Straightforward Access to α-Methylamines through Cross-Metathesis

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Abstract: A two-step procedure involving cross-metathesis and reductive amination enables easy access to α-methylamines and α,α′-dimethyldiamines from a wide variety of terminal olefins.

Key words: amines, alkenes, metathesis, ruthenium, hydrogenation

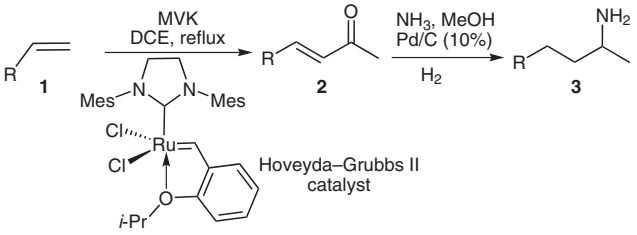
Amines are compounds of prime importance with a broad spectrum of applications ranging from corrosion inhibitors to synthetic intermediates in pharmaceutical or agrochemical industries.[1]

Our group is currently investigating kinetic resolution (KR) of amines with the objective to devise a versatile dynamic kinetic resolution (DKR) method for amines in which the stereocenter is directly adjacent to the amine moiety.[2] Selective chemoenzymatic DKR could be achieved by the association of radical racemization[3] with enzymatic resolution by either lipases or proteases to prepare either *R*-[4] or *S*-acylated[5] amines.

Primary α-methylamines are very good substrates in KR,[6] because the steric discrimination between the two alkyl groups at the stereogenic center is maximized by the presence of the smallest alkyl in the series, namely the methyl group.[7]

To make a wide diversity of functionalized α-methylamines available for DKR studies, a straightforward synthesis needed to be developed. There are numerous methodologies to synthesize primary amines, and it is impossible to list them all here.[8] The reductive amination of ketones,[9] the addition of organometallic species to imine equivalents,[10] or the reduction of nitro[11] groups can be cited as examples among many.

Over the past ten years, olefin metathesis has emerged as a powerful synthetic tool.[12] We wanted to use the advantage of the compatibility of this reaction with a variety of functional groups to design a short route to primary α-methylamines. Our approach is depicted in Scheme 1. A cross-metathesis (CM) reaction between a terminal alkene **1** and methyl vinyl ketone should lead to the α,β-unsaturated ketone **2**. The second-generation Hoveyda–Grubbs catalyst was selected because of its ability to catalyze metathesis reactions of electron-deficient substrates.[12] Reductive amination of **2** should afford α-methylamines **3**. Therefore, this strategy should provide a rapid access to α-methylamines from the wide pool of commercially available or easily synthesized functionalized olefins.



Scheme 1 Cross-metathesis–reductive-amination sequence used for the synthesis of α-methylamines

The reaction of alkene **1** (1 equiv) with methyl vinyl ketone (3 equiv) in the presence of a catalytic amount (3 mol%) of the Hoveyda–Grubbs II catalyst, in 1,2-dichloroethane at reflux,[13] afforded the desired α,β-unsaturated ketone **2** together with the methyl vinyl ketone dimer. Yields ranged from 60 to 92%. As expected, CM with methyl vinyl ketone proceeded with total selectivity in favor of the *E*-isomer; at this temperature no trace of the *Z*-isomer was detected.[14]

