major signals) δ 174.22, 167.01, 63.79, 51.34, 39.76, 33.94, 29.07, 28.81, 26.48, 26.29, 24.78.

IR (neat, cm⁻¹) 2928, 2854, 1735, 1528, 806.

TLC (3:1, major spot) hexane/Et₂O, UV & permanganate, R_f = 0.71.

HRMS decomposes to ester **4**.

Synthesis of Ester 4 The solution of crude *N*-nitrosoamide **3** (0.1 M in EtOAc) was warmed in an oil bath (40 °C, 12 h). Volatiles were removed under reduced pressure to yield crude ester **4** (1.61 g, 98% mass recovery, full consumption of starting material, 7:1 rearrangement / elimination, yellow oil), which was used directly in the

subsequent reaction. For analysis, an aliquot was purified by column chromatography (silica gel, 10:1 hexane/Et₂O) to yield pure ester **4**. The product ratio was determined by integration of the ¹H NMR spectrum of the crude material.

¹H NMR (CDCl₃, 200 MHz) δ 5.94 (s, 1H, Cl₂CH), 4.27 (t, *J* = 6.6 Hz, 2H, O–CH₂), 3.67 (s, 3H, OMe), 2.30 (t, *J* = 7.5 Hz, 2H, O=C–CH₂), 1.79–1.53 (m, 4H, 2 x CH₂), 1.46–1.17 (m, 12H, (CH₂)₆).

¹³C NMR (CDCl₃, 50 MHz) δ 174.29, 164.59, 67.70, 64.33, 51.44, 34.06, 29.31, 29.25, 29.16, 29.07, 29.03, 28.21, 25.55, 24.89.

IR (neat, cm^{–1}) 2927, 2855, 1763, 1737, 1463, 1436, 1279, 1166, 814.

TLC (8:1) hexane/Et₂O, permanganate, *R_f* = 0.41.

HRMS calculated for [C₁₄H₂₄Cl₂O₄H]⁺, requires *m/z* = 327.1130, found *m/z* = 327.1129 (ESI).

Terminal alkene **4a** is the major elimination product, and a trace amount of internal alkene **4b** is also observed. For analysis, an aliquot was purified by column chromatography. An inseparable mixture of the alkenes was isolated (silica gel, 10:1 hexane/Et₂O, co-eluting). Compound analysis is consistent with published data.¹

Terminal alkene **4a**:

¹H NMR (major signals) (CDCl₃, 200 MHz) δ 5.81 (ddt, 1H, *J_t* = 6.6 Hz, *J_d* = 10.1, 16.7 Hz, CH=C), 5.06–4.87 (m, 2H, CH₂=C), 3.67 (s, 3H, OMe), 2.31 (t, *J* = 7.5 Hz, 2H, O=C–CH₂), 2.04 (q, *J* = 6.5 Hz, 2H, CH₂–C=C), 1.76–1.50 (m, 2H, CH₂), 1.50–1.07 (m, 10 H, (CH₂)₅).

TLC (10:1) hexane/Et₂O, permanganate, *R_f* = 0.49.

Internal alkene **4b**:

¹H NMR (minor signals) (CDCl₃, 200 MHz) δ 5.46–5.35 (m, 2H, CH=CH), other signals overlap with those of terminal alkene **4a**.

TLC (10:1) hexane/Et₂O, permanganate, *R_f* = 0.49 (overlapping alkene **4a**).

Synthesis of alcohol 5 Into a flask were added crude ester **4** (4.92 mmol, 1 equiv), MeOH (25 mL, 0.2 M), and TEA (1.40 mL, 9.84 mmol, 2 equiv). The mixture was stirred (2 h), diluted with potassium phosphate monobasic (1 M aqueous, pH 5, 10 mL) and water (25 mL), extracted with EtOAc (40 + 20 + 10 mL), and dried with sodium sulfate. Volatiles were removed under reduced pressure, and the crude material was purified by column chromatography (50 mL silica gel, [3:1 to 2:1] hexane/EtOAc) to yield alcohol **5** (0.721 g, 3.35 mmol, 66% yield from amine **1**, colorless oil). Compound analysis is consistent with published data.²

¹H NMR (CDCl₃, 200 MHz) δ 3.67 (s, 3H, OMe), 3.67–3.59 (m, 2H, O–CH₂), 2.30 (t, *J* = 7.5, O=C–CH₂), 1.70–1.47 (m, 4H, 2 x CH₂), 1.42–1.20 (m, 12H, (CH₂)₆).

TLC (2:1) hexane/EtOAc, permanganate, *R_f* = 0.36.

¹ Compound data from: Condorelli, G. G.; Motta, A.; Fragala, I. L.; Giannazzo, F.; Raineri, V.; Caneschi, A.; Gatteschi, D. *Angew. Chem., Int. Ed.* **2004**, *43*, 4081–4084.

² Compound data from: Miyamoto, K.; Sei, Y.; Yamaguchi, K.; Ochiai, M. *J. Am. Chem. Soc.* **2009**, *131*, 1382–1383.

2.5 Amine-to-Alcohol Reactions from the Substrate Scope Table

Synthesis of 1-nonanol (7) The standard procedure was followed beginning with nonylamine (**6**, 500 mg, 3.49 mmol, 1 equiv). To minimize loss of material into the aqueous washes, the workup of the nitrosylation step was modified to use 1:1 mixtures of brine and 10% sodium carbonate for the base washes and a 1:1 mixture of brine and water for the final wash. The crude product was purified by column chromatography (3:2 hexane/Et₂O, 40 mL silica gel) to yield 1-nonanol (**7**, 282 mg, 1.97 mmol, 56% yield). Prolonged exposure to high vacuum was avoided due to the product's moderate volatility (BP = 214 °C). Compound analysis is consistent with data from commercially available material.³

¹H NMR (CDCl₃, 200 MHz) δ 3.64 (t, J = 6.5 Hz, 2H, O–CH₂), 1.66–1.46 (m, 2H, O–C–CH₂), 1.43–1.12 (m, 12H, (CH₂)₆), 0.89 (t, J = 6.9 Hz, 3H, CH₃).

TLC (3:2) hexane/Et₂O, permanganate, R_f = 0.34.

