A Novel Method for Preparing Isocyanides from N-Substituted Formamides with Chlorophosphate Compounds

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Abstract: Treatment of N-substituted formamides with chlorophosphate compounds such as $PhOPOCl_2$, $EtOPOCl_2$, Me_2NPOCl_2, and $(PhO)_2POCl$ and tertiary amines such as triethylamine, pyridine, and *N*,*N*-diisopropylethylamine produced the corresponding isocyanides in high yields. This method can be used to prepare various alkyl and aryl isocyanides.

Key words: isocyanide, isonitrile, formamide, dehydration, dichlorophosphate, monochlorophosphate

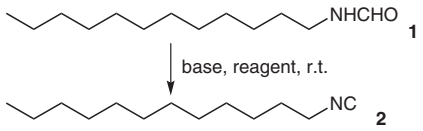
Isocyanide is an important reactant for Passerini[1] and Ugi[2] multicomponent reactions[3] and has the ability to function as a bonding partner for metals in complexes.[3a] In addition, various biologically active isocyanides have been isolated[4] and synthesized.[5] The standard procedure for preparing isocyanides is dehydration of the corresponding formamides.[3a,6] The most common dehydrating agents are $POCl_3$ and TsCl, but a variety of dehydrating reagents have been used for this reaction. However, these methods have some drawbacks related to toxicity and scope. $POCl_3$ is known as a specific controlled poisonous substance under the Poisonous and Deleterious Substances Control Law in Japan,[7] although most isocyanides are prepared using this reagent. On the other hand, there is often no reaction observed using TsCl for dehydration of *N*-aryl-substituted formamides into the corresponding phenyl isocyanides, although it is comparatively nontoxic.

Recently, Kuo et al. reported an efficient method for dehydrating amides into the corresponding nitriles using ethyl dichlorophosphate ($EtOPOCl_2$) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).[8] Their study prompted us to use the same conditions to dehydrate N-substituted formamides into isocyanides because the same conditions are used for dehydration of caroboxamides and N-substituted formamides.[6d–f,9] This paper reports on a mild and efficient method for preparing isocyanides from N-substituted formamides using chlorophosphate compounds and tertiary amines.

The results for the reaction of *N*-dodecylformamide (**1**) with a variety of chlorophosphate compounds and bases are summarized in Table 1. An initial study was performed in which formamide **1** was treated with $EtOPOCl_2$ and DBU in CH_2Cl_2, which is the best condition for converting primary amides into nitriles. Although the desired reaction produced moderate yields, the starting material was recovered (Table 1, entry 1). Longer reaction times and larger amounts of DBU did not increase the yield, in contrast to the dehydration of primary amides. Further studies to establish optimal reaction conditions showed that dodecyl isocyanide (**2**) was obtained from **1** in high yields with $PhOPOCl_2$, $EtOPOCl_2$, MeN_2POCl_2, and $(PhO)_2POCl$ as dehydrating reagents and Et_3N, DIPEA, and pyridine as bases (entries 2–7). The reaction was carried out with 1.2–2.0 equivalents of chlorophosphate and a tertiary amine under neat conditions. In all cases, **2** was obtained with no significant by-products, but the reaction proceeded more effectively with $PhOPOCl_2$ and $EtOPOCl_2$ than MeN_2POCl_2 and $(PhO)_2POCl$ (entries 2–5). DIPEA and pyridine promoted the desired reaction with $PhOPOCl_2$ as well as Et_3N (entries 6–7).

The results for the reaction of *N*-(4-heptylphenyl)formamide (**3**) with a variety of chlorophosphate compounds and bases are summarized in Table 2. It is known that the

Table 1 Reaction of *N*-Dodecylformamide (**1**) with Various Bases and Dehydrating Reagents



Entry[a]	Base	Reagent	Time (h)	Yield (%)[b]
1[c]	DBU	$EtOPOCl_2$ (2.0 equiv)	24	39 (28)[d]
2	Et_3N	$PhOPOCl_2$ (1.2 equiv)	1	89
3	Et_3N	$EtOPOCl_2$ (1.2 equiv)	1	87
4	Et_3N	Me_2NPOCl_2 (2.0 equiv)	24	82
5	Et_3N	$(PhO)_2POCl$ (1.2 equiv)	24	84
6	DIPEA	$PhOPOCl_2$ (1.2 equiv)	1	85
7	pyridine	$PhOPOCl_2$ (1.2 equiv)	1	90