To investigate the scope of this reaction, the alkene functionalization was varied (Table 1). Terminal unfunctionalized olefins **1a** and **1b** (entries 1 and 2) and the conjugated alkene **1f** (entry 6) gave very good yields. It was also possible to perform the reaction on **1c** or **1i** without protection of the alcohol group (entries 3 and 9). Other functional groups such as esters **1d** and **1g** (entries 4 and 7), sulfone **1e** (entry 5), and acetal **1h** (entry 8) gave the corresponding ketones in slightly lower yields (63–90%). α,ω-Terminal dienes **1i** and **1j** could similarly be used as substrates (entries 9 and 10). It must be emphasized that a cyclopentene resulting from ring-closing metathesis from **1i** was not detected, although it is expected be an intermediate in the formation of **2i**.[15,16] The reactions of dienes **1i** and **1j** led to double CM products **2i** and **2j** in quite good yields. Ring-opening cross-metathesis (RO-CM)[16] of cyclooctene (**1k**) led to the expected diketone **2k** in very good yield (entry 11). During the RO-CM step of cyclooctene (**1k**), six carbon atoms were incorporated into the chain, whereas with linear diene **1j** only four carbon

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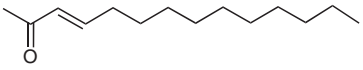
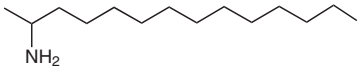
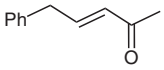
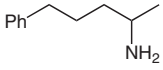
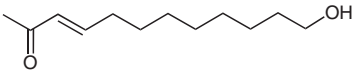
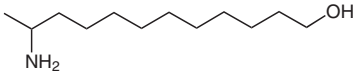
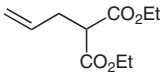
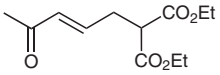
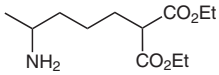
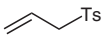
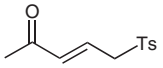
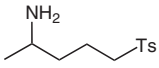
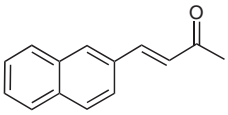
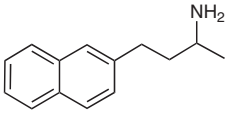
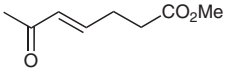
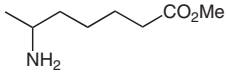
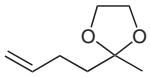
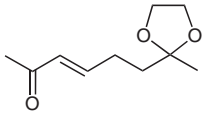
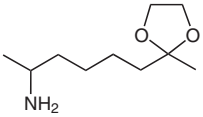
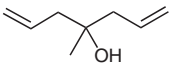
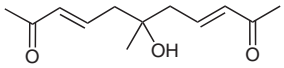
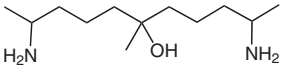
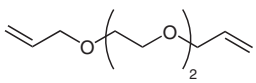
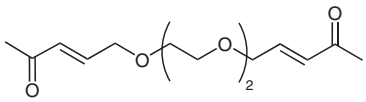
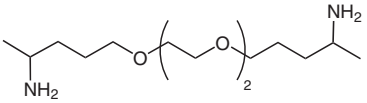
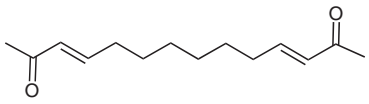
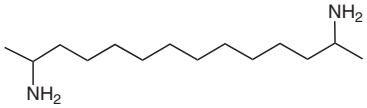
Table 1 Synthesis of α-Methylamines from Various Functionalized Alkenes

Entry	Alkene **1**	Ketone **2**	Yield (%)	Amine **3**	Yield (%)
1	**1a** dodec-1-ene	**2a** 	92	**3a** 	90[b]
2	**1b** allylbenzene	**2b** 	81	**3b** 	93[b]
3	**1c** dec-9-en-1-ol	**2c** 	86	**3c** 	69[c]
4	**1d** 	**2d** 	70	**3d** 	57[c,d]
5	**1e** 	**2e** 	67	**3e** 	54[c]
6	**1f** 2-vinylnaphthalene	**2f** 	81	**3f** 	82[c]
7	**1g** 	**2g** 	63[a]	**3g** 	71[c]
8	**1h** 	**2h** 	90[a]	**3h** 	77[c]
9	**1i** 	**2i** 	60	**3i** 	84[b]
10	**1j** 	**2j** 	63	**3j** 	89[b]
11	**1k** cyclooctene	**2k** 	92	**3k** 	69[b]

[a] Partially contaminated with MVK dimer.
[b] Product can be used without further purification.
[c] Purified on a short pad of silica.
[d] An NH_3/EtOH solution was used.

atoms were introduced (entry 10, **2j**). This provides a fast entry to fatty alkylamines.

