One-pot Synthesis of Cationic Amphiphiles from n-Alcohols and Allyl alcohols

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General Methods:

1H NMR spectra were run on Bruker Advance DPX 300 MHz in CDCl3, 13C NMR spectra were recorded at 75 MHz and 50 MHz in CDCl3. COSY, HMBC, HSQC spectras were recorded at 300 MHz in CDCl3. Chemical shifts are reported as values in ppm relative to CHCl3 (7.26) in CDCl3. TMS was used as internal standard. ESI mass spectra were recorded on JEOL SX 102/DA-6000. Chromatography was executed with silica gel (100-200 mesh) using mixtures of methanol and chloroform as eluants. Methanol and chloroform were dried and purified by distillation prior to use.
Experimental Procedures:

**Synthesis of alkylated triethylaminium compounds (2a-2d and 2j-2l)**

*Representative procedure for the preparation of N,N,N-triethyltridecan-1-aminium chloride (2a):* A solution of 1a (5.0 g, 25.0 mmol) in dichloromethane (10 mL) and triethylamine (10 mL) was added drop wise to a stirred solution of POCl₃ (7.6 g, 50.0 mmol) in dichloromethane (10 mL) at 0°C. After stirring the solution for 1 h, a solution of N,N-diethyl ethanolamine (4.4 g, 37.5 mmol) in triethylamine (10 mL) was added. The whole reaction mixture was stirred for 1 h at 0°C followed by 2 h at room temperature. Water was added to the reaction mixture and stirred for additional 30 min. 10% solution of citric acid and methanol-water (1:1) was added to the reaction mixture
and extracted into chloroform (3 x 100 mL). The combined organic layer was washed with methanol-water (1:1) and dried over anhyd. Na₂SO₄. The solvent was evaporated under reduced pressure and the crude product was chromatographed on silica gel as stationary phase and CHCl₃+MeOH+H₂O as mobile phase to afford the compound 2a (4.26 g, 60%). ESI-MS m/z: 284.4; ¹H NMR (CDCl₃, 300 MHz) δ 3.60-3.03 (m, 8H), 1.43 (m, 2H), 1.18-1.04 (m, 29H), 0.70 (t, J = 6.2 Hz, 3H); ¹³C NMR (CDCl₃, 50 MHz) δ 57.6, 53.6 (3C), 32.2, 30.0 (6C), 29.8, 29.7, 29.5, 26.8, 26.1, 23.0, 22.2, 14.4.

**Synthesis of alkylated pyridinium compounds (2f-2h and 2m-2o)**

Representative procedure for the preparation of 1-nonylpyridinium chloride (2f): A solution of 1f (5.0 g, 26.9 mmol) in dichloromethane (10 mL) and pyridine (10 mL) was added drop wise to the stirred solution of POCl₃ (8.25 g, 53.7 mmol) in dichloromethane (10 mL) at 0°C. After stirring for 1 h, a solution of N,N-diethyl-
Supporting Information

ethanolamine (4.7 g, 40.3 mmol) in pyridine (10 mL) was then added at 0ºC. The whole reaction mixture was stirred for 1 h at 0ºC followed by 2 h at room temperature. Water was added to the reaction mixture and stirred for additional 30 min. 10% solution of citric acid and methanol-water (1:1) was added in the reaction mixture and extracted into chloroform (2 x 100mL). The combined organic layer was washed with methanol-water (1:1) and dried over anhyd. Na₂SO₄. The solvent was evaporated under reduced pressure and the crude product was chromatographed on silica gel as stationary phase and CHCl₃+MeOH+H₂O as mobile phase to afford the compound 2f (3.67 g, 55%). ESI-MS m/z: 248.3; ¹H NMR (CD₃OD, 200 MHz) δ 9.04 (d, J = 5.8 Hz, 2H), 8.61 (t, J = 7.7 Hz, 1H), 8.13 (t, J = 6.9 Hz, 2H), 4.66 (t, J = 7.6, 2H), 2.03 (t, J = 6.9, 2H), 1.38-1.28 (m, 18H), 0.89 (t, J = 6.7, 3H); ¹³C NMR (CD₃OD, 50 MHz) δ 145.9, 145.0 (2C), 128.6 (2C), 62.2, 32.1, 31.5, 29.7 (2C), 29.6, 29.5, 29.1, 26.2, 22.7, 13.5.