[a] The reactions were carried out at r.t. with formamide **1** (0.5 mmol) and a chlorophosphate compound (1.2–2.0 equiv) in a tertiary amine (1 mL).
[b] Isolated yields.
[c] The reaction was carried out at r.t. with 3.0 equiv of DBU in CH_2Cl_2 (1 mL).
[d] Yield of the recovered starting material in parentheses.

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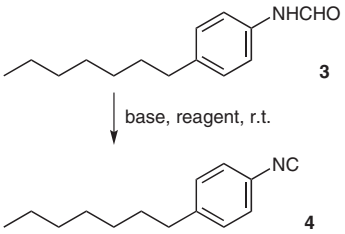
reaction condition with TsCl and pyridine, which is one of the most common methods for preparing isocyanide from the corresponding formamide, is inefficient for dehydration of *N*-phenylformamide compounds into the corresponding isocyanides, although there is no report on this. No product was observed for the reaction of formamide **3** with TsCl and pyridine (Table 2, entry 1). In addition, 4-*n*-heptylphenyl isocyanide (**4**) was obtained in moderate yield when formamide **3** was treated with DBU and $PhOPOCl_2$ as for the dehydration of formamide **1** (entry 2). In contrast, isocyanide **4** was obtained from **3** in high yields with $PhOPOCl_2$ and Et_3N under neat conditions, although longer reaction times were needed compared for the dehydration of formamide **1** (entry 3). The reaction, however, proceeded more efficiently when CH_2Cl_2 was used as the solvent (entry 4). These results suggest that the use of a solvent is beneficial when preparing phenyl isocyanides. Isocyanide **4** was also obtained in high yields with $EtOPOCl_2$, MeN_2POCl_2, and $(PhO)_2POCl$ as the dehydrating reagent, although $EtOPOCl_2$ was more efficient than the others (entries 5–7). DIPEA promoted the desired reaction with $PhOPOCl_2$ as well as Et_3N, whereas the reaction with pyridine was less effective than those with Et_3N and DIPEA (entries 8, 9).

The scope of this reaction was investigated under the optimized conditions. Table 3 presents the results of the reaction of *N*-aliphatic-substituted formamides with $PhOPOCl_2$ or $EtOPOCl_2$ in Et_3N. All the formamides examined gave high yields of the corresponding isocyanides. Various functional groups, such as alkene, ester, ether, amide, and imide, were only slightly affected under these conditions (Table 3, entries 1–7). In addition, isocyanides containing halogens were also obtained in high yields (entries 8–11). However, substrates with a free hydroxy or amine group produced messy products (data not shown). This problem could be resolved using a protective group (entries 2, 5–7). The results suggest that formyl or *tert*-butyldimethylsilyl (TBS) groups were effective as protecting groups of alcohols, and Boc or Fmoc groups were effective as a protective group of amines.

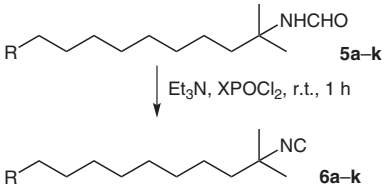
Table 2 Reaction of *N*-(4-Heptylphenyl)formamide (**3**) with Various Bases and Dehydrating Reagents



Entry[a]	Base	Reagent	Time (h)	Yield (%)[b]
1[c]	pyridine	TsCl (2.0 equiv)	24	n.r.
2[d]	DBU	$PhOPOCl_2$ (1.2 equiv)	24	49 (38)[e]
3	Et_3N[f]	$PhOPOCl_2$ (1.2 equiv)	24	83 (9)[e]
4	Et_3N	$PhOPOCl_2$ (1.2 equiv)	2	99
5	Et_3N	$EtOPOCl_2$ (1.2 equiv)	2	99
6	Et_3N	Me_2NPOCl_2 (2.0 equiv)	24	86
7	Et_3N	$(PhO)_2POCl$ (1.2 equiv)	24	80
8	DIPEA	$PhOPOCl_2$ (1.2 equiv)	24	86 (11)[e]
9	pyridine	$PhOPOCl_2$ (2.0 equiv)[g]	24	27 (63)[e]