Synthesis of alcohol 9 The standard procedure was followed beginning with 3-phenylpropylamine (**8**, 500 mg, 3.70 mmol, 1 equiv). The crude product was purified by column chromatography (1:1 hexane/Et₂O, 40 mL silica gel) to yield alcohol **9** (254 mg, 1.88 mmol, 50% yield). Compound analysis is consistent with data from commercially available material.⁴

¹H NMR (CDCl₃, 200 MHz) δ 7.34–7.14 (m, 5H, Ar), 3.68 (t, J = 6.3, 2H, O–CH₂), 2.72 (t, J = 7.6 Hz, 2H, Ar–CH₂), 1.91 (pent, J = 7.0, 2H, CH₂), 1.26 (brs, 1H, OH).

TLC (1:1) hexane/Et₂O, permanganate, R_f = 0.31.

Synthesis of alcohol 11 The standard procedure was followed beginning with amine **10** (491 mg, 2.22 mmol, 1 equiv). The crude product was purified by column chromatography (2:1 hexane/EtOAc, 40 mL silica gel) to yield alcohol **11** (256 mg, 1.16 mmol, 52% yield). Compound analysis is consistent with published data.⁵

¹H NMR (CDCl₃, 200 MHz) δ 7.39–7.31 (m, 5H, Ar), 5.12 (s, 2H, Bn), 3.64 (t, J = 6.4 Hz, 2H, CH₂–O), 2.38 (t, J = 7.4 Hz, 2H, O=C–CH₂), 1.79–1.24 (m, 6H, (CH₂)₃).

TLC (2:1) hexane/EtOAc, permanganate, R_f = 0.18.

³ Compound data from: www.sigmaaldrich.com

⁴ Compound data from: Chen, G.; Fu, C.; Ma, S. *Tetrahedron* **2006**, 62, 4444–4452.

⁵ Compound data from: Samori, C.; Ali-Boucetta, H.; Sainz, R.; Guo, C.; Toma, F.; Fabbro, C.; de Ros, T.; Prato, M.; Kostarelos, K.; Bianco, A. *Chem. Comm.* **2010**, 46, 1494–1496.

Synthesis of alcohol 13 The standard procedure was followed beginning with amine **12** (1.06 g, 3.71 mmol, 1 equiv). The crude product was purified by column chromatography (2:1 EtOAc/hexane, 40 mL silica gel) to yield alcohol **13** (487 mg, 1.71 mmol, 46% yield).

¹H NMR (CDCl₃, 200 MHz) δ 3.64 (t, J = 6.6 Hz, 2H, O–CH₂), 3.32–3.13 (m, 4H, CH₂–N–CH₂), 2.28 (t, J = 7.5 Hz, 2H, O=C–CH₂), 1.76–1.44 (m, 6H, 2 x CH₂–C–N, CH₂–C–O), 1.44–1.20 (m, 14H, (CH₂)₇), 0.90 (q, J = 7.5 Hz, 6H, 2 x CH₃).

¹³C NMR (CDCl₃, 50 MHz) δ 172.58, 62.10, 49.30, 47.12, 32.75, 32.39, 29.07, 25.46, 25.16, 21.92, 20.55, 10.94, 10.84.

IR (neat, cm^{–1}) 3428, 2925, 1624, 1464, 1425.

TLC (1:1) hexane/EtOAc, permanganate, R_f = 0.33.

HRMS calculated for [C₁₇H₃₅NO₂H]⁺, requires m/z = 286.2746, found m/z = 286.2748 (ESI).

Synthesis of alcohol 15 The standard procedure was followed beginning with amine **14** (332 mg, 1.24 mmol, 1 equiv). The crude product was purified by column chromatography (3:1 hexane/Et₂O, 40 mL silica gel) to yield alcohol **15** (148 mg, 0.569 mmol, 46% yield). Compound analysis is consistent with published data.⁶

¹H NMR (CDCl₃, 200 MHz) δ 3.73–3.60 (m, 4H, 2 x O–CH₂), 1.68–1.30 (m, 9 H, (CH₂)₃, 3 x iPr), 1.10–1.04 (brs, 18 H, 3 x iPr).

TLC (3:1) hexane/Et₂O, permanganate, R_f = 0.28.

Synthesis of alcohol 17 The standard procedure was followed beginning with amine **16** (308 mg, 1.57 mmol, 1 equiv). The crude product was purified by column chromatography (2:1 EtOAc/hexane, 30 mL silica gel) to yield alcohol **17** (230 mg, 1.16 mmol, 74% yield). Compound analysis is consistent with published data.⁷

¹H NMR (CDCl₃, 200 MHz) δ 8.20 (d, J = 9.2 Hz, 2H, Ar), 6.97 (d, J = 9.3 Hz, 2H, Ar), 4.22 (t, J = 6.2 Hz, 2H, Ar–O–CH₂), 3.88 (t, J = 6.0 Hz, 2H, O–CH₂), 2.09 (pent, J = 6.0 Hz, 2H, C–CH₂–C), 1.52 (bs, 1H, OH).

TLC (2:1) EtOAc/hexane, permanganate, R_f = 0.34.

Synthesis of alcohol 19 The standard procedure was followed beginning with 2-ethylhexylamine (**18**, 500 mg, 3.87 mmol, 1 equiv). To minimize loss of material into the aqueous washes, the workup of the nitrosylation step was

⁶ Compound data from: Crimmins, M. T.; Vanier, G. S. *Org. Lett.* **2006**, 8, 2887–2890.

⁷ Compound data from: Steel W. H.; Damkaci, F.; Nolan, R.; Walker, R. A. *J. Am. Chem. Soc.* **2002**, 124, 4824–4831.

modified to use 1:1 mixtures of brine and 10% sodium carbonate for the base washes and a reduced amount of potassium phosphate monobasic for the final wash. Similarly, the workup of the hydrolysis step was modified to use a dilution of 50% brine rather than water. The crude product was purified by column chromatography (3:2 hexane/Et₂O, 50 mL silica gel) to yield alcohol **19** (247 mg, 1.89 mmol, 49% yield). Prolonged exposure to high vacuum was avoided due to the product's moderate volatility (BP = 180 °C). Compound analysis is consistent with data from commercially available material.⁸

¹H NMR (CDCl₃, 600 MHz) δ 3.55 (d, J = 5.4 Hz, 2H, O–CH₂), 1.44–1.24 (m, 9H, CH, 4 x CH₂), 0.90 (t, J = 7.4 Hz, 6H, 2 x CH₃).

TLC (3:2) hexane/ether, permanganate, R_f = 0.46.

