Supplementary information

A more sustainable and highly practicable synthesis of aliphatic isocyanides

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General information

Nuclear Magnetic Resonance Spectroscopy (NMR):

$^1$H- and $^{13}$C-NMR spectra were recorded on BRUKER Avance DPX spectrometers (Billerica, MA) with a 5-mm dual proton/carbon probe (300 and 400 MHz) and on a Bruker Avance III with a 5 mm $z$-gradient cryogenically cooled probe head (CPTCI, 600 MHz $^1$H/75.5 MHz). Unless otherwise stated, all spectra were measured at ambient temperature. The chemical shift for $^1$H-MR spectra was reported in parts per million (ppm) and referenced to characteristic solvents of partly deuterated solvents e.g. CDCl$_3$ at 7.26 ppm. $^{13}$C-MR spectra were reported in ppm relative to characteristic signals of partly deuterated solvents, e.g. the centroid peak of the CDCl$_3$ triplet at 77.2 ppm. The spin multiplicity and corresponding signal patterns were abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext. = sextet, m = multiplet and br = broad signal. Coupling constants $J$ were noted in Hz. Furthermore, 2D-NMR methods, e.g. heteronuclear multiple quantum coherence (HMQC), heteronuclear single quantum coherence (HSQC), heteronuclear multiple bond correlation (HMBC) and correlated spectroscopy (COSY) were carried out, if necessary, for signal assignment and structure elucidation. If conformers (rotamers) of a substance could be observed due to restricted rotation, all species which could be assigned clearly were labelled with additional appendices (a, b, c, etc.). Hereby, the main conformer was labelled with the appendix “a”, the second conformer with appendix “b” and so on.

Mass Spectrometry (MS):

Fast-atom-bombardment (FAB) and electron ionization (EI) spectra were recorded utilizing a Finnigan MAT 95 mass spectrometer. A Q Exactive (Orbitrap) mass spectrometer (Thermo Fisher Scientific, San Jose, CA, USA) equipped with a HESI II probe was employed to record high resolution electrospray ionization–MS (ESI-MS). Calibration was carried out in the $m/z$ range 74–1,822 using premixed calibration solutions (Thermo Fisher Scientific). A constant spray voltage of 4.7 kV and a dimensionless sheath gas of 5 were employed. The S-lens RF level was set to 62.0, while the capillary temperature was set to 250 °C. All samples were dissolved at a concentration of 0.05 mg mL$^{-1}$ in a mixture of THF and MeOH (3:2) doped with 100 pmol sodium trifluoroacetate and injected with a flow of 5 µl min$^{-1}$.

Column chromatography;

TLC silica gel F254 (Sigma Aldrich) and solvents, which had HPLC-purity, were used.

Infrared Spectroscopy (IR):

Infrared spectra (IR) were recorded on a BRUKER Alpha-p instrument applying ATR-technology (ATR = Attenuated Total Reflection) in a frequency range from 3998 to 374 cm$^{-1}$. The band intensities were characterized in relation to the most intense signal as follows: s = strong, m = medium, w = weak. In addition, broad signals were expressed by the term: br = broad

Gas Chromatography (GC):

Gas chromatography (GC) was performed on a Bruker 430 GC instrument equipped with capillary column FactorFour™ VF-5 ms (30.0 m x 0.25 mm x 0.25 µm), using flame ionization detection (FID). The oven temperature program was: initial temperature 95 °C, hold for 1 min, ramp at 15 °C min$^{-1}$ to 220 °C, hold for 4 min, ramp at 15 °C min$^{-1}$ to 300 °C, hold for 2 min, ramp at 15 °C min$^{-1}$ to 325 °C, hold for 3 min. Measurements were performed in split-split mode using nitrogen as the carrier gas (flow rate 30 ml min$^{-1}$).

Size Exclusion Chromatography (SEC):

SEC measurements were performed on a SHIMADZU Size Exclusion Chromatography (SEC) system equipped with a SHIMADZU isocratic pump (LC-20AD), a SHIMADZU refractive index detector (24°C) (RI-D-20A), a SHIMADZU autosampler (SIL-20A) and a VARIAN column oven (510, 50°C). For separation, a three-column setup was used with one SDV 3 µm, 8×50 mm precolumn and two SDV 3 µm, 1000 Å, 3×300 mm columns supplied by PSS, Germany. Tetrahydrofuran (THF) stabilized with 250 ppm butylated hydroxytoluene (BHT, ≥99.9%) supplied by SIGMA-ALDRICH was used at a flow rate of 1.0 mL min$^{-1}$. Calibration was carried out by injection of eight narrow polymethylmethacrylate standards ranging from 102 to 58300 kDa.

Thin Layer Chromatography (TLC):

For TLC analysis, precoated aluminium foils with fluorescence indicator from MERCK (TLC Silica gel 60, F254, layer thickness: 0.25 mm) were employed as stationary phase. The spots were firstly visualized by fluorescence quenching under UV-light ($\lambda = 254$ nm), fluorescence ($\lambda = 365$ nm), and by staining with Seebach reagent: solution of 2.50 g cerium(IV) sulfate
tetrahydrate (Ce(SO\(_4\))\(_2\) \times 4 \text{H}_2\text{O}), 6.25 g ammonium heptamolybdate tetrahydrate (NH\(_4\))\(_6\)Mo\(_7\)O\(_{24}\) \times 4 \text{H}_2\text{O}), 225 mL water and 25.0 mL concentrated sulfuric acid. Or vanillin: solution of 15 g vanillin and 2.5 mL concentrated sulfuric acid in 250 mL ethanol.
**Materials:**

All chemicals were used as received, if not mentioned otherwise. All solvents used in HPLC grade or higher apart from dichlormethane and diethylether which were technical grade and thus, were distilled beforehand.