[a] The reactions were carried out at r.t. with formamide **3** (0.5 mmol) and a chlorophosphate compound (1.2–2.0 equiv) in a tertiary amine (0.5 mL) and CH_2Cl_2 (0.5 mL).
[b] Isolated yields. n.r. = no reaction.
[c] The reaction was carried out with 2.0 equiv of TsCl in pyridine (1 mL).
[d] The reaction was carried out with 3.0 equiv of DBU in CH_2Cl_2 (1 mL).
[e] Yield of the recovered starting material in parentheses.
[f] The reaction was carried out in Et_3N (1 mL) without CH_2Cl_2.
[g] $PhOPOCl_2$ (2.0 equiv) was used.

Table 3 Reactions of Various N-Aliphatic-Substituted Formamides **5a–k** with Et_3N and $PhOPOCl_2$ or $EtOPOCl_2$



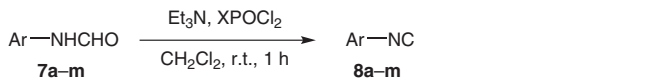
Entry[a]	R	Yield (%, X = Ph)[b]	Yield (%, X = Et)[b]
1	CH_2=CH (**5a**)	92	91
2	H(C=O)OCH_2CH_2 (**5b**)	97	94
3	$MeOCH_2CH_2$ (**5c**)	90	83
4	phthalimide-CH_2 (**5d**)	96	94
5	$TBSOCH_2CH_2$ (**5e**)	92	89
6	$FmocNHCH_2CH_2$ (**5f**)	82	85
7	$BocNHCH_2CH_2$ (**5g**)	92	95
8	FCH_2CH_2 (**5h**)	85	85
9	$ClCH_2CH_2$ (**5i**)	89	90
10	$BrCH_2CH_2$ (**5j**)	87	86
11	ICH_2CH_2 (**5k**)	89	90

[a] The reactions were carried out at r.t. for 1 h with 1.2 equiv of $PhOPOCl_2$ or $EtOPOCl_2$ in Et_3N (1 mL).
[b] Isolated yields.

Table 4 shows the results of the reaction of *N*-aryl-substituted formamides with $PhOPOCl_2$ or $EtOPOCl_2$ in a 1:1 mixture of Et_3N and CH_2Cl_2. Three structural isomers of *N*-benzyloxyphenylformamides and *N*-ethoxycarbonylphenylformamides gave the corresponding isocyanides in high yields (Table 4, entries 1–6). These results indicate that substitution patterns on the benzene rings did not

significantly affect the progression of this reaction. *N*-Phenyl-substituted formamides with bromine, iodine, or nitro group on the aromatic ring also gave the corresponding isocyanides in high yields (entries 7–9). However, a decrease in reactivity was observed when an electron-withdrawing group, such as a nitro group, was substituted on the benzene ring (entry 9). On the other hand, isocyanopyridine was also obtained from the corresponding *N*-pyridinylformamide in high yield (entry 13). Entries 11–13 show the results of *N*-aryl-substituted formamides with two or three substituents. The desired isocyanides were also obtained in high yields in those cases. It should be noted that *N*-aryl-substituted formamide with methoxy and nitro groups produced the corresponding isocyanide even though there was a nitro group on the benzene ring (entry 11). These results suggest that reactivity depends on and varies according to the combination of substituents when more than one functional group is present.