⁸ Compound data from: www.sigmaaldrich.com

2.6 Synthesis of Amine Substrates from the Substrate Scope Table

Synthesis of ester hydrochloride 1b Into a flask were added 11-aminoundecanoic acid (**1a**, 10.0 g, 49.7 mmol, 1 equiv) and MeOH (50 mL, 1 M). The mixture was cooled in an ice bath (0 °C). Thionyl chloride (7.25 mL, 99.4 mmol, 2 equiv) was added dropwise. The mixture was heated to reflux (3 h), allowed to cool to ambient temperature, and diluted with EtOAc (100 mL, producing white precipitate). Solids were isolated by vacuum filtration and dried under vacuum to yield pure ester hydrochloride **1b** (8.45 g, 33.6 mmol, 68% yield, white solid), which was used directly in the next step.

Synthesis of ester 1 Into a flask were added ester hydrochloride **1b** (4.00 g, 15.9 mmol, 1 equiv) and sodium carbonate (10% aqueous, 60 mL). The mixture was stirred (5 min) and extracted with EtOAc (50 + 40 + 20 mL). The combined organic phase was dried with sodium sulfate. Volatiles were removed under reduced pressure to yield pure ester **1** (3.20 g, 14.9 mmol, 94% yield, translucent oil). Compound analysis is consistent with published data.⁹

¹H NMR (CDCl₃, 200 MHz) δ 3.67 (s, 3H, OMe), 2.68 (t, J = 6.6 Hz, 2H, N-CH₂), 2.31 (t, J = 7.5 Hz, 2H, O=C-CH₂), 1.71–1.52 (m, 2H, CH₂), 1.50–1.07 (m, 16H, NH₂, (CH₂)₇).

Nonylamine (**8**), 3-phenylpropylamine (**10**), and 2-ethylhexylamine (**18**) are commercially available.

Synthesis of ester 10 Into a flask were added 6-aminohexanoic acid (**10a**, 1.32 g, 10.1 mmol, 1 equiv), toluene (25 mL, 0.4 M), benzyl alcohol (3.67 mL, 35.3 mmol, 3.5 equiv), and p-toluenesulfonic acid hydrate (3.00 g, 15.2 mmol, 1.5 equiv). Using a Dean-Stark apparatus the mixture was heated to reflux (18 h) and allowed to cool to ambient temperature (producing white precipitate). Solids were isolated by vacuum filtration, washed with ether, and dried under vacuum to yield crude tosylate salt **10b** (3.00 g, 7.63 mmol, 76% crude yield), which was used directly in the next step. Compound analysis is consistent with published data.¹⁰

¹H NMR (D₂O, 200 MHz) δ 7.72 (d, J = 8.0 Hz, 2H, Ts), 7.49–7.44 (m, 5H, Bn), 7.39 (d, J = 8.0 Hz, 2H, Ts), 5.20 (s, 2H, Bn), 2.97 (t, J = 6.9 Hz, 2H, CH₂-N), 2.49 (t, J = 7.5 Hz, 2H, O=C-CH₂), 1.66 (pent, J = 7.4 Hz, 4H, 2 x CH₂), 1.50–1.28 (m, 2H, CH₂).

Into an extraction funnel were added one third of crude tosylate salt **10b** (1.00 g, 2.54 mmol) and sodium carbonate (10% aqueous, 50 mL). The mixture was mixed until homogeneous, extracted with EtOAc (3 x 30 mL), and dried with sodium sulfate. Volatiles were removed under reduced pressure to yield ester **10** (491 mg, 2.22 mmol, 66% yield from acid **10a**).

⁹ Compound data from: Moon, K.-S.; Lee, E.; Lim, Y.-B.; Lee, M. *Chem. Commun.* **2008**, 4001–4003.

¹⁰ Compound data from: Machida, S.; Kato, N.; Harada, K.; Ohkanda, J. *J. Am. Chem. Soc.* **2010**, 133, 985–963

¹H NMR (CDCl₃, 200 MHz) δ 7.46–7.29 (m, 5H, Ar), 5.11 (s, 2H, O–CH₂), 2.67 (t, J = 6.7 Hz, 2H, CH₂–N), 2.37, (t, J = 7.4 Hz, 2H, CH₂–C=O), 1.67 (pent, J = 7.3 Hz, CH₂–C–N), 1.55–1.25 (m, 4H, (CH₂)₂), 1.25 (brs, 2H, NH₂).

Synthesis of carbamate 12b Into a flask were added 11-aminoundecanoic acid (**12a**, 1.00 g, 4.97 mmol, 1 equiv) and dioxane (6.2 mL, 0.8 M). Sodium hydroxide (0.19 g, 5.0 mmol, 1 equiv) was dissolved in water (10 mL, 0.8 M) and added to the dioxane solution. The mixture was cooled in an ice bath (0 °C, 20 min). Di-*tert*-butyl dicarbonate (1.19 g, 5.46 mmol, 1.1 equiv) was dissolved in dioxane (6.2 mL) and added. The suspension was stirred vigorously and allowed to gradually warm to ambient temperature (26 h). Volatiles were removed under reduced pressure. The residue was dissolved in a mixture of water (40 mL) and saturated sodium bicarbonate (10 mL), washed with EtOAc (2 x 30 mL), acidified with sodium bisulfate (1 M, 30 mL, to pH 2), extracted with EtOAc (40 mL plus 2 x 30 mL), and dried with sodium sulfate. Volatiles were removed under reduced pressure to yield pure carbamate **12b** (1.16 g, 3.85 mmol, 79% yield), which was used directly in the next step. Compound analysis is consistent with published data.¹¹

¹H NMR (CDCl₃, 200 MHz) δ 4.51 (brs, 1H, NH), 3.10 (q, J = 6.6 Hz 2H, N–CH₂), 2.35 (t, J = 7.3 Hz, 2H, O=C–CH₂), 1.69–1.55 (m, 2H, N–C–CH₂), 1.44 (s, 9H, Boc), 1.38–1.22 (m, 14H, (CH₂)₇).

Synthesis of amide 12d Into a flask were added carbamate **12b** (1.16 g, 3.85 mmol, 1 equiv), DCM (3.9 mL, 1 M), dipropylamine (**12c**, 0.56 mL, 7.74 mmol, 2 equiv), EDC hydrochloride (1.48 g, 7.73 mmol, 2 equiv), and HOBT hydrate (0.59 g, 3.87 mmol, 1 equiv). The mixture was stirred (24 h), diluted with sodium bisulfate (1 M, 50 mL), and extracted with ether (2 x 50 mL + 25 mL). The combined organic phases were washed with sodium carbonate (10%, 70 mL) and dried with sodium sulfate. Volatiles were removed under reduced pressure to yield pure amide **12d** (1.42 g, 3.69 mmol, 95% yield), which was used directly in the next step.