Adamantly amine (Alfar Aesar 98 %), 4-aminobenzoic acid (Alfar Aesar 99 %), amino decane (Alfar Aesar, 97 %), amino octadecane (TCI >85 %), 11-aminoundecanoic acid (Aldrich Chemistry, 97 %), benzyl amine (Merck kGaA, >99 %), cyclohexyl amine (Aldrich Chemistry, 99 %), 1,12-diamino dodecane (Aldrich Chemistry 98 %), 1,5-diamino pentane (ACROS Organics, 98 %), ethyl formate (ACROS 98+ %), formic acid (ACROS Organics 99 %), heptanal (Aldrich 95 %), 6-hydroxyhexyl amine (TCI >97 %), pyridine (Fisher Scientific UK, 99.9 %), oleylamine (Sigma-Aldrich, >98 %), para-toluenesulfonyl chloride (Sigma-Aldrich ≥98 %), sebacic acid (Aldrich Chemistry 99 %), sodium sulphate (dry, Bernd Kraft), thionyl chloride (ACROS Organics 99.5+ %), tetradecane (Sigma-Aldrich, ≥99 %).
Synthesis and characterization of $N$-formamides

General synthesis of aliphatic $N$-formamides

The corresponding aliphatic amine (30.0 mmol, 1.00 eq.) and ethyl formate (24.2 mL, 22.2 g, 300 mmol, 10.0 eq.) were heated under reflux overnight. Afterwards, remaining ethyl formate and ethanol were removed under reduced pressure and the crude product was used without further purification or analysis.

Exceptions:

Adamantyl $N$-formamide

Adamantyl amine, chloroform and ethyl formate were heated under reflux for 48 hours. Afterwards, remaining ethyl formate, chloroform and ethanol were removed under reduced pressure and the crude product was used without further purification or analysis.

$N$-(6-Hydroxyhexyl)formamide

6-Amino hexane-1-ol (5.00 g, 42.7 mmol, 1.00 eq.) and ethyl formate (34.4 mL, 34.6 g, 427 mmol, 10.0 eq.) were heated under reflux for 20 hours. Afterwards, remaining ethyl formate and ethanol were removed under reduced pressure, and the crude mixture was stored for two weeks at room temperature. The product crystallized from the solution and was obtained as white solid (1.70 g, 11.7 mmol) in a yield of 27% after filtration and washing with cyclohexane and ethyl acetate. 

$R_f = 0.16$ (cyclohexane/ethyl acetate, 1:1) visualized via Seebach staining solution.

$^1$H-NMR (500 MHz, DMSO-$d_6$) δ/ppm = 7.98-7.91 (m, 2H, NH, CH, $^1$), 4.34 (t, $^3J = 5.1$ Hz, 2H, CH$_2$, $^2$), 3.40-3.35 (m, 2H, CH$_2$, $^3$), 3.07 (q, $^3J = 6.5$ Hz, 2H, CH$_2$, $^4$), 1.43-1.37 (m, 2H, CH$_2$, $^5$), 1.31-1.25 (m, 4H, CH$_2$, $^6$).

$^{13}$C-NMR (126 MHz, DMSO-$d_6$) δ/ppm = 164.5, 160.9, 60.7, 40.8, 37.1, 32.5, 31.0, 29.1, 26.3, 25.8, 25.2.
El-MS m/z: [M-H]^+ calculate for \([C_7H_{14}O_2N_1]^{+}\) = 144.1025, found: 144.1025, Δ = 0.0752 mmu.

IR (ATR platinum diamond): \(\nu/\text{cm}^{-1}\) = 3374.0 (m), 3307.8 (s), 3035.1 (w), 2933.6 (m), 2854.5 (m), 1640.4 (s), 1523.9 (s), 1463.8 (m), 1362.9 (s), 1282.7 (m), 1240.9 (m), 1215.4 (w), 1107.2 (w), 1062.1 (m), 1048.0 (s), 1024.8 (m), 1005.6 (m), 975.4 (m), 781.9 (m), 738.8 (w), 705.3 (s), 638.2 (s).
11-Formamidoundecanoic acid

11-Aminoundecanoic acid (25.1 g, 125 mmol, 1.00 eq.) was suspended in ethyl formate (101 mL, 92.6 g, 1.25 mol, 10.0 eq.) and DMF (50 mL), and was stirred at 75 °C until a clear solution was formed (mostly 20 – 26 h). After the reaction was finished, the solvent was removed under reduced pressure and the product was used without further purification. The product was obtained as white solid (28.7 g, 125 mmol) in quantitative yield.