All the ketones were then submitted to reductive amination in a three molar solution of ammonia in methanol in the presence of palladium (10%) on activated carbon under a hydrogen atmosphere (8 bar). To avoid the formation of side products resulting from competitive Michael addition, the reduction of the double bond had to be fast. Under the above conditions, amines and diamines were obtained in good yields. No aminolysis of ester groups or cyclization into lactams was detected (entries 4 and 7). The presence of the methyl vinyl ketone dimer did not interfere with the reductive amination step (entries 7 and 8), and its reductive amination product was not detected after purification. The products were recovered by either simple filtration over Celite or after flash chromatography on a short column of silica. According to the same procedure, diketones **2i–k** led very cleanly to α,α′-dimethyldiamines **3i–k** (entries 9–11).

In conclusion, this two-step procedure offers an easy and efficient access to α-methylamines. Its ease of use makes it competitive with the approaches already reported in the literature. Furthermore, this methodology applies to dienes and cycloolefins and allows the synthesis of symmetrical α,α′-dimethyldiamines, which are very interesting candidates for further DKR studies.[17]

All reactions were carried out in dry glassware and by using magnetic stirring and a positive pressure of argon. Commercially available solvents were used as purchased, without further purification.

Dry state adsorption and purification were performed on Macherey Nagel silica gel 60 Å (70–230 mesh). Analytical TLC was performed on precoated silica gel plates. Visualization was accomplished by UV (254 nm) and with phosphomolybdic acid in ethanol. ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively, on a Bruker spectrometer. Signals due to residual undeuterated solvent (^{1}H NMR, $CDCl_3$, δ = 7.27) or to the solvent (^{13}C NMR, $CDCl_3$, δ = 77.0) served as the internal standards. DEPT 135 was used for ^{13}C spectral assignment. HRMS (TOF, ES+) was carried out on a QStar Elite (Applied Biosystems SCIEX) mass spectrometer. MVK was distilled prior to use. Alkenes **1a**–**d**, **1f**, **1i**, and **1k** and the ruthenium catalyst were commercially available. Alkenes **1e**[18] and **1h**[19] were prepared according to literature procedure. Alkene **1g** was prepared by esterification of the commercially available corresponding carboxylic acid. Alkene **1j** was obtained by a standard allylation procedure (NaH/THF).

Ketones 2 by Cross-Metathesis; General Procedure

The catalyst (3 mol%) was added to a 0.1 M soln of alkene **1** (1 mmol) and MVK (3 mmol) in DCE. The mixture was stirred at reflux for 0.5–1 h (TLC monitoring). Then the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (silica gel, EtOAc–pentane); this afforded pure ketone **2**.

(*E*)-Tetradec-3-en-2-one (2a)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.76 (dt, *J* = 15.9, 7.0 Hz, 1 H), 6.02 (dt, *J* = 15.9, 1.5 Hz, 1 H), 2.22–2.12 (m, 2 H), 2.19 (superimposed s, 3 H), 1.49–1.35 (m, 2 H), 1.34–1.14 (m, 14 H), 0.83 (t, *J* = 6.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.9 (C=O), 148.9 (HC=), 131.6 (HC=), 32.8 (CH_2), 32.2 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 28.4 (CH_2), 27.1 (CH_3), 23.0 (CH_2), 15.4 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{27}O$: 211.2056; found: 211.2050.