¹H NMR (CDCl₃, 200 MHz) δ 4.50 (brs, 1H, NH), 3.32–3.13 (m, 4H, CH₂–N–CH₂), 3.10 (q, J = 6.6 Hz, 2H, O=C–N–CH₂), 2.28 (t, J = 7.5 Hz, 2H, O=C–CH₂), 1.68–1.40 (m, 6H, 3 x N–C–CH₂), 1.44 (s, 9H, Boc), 1.38–1.22 (m, 14H, (CH₂)₇), 0.90 (q, J = 7.5 Hz, 6H, 2 x CH₃).

¹³C NMR (CDCl₃, 50 MHz) δ 172.13, 155.61, 77.97, 49.09, 46.92, 40.09, 32.56, 29.57, 28.93, 27.92, 26.29, 24.99, 21.82, 20.45, 10.86, 10.71.

IR (thin film, cm⁻¹) 3335, 2927, 1698, 1631, 1176.

TLC (1:1) hexane/EtOAc, permanganate, R_f = 0.57.

HRMS calculated for [C₂₂H₄₄N₂O₃H]⁺, requires m/z = 385.3430, found m/z = 385.3429 (ESI).

Synthesis of amine 12 Into a flask were added carbamate **12d** (1.42 g, 3.69 mmol, 1 equiv), DCM (21 mL, 0.2 M), and TFA (8 mL). The mixture was stirred (2 h), and volatiles were removed under reduced pressure (toluene

¹¹ Compound data from: Amara, N.; Mashiach, R.; Amar, D.; Krief, P.; Spieser, S. A. H.; Bottomley, M. J.; Aharoni, A.; Meijler, M. M. *J. Am. Chem. Soc.* **2009**, *131*, 10610–10619.

azeotrope). The crude oil was diluted with a mixture of sodium carbonate (10% aqueous, 30 mL) and brine (25 mL), extracted with EtOAc (30 mL + 2 x 20 mL), and dried with sodium sulfate. Volatiles were removed under reduced pressure to yield free amine **12** (1.06 g, 3.69 mmol, 100% yield).

¹H NMR (CDCl₃, 200 MHz) δ 4.50 (brs, 2H, NH₂), 3.32–3.13 (m, 4H, CH₂–N–CH₂), 2.77 (t, J = 7.2 Hz, 2H, CH₂–N), 2.28 (t, J = 7.5 Hz, 2H, O=C–CH₂), 1.68–1.43 (m, 4H, 2 x CH₂–C–N), 1.43–1.20 (m, 14H, (CH₂)₇), 0.90 (q, J = 7.5 Hz, 4H, 2 x CH₃).

¹³C NMR (CDCl₃, 50 MHz) δ 171.51, 48.56, 46.38, 40.71, 31.98, 28.41, 25.82, 24.47, 21.30, 19.92, 10.26, 10.15.

IR (thin film, cm⁻¹) 2927, 1641, 1464, 1427.

HRMS calculated for [C₁₇H₃₆N₂OH]⁺, requires m/z = 285.2906, found m/z = 258.2909 (ESI).

Synthesis of silyl ether 14 Into a flask were added 5-amino-1-pentanol (**14b**, 1.00 g, 9.69 mmol, 1 equiv), DCM (39 mL, 0.25 M), and imidazole (956 mg, 14.1 mmol, 1.5 equiv). Triisopropylsilyl chloride was added dropwise to the mixture (5 min). The mixture was stirred at ambient temperature (140 h, evaporating most of the DCM, shorter reaction time is likely sufficient), diluted with a mixture of brine and water (1:1, 100 mL), and extracted with ether (2 x 50 mL + 30 mL). The combined organic phase was washed with sodium carbonate (5% aqueous, 50 mL) and dried with sodium sulfate. Volatiles were removed under reduced pressure to yield impure silyl ether **14** (2.08 g, 83% mass recovery), a fraction of which was used crude for the next step. (Since amine **14** is difficult to purify directly, it was protected as a benzyl carbamate, purified, and deprotected.)

Synthesis of benzyl carbamate 14c Into a flame dried flask were added 86% of crude silyl ether **14** (6.92 mmol, 1 equiv), DCM (43 mL, 0.2 M), and TEA (2.12 mL, 15.2 mmol, 2.2 equiv). The flask was capped with a rubber septum and vented through a syringe packed with anhydrous calcium sulfate. Benzyl chloroformate (0.99 mL, 6.96 mmol, 1 equiv) was added dropwise (over 5 min). The mixture was stirred (18 h), the organic layer was washed with sodium phosphate (1 M aqueous, pH 5, 50 mL). The aqueous phase was further extracted with DCM (2 x 50 mL), and the combined organic phases were washed with sodium bicarbonate (saturated aqueous, 65 mL) and dried with sodium sulfate. Volatiles were removed under reduced pressure, and the crude material was purified by column chromatography (3:1 hexane/Et₂O, 100 mL silica gel) to yield pure carbamate **14c** (640 mg, 1.63 mmol, 23% yield, plus additional impure material).

¹H NMR (CDCl₃, 200 MHz) δ 7.41–7.29 (m, 5H, Ar), 5.10 (s, 2H, Bn), 4.72 (brs, 1H, NH), 3.67 (t, J = 6.1 Hz, 2H, O–CH₂), 3.20 (q, J = 6.3 Hz, 2H, N–CH₂), 1.64–1.22 (m, 9 H, (CH₂)₃, 3 x iPr), 1.10–1.00 (brs, 18 H, 3 x iPr).

¹³C NMR (CDCl₃, 50 MHz) δ 156.37, 136.65, 128.46, 128.04, 66.53, 63.12, 41.08, 32.53, 29.74, 23.03, 17.98, 11.96.

IR (neat, cm⁻¹) 2941, 2864, 1701, 1520, 1463, 1102, 908, 882.

TLC (3:1) hexane/Et₂O, permanganate, R_f = 0.51.

HRMS calculated for [C₂₂H₃₉NO₃SiH]⁺, requires m/z = 394.2777, found m/z = 394.2772 (ESI).