\[ ^1H\text{-NMR} \ (500 \text{ MHz, DMSO-}d_6) \delta/\text{ppm} = 11.93 \ (\text{br, } 1H, \text{ COOH, } 1), \ 7.98 – 7.91 \ (\text{m, } 2H, \text{ CH, NH, } 2), \ 3.08 – 3.04 \ (\text{m, } 2H, \text{ CH}_2, 3), \ 2.19 \ (t, \ J = 7.4 \text{ Hz, } 2H, \text{ CH}_2, 4), \ 1.51 – 1.36 \ (\text{m, } 4H, \text{ CH}_2, 5), \ 1.25 \ (\text{m, } 12H, \text{ CH}_2, 6). \]

\[ ^{13}C\text{-NMR} \ (126 \text{ MHz, DMSO-}d_6) \delta/\text{ppm} = 174.6, \ 164.5, \ 160.9, \ 37.1, \ 33.7, \ 30.9, \ 29.0, \ 29.0, \ 28.9, \ 28.9, \ 27.8, \ 28.8, \ 28.7, \ 28.6, \ 28.6, \ 26.4, \ 25.9, \ 24.5. \]

\[ \text{FAB-HRMS} \ m/z: \ [M+H]^+ \text{ calculated for } [C_{12}H_{24}NO_3] \ 230.1756, \text{ found: } 230.1755 \ \Delta = -0.107 \text{ mmu.} \]

\[ \text{IR} \ (\text{ATR platinum diamond}): \ \nu/\text{cm}^{-1} = 3358.8 \ (\text{w}), \ 2938.6 \ (\text{w}), \ 2918.6 \ (\text{s}), \ 2849.3 \ (\text{w}), \ 2577.6 \ (\text{w}), \ 1720.9 \ (\text{s}), \ 1646.7 \ (\text{w}), \ 1626.3 \ (\text{s}), \ 1525.6 \ (\text{m}), \ 1470.7 \ (\text{m}), \ 1438.2 \ (\text{m}), \ 1409.8 \ (\text{w}), \ 1362.8 \ (\text{s}), \ 1319.3 \ (\text{w}), \ 1293.7 \ (\text{w}), \ 1273.4 \ (\text{m}), \ 1243.3 \ (\text{m}), \ 1206.6 \ (\text{m}), \ 1177.5 \ (\text{s}), \ 1108.8 \ (\text{w}), \ 1054.9 \ (\text{w}), \ 933.6 \ (\text{m}), \ 896.5 \ (\text{w}), \ 806.3 \ (\text{w}), \ 765.2 \ (\text{w}), \ 740.2 \ (\text{w}), \ 718.8 \ (\text{s}), \ 662.5 \ (\text{m}), \ 548.0 \ (\text{w}), \ 529.4 \ (\text{w}), \ 448.3 \ (\text{s}). \]
General Synthesis of Aromatic N-formamides

Methyl-4-formamidobenzoate

In a flask equipped with a Dimroth-cooler, methyl 4-aminobenzoate (9.82 g, 65.0 mmol, 1.00 eq.) was dissolved in formic acid (9.80 mL, 12.0 g, 260 mmol, 4.00 eq.) and was heated to 60°C for 24 h. Afterwards, formic acid and water were removed under reduced pressure and the product (11.0 g, 61.4 mmol) was obtained as white powder in a yield of 95% without further purification.

$R_f = 0.13$ (cyclohexane/ethyl acetate, 2:1) visualized via UV quenching at 254 nm, vanillin and Seebach staining solution.

$^1$H-NMR (500 MHz, DMSO-$d_6$) δ/ppm = 10.56 (s, 1H, CH, $^a_1$), 10.47 (d, $^3J = 10.7$ Hz, 1H, CH, $^b_1$), 8.97 (d, $^3J = 10.7$ Hz, 1H, NH, $^b_2$), 8.35 (d, $^3J = 1.7$ Hz, 1H, NH, $^a_2$), 7.93 - 7.88 (m, 2H, aromatic, $^a_3, b_3$), 7.71 (d, $^3J = 8.8$ Hz, 2H, aromatic, $^a_4$), 7.31 (d, $^3J = 8.6$ Hz, 2H, aromatic, $^{14}$), 3.81 (s, 3H, CH$_3$, $^5$).

$^{13}$C-NMR (126 MHz, CDCl$_3$) δ/ppm = 165.8, 163.2, 162.6, 160.2, 142.5, 130.8, 130.4, 124.4, 118.7, 116.5, 51.9.

EI-HRMS m/z: [M]$^+$ calculated for [C$_9$H$_9$O$_3$N$_1$]$^+$ = 179.0582, found: 179.0584, $\Delta = 0.1270$ mmu.

IR (ATR platinum diamond): $\tilde{v}$/cm$^{-1}$ = 3182.0 (w), 3052.5 (w), 2961.9 (w), 2883.8 (w), 1715.5 (s), 1610.6 (s), 1522.1 (m), 1437.8 (m), 1419.3 (m), 1273.2 (s)1188.9 (s), 1038.7 (m), 1016.1 (m), 962.6 (m), 884.5 (m), 847.4 (s), 816.6 (s), 763.1 (s), 687.0 (s), 635.6 (m), 522.5 (s), 506.0 (m), 479.3 (w), 456.6 (m).
Synthesis of other compounds

**Methyl-4-aminobenzoate**

4-Aminobenzoic acid (20.0 g, 146 mmol, 1.00 eq.) was dissolved in methanol (594 mL, 468 g, 14.6 mol, 100 eq.) and the mixture was cooled with an ice bath to 0°C. Subsequently, thionyl chloride (31.7 mL, 52.0 g, 438 mmol, 3.00 eq.) was added dropwise and the solution was stirred at room temperature overnight. The solution was neutralized with saturated NaHCO₃-solution and then K₂CO₃ was added till a pH-value of eight was acquired. Precipitating salts were dissolved by addition of water. Afterwards the organic phase was extracted with DCM (7 × 150 mL) and the combined organic layers were dried over sodium sulfate and filtered off. The product (22.0 g, 146 mmol) was obtained as slightly yellow crystals after removing the solvent under reduced pressure in quantitative yield.