Table 4 Reactions of Various *N*-Aryl-Substituted Formamides **7a–m** with Et_3N and $PhOPOCl_2$ or $EtOPOCl_2$



Entry[a]	Ar	Yield (%, X = Ph)[b]	Yield (%, X = Et)[b]
1	2-$BnOC_6H_4$ (**7a**)	88	93
2	3-$BnOC_6H_4$ (**7b**)	96	88
3	4-$BnOC_6H_4$ (**7c**)	84	87
4	2-$EtO_2CC_6H_4$ (**7d**)	86	88[c]
5	3-$EtO_2CC_6H_4$ (**7e**)	87	82[c]
6	4-$EtO_2CC_6H_4$ (**7f**)	88	87[c]
7	4-BrC_6H_4 (**7g**)	86	85
8	4-IC_6H_4 (**7h**)	89[d]	87[d]
9	4-$O_2NC_6H_4$ (**7i**)	80 (15)[e,f,g]	78 (18)[e,f,g]
10	2-MeO-4-$O_2NC_6H_3$ (**7j**)	88[c]	89[c]
11	3,5-$(MeO)_2C_6H_3$ (**7k**)	94	94
12	3,4,5-$(MeO)_3C_6H_2$ (**7l**)	88	90
13	6-BnO-2-pyridinyl (**7m**)	90	83

[a] The reactions were carried out at r.t. with 1.2 equiv of $PhOPOCl_2$ or $EtOPOCl_2$ in a 1:1 mixture of Et_3N and CH_2Cl_2 (1.0 mL).
[b] Isolated yields.
[c] Amount of reagent used: 1.5 equiv.
[d] Amount of reagent used: 2.0 equiv.

In conclusion, we have developed a mild and efficient method of converting N-substituted formamides to the corresponding isocyanides. We believe this method provides a convenient and useful way to prepare various isocyanides.

NMR spectra were obtained in $CDCl_3$ on a JEOL alpha-600 spectrometer. All ^1H NMR spectra are reported in ppm relative to TMS. All ^{13}C NMR spectra are reported in ppm relative to the central line of the triplet for $CDCl_3$ at 77.0 ppm. IR spectra were recorded on a JEOL WINSPEC-50 spectrometer. Electrospray ionization (ESI) and direct analysis in real time (DART) mass spectra were recorded on a JEOL JMS-T100 mass spectrometer. Chromatographic separations were carried out on a silica gel column (Fuji Silysia Chemical BW-127ZH; 100–270 mesh or Kanto Chemical 60N; 63–210 μm), unless otherwise stated. Analytical and spectral data for compounds **2**,[10] **6a**,[11] **6d**,[12] **7d**,[13] **8d**,[14] **8f**,[15] **8g**,[15] and **8i**[16] were identical to the data reported in the literature. Compounds **1**,[10] **7h**,[17] and **7i**[18] were prepared according to literature procedures.

N-(4-Heptylphenyl)formamide (3)

p-TsOH monohydrate (40 mg, 0.23 mmol) was added to a solution of 4-heptylaniline (1.01 g, 5.26 mmol) in ethyl formate (4 mL). After refluxing the reaction mixture for 14 h, EtOAc (150 mL) was added. The organic layer was washed with sat. aq $NaHCO_3$ (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:3) to yield formamide **3** (863 mg, 75%) as a yellow oil.

IR (neat): 3294 (br), 2954, 2922, 2848, 1645, 1537, 1468, 1379, 1234, 1217 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.63 (1 H, d, *J* = 11 Hz), 7.93 (1 H, br s), 7.44–6.99 (4 H, m), 2.58 (2 H, dd, *J* = 8.6, 7.2 Hz), 1.61–1.26 (10 H, m), 0.88 (3 H, t, *J* = 6.6 Hz); δ (minor) = 8.35 (1 H, s), 7.93 (1 H, br s), 7.44–6.99 (4 H, m), 2.58 (2 H, dd, *J* = 8.6, 7.2 Hz), 1.61–1.26 (10 H, m), 0.88 (3 H, t, *J* = 6.6 Hz).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 162.6, 140.3, 134.4, 129.6, 119.2, 35.3, 31.8, 31.5, 29.2, 29.2, 22.6, 14.1; δ (minor) = 158.8, 139.7, 134.1, 129.0, 120.0, 35.4, 31.8, 31.5, 29.2, 29.2, 22.6, 14.1.

HRMS (ESI): *m/z* $(M + Na)^+$ calcd for $C_{14}H_{21}NO$ + Na: 242.1521; found: 242.1519.