Synthesis of amine 14 Into a flask were added carbamate **14c** (585 mg, 1.49 mmol, 1 equiv) and MeOH (5 mL). Into another flask was added palladium on carbon (10% Pd, 75 mg, 50 mg/mmol substrate). The palladium-containing flask was capped with a septum and flushed with nitrogen. MeOH (2.5 mL) was added by syringe, the flask was uncapped, and the slurry was transferred to the substrate-containing flask (final concentration = 0.2 M). The mixture was capped and flushed with nitrogen (5 min). A hydrogen-filled balloon was attached such that its needle remained submerged, the flask was flushed briefly with hydrogen (30 sec), and the reaction was stirred at ambient temperature under the balloon's pressure (4 h). The balloon was removed, and the flask was flushed with nitrogen. The mixture was filtered through Celite (MeOH chase), and volatiles were removed under reduced pressure to yield pure amine **14** (373 mg, 1.44 mmol, 96% yield).

¹H NMR (CDCl₃, 200 MHz) δ 3.68 (t, J = 6.3 Hz, 2H, O–CH₂), 2.70 (t, J = 6.6 Hz, 2H, N–CH₂), 1.78–1.64 (brs, 2H, NH₂), 1.64–1.26 (m, 9H, (CH₂)₃, 3 x iPr), 1.11–0.99 (brs, 18H, 3 x iPr).
¹³C NMR (CDCl₃, 50 MHz) δ 63.22, 41.86, 33.01, 32.74, 23.06, 17.97, 11.95.
IR (neat, cm^{–1}) 2940, 2865, 1463, 1103, 882.
HRMS calculated for [C₁₄H₃₃NOSiH]⁺, requires m/z = 260.2410, found m/z = 260.2411 (ESI).

Synthesis of ether **16** Into a flame-dried flask was added sodium hydride (320 mg, 13.3 mmol, 1 equiv). The flask was capped with a rubber septum, maintained under a nitrogen atmosphere, and cooled in an ice bath (0° C). DMF (8.8 mL, 1.5 M) was added. 3-Aminopropanol (**16a**, 1.00 g, 13.3 mmol, 1 equiv) was dissolved in DMF (4.4 mL) and added dropwise to the reaction (over 5 min, producing gas). The mixture was stirred (additional 5 min). 4-Fluoronitrobenzene (**16b**, 1.88 g, 13.3 mmol, 1 equiv) was dissolved in DMF (4.4 mL) and added dropwise to the reaction (over 5 min, becoming bright orange, final concentration = 0.8 M). The mixture was stirred (10 min), allowed to warm to ambient temperature, stirred (additional 3 h), diluted with water (150 mL), acidified with sodium bisulfate (1 M aqueous, 40 mL, to pH 2), washed with ether (2 x 50 mL), basified with sodium hydroxide (1 M aqueous, 20 mL, plus 600 mg solid), extracted with ether (3 x 50 mL), and dried with sodium sulfate. Volatiles were removed under reduced pressure to yield crude ether **16** (1.42 g, 7.24 mmol, 54% crude yield), which was used directly in the next step. (Since amine **16** is difficult to purify, it was protected as a carbamate, purified, and deprotected.)

Synthesis of carbamate **16c** Into a flask were added crude amine **16** (1.22 g, 6.19 mmol, 1 equiv), dioxane (8.2 mL), water (8.2 mL), and sodium hydroxide (248 mg, 6.19 mmol, 1 equiv). The flask was stirred in an ice bath (0° C). Di-*tert*-butyl dicarbonate (1.49 g, 6.81 mmol, 1.1 equiv) was dissolved in dioxane (8.2 mL) and added to the reaction (final concentration = 0.3 M). The mixture was stirred and allowed to gradually warm to ambient temperature (19 h). Volatiles were removed under reduced pressure. The residue was dissolved in sodium carbonate (10% aqueous, 100 mL), extracted with EtOAc (3 x 50 mL), washed with potassium phosphate monobasic (1 M aqueous, pH 5, 50 mL), and dried with sodium sulfate. Volatiles were removed under reduced pressure, and the crude material was purified by column chromatography (1:1 hexane/Et₂O, 40 mL silica gel) to yield pure carbamate **16c** (1.54 g, 5.20 mmol, 84% yield).

¹H NMR (CDCl₃, 200 MHz) δ 8.20 (d, J = 9.2 Hz, 2H, Ar), 6.96 (d, J = 9.2 Hz, 2H, Ar), 4.67 (brs, 1H, NH), 4.11 (t, J = 6.2 Hz, 2H, O–CH₂), 3.34 (q, J = 6.5 Hz, 2H, N–CH₂), 1.97 (pent, J = 6.5 Hz, 2H, CH₂), 1.44 (s, 9H, (CH₃)₃).

TLC (1:1) hexane/EtOAc, permanganate, R_f = 0.28.

Synthesis of amine **16** Into a flask were added carbamate **16c** (1.54 g, 5.20 mmol, 1 equiv), DCM (29 mL), and TFA (5 mL) and the mixture (final concentration = 0.2 M, 6:1) was stirred (1.5 h). Volatiles were removed under reduced pressure (3 x toluene azeotrope). The residue was dissolved in sodium carbonate (saturated aqueous, 100 mL) and brine (20 mL), extracted with ether (3 x 50 mL), and dried with sodium sulfate. Volatiles were removed under reduced pressure to yield pure amine **16** (719 mg, 3.67 mmol, 70% yield). Compound analysis is consistent with published data.¹²

¹H NMR (CDCl₃, 200 MHz) δ 8.20 (d, J = 9.2 Hz, 2H, Ar), 6.96 (d, J = 9.2 Hz, 2H, Ar), 4.16 (t, J = 6.2 Hz, 2H, O–CH₂), 2.93 (q, J = 6.3 Hz, 2H, N–CH₂), 1.97 (pent, J = 6.5 Hz, 2H, CH₂), 1.22 (brs, 2H, NH₂).

¹² Compound data from: Nakhara, S.; Minami, S. Liquid Crystal Aligning Agent. PCT Int. Appl., 2010-053128, May, 14, 2010.

2.7 Formation of Imidoyl Trifluoroacetate 28

Formation of imidoyl trifluoroacetate 28 The standard nitrosylation procedure (see section 2.9) was followed using benzamide **27** and a solvent mixture of 5:1:1 EtOAc / trifluoroacetic acid / trifluoroacetic anhydride. Imidoyl trifluoroacetate **28** was recovered as the major product (>95% conversion). Since the product is not fully stable to silica gel, it was analyzed crude. Similar imidoyl trifluoroacetates have been previously reported.¹³

¹H NMR (CDCl_3 , 200 MHz, major signals) δ 7.83–7.41 (m, 5H, Ar), 3.73 (t, J = 7.6 Hz, 2H, N–CH₂), 3.66 (s, 3H, OMe), 2.29 (t, J = 7.5 Hz, 2H, O=C–CH₂), 1.71–1.47 (m, 4H, 2 x CH₂), 1.34–1.13 (m, 12H, (CH₂)₆).