(*E*)-5-Phenylpent-3-en-2-one (2b)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.17 (m, 5 H), 6.94 (dt, *J* = 15.9, 6.8 Hz, 1 H), 6.10 (dt, *J* = 15.9, 1.5 Hz, 1 H), 3.56 (br d, *J* = 6.8 Hz, 2 H), 2.26 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.9 (C=O), 146.7 (HC=), 138.0 (C=), 132.4 (HC=), 129.2 (HC=), 129.1 (HC=), 127.2 (HC=), 39.2 (CH_2), 27.3 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{13}O$: 161.0961; found: 161.0960.

(*E*)-12-Hydroxydodec-3-en-2-one (2c)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.81 (dt, *J* = 16.0, 6.8 Hz, 1 H), 6.08 (dt, *J* = 16.0, 1.5 Hz, 1 H), 3.66 (t, *J* = 6.6 Hz, 2 H), 2.28–2.18 (m, 2 H), 2.25 (s, 3 H), 1.60–1.45 (m, 5 H), 1.33 (m, 8 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.2 (C=O), 149.0 (HC=), 131.7 (HC=), 63.3 (CH_2), 33.1 (CH_2), 32.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 28.4 (CH_2), 27.2 (CH_3), 26.1 (CH_2).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{23}O_2$: 199.1693; found: 199.1696.

Diethyl 2-[(*E*)-4-Oxopent-2-enyl]malonate (2d)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.75 (dt, *J* = 16.0, 7.0 Hz, 1 H), 6.13 (dt, *J* = 16.0, 1.3 Hz, 1 H), 4.23 (ABX_3, 4 H), 3.50 (t, *J* = 7.3 Hz, 1 H), 2.81 (td, *J* = 7.3, 1.5 Hz, 2 H), 2.24 (s, 3 H), 1.27 (t, *J* = 7.2 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.4 (C=O), 168.7 (C=O), 143.2 (HC=), 133.5 (HC=), 62.1 (CH_2), 51.0 (CH), 31.7 (CH_2), 27.4 (CH_3), 14.4 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{19}O_5$: 243.1227; found: 243.1224.

(*E*)-5-Tosylpent-3-en-2-one (2e)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.3 Hz, 2 H), 7.38 (d, *J* = 8.3 Hz, 2 H), 6.63 (dt, *J* = 15.9, 7.7 Hz, 1 H), 6.05 (dt, *J* = 15.9, 1.1 Hz, 1 H), 3.94 (dd, *J* = 7.7, 1.1 Hz, 2 H), 2.47 (s, 3 H), 2.27 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.4 (C=O), 145.8 (C=), 138.1 (HC=), 135.6 (C=), 132.2 (HC=), 130.4 (HC=), 128.7 (HC=), 59.9 (CH_2), 27.7 (CH_3), 22.1 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{12}H_{18}NO_3S$: 256.1002; found: 256.1003.

(*E*)-4-(2-Naphthyl)but-3-en-2-one (2f)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99 (br s, 1 H), 7.92–7.83 (m, 3 H), 7.71 (d, *J* = 16.3 Hz, 1 H), 7.70 (dd, *J* = 8.8, 1.8 Hz, 1 H), 7.58–7.51 (m, 2 H), 6.86 (d, *J* = 16.3 Hz, 1 H), 2.45 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.7 (C=O), 143.9 (HC=), 134.7 (C=), 133.7 (C=), 132.3 (C=), 130.7 (HC=), 129.2 (HC=), 129.0 (HC=), 128.2 (HC=), 127.8 (HC=), 127.7 (HC=), 127.2 (HC=), 123.9 (HC=), 28.0 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{13}O$: 197.0961; found: 197.0957.