R₁ = 0.45 (cyclohexane/ethyl acetate, 2:1) visualized via UV quenching at 254 nm.

**¹H-NMR** (500 MHz, DMSO-d₆) δ/ppm = 7.65 (d, J = 8.7 Hz, 2H, aromatic, ¹), 6.58 (d, J = 8.7 Hz, 2H, aromatic, ²), 5.97 (s, 2H, NH, ³), 3.73 (s, 3H, CH₃, ⁴).

**¹³C-NMR** (126 MHz, CDCl₃) δ/ppm = 166.4, 153.5, 131.1, 115.8, 112.7, 51.2.

**EI-HRMS** m/z: [M]+ calculated for [C₈H₉O₂N₁]⁺ = 151.0633, found: 151.0634, Δ = 0.0897 mmu.

**IR** (ATR platinum diamond): ν/cm⁻¹ = 3406.2 (w), 3334.2 (m), 3229.3 (w), 2943.4 (w), 1680.5 (s), 1633.2 (m), 1594.1 (s), 1513.9 (m), 1433.7 (m), 1312.3 (3), 1281.5 (s), 1197.1 (w), 1174.5 (m), 1116.9 (s), 1077.8 (m), 849.5 (w), 767.2 (s), 697.3 (m), 586.2 (w), 506.0 (m).
Benzyl 11-formamidoundecanoate

11-Formamidoundecanoic acid (22.9 g, 100 mmol, 1.00 eq.) was suspended DCM (50 mL) and DIPEA (19.6 mL, 14.9 g, 115 mmol, 1.15 eq.) was added. Under stirring, benzyl bromide (17.8 mL, 25.7 g, 150 mmol, 1.50 eq.) in DCM (25 mL) was slowly added via a dropping funnel. The reaction mixture was stirred overnight at room temperature. After full conversion was indicated via TLC, triethylamine (7.62 mL, 5.57 g, 55.0 mmol, 0.55 eq.) was added and the reaction was stirred for another hour. Afterwards water (150 mL) was added, the phases were separated, and the aqueous phase was extracted with DCM (3 × 75 mL). The combined organic extracts were washed with water (3 × 150 mL). The combined organic extracts were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The product was obtained as a slightly yellow solid (32.6 g, 102%) and was used without further purification. The analytical data is according to the literature.

$R_f = 0.25$ (cyclohexane/ethyl acetate, 1:2) visualized via UV quenching at 254 nm and Seebach staining solution.

$^1$H-NMR (500 MHz, CDCl$_3$) δ/ppm = 8.15 (s, 1H, CH$_{1a}$), 8.03 (d, $^3J = 7$ Hz, 1H, CH$_{1b}$), 7.37 – 7.26 (m, 5H, aromatic), 5.65 (br, 1H, NH$_3$), 5.11 (s, 2H, CH$_2$$_4$), 3.28 (m, 2H, CH$_2$$_5$), 3.19 (m, 2H, CH$_2$$_6$), 2.34 (t, $^3J = 7.5$ Hz, 2H, CH$_2$$_6$), 1.63 (p, $^3J = 7.5$ Hz, 2H, CH$_2$$_7$), 1.28 – 1.25 (m, 12H, CH$_2$$_9$).


FAB-HRMS m/z: [M+H]$^+$ calculated for [C$_{19}$H$_{30}$NO$_3$]$^+$ = 320.2220, found: 320.2222, Δ = -0.20 mmu.

IR (ATR platinum diamond): $\nu$/cm$^{-1}$ = 3265.7 (w), 3069.9 (w), 2914.9 (m), 2877.4 (w), 2848.4 (w), 1731.9 (m), 1652.5 (s), 1556.6 (w), 1496.9 (w), 1407.0 (m), 1450.7 (w), 1417.4 (w), 1380.1 (m), 1351.6 (w), 1330.2 (w), 1300.0 (w), 1268.0 (w), 1246.6 (w), 1234.2 (w), 1213.3 (w), 1200.1 (w), 1160.5 (s), 1108.8 (w), 1083.2 (w), 1055.3 (w), 1029.2 (w), 997.2 (w), 938.8 (m), 923.5 (w), 903.9 (w), 866.6 (w), 825.6 (w), 806.7 (w), 753.5 (m), 718.8 (w), 695.9 (s), 609.4 (w), 520.1 (m), 487.6 (w), 451.7 (m).
Synthesis Procedure for P-3CR polymer 16

Using column purified diisocyanide 9

Decanedioic acid 14 (405 mg, 2.00 mmol, 1.00 eq.), heptanal 15 (1.69 mL, 1.37 mg, 0.12 mmol, 6.00 eq.) and 1,12-diisocyanododecane 9 (441 mg, 2.00 mmol, 1.00 eq.) were stirred under argon atmosphere at room temperature for 24 hours. The obtained solid was dissolved in DCM (3 mL) and was then precipitated into diethylether (75 mL). Polymer 16 (886 mg, $M_n = 10517$ Da, $M_w = 16760$ Da, PDI = 1.59) was obtained after filtration and removal of remaining solvent under reduced pressure as a brownish highly viscous oil in a yield of 67% (in correspondence to the theoretical, maximal mass of the polymer).