**Synthesis of alkylated N-methylpiperidinium compound (2e)**

\[
\begin{array}{c}
\begin{array}{c}
\text{1e} \\
\text{OH}
\end{array} \\
\quad \\
\text{15}
\end{array}
\text{POCl}_3\quad \text{dichloromethane} \\
\text{N-methyl piperidine, 0 ºC.} \\
\begin{array}{c}
\begin{array}{c}
\text{15} \\
\text{N}
\end{array} \\
\text{2e}
\end{array}
\text{N,N-diethylethanolamine} \\
\text{0 ºC- rt.}
\end{array}
\]

A solution of 1e (5.0 g, 18.5 mmol) in dichloromethane (10 mL) and N-methyl piperidine (10 mL) was added drop wise to a stirred solution of POCl₃ (5.7 g, 37.0 mmol) in dichloromethane (10 mL) at 0ºC. After stirring the solution for 1 h, a solution of N,N-diethylethanolamine (3.2 g, 27.8 mmol) in N-methylpiperidine (10 mL) was added. The whole reaction mixture was stirred for 1 h at 0ºC followed by 2 h at room temperature. 5 mL of Water was added dropwise to the reaction mixture and stirred for additional 30
min. 10% solution of citric acid (10 mL) and methanol-water (1:1) was added to the reaction mixture and extracted into chloroform (3 x 100 mL). The combined organic layer was washed with methanol-water (1:1) and dried over anhyd. Na₂SO₄. The solvent was evaporated under reduced pressure and the crude product was chromatographed on silica gel as stationary phase and CHCl₃+MeOH+H₂O as mobile phase to afford the compound 2e (3.12 g, 48 %). ¹H NMR (CDCl₃, 200 MHz) δ 3.32-3.18 (m, 6H), 3.01 (s, 3H), 1.72-1.54 (m, 9H), 1.05 (m, 29H), 0.67 (t, J = 6.8, 3H); ¹³C NMR (CDCl₃, 50 MHz) δ 62.0, 61.1 (3C), 49.5, 32.1, 30.0 (8C), 29.9 (3C), 29.6, 26.7, 22.9, 22.1, 20.9, 20.3, 14.3.

**Synthesis of alkylated N, N-dimethylaminopyridine compound (2i)**

A solution of 1f (5.0 g, 26.8 mmol) in dichloromethane (10 mL) and N,N-dimethylaminopyridine (DMAP) (10 mL) was added drop wise to a stirred solution of POCl₃ (8.3 g, 53.7 mmol) in dichloromethane (10 mL) at 0°C. After stirring the solution for 1 h, a solution of N,N-diethyl ethanolamine (4.7 g, 40.3 mmol) in N,N-dimethylaminopyridine (10 mL) was added. The whole reaction mixture was stirred for 1 h at 0°C followed by 2 h at room temperature. 5 mL of water was added dropwise to the reaction mixture and stirred for additional 30 min. 10% solution of citric acid (10 mL) and methanol-water (1:1) was added to the reaction mixture and extracted into chloroform (3 x 100 mL). The combined organic layer was washed with methanol-water (1:1) and dried over anhyd. Na₂SO₄. The solvent was evaporated under reduced pressure and the crude product was chromatographed on silica gel as stationary phase and CHCl₃+MeOH+H₂O.
as mobile phase to afford the compound 2i (4.4 g, 57 %). ESI-MS m/z: 291.4; \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 300 MHz) \(\delta\) 7.96 (d, \(J = 7.6\) Hz, 2H), 6.66 (d, \(J = 7.3\) Hz, 2H), 3.42 (d, \(J = 10.68\) Hz, 2H), 3.07 (s, 6H), 1.47-1.43 (m, 14H), 1.47-1.09 (m, 18H), 0.71 (t, \(J = 6.8\), 3H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}+CD\textsubscript{3}OD, 50 MHz) \(\delta\) 157.3, 139.2 (2C), 106.6 (2C), 65.9, 39.7 (2C), 31.77 (5C), 29.5 (2C), 29.2, 25.6, 22.5, 13.8.
Fig. 1: $^1$H-spectrum of 2a (300 MHz, CDCl$_3$)