(*E*)-Methyl 6-Oxohept-4-enoate (2g)

^{1}H NMR (300 MHz, $CDCl_3$) (mixture with (*E*)-hex-3-ene-2,5-dione): δ = 6.80 (dt, *J* = 16.0, 6.4 Hz, 1 H), 6.11 (dt, *J* = 16.0, 1.5 Hz, 1 H), 3.70 (s, 3 H), 2.60–2.45 (m, 4 H), 2.25 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.7 (C=O), 173.0 (C=O), 146.0 (HC=), 132.1 (HC=), 52.1 (CH_3), 32.5 (CH_2), 27.7 (CH_2), 27.3 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_8H_{13}O_3$: 157.0859; found: 157.0855.

(*E*)-6-(2-Methyl-1,3-dioxolan-2-yl)hex-3-en-2-one (2h)

^{1}H NMR (300 MHz, $CDCl_3$) (mixture with (*E*)-hex-3-ene-2,5-dione): δ = 6.80 (dt, *J* = 15.9, 6.8 Hz, 1 H), 6.11 (br d, *J* = 15.9 Hz, 1 H), 4.00–3.85 (m, 4 H), 2.33 (pseudo q, *J* = 7.7 Hz, 2 H), 2.21 (s, 3 H), 1.8 (m, 2 H), 1.31 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.7 (C=O), 149.3 (HC=), 132.2 (HC=), 110.4 (C), 65.8 (2 × CH_2), 38.4 (CH_2), 28.1 (CH_2), 27.8 (CH_3), 25.1 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{10}H_{20}NO_3$: 202.1438; found: 202.1437.

(3*E*,8*E*)-6-Hydroxy-6-methylundeca-3,8-diene-2,10-dione (2i)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.83 (dt, *J* = 16.0, 7.6 Hz, 2 H), 6.16 (dt, *J* = 16.0, 1.1 Hz, 2 H), 2.43 (m, 4 H), 2.43 (s, 6 H), 1.28 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.7 (C=O), 143.0 (HC=), 134.7 (HC=), 45.5 (CH_2), 27.7 (CH_3), 27.6 (2 × CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{19}O_3$: 211.1329; found: 211.1330.

(3*E*,14*E*)-6,9,12-Trioxaheptadeca-3,14-diene-2,16-dione (2j)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.80 (dt, *J* = 16.2, 4.5 Hz, 2 H), 6.32 (dt, *J* = 16.2, 1.7 Hz, 2 H), 4.24 (dd, *J* = 4.5, 1.7 Hz, 4 H), 3.69 (m, 8 H), 2.29 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.6 (C=O), 143.4 (HC=), 130.8 (HC=), 71.1 (CH_2), 70.8 (CH_2), 70.4 (CH_2), 27.6 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{23}O_5$: 271.1540; found: 271.1533.

(3*E*,11*E*)-Tetradeca-3,11-diene-2,13-dione (2k)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.79 (dt, *J* = 16.0, 6.8 Hz, 2 H), 6.10 (dt, *J* = 16.0, 1.5 Hz, 2 H), 2.30–2.15 (m, 4 H), 2.28 (superimposed s, 6 H), 1.57–1.40 (m, 4 H), 1.40–1.29 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 199.0 (C=O), 148.7 (HC=), 131.7 (HC=), 32.7 (CH_2), 29.3 (CH_2), 28.3 (CH_2), 27.2 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{23}O_2$: 223.1693; found: 223.1691.

Amines 3 by Reductive Amination of Ketones 2; General Procedure

Pd/C (10%, 80 mg) was added to a 0.05 M soln of ketone **2** (1 mmol) in a 3 M soln of NH_3 in MeOH. The mixture was stirred overnight at r.t. under H_2 pressure (8 bar). After filtration over Celite, the residue was purified by flash chromatography on a short column of silica gel (MeOH–Et_3N–CH_2Cl_2, 1.6:1.6:96.8); this afforded pure amine **3**.