Using diisocyanide 9 purified by washing

Decanedioic acid 14 (405 mg, 2.00 mmol, 1.00 eq.), heptanal 15 (1.69 mL, 1.37 mg, 0.12 mmol, 6.00 eq.) and 1,12-diisocyanododecane 9 (441 mg, 2.00 mmol, 1.00 eq.) were stirred under argon atmosphere at room temperature for 24 h. The obtained solid was dissolved in DCM (3 mL) and was then precipitated with diethylether (75 mL). Polymer 16 (886 mg, $M_n = 10517$ Da, $M_w = 16760$ Da, PDI = 1.59) was obtained after filtration and removal of remaining solvent under reduced pressure as a brownish highly viscous oil in a yield of 63% (in correspondence to the theoretical, maximal mass of the polymer).

$^1$H-NMR (500 MHz, CDCl$_3$) δ/ppm = 6.06 (br, 2H, NH, 1), 5.17-5.13 (m, 2H, CH, 2), 3.27-3.21 (m, 4H, CH$_2$, 3), 2.38 (t, $^3J = 7.5$ Hz, 4H, CH$_2$, 4), 1.88-1.75 (m, 4H, CH$_2$, 5), 1.68-1.59 (m, 4H, CH$_2$, 6), 1.52-1.44 (m, 4H, CH$_2$, 7), 1.35-1.24 (m, 40H, CH$_2$, 8), 0.86 (t, $^3J = 7.0$ Hz, CH$_3$, 9).

$^{13}$C-NMR (126 MHz, DMSO-d$_6$) δ/ppm = 172.6, 170.0, 74.1, 39.4, 34.4, 32.1, 31.8, 29.7, 29.2, 29.0, 27.0, 25.0, 24.8, 22.7, 14.2.
IR (ATR platinum diamond): ν/cm⁻¹ = 3291.3 (w), 2923 (s), 2853.7 (m), 1741.3 (m), 1653.3 (s), 1538.3 (m), 1464.0 (m), 1375.7 (w), 1236.9 (m), 1161.6 (m), 1095.5 (m), 723.0 (w).

**GPC:** Red curve: Passerini-polymer 16 when 1, 12-diisocyano dodecane 9 was used which was purified by flash column chromatography beforehand. $M_n = 10517$ Da, $M_w = 16760$, $Đ = 1.59$.

Black curve: Passerini-polymer 16 when 1, 12-diisocyano dodecane 9 was used which was purified by washing beforehand. $M_n = 8328$ Da, $M_w = 12615$, $Đ = 1.51$. 

![Graph showing IR spectra and GPC traces](image-url)
GC-Screening, synthesis and characterization of isocyanides

General isocyanide screening with internal standard (3.00 mmol scale)

In order to determine the concentration of isocyanooctadecane in the GC screening experiments, a gas chromatography calibration curve with tetradecane as internal standard (IS) was compiled by measuring six samples.

Table S1: Six sample of different concentrations of isocyanide 2 and the same concentration of IS were measured and the ratio of the area of the isocyanide 2 and the area of IS were calculated.

<table>
<thead>
<tr>
<th>Sample</th>
<th>A(2)</th>
<th>A(IS)</th>
<th>c(2) / mg/mL</th>
<th>c(IS) / mg/mL</th>
<th>c(2) / c(IS)</th>
<th>A(2) / A(IS)</th>
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<td>0.100</td>
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<tr>
<td>4</td>
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<td>0.100</td>
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</tr>
<tr>
<td>5</td>
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<td>0.100</td>
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</tr>
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<td>6</td>
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<td>5.85</td>
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</tbody>
</table>

Figure 1: Calibration curve calculated using a linear fit (red line). The obtained slope was 0.0989 and the R²-value was 0.996.

In a typical GC screening experiment, 3.00 mmol of N-formamido octadecane was dissolved in a solvent (various amount) and then, reacted with a dehydrating agent (various amounts) in presence of a base (various amounts) and a given amount of tetradecane (mostly 10 mol%). Samples were taken after different reactions times and the resulting areas of the signals of tetradecane and the product 2 were determined to calculate the yield of each specific reaction condition applying the following formulas:
\[ R_{x/is} = \frac{A_x/A_{is}}{c_x/c_{is}} \]

\( R_{x/is} \) is the slope of the calibration curve, whereas \( A_{is} \), \( A_x \), \( c_x \) and \( c_{is} \) correspond to the measured area and concentration of standard (is) and analyte (x).

\[ c_x = \frac{c_x}{c_{is}} c_{is} \]

As the amount of internal standard and therefore its concentration is known, the unknown concentration of analyte (x) and the corresponding yield can be calculated, respectively.