Fig. 2: $^{13}$C-NMR Spectrum of 2a (50 MHz, CDCl$_3$)
Fig. 3: Mass (ESI) Spectrum of 2a

Fig. 4: $^1$H-spectrum of 2b (300 MHz, CDCl$_3$)
Fig. 5: $^{13}$C-NMR Spectrum of 2b (75 MHz, CDCl$_3$)

Fig. 6: $^{13}$C DEPT 135-NMR Spectrum of 2b (75 MHz, CDCl$_3$)
Supporting Information

Fig. 7: COSY (\(^1\text{H} \rightarrow \text{H}\))-NMR Spectrum of \(2\text{b}\) (300 MHz, CDCl\(_3\))

Fig. 8: HSQC (\(^1\text{H} \rightarrow ^{13}\text{C}\))-NMR Spectrum of \(2\text{b}\) (300 MHz, CDCl\(_3\))
Fig. 9: HMBC (\textsuperscript{1}H→\textsuperscript{13}C)-NMR Spectrum of 2b (300 MHz, CDCl\textsubscript{3})

Fig. 10: Mass (ESI)-Spectrum of 2b
Fig. 11: $^1$H-NMR Spectrum of 2c (200 MHz, CDCl$_3$)

Fig. 12: $^{13}$C-NMR Spectrum of 2c (50 MHz, CDCl$_3$)
Supporting Information

Fig. 13: Mass (ESI) Spectrum of 2c

Fig. 14: $^1$H-NMR Spectrum of 2d (200 MHz, CDCl$_3$)
**Fig. 15:** $^{13}$C-NMR Spectrum of 2d (50 MHz, CDCl$_3$)

**Fig. 16:** Mass (ESI) Spectrum of 2d
**Fig. 17:** $^1$H-NMR Spectrum of 2e (200 MHz, CDCl$_3$)

**Fig. 18:** $^{13}$C-NMR Spectrum of 2e (50 MHz, CDCl$_3$)
Fig. 19: $^1$H-NMR Spectrum of 2f (200 MHz, CD$_3$OD)

Fig. 20: $^{13}$C-NMR Spectrum of 2f (50 MHz, CD$_3$OD)
Fig. 21: $^{13}$C-DEPT 135 NMR Spectrum of 2f (50 MHz, CD$_3$OD)

Fig. 22: $^{13}$C-DEPT 90 NMR Spectrum of 2f (50 MHz, CD$_3$OD)
Fig. 23: Mass (ESI) Spectrum of 2f

Fig. 24: $^1$H-NMR Spectrum of 2g (300 MHz, CDCl$_3$)
Fig. 25: $^{13}$C-NMR Spectrum of 2g (75 MHz, CDCl$_3$)

Fig. 26: $^{13}$C-DEPT 135 NMR Spectrum of 2g (75 MHz, CDCl$_3$)
Fig. 27: $^{13}$C DEPT 90-NMR Spectrum of 2g (75 MHz, CDCl$_3$)

Fig. 28: COSY (\textsuperscript{1}H→\textsuperscript{1}H)-NMR Spectrum of 2g (300 MHz, CDCl$_3$)
Supporting Information

Fig. 29: Mass (ESI) Spectrum of 2g

Fig. 30: $^1$H-NMR Spectrum of 2h (300 MHz, CDCl$_3$)
Fig. 31: $^{13}$C-NMR Spectrum of 2h (75 MHz, CDCl$_3$)