N-(1,1-Dimethylundec-10-enyl)formamide (5a)

TMSCN (8.2 mL, 116 mmol) and H_2SO_4 (5 mL, 93.8 mmol) were successively added to a solution of 2-methyldode-11-en-2-ol[10] (10.8 g, 38.7 mmol) in AcOH (20 mL) at 0 °C. After stirring the reaction mixture at r.t. for 2 d, 10% NaOH (200 mL) was added, and the resultant mixture was extracted with EtOAc (500 mL). The combined extracts were washed with H_2O (100 mL) and brine (150 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:2) to yield **5a** (1.86 g, 79%) as a colorless oil.

IR (neat): 3286 (br), 3061, 2972, 2926, 2854, 2754, 1664, 1541, 1466, 1387, 1365, 1263 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.22 (1 H, d, *J* = 13.0 Hz), 5.85–5.71 (2 H, m), 5.02–4.91 (2 H, m), 2.07–2.01 (2 H, m), 1.80–1.22 (20 H, m); δ (minor) = 8.05 (1 H, d, *J* = 1.5 Hz), 5.85–5.71 (1 H, m), 5.19 (1 H, br s), 5.02–4.97 (2 H, m), 2.07–2.01 (2 H, m), 1.80–1.22 (20 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 160.4, 139.1, 114.1, 52.8, 43.8, 29.9, 29.5, 29.4, 29.1, 28.9, 28.7, 27.0, 23.8; δ (minor) = 162.9, 139.2, 114.1, 54.0, 40.6, 33.7, 29.8, 29.4, 29.4, 29.0, 28.9, 27.0, 23.8.

HRMS (ESI): *m/z* $(M + Na)^+$ calcd for $C_{14}H_{27}NO$ + Na: 248.1990; found: 248.1978.

N-(11-Bromo-1,1-dimethylundecyl)formamide (5j)

TMSCN (4.0 mL, 32.3 mmol) and H_2SO_4 (2.3 mL, 43.2 mmol) were successively added to a solution of 12-bromo-2-methylunde-

can-2-ol[11] (3.08 g, 10.7 mmol) in AcOH (10 mL) at 0 °C. After stirring the reaction mixture at r.t. for 2 d, sat. aq 10% NaOH (50 mL) was added at 0 °C, and the resultant mixture was extracted with EtOAc (400 mL). The combined extracts were washed with H_2O (100 mL) and brine (150 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:1) to yield **5j** (3.32 g, 98%) as a colorless oil.

IR (neat): 3275 (br), 2968, 2924, 2854, 2754, 1664, 1537, 1468, 1387, 1365, 1263 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.23 (1 H, d, *J* = 13 Hz), 5.63 (1 H, br s), 3.41 (2 H, t, *J* = 6.6 Hz), 1.85 (2 H, quint, *J* = 7.3 Hz), 1.70–1.23 (22 H, m); δ (minor) = 8.05 (1 H, d, *J* = 2.2 Hz), 5.14 (1 H, br s), 3.41 (2 H, t, *J* = 6.6 Hz), 1.85 (2 H, quint, *J* = 7.3 Hz), 1.70–1.23 (22 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 160.4, 52.8, 43.8, 34.0, 32.8, 29.8, 29.5, 29.4, 28.7, 28.1, 27.1, 24.0, 23.8; δ (minor) = 162.9, 54.1, 40.6, 34.0, 32.8, 29.8, 29.5, 29.4, 28.7, 28.1, 27.1, 24.0, 23.8.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{14}H_{28}BrNO$ + Na: 328.1252; found: 328.1246.

N-(11-Formyloxy-1,1-dimethylundecyl)formamide (5b)

Et_3N (463 μL, 3.24 mmol) and formic acid (126 μL, 3.24 mmol) were successively added to a solution of formamide **5j** (341 mg, 1.11 mmol) in DMF (10 mL). After stirring the reaction mixture at 80 °C for 3 h, brine (50 mL) was added, and the resultant mixture was extracted with EtOAc (150 mL). The combined extracts were washed with sat. aq $NaHCO_3$ (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:1) to yield formamide **5b** (227 mg, 76%) as a colorless oil.