**General isocyanide synthesis in DCM (5.00 mmol scale)**

The formamide (5.00 mmol, 1.00 eq.) was dissolved in DCM (5 mL) and pyridine (15.0 mmol, 3.00 eq.) was added. Subsequently, \( p \)-TsCl (7.50 mmol, 1.50 eq.) was added under cooling with a water bath. The cooling was removed, and the reaction mixture was stirred until full conversion (monitored via TLC, average reaction time of 2 hours) was observed. Afterwards, aqueous Na\(_2\)SO\(_4\)-solution (5 mL, 20 wt%) was added and the biphasic mixture was stirred for another 30 minutes. Water (10 mL) and DCM (10 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 \( \times \) 5 mL), the organic extracts were combined and washed with water (3 \( \times \) 5 mL) and saturated sodium chloride solution (2 \( \times \) 5 mL). The organic extract was dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. Further purification was not necessary in many cases. Nevertheless, purification by flash column chromatography (mixture of cyclohexane and ethyl acetate) could be applied to obtain the product in higher purity.

**General isocyanide synthesis in DMC (5.00 mmol scale)**

The formamide (5.00 mmol, 1.00 eq.) was dissolved in DCM (5 mL) and pyridine (15.0 mmol, 3.00 eq.) was added. Subsequently, \( p \)-TsCl (7.50 mmol, 1.50 eq.) was added under cooling with a water bath. The cooling was removed, and the reaction mixture was stirred until full conversion (monitored via TLC, average reaction time of 24 hours) was observed. Afterwards, aqueous Na\(_2\)SO\(_4\)-solution (5 mL, 20 wt%) were added and the biphasic mixture was stirred for another 30 minutes. Water (10 mL) and DMC (10 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DMC (3 \( \times \) 5 mL), the organic extracts were combined and washed with water (3 \( \times \) 5 mL) and saturated sodium chloride solution (2 \( \times \) 5 mL). The organic extract was dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. Further purification was not necessary in many cases. Nevertheless, purification by flash column chromatography (mixture of cyclohexane and ethyl acetate) could be applied to obtain the product in higher purity.)
1-Isocyano octadecane 2

Obtained as rose solid in a yield of 96 % (DCM) or 89 % (DMC).

\(R_f = 0.47\) (cyclohexane/ethyl acetate, 15:1) visualized via UV quenching at 254 nm and vanillin staining solution.

\(^1H\)-NMR (500 MHz, CDCl\(_3\)) \(\delta/\text{ppm} = 3.31 \ (\text{tt}, \ ^3J = 6.8 \text{ Hz}, \ ^2J = 1.8 \text{ Hz}, \ 2\text{H}, \ \text{CH}_2, \ ^1), 1.61 \ (\text{m}, \ 2\text{H}, \ \text{CH}_2, \ ^3), 1.36 \ (\text{t}, \ ^3J = 7.0 \text{ Hz}, \ 2\text{H}, \ \text{CH}_3, \ ^3), 1.23-1.19 \ (\text{m}, \ 30\text{H}, \ \text{CH}_2, \ ^4), 0.81 \ (\text{t}, \ ^3J = 7.0 \text{ Hz}, \ 3\text{H}, \ \text{CH}_3, \ ^5).

\(^{13}C\)-NMR (126 MHz, CDCl\(_3\)) \(\delta/\text{ppm} = 155.7 \ (\text{t}), 41.7 \ (\text{t}), 32.1, 29.8, 29.7, 29.5, 29.3, 28.9, 26.5, 22.8, 14.3.

EI-HRMS m/z: [M]+ calculated for \([C_{19}H_{37}N_1]^+ = 279.2925\), found: 279.2926, \(\Delta = 0.1324\) mmu.

IR (ATR platinum diamond): \(\nu/\text{cm}^{-1} = 2912.6 \ (s), 2848.8 \ (s), 2151.5 \ (m), 1470.7 \ (m), 717.9 \ (m).\)
1-Isocyno dodecane 3

Obtained as yellow liquid in a yield of 90% (DCM) and 94% (DMC).

$R_f = 0.58$ (cyclohexane/ethyl acetate, 15:1) visualized via UV quenching at 254 nm and vanillin staining solution (orange).

$^1$H-NMR (500 MHz, CDCl$_3$) $\delta$/ppm = 3.37 (tt, $^3J = 6.8$ Hz, $^2J = 1.9$ Hz, 2H, CH$_2$, 1), 1.70-1.62 (m, 2H, CH$_2$, 1), 1.42 (quint, $^3J = 7.3$ Hz, 2H, CH$_2$, 2), 1.30-1.26 (m, 16H, CH$_2$, 4), 0.87 (t, $^3J = 7.0$ Hz, CH$_3$, 5).

$^{13}$C-NMR (126 MHz, CDCl$_3$) $\delta$/ppm = 155.7 (t), 41.7 (t), 32.0, 29.7, 29.6, 29.5, 29.4, 29.2, 28.8, 26.4, 22.8, 14.2.

EI-HRMS m/z: [M-H]$^-$ calculated for [C$_{13}$H$_{24}$N$_1$]$^-$ = 194.1909, found: 194.1909, $\Delta = 0.0392$ mmu.

IR (ATR platinum diamond): $\nu$/cm$^{-1}$ = 2922.9 (s), 2852.9 (s), 2145.4 (s), 1458.3 (m).
(Z)-1-Isocyanoctadec-9-ene 4

Was obtained as yellowish oil in a yield of 97 % (DCM) and 98 % (DMC)
$R_f = 0.70$ (cyclohexane/ethyl acetate, 9:1) visualized via vanillin staining solution (yellow/orange to brown).