¹³C NMR (CDCl_3 , 50 MHz, major signals) δ 174.34, 172.55, 160.16 (q, J = 39.3 Hz), 133.98, 132.30, 129.42, 129.04, 115.58 (q, J = 286 Hz), 51.43, 47.73, 34.03, 29.17, 28.30, 26.90, 24.86.

IR (neat, cm^{-1}) 2926, 2853, 1736, 1719, 1704, 1388, 1165, 1088, 669.

TLC (3:1) hexane/EtOAc, permanganate, R_f = 0.69 (partial decomposition).

HRMS Decomposes to starting amide **27** (ESI).

¹³ For formation of a similar compound: Nagubandi, S.; Fodor, G. *Heterocycles* **1981**, *15*, 165–177.

2.8 Synthesis of Amide Substrates for Mechanistic Studies and Supporting Table S3

Synthesis of benzamide 27 Into a flask were added benzoic acid (**27a**, 660 mg, 5.40 mmol, 1 equiv), amine hydrochloride **1b** (1.50 g, 6.0 mmol, 1.1 equiv), EDC hydrochloride (1.60 g, 8.33 mmol, 1.5 equiv), hydroxybenzotriazole hydrate (1.24 g, 8.33 mmol, 1.5 equiv), DCM (18 mL, 0.3 M), and TEA (2.00 mL, 14.0 mmol, 2.6 equiv). The mixture was stirred (20 h), diluted with EtOAc (60 mL), washed with a 1:1 mixture (120 mL) of sodium carbonate (10% aqueous) and brine, then with a 1:1 mixture (120 mL) of sodium bisulfate (1 M aqueous) and brine, and then with a 1:1 mixture (120 mL) of water and brine, and dried with sodium sulfate. Volatiles were removed under reduced pressure to yield pure benzamide **27** (1.22 g, 3.74 mmol, 69% yield).

¹H NMR (CDCl₃, 200 MHz) δ 7.75 (d, J = 7.7 Hz, 2H, Ar), 7.51–7.36 (m, 3H, Ar), 6.09 (brs, 1H, NH), 3.66 (s, 3H, OMe), 3.45 (q, J = 7.0 Hz, 2H, N–CH₂), 2.30 (t, J = 7.5 Hz, 2H, O=C–CH₂), 1.70–1.51 (m, 4H, 2 x CH₂), 1.44–1.19 (m, 12H, (CH₂)₆).

¹³C NMR (CDCl₃, 50 MHz) δ 174.06, 167.39, 134.56, 130.86, 128.06, 126.77, 51.14, 39.87, 33.78, 29.35, 29.05, 28.94, 28.81, 26.73, 24.64.

IR (neat, cm^{−1}) 3375, 2918, 2849, 1723, 1634, 1522, 1175, 714.

TLC (3:1) hexane/EtOAc, UV, R_f = 0.39.

HRMS calculated for [C₁₉H₂₉NO₃H]⁺, requires m/z = 320.2226, found m/z = 320.2226 (ESI).

Synthesis of acetamide S5 Into a flask were added amine **1** (1.47 g, 6.82 mmol, 1 equiv), EtOAc (10 mL, 0.7 M), and acetic anhydride (0.97 mL, 10.2 mmol, 1.5 equiv). The mixture was stirred (22 h). Volatiles were removed under reduced pressure to yield pure acetamide **S5** (1.73 g, 6.75 mmol, 99% yield, white solid).

¹H NMR (CDCl₃, 200 MHz) δ 5.45 (brs, 1H, NH), 3.67 (s, 3H, OMe), 3.23 (q, J = 6.7 Hz, 2H, N–CH₂), 2.31 (t, J = 7.5 Hz, 2H, O=C–CH₂), 1.98 (s, 3H, O=C–CH₃), 1.69–1.39 (m, 4H, 2 x CH₂), 1.39–1.20 (m, 12H, (CH₂)₆).

¹³C NMR (CDCl₃, 50 MHz) δ 174.28, 169.93, 51.40, 39.63, 34.05, 29.56, 29.37, 29.16, 26.84, 24.88, 23.31.

IR (neat, cm^{−1}) 3286, 2914, 2848, 1730, 1636, 1556, 1177, 719, 608.

HRMS calculated for [C₁₄H₂₇NO₃H]⁺, requires m/z = 258.2069, found m/z = 258.2062 (ESI).

Synthesis of amide S6 Into a flask were added amine **1** (1.00 g, 4.65 mmol, 1 equiv), EtOAc (5 mL, 1 M), and isobutyric anhydride (1.20 mL, 6.97 mmol, 1.5 equiv, stench). The mixture was stirred (6 h), diluted with EtOAc (30 mL), washed with sodium carbonate (10% aqueous, 30 mL), and dried with sodium sulfate. Volatiles were removed under reduced pressure, the crude product was purified by recrystallization (20 mL hot hexane), and the isolated solid was dried under vacuum to yield pure amide **S6** (1.02 g, 3.57 mmol, 77% yield, white solid).

¹H NMR (CDCl₃, 200 MHz) δ 5.42 (brs, 1H, NH), 3.66 (s, 3H, OMe), 3.24 (q, J = 6.5 Hz, 2H, N–CH₂), 2.41–2.45 (m, 3H, iPr, O=C–CH₂), 1.68–1.40 (m, 4H, 2 x CH₂), 1.36–1.20 (m, 12H, (CH₂)₆), 1.15 (d, J = 7.5 Hz, 6H, iPr).

¹³C NMR (CDCl₃, 50 MHz) δ 176.84, 174.05, 51.14, 39.10, 35.23, 33.80, 29.40, 29.03, 26.64, 24.76, 19.43.
IR (neat, cm⁻¹) 3301, 2919, 2852, 1731, 1635, 1542, 1172.
HRMS calculated for [C₁₆H₃₁NO₃H]⁺, requires m/z = 286.2382, found m/z = 286.2378 (ESI).

Synthesis of trifluoroacetamide S7 Into a flask were added amine **1** (1.41 g, 6.55 mmol, 1 equiv), EtOAc (10 mL, 0.7 M), and ethyl trifluoroacetate (**S7a**, 1.17 mL, 9.83 mmol, 1.5 equiv). The mixture was stirred (22 h). Volatiles were removed under reduced pressure to yield pure trifluoroacetamide **S7** (2.02 g, 6.50 mmol, 99% yield). Compound analysis is consistent with published data.¹⁴

¹H NMR (CDCl₃, 200 MHz) δ 6.27 (brs, 1H, NH), 3.67 (s, 3H, OMe), 3.36 (q, J = 6.7 Hz, 2H, N-CH₂), 2.30 (t, J = 7.4 Hz, 2H, O=C-CH₂), 1.73–1.47 (m, 4H, 2 x CH₂), 1.43–1.13 (m, 12H, (CH₂)₆).