IR (neat): 3382 (br), 2948, 2902, 2752, 1740, 1537, 1468, 1387, 1078, 1047 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.23 (1 H, d, *J* = 13 Hz), 8.06 (1 H, s), 5.72 (1 H, br s), 4.16 (2 H, t, *J* = 6.6 Hz), 1.74–1.20 (24 H, m); δ (minor) = 8.06 (1 H, s), 8.05 (1 H, d, *J* = 2.2 Hz), 5.20 (1 H, br s), 4.16 (2 H, t, *J* = 6.6 Hz), 1.74–1.20 (24 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$) δ (major) = 161.2, 160.4, 64.1, 52.8, 43.8, 40.6, 29.8, 29.5, 29.4, 28.7, 28.5, 27.0, 25.8, 23.7; δ (minor) = 162.9, 161.2, 64.1, 54.0, 43.8, 40.6, 29.9, 29.5, 29.1, 28.7, 28.5, 27.0, 25.8, 24.0.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{15}H_{29}NO_3$ + Na: 294.2045; found: 294.2046.

N-(1,1-Dimethyl-11-methoxyundecyl)formamide (5c)

NaOMe (529 mg, 9.78 mmol) was added to a solution of formamide **5j** (1.00 g, 3.26 mmol) in MeOH (10 mL). After stirring the reaction mixture at r.t. for 18 h, H_2O (30 mL) was added, and the resultant mixture was extracted with EtOAc (200 mL). The combined extracts were washed with H_2O (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:1) to yield **5c** (532 mg, 63%) as a colorless oil.

IR (neat): 3298 (br), 2970, 2926, 2854, 2752, 1668, 1537, 1462, 1387, 1313, 1259, 1120, 1047 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.23 (1 H, d, *J* = 13 Hz), 5.64 (1 H, br s), 3.40–3.30 (5 H, m), 1.71–1.63 (2 H, m), 1.60–1.52 (2 H, m), 1.38–1.20 (20 H, m); δ (minor) = 8.05 (1 H, s), 5.15 (1 H, br s), 3.40–3.30 (5 H, m), 1.60–1.52 (2 H, m), 1.52–1.45 (2 H, m), 1.38–1.20 (20 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 160.4, 72.9, 58.5, 54.0, 40.6, 29.9, 29.6, 29.6, 29.5, 29.4, 28.7, 27.0, 26.1, 23.8; δ (minor) = 162.9, 73.0, 58.5, 54.0, 40.6, 29.9, 29.6, 29.6, 29.5, 29.4, 28.7, 27.0, 26.1, 24.0.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{15}H_{31}NO_2$ + Na: 280.2252; found: 280.2252.

2-(11-Formamino-11-methyldodecyl)isoindole-1,3-dione (5d)

Phthalimide potassium salt (14.3 g, 77.2 mmol) was added to a solution of formamide **5j** (15.3 g, 50.0 mmol) in DMF (30 mL). After stirring the reaction mixture at 80 °C for 28 h, H_2O (30 mL) was added, and the resultant mixture was extracted with EtOAc (300 mL). The combined extracts were washed with aq 5% KOH (100 mL), H_2O (50 mL), and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:2) to yield **5d** (13.8 g, 74%) as a colorless oil.

IR (neat): 3304 (br), 3057, 2968, 2933, 2854, 2756, 1772, 1719, 1687, 1535, 1468, 1336, 1036 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.22 (1 H, d, *J* = 13 Hz), 7.86–7.69 (4 H, m), 5.62 (1 H, d, *J* = 11.0 Hz), 3.67 (2 H, t, *J* = 7.3 Hz), 1.70–1.63 (2 H, m), 1.63–1.59 (2 H, m), 1.37–1.22 (20 H, m); δ (minor) = 8.05 (1 H, d, *J* = 1.5 Hz), 7.86–7.69 (4 H, m), 5.15 (1 H, m), 3.67 (2 H, t, *J* = 7.3 Hz), 1.70–1.63 (2 H, m), 1.63–1.59 (2 H, m), 1.37–1.22 (20 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 168.5, 160.4, 133.8, 132.2, 123.1, 54.1, 43.8, 38.1, 29.9, 29.5, 29.4, 29.4, 29.4, 29.1, 28.7, 27.0, 23.8; δ (minor) = 168.5, 162.9, 133.8, 132.2, 123.1, 52.8, 40.7, 38.1, 29.8, 29.5, 29.4, 29.4, 29.4, 29.1, 28.6, 26.8, 24.0.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{22}H_{32}N_2O_3$ + Na: 395.2311; found: 395.2306.