Tetradecan-2-amine (3a)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.87 (sext, *J* = 6.0 Hz, 1 H), 1.85 (br s, 2 H), 1.45–1.15 (m, 22 H), 1.05 (d, *J* = 6.0 Hz, 3 H), 0.87 (t, *J* = 6.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 47.3 (CH), 40.5 (CH_2), 32.3 (CH_2), 30.1 (CH_2), 30.0 (br, 5 × CH_2), 29.7 (CH_2), 26.8 (CH_2), 24.2 (CH_3), 23.1 (CH_2), 14.5 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{32}N$: 214.2529; found: 214.2525.

5-Phenylpentan-2-amine (3b)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.10 (m, 5 H), 2.92 (sext, *J* = 6.4 Hz, 1 H), 2.63 (t, *J* = 7.6 Hz, 2 H), 2.08 (br s, 2 H), 1.65 (m, 2 H), 1.39 (m, 2 H), 1.08 (d, *J* = 6.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.8 (C=), 128.8 (HC=), 128.7 (HC=), 126.1 (HC=), 47.3 (CH), 39.7 (CH_2), 36.4 (CH_2), 28.7 (CH_2), 23.9 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{18}N$: 164.1434; found: 164.1436.

11-Aminododecan-1-ol (3c)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.5 (br s, 3 H), 3.62 (t, *J* = 6.6 Hz, 2 H), 3.09 (sext, *J* = 6.4 Hz, 1 H), 1.62–1.45 (m, 4 H), 1.42–1.24 (m, 14 H), 1.22 (d, *J* = 6.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 63.2 (CH_2), 45.7 (CH), 33.2 (CH_2), 30.0 (CH_2), 29.9 (2 × CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 26.6 (CH_2), 26.1 (CH_2), 23.1 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{28}NO$: 202.2165; found: 202.2164.

Diethyl 2-(4-Aminopentyl)malonate (3d)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.40 (br s, 2 H), 4.15 (q, *J* = 7.2 Hz, 4 H), 3.30 (t, *J* = 7.5 Hz, 1 H), 3.11 (sext, *J* = 6.3 Hz, 1 H), 1.86 (q, *J* = 7.5 Hz, 2 H), 1.68–1.32 (m, 4 H), 1.23 (t, *J* = 7.2 Hz, 6 H), 1.21 (d, *J* = 6.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.7 (C=O), 61.7 (CH_2), 52.2 (CH), 47.8 (CH), 37.0 (CH_2), 28.7 (CH_2), 24.1 (CH_2), 21.1 (CH_3), 14.4 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{24}NO_4$: 246.1700; found: 246.1698.

5-Tosylpentan-2-amine (3e)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.3 Hz, 2 H), 7.34 (d, *J* = 8.3 Hz, 2 H), 3.60 (t, *J* = 7.9 Hz, 2 H), 2.86 (sext, *J* = 6.4 Hz, 1 H), 2.43 (s, 3 H), 1.83 (br s, 2 H), 1.80–1.67 (m, 2 H), 1.42–1.32 (m, 2 H), 1.03 (d, *J* = 6.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.0 (C=), 136.5 (C=), 130.3 (HC=), 128.4 (HC=), 56.6 (CH_2), 46.9 (CH), 38.4 (CH_2), 24.0 (CH_3), 22.0 (CH_3), 20.1 (CH_2).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{20}NO_2S$: 242.1209; found: 242.1208.

4-(2-Naphthyl)butan-2-amine (3f)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.97 (m, 3 H), 7.65 (br s, 1 H), 7.52–7.40 (m, 2 H), 7.36 (dd, *J* = 8.5, 1.7 Hz, 1 H), 2.99 (sext, *J* = 6.3 Hz, 1 H), 2.85 (m, 2 H), 1.88 (br s, 2 H), 1.79 (m, 2 H), 1.17 (d, *J* = 6.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.2 (C=), 134.1 (C=), 132.4 (C=), 128.3 (HC=), 128.0 (HC=), 127.8 (HC=), 127.7 (HC=), 126.7 (HC=), 126.3 (HC=), 125.5 (HC=), 47.0 (CH), 41.9 (CH_2), 33.3 (CH_2), 24.3 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{18}N$: 200.1434; found: 200.1441.