$^1$H-NMR-spectra is in accordance with the literature.$^3$
**Benzyl 11-isocyanoundecanoate 5**

Obtained as yellowish liquid in a yield of 97% (DCM) and 87% (DMC)

$R_f = 0.63$ (cyclohexane/ethyl acetate, 9:1) visualized via UV quenching at 254 nm and vanillin staining solution (brown).

**$^1$H-NMR** (500 MHz, CDCl$_3$) $\delta$/ppm = 7.37-7.30 (m, 5H, aromatic, 1$^\text{st}$), 5.11 (s, 2H, CH$_2$, 2$^\text{nd}$), 3.35 (tt, $^1J = 6.8$ Hz, $^2J = 1.9$ Hz, 2H, CH$_2$, 3$^\text{rd}$), 2.35 (t, $^1J = 7.5$ Hz, 2H, CH$_2$, 4$^\text{th}$) 1.69-1.61 (m, 4H, CH$_2$, 5$^\text{th}$), 1.41 (quint, $^1J = 7.3$ Hz, 4H, CH$_2$, 6$^\text{th}$), 1.33-1.28 (m, 10H, CH$_2$, 7$^\text{th}$).

**$^{13}$C-NMR** (126 MHz, CDCl$_3$) $\delta$/ppm = 173.6, 155.7 (br), 136.1, 128.5, 128.1, 66.0, 41.5 (t), 34.3, 29.3, 29.1, 29.0, 28.6, 26.3, 24.9.

**EI-HRMS** m/z: [M]$^+$ calculated for [C$_{19}$H$_{27}$O$_2$N$_1$]$^+$ = 301.2042, found: 301.2043, $\Delta = 0.1494$ mmu.

**IR (ATR platinum diamond):** $\nu$/cm$^{-1}$ = 2924.9 (s), 2855.0 (s), 2145.4 (m), 1734.0 (s), 1454.2 (m), 1162.2 (s), 736.4 (s), 697.3 (s).
6-Isocyanohexyl benzenesulfonate 6

Obtained as brown oil a yield of 53 % (DCM) and 68 % (DMC).

$R_f = 0.69$ (cyclohexane/ethyl acetate, 2:1) visualized via vanillin staining solution (orange).

$^1$H-NMR (500 MHz, CDCl$_3$) $\delta$/ppm = 7.79 ($d$, $^3J = 8.4$ Hz, 2H, aromatic, 1), 7.35 ($d$, $^3J = 8.0$ Hz, 2H, aromatic, 2), 4.03 ($t$, $^3J = 6.3$ Hz, 2H, CH$_2$), 3.35 ($tt$, $^3J = 6.6$ Hz, $^2J = 1.9$ Hz, 2H, CH$_2$), 2.45 (s, 3H, CH$_3$), 1.69-1.61 (m, 4H, CH$_2$), 1.44-1.33 (m, 4H, CH$_3$).

$^{13}$C-NMR (126 MHz, CDCl$_3$) $\delta$/ppm = 156.1 (t), 144.9, 133.2, 130.0, 128.0, 70.3, 41.5 (t), 29.0, 28.8, 25.8, 24.8, 21.8.

EI-HRMS m/z: [M]$^+$ calculated for [C$_{14}$H$_{19}$O$_3$N$_3$S]$^+$ = 281.1086, found: 281.1086, $\Delta = 0.0435$ mmu.

IR (ATR platinum diamond): $\nu$/cm$^{-1}$ = 2938.0 (w), 2862.9 (w), 2147.8 (w), 1597.7 (w), 1454.3 (w), 1353.4 (m), 1306.6 (w), 1187.9 (m), 1173.0 (s), 1096.5 (w), 1019.1 (w), 956.7 (m), 917.6 (m), 814.1 (m), 749.0 (w), 725.1 (w), 688.0 (w), 662.0 (s), 575.2 (m), 553.2 (s).
1,5-Diisocyno pentane 7

Obtained as brownish liquid in a yield of 48 % (DCM) and 82 % (DMC).

\( R_f = 0.48 \) (cyclohexane/ethyl acetate, 2:1) visualized via UV quenching at 254 nm and vanillin staining solution (orange).

\(^1\text{H-NMR} \) (500 MHz, CDCl\(_3\) \( \delta /\text{ppm} = 3.37 \) (tt, \( ^3J = 6.5 \) Hz, \( ^2J = 2.0 \) Hz, 4H, CH\(_2\)), 1.71-1.64 (m, 4H, CH\(_2\)), 1.58-1.52 (m, 2H, CH\(_2\)).

\(^{13}\text{C-NMR} \) (126 MHz, CDCl\(_3\) \( \delta /\text{ppm} = 156.3 \) (t), 41.3 (t), 28.2, 23.3).

EI-HRMS m/z: \([\text{M-H}]^+ \) calculated for \([\text{C}_7\text{H}_9\text{N}_2]^+ = 121.0765\), found: 121.0766, \( \Delta = 0.0416 \) mmu.

IR (ATR platinum diamond): \( \nu /\text{cm}^{-1} = 2922.7 \) (s), 2852.9 (s), 2145.4 (m), 1464.5 (m), 1352.4 (w), 722.0 (w).
1,10-Diisocyanido decane 8

Obtained as yellow liquid in a yield of 93 % (DCM) and 89 % (DMC).

$R_f = 0.44$ (cyclohexane/ethyl acetate, 4:1) visualized via UV quenching at 254 nm and vanillin staining solution (orange).