Fig. 32: Mass (ESI) Spectrum of 2h
Fig. 33: $^1$H-NMR Spectrum of 2i (300 MHz, CDCl$_3$)

Fig. 34: $^{13}$C-NMR Spectrum of 2i (50 MHz, CDCl$_3$)
**Fig. 35:** Mass Spectrum of 2i

**Fig. 36:** $^1$H-NMR Spectrum of 2j (200 MHz, CDCl$_3$)
Fig. 37: $^{13}$C-NMR Spectrum of 2j (50 MHz, CDCl$_3$)

Fig. 38: Mass (ESI) Spectrum of 2j
Fig. 39: $^1$H-NMR Spectrum of $2k$ (200 MHz, CDCl$_3$)

Fig. 40: $^{13}$C-NMR Spectrum of $2k$ (50 MHz, CDCl$_3$)
Supporting Information

**Fig. 41:** Mass (ESI) Spectrum of 2k

**Fig. 42:** $^1$H-NMR Spectrum of 2l (200 MHz, CDCl$_3$)
Fig. 43: $^{13}$C-NMR Spectrum of 2l (50 MHz, CDCl$_3$)

Fig. 44: $^{13}$C-DEPT 135-NMR Spectrum of 2l (50 MHz, CDCl$_3$)
**Fig. 45:** $^{13}$C-DEPT 90-NMR Spectrum of 2l (50 MHz, CDCl$_3$)

**Fig. 46:** Mass (ESI) Spectrum of 2l
**Fig. 47:** \(^1\)H-NMR Spectrum of \(2m\) (200 MHz, CDCl\(_3\))

**Fig. 48:** \(^{13}\)C-NMR Spectrum of \(2m\) (75 MHz, CDCl\(_3\))
Fig. 49: $^{13}$C-DEPT 135-NMR Spectrum of 2m (75 MHz, DMSO-D$_6$)

Fig. 50: $^{13}$C-DEPT 90 NMR Spectrum of 2m (75 MHz, DMSO-D$_6$)
Supporting Information

Fig. 51: COSY (\textsuperscript{1}H→\textsuperscript{1}H)-NMR Spectrum of 2m (300 MHz, DMSO-D\textsubscript{6})

Fig. 52: HSQC (\textsuperscript{1}H→\textsuperscript{13}C)-NMR Spectrum of 2m (300 MHz, DMSO-D\textsubscript{6})
Supporting Information

Fig. 53: HMBC ($^1$H→$^{13}$C)-NMR Spectrum of 2m (300 MHz, DMSO-D$_6$)

Fig. 54: Mass (ESI) Spectrum of 2m
Fig. 55: $^1$H-NMR Spectrum of $2n$ (300 MHz, DMSO-D$_6$)

Fig. 56: $^{13}$C-NMR Spectrum of $2n$ (75 MHz, DMSO-D$_6$)
Fig. 57: $^{13}$C-DEPT 135-NMR Spectrum of $2n$ (75 MHz, DMSO-D$_6$)

Fig. 58: $^{13}$C-DEPT 90-NMR Spectrum of $2n$ (75 MHz, DMSO-D$_6$)
Supporting Information

**Fig. 59:** Mass (ESI) Spectrum of 2n

**Fig. 60:** $^1$H-NMR Spectrum of 2o (300 MHz, CDCl$_3$+CD$_3$OD)
Fig. 61: $^{13}$C-NMR Spectrum of $2o$ (75 MHz, CDCl$_3$+CD$_3$OD)

Fig. 62: $^{13}$C-DEPT 135-NMR Spectrum of $2o$ (75 MHz, CDCl$_3$+CD$_3$OD)
Fig. 63: $^{13}$C-DEPT 90-NMR Spectrum of 2o (75 MHz, CDCl$_3$+CD$_3$OD)

Fig. 64: Mass (ESI) Spectrum of 2o