TLC (3:1) hexane/EtOAc, permanganate, R_f = 0.64.

¹⁴ Compound data from: Miyamoto, K.; Sei, Y.; Yamaguchi, K.; Ochiai, M. *J. Am. Chem. Soc.* **2009**, *131*, 1382–1383.

2.9 Synthesis of *N*-Nitrosoamides for Supporting Tables S1 and S2

Standard nitrosylation procedure Into a vial were added the required amide (150 mg) and the required solvent mixture (typically 0.3 M in 5:1 acetic anhydride / acetic acid unless specified otherwise). The vial was capped with a rubber septum, sealed with tape, and stirred in an ice bath (0 °C, 15 min). To the mixture was added solid sodium nitrite (2 equiv, creating a blue solution and slowly evolving brown gas). The vial was capped with a rubber septum, sealed with tape, vented with a syringe packed with anhydrous calcium sulfate, and stirred (2 h). To the mixture was added additional sodium nitrite (2 equiv). The mixture was stirred (additional 4 h), diluted with EtOAc (5 mL), washed with cold water (5 mL) and then cold sodium carbonate (10% aqueous, 3 x 5 mL), diluted with cold sodium carbonate (10% aqueous, 5 mL), and stirred rapidly (30 min, to quench any remaining anhydride). The organic phase was isolated, washed with potassium phosphate monobasic (1 M aqueous, pH 5, 5 mL), and dried with sodium sulfate. Volatiles were removed under reduced pressure to yield the crude product, which was analyzed by ¹H NMR to determine the conversion and product distribution. Crude *N*-nitrosoamides **S1–S3** were pure enough to not require additional purification.

S1

¹H NMR (CDCl₃, 200 MHz) δ 3.74 (t, *J* = 7.2 Hz, 2H, N–CH₂), 3.67 (s, 3H, OMe), 2.76 (s, 3H, Ac), 2.30 (t, *J* = 7.5, 2H, O=C–CH₂), 1.70–1.52 (m, 2H, CH₂), 1.41–1.12 (m, 14H, (CH₂)₇).

¹³C NMR (CDCl₃, 50 MHz) δ 174.60, 174.36, 51.45, 38.68, 34.07, 29.26, 29.14, 29.08, 28.99, 26.87, 26.67, 24.90, 22.52.

IR (neat, cm^{–1}) 2927, 2855, 1732, 1504, 1115, 952.

TLC (3:1) hexane/Et₂O, UV & permanganate, *R_f* = 0.55.

HRMS Decomposes to ester **S1a** (ESI).

S2

¹H NMR (CDCl₃, 200 MHz) δ 3.88 (sept, *J* = 6.8 Hz, 1H, iPr), 3.74 (t, *J* = 6.7 Hz, 2H, N–CH₂), 3.67 (s, 3H, OMe), 2.30 (t, *J* = 7.5 Hz, 2H, O=C–CH₂), 1.69–1.52 (m, 2H, CH₂), 1.31 (d, *J* = 6.9 Hz, 6H, iPr), 1.27–1.11 (m, 14H, (CH₂)₆).

¹³C NMR (CDCl₃, 200 MHz) δ 181.02, 174.35, 51.44, 38.73, 34.06, 32.62, 29.26, 29.11, 28.99, 26.80, 26.60, 24.89, 19.15.

IR (neat, cm^{–1}) 2928, 2855, 1735, 1502, 1170, 1002.

TLC (3:1) hexane/Et₂O, UV & permanganate, *R_f* = 0.75.

HRMS Decomposes to ester **S2a** (ESI).

S3

To allow better solubility of the substrate, the reaction to make *N*-nitrosobenzamide **S3** was run at 0.13 M.

¹H NMR (CDCl₃, 200 MHz) δ 7.75 (d, J = 7.8 Hz, 2H, Ar), 7.64–7.42 (m, 3H, Ar), 3.93 (t, J = 7.4 Hz, 2H, N-CH₂), 3.67 (s, 3H, OMe), 2.30 (t, J = 7.6 Hz, O=C-CH₂), 1.70–1.41 (m, 4H, 2 x CH₂), 1.38–1.14 (m, 12H, (CH₂)₆).

¹³C NMR (CDCl₃, 50 MHz) δ 174.32, 173.13, 133.12, 132.37, 130.60, 128.12, 51.45, 39.73, 34.10, 29.29, 29.17, 26.98, 26.75, 24.93.

IR (neat, cm⁻¹) 2926, 2855, 1737, 1702, 1504, 1352, 1168, 1001, 715.

TLC (3:1) hexane/Et₂O, UV & permanganate, R_f = 0.50.

HRMS (minor signal) calculated for [C₁₉H₂₈N₂O₄H]⁺, requires m/z = 349.2127, found m/z = 349.2129 (ESI). The majority of the material decomposes to ester **S3a**.

S4

N-Nitrosotrifluoroacetamide **S4** was not observed, as it rearranges spontaneously at ambient temperature.

2.10 Thermal Rearrangements of *N*-Nitrosoamides for Supporting Tables S1 and S2

Standard rearrangement procedure Into a flask were added the crude *N*-nitrosoamide and the solvent (0.1 M, toluene unless specified otherwise). Using an oil bath, the mixture was heated to the indicated temperature for the indicated time (typically 5 or 24 hours). Volatiles were removed under reduced pressure, and the crude mixture was analyzed by ^1H NMR to assess conversion and product distribution.

^1H NMR (CDCl_3 , 200 MHz) δ 4.05 (t, J = 6.7 Hz, 2H, O-CH₂), 3.67 (s, 3H, OMe), 2.30 (t, J = 7.5 Hz, 2H, O=C-CH₂), 2.05 (s, 3H, O=C-CH₃), 1.70–1.50 (m, 4H, 2 x CH₂), 1.35–1.21 (m, 12H, (CH₂)₆).

^{13}C NMR (CDCl_3 , 50 MHz) δ 173.65, 170.55, 64.11, 50.91, 33.62, 28.85, 28.26, 25.54, 24.55, 20.50.

IR (neat, cm^{-1}) 2926, 2855, 1736, 1234.

TLC (3:1) hexane/EtOAc, permanganate, R_f = 0.68.