Methyl 6-Aminoheptanoate (3g)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.60 (br s, 2 H), 3.65 (s, 3 H), 3.20 (sext, *J* = 6.4 Hz, 1 H), 2.30 (t, *J* = 7.4 Hz, 2 H), 1.80–1.50 (m, 4 H), 1.49–1.33 (m, 2 H), 1.25 (d, *J* = 6.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.2 (C=O), 51.9 (CH_3), 48.2 (CH), 35.8 (CH_2), 34.0 (CH_2), 25.5 (CH_2), 24.8 (CH_2), 19.9 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_8H_{18}NO_2$: 160.1332; found: 160.1330.

6-(2-Methyl-1,3-dioxolan-2-yl)hexan-2-amine (3h)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.98–3.80 (m, 4 H), 2.85 (sext, *J* = 6.1 Hz, 1 H), 1.89 (br s, 2 H), 1.64–1.56 (m, 2 H), 1.42–1.20 (m, 6 H), 1.26 (superimposed s, 3 H), 1.02 (d, *J* = 6.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 110.4 (C), 64.9 (2 × CH_2), 47.2 (CH), 40.3 (CH_2), 39.5 (CH_2), 26.9 (CH_2), 24.5 (CH_2), 24.1 (2 × CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{22}NO_2$: 188.1645; found: 188.1642.

2,10-Diamino-6-methylundecan-6-ol (3i)

^{1}H NMR (300 MHz, $CDCl_3$) (mixture of diastereomers): δ = 2.91 (sext, *J* = 6.2 Hz, 2 H), 2.00–1.80 (br s, 5 H), 1.50–1.25 (m, 12 H), 1.17 (s, 3 H), 1.08 (d, *J* = 6.2 Hz, 6 H).

^{13}C NMR (75 MHz, CD_3OD): δ = 72.5 (C), 48.0 (CH), 42.0 (CH_2), 41.9 (CH_2), 41.8 (CH_2), 41.8 (CH_2), 37.3 (CH_2), 26.2 (CH_3), 26.1 (2 × CH_3), 26.0 (CH_3), 20.6 (CH_2), 19.7 (CH_3).

Because of the presence of phthalate residues in the mass spectrometer interfering with the mass determination of **3i**, HRMS analysis had to be performed after derivatization in bis(trifluoroacetamide) with *N*-methylbis(trifluoroacetamide) (3 equiv).

HRMS (TOF, ES+): *m*/*z* [M + NH_4]$^+$ calcd for $C_{16}H_{26}N_3O_3F_6$: 426.2186; found: 426.2188.

5-{2-[2-(4-Aminopentyloxy)ethoxy]ethoxy}pentan-2-amine (3j)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.00 (br s, 4 H), 3.60 (m, 8 H), 3.49 (t, *J* = 6.2 Hz, 4 H), 3.07 (m, 2 H), 1.70–1.45 (m, 8 H), 1.17 (d, *J* = 5.5 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 71.6 (CH_2), 70.7 (CH_2), 70.4 (CH_2), 47.5 (CH), 35.4 (CH_2), 26.6 (CH_2), 22.5 (CH_3).

HRMS (TOF, ES+): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{33}N_2O_3$: 277.2486; found: 277.2491.

Tetradecane-2,13-diamine (3k)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.84 (sext, *J* = 6.2 Hz, 2 H), 2.00–1.85 (br s, 4 H), 1.35–1.20 (m, 20 H), 1.03 (d, *J* = 6.2 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 48.1 (CH), 39.5 (CH_2), 30.2 (br, CH_2), 30.0 (br, CH_2), 26.8 (CH_2), 23.3 (CH_3).

HRMS (TOF, ES+): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{33}N_2$: 229.2638; found: 229.2634.

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