$^1$H-NMR (500 MHz, CDCl$_3$) $\delta$/ppm = 3.37 (tt, $^3J = 6.8$ Hz, $^2J = 1.8$ Hz, 4H, CH$_2$), 1.69-1.62 (m, 4H, CH$_2$), 1.42 (quint, $^3J = 7.1$ Hz, 4H, CH$_2$), 1.31-1.29 (m, 8H, CH$_2$).

$^{13}$C-NMR (126 MHz, CDCl$_3$) $\delta$/ppm = 155.8 (br), 41.6 (t), 29.2, 29.1, 28.7, 26.3.

EI-HRMS m/z: [M-H]$^+$ calculated for $[C_{12}H_{19}N_2]^+$ = 191.1548, found: 191.1547, $\Delta = 0.1013$ mmu.

IR (ATR platinum diamond): $\nu$/cm$^{-1}$ = 2927.0 (s), 2857.0 (s), 2145.4 (s), 1454.2 (m), 1351.4 (w).
1,12-Diisocyanododecane 9

Obtained as yellow liquid in a yield of 87 % (DCM) and 97 % (DMC)

$R_f = 0.44$ (cyclohexane/ethyl acetate, 9:1) visualized via UV quenching at 254 nm and vanillin staining solution (orange).

$^1$H-NMR (500 MHz, CDCl$_3$) $\delta$/ppm = 3.36 (tt, $^3J = 6.8$ Hz, $^2J = 1.9$ Hz, 4H, CH$_2$, $^1$), 1.68-1.62 (m, 4H, CH$_2$, $^2$), 1.41 (quint, $^3J = 7.3$ Hz, 4H, CH$_2$, $^3$), 1.3-1.23 (m, 12H, CH$_2$, $^4$).

$^{13}$C-NMR (126 MHz, CDCl$_3$) $\delta$/ppm = 155.6 (br), 41.6 (t), 29.4, 29.3, 29.1, 28.7, 26.3.

EI-HRMS m/z: [M-H]$^+$ calculated for [C$_{14}$H$_{23}$N$_2$]$^+$ = 219.1861, found: 219.1863, $\Delta = 0.2013$ mmu.

IR (ATR platinum diamond): $\nu$/cm$^{-1}$ = 2924.9 (s), 2855.0 (s), 2145.4 (s), 1456.3 (m).
1-Isocyno cyclohexane 10

Was obtained as yellowish liquid in a yield of 67 % (DCM) and 68 % (DMC) 
$R_f = 0.57$ (cyclohexane/ethyl acetate, 9:1) visualized via UV quenching at 254 nm, Seebach staining solution and vanillin staining solution (orange). 
$^1$H-NMR-spectra was in accordance with the literature. 

1-Isocyno methylbenzene 11

Was obtained as dark brown liquid in a yield of 67 % (DCM) and 68 % (DMC) 
$R_f = 0.66$ (cyclohexane/ethyl acetate, 10:1) visualized via Seebach staining solution and vanillin staining solution (orange). 
$^1$H-NMR-spectra is in accordance with the literature. 

1-Isocyno adamantane 12

Was obtained white solid in a yield of 79 % (DCM) and 78 % (DMC) 
$R_f = 0.83$ (cyclohexane/ethyl acetate, 4:1) visualized via vanillin staining solution (orange). 
$^1$H-NMR-spectra is in accordance with the literature.
Methyl 4-isocyanobenzoate 13

The Methyl-4-formamidobenzoate (1.00 g, 5.58 mmol, 1.00 eq.) was dissolved in DCM (5.58 mL) and pyridine (1.50 mL, 19.0 mmol, 3.40 eq.) was added. Subsequently, p-TsCl (1.81 g, 9.49 mmol, 1.70 eq.) was added under cooling with a water bath. The cooling was removed, and the reaction mixture was stirred for 165 minutes. Afterwards, aqueous, saturated Na2SO4-solution (24 mL) were added and the biphasic mixture was stirred for another 30 minutes. Water (10 mL) and DCM (10 mL) were added, and the organic phase was separated. The aqueous phase was extracted with DCM (3 × 5 mL). The organic layers were dried over sodium sulfate, filtered and the solvent was removed under reduced pressure. The product was obtained as black solid (120 mg, 0.740 mmol) after purification by column chromatography (cyclohexane / ethyl acetate, 3:1) in a yield of 13%.

1H-NMR (400 MHz, DMSO-d6) δ/ppm = 8.02 (d, 3J = 8.5 Hz, 2H, aromatic, 1), 7.69 (d, 3J = 8.5 Hz, 2H, aromatic, 2), 3.86 (s, 3H, CH3).

13C-NMR (101 MHz, DMSO-d6) δ/ppm = 166.6, 164.9, 130.6, 130.5, 129.2, 126.9.

EI-HRMS m/z: [M]+ calculated for [C9H7O2N1]+ = 161.0477, found: 161.0475, Δ = -0.1514 mmu.
IR (ATR platinum diamond): ν/cm⁻¹ = 3088.2 (w, br), 2952.8 (w), 2127.9 (s), 1715.5 (s), 1604.6 (m), 1504.1 (w), 1428.2 (m), 1272.2 (s), 1168.6 (m), 1102.9 (s), 1017.8 (m), 955.2 (m), 864.9 (s), 833.1 (m), 760.3 (s), 686.4 (m), 637.1 (w), 571.5 (m), 513.0 (m), 448.4 (w).
**Literature**