HRMS calculated for $[\text{C}_{14}\text{H}_{26}\text{O}_4\text{H}]^+$, requires m/z = 259.1909, found m/z = 259.1904 (ESI).

^1H NMR (CDCl_3 , 200 MHz) δ 4.05 (t, J = 6.7 Hz, 2H, O-CH₂), 3.67 (s, 3H, OMe), 2.54 (sept, J = 7.0 Hz, 1H, iPr), 2.31 (t, J = 7.5 Hz, 2H, O=C-CH₂), 1.70–1.51 (m, 4H, 2 x CH₂), 1.36–1.24 (m, 12H, (CH₂)₆), 1.16 (d, J = 7.0 Hz, 6H, iPr).

^{13}C NMR (CDCl_3 , 50 MHz) δ 176.81, 173.87, 64.05, 51.10, 33.77, 28.97, 28.40, 25.65, 24.69, 18.76.

IR (neat, cm^{-1}) 2928, 2855, 1735, 1193, 1157.

TLC (3:1) hexane/EtOAc, permanganate, R_f = 0.69.

HRMS calculated for $[\text{C}_{16}\text{H}_{30}\text{O}_4\text{H}]^+$, requires m/z = 287.222, found m/z = 287.2214 (ESI).

^1H NMR (CDCl_3 , 200 MHz) δ 8.05 (d, J = 7.5 Hz, 2H, Ar), 7.62–7.37 (m, 3H, Ar), 4.32 (t, J = 6.6 Hz, 2H, O-CH₂), 3.67 (s, 3H, OMe), 2.30 (t, J = 7.5 Hz, 2H, O=C-CH₂), 1.84–1.51 (m, 4H, 2 x CH₂), 1.51–1.17 (m, 12H, (CH₂)₆).

^{13}C NMR (CDCl_3 , 50 MHz) δ 174.32, 166.67, 132.77, 130.48, 129.51, 128.29, 65.10, 51.44, 34.08, 29.22, 28.68, 26.01, 24.93.

IR (neat, cm^{-1}) 2927, 2855, 1738, 1717, 1271, 1109, 710.

TLC (15:1) hexane/EtOAc, UV & permanganate, R_f = 0.30.

HRMS calculated for $[\text{C}_{19}\text{H}_{28}\text{O}_4\text{H}]^+$, requires m/z = 321.2066, found m/z = 321.2060 (ESI).

S4a

¹H NMR (CDCl₃, 200 MHz) δ 4.35 (t, J = 6.7 Hz, 2H, O–CH₂), 3.67 (s, 3H, OMe), 2.31 (t, J = 7.5 Hz, 2H, O=C–CH₂), 1.82–1.50 (m, 4H, 2 x CH₂), 1.50–1.22 (m, 12H, (CH₂)₆).

¹³C NMR (CDCl₃, 50 MHz) δ 174.01, 157.35 (q, J = 41.9 Hz), 114.46 (q, J = 286 Hz), 68.09, 51.12, 33.85, 29.11, 27.94, 25.33, 24.77.

IR (neat, cm^{–1}) 2929, 2857, 1784, 1738, 1217, 1144.

TLC (5:1) hexane/EtOAc, permanganate, R_f = 0.78 (partial decomposition on TLC plate).

HRMS calculated for [C₁₄H₂₃F₃O₄Na]⁺, requires m/z = 335.1446, found m/z = 335.1445 (ESI).

3. NMR Spectra

¹H NMR Spectrum of 1

¹H NMR Spectrum of 2

CCCCCCCCCCCCCCCC(=O)OCC(=O)C(Cl)Cl

1H NMR spectrum (DMSO-d₆) of 1-(11-chloro-11-oxododecyl)pyrrolidine. The spectrum shows a broad peak at ~7.2 ppm (NH), a multiplet at ~4.2 ppm (CH₂-O), a multiplet at ~2.5 ppm (CH₂-CH₂), and a triplet at ~1.2 ppm (CH₃). Solvent peaks for DMSO-d₆ are visible at ~2.5 and ~2.9 ppm.

COC(=O)CCCCCCCCCN(C(=O)Cl)C(=O)Cl

1.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.

¹³C NMR Spectrum of 3

¹H NMR Spectrum of 4

¹³C NMR Spectrum of 4

¹H NMR Spectrum of 4a (contaminated with some 4b)

¹H NMR Spectrum of 5

¹H NMR Spectrum of 7

¹H NMR Spectrum of 9

¹H NMR Spectrum of 10b

¹H NMR Spectrum of 10

¹H NMR Spectrum of 11

Chemical structure: CCCCCCCCC(=O)O (1-octanecarboxylic acid) with a Boc group attached to the nitrogen atom.

¹H NMR spectrum (CDCl₃) showing peaks at approximately 11.5 (broad, 1H), 7.2 (sharp, 1H), 4.5 (broad, 1H), 3.1 (triplet, 2H), 2.3 (triplet, 2H), 1.5 (multiplet, 4H), and 1.2 (triplet, 3H).

^1H NMR Spectrum of 12d

^{13}C NMR Spectrum of 12d

^1H NMR Spectrum of 12

^{13}C NMR Spectrum of 12

^1H NMR Spectrum of 13

^{13}C NMR Spectrum of 13

¹H NMR Spectrum of 14c

¹³C NMR Spectrum of 14c

¹H NMR Spectrum of 14

¹³C NMR Spectrum of 14

¹H NMR Spectrum of 15

¹H NMR Spectrum of 16c

¹H NMR Spectrum of 16

¹H NMR Spectrum of 17

¹H NMR Spectrum of 19

¹H NMR Spectrum of 27

¹³C NMR Spectrum of 27

¹H NMR Spectrum of 28 (crude)

¹³C NMR Spectrum of 28 (crude)

¹H NMR Spectrum of S1

¹³C NMR Spectrum of S1

¹H NMR Spectrum of S1a

^{13}C NMR Spectrum of S1a

^1H NMR Spectrum of S2

¹³C NMR Spectrum of S2

¹H NMR Spectrum of S2a

¹³C NMR Spectrum of S2a

¹H NMR Spectrum of S3

¹³C NMR Spectrum of S3

¹H NMR Spectrum of S3a

¹³C NMR Spectrum of S3a

¹H NMR Spectrum of S4a

¹³C NMR Spectrum of S4a

¹H NMR Spectrum of S5

^{13}C NMR Spectrum of S5

^1H NMR Spectrum of S6

^{13}C NMR Spectrum of S6

^1H NMR Spectrum of S7