N-(11-Hydroxy-1,1-dimethylundecyl)formamide (9)

Aq 10% K_2CO_3 (20 mL) was added to a solution of formamide **5b** (4.45 g, 16.4 mmol) in MeOH (30 mL), and the reaction mixture was stirred at r.t. for 5 h. After concentration of the mixture, brine (50 mL) was added, and the resultant mixture was extracted with EtOAc (300 mL). The combined extracts were washed with H_2O (100 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:2) to yield **9** (3.43 g, 86%) as a colorless oil.

IR (neat): 3282 (br), 2926, 2856, 2756, 1670, 1543, 1468, 1387, 1267, 1057 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.23 (1 H, d, *J* = 12.4 Hz), 5.56 (1 H, br s), 3.64 (2 H, q, *J* = 6.6 Hz), 1.70–1.22 (24 H, m); δ (minor) = 8.04 (1 H, d, *J* = 1.5 Hz), 5.13 (1 H, br s), 3.64 (2 H, q, *J* = 6.6 Hz), 1.70–1.22 (24 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 160.3, 67.6, 52.7, 43.5, 32.6, 29.4, 29.4, 29.3, 29.2, 28.4, 25.6, 23.8, 23.6; δ (minor) = 160.6, 62.6, 52.7, 43.4, 29.8, 29.6, 29.3, 29.3, 29.2, 26.8, 25.6, 23.8, 23.6.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{14}H_{29}NO_2$ + Na: 266.2096; found: 266.2096.

N-(1,1-Dimethyl-11-*tert*-butyldimethylsilyloxyundecyl)formamide (5e)

Imidazole (560 mg, 8.23 mmol) and TBSCl (743 mg, 4.93 mmol) were successively added to a solution of formamide **9** (1.02 g, 4.11 mmol) in DMF (10 mL). After stirring the reaction mixture at r.t. for 60 h, sat. aq NH_4Cl (50 mL) was added, and the resultant mixture was extracted with EtOAc (300 mL). The combined extracts were washed with aq 1 M HCl (100 mL), sat. aq $NaHCO_3$ (50 mL), and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced

pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:3) to yield **5e** (1.14 g, 77%) as a colorless oil.

IR (neat): 3292 (br), 3055, 2927, 2956, 2752, 1668, 1539, 1471, 1387, 1254, 1099, 1007 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.23 (1 H, d, *J* = 12.4 Hz), 5.13 (1 H, br s), 3.60 (2 H, t, *J* = 7.3 Hz), 1.70–1.47 (6 H, m), 1.33–1.24 (18 H, m), 0.90 (9 H, s) 0.05 (6 H, s); δ (minor) = 8.05 (1 H, d, *J* = 12.4 Hz), 5.59 (1 H, br s), 3.60 (2 H, t, *J* = 7.3 Hz), 1.70–1.47 (6 H, m), 1.33–1.24 (18 H, m), 0.90 (9 H, s), 0.05 (6 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 160.4, 63.1, 52.6, 43.6, 29.8, 29.5, 29.4, 29.4, 29.3, 26.8, 25.8, 25.6, 23.9, 23.7, 18.2, –5.39; δ (minor) = 163.1, 63.1, 53.8, 32.7, 29.7, 29.5, 29.4, 29.3, 28.4, 26.8, 25.8, 25.6, 23.9, 23.7, 18.2, –5.39.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{20}H_{43}NO_2Si$ + Na: 380.2961; found: 380.2961.

Carbamic Acid *N*-(11-Formamino-11-methyldodecyl) (9*H*-Fluoren-9-yl)methyl Ester (5f)

Hydrazine monohydrate (1.73 mL, 35.0 mmol) was added to a solution of **5d** (5.93 g, 15.9 mmol) in MeOH (20 mL). After refluxing the reaction mixture for 20 h, brine (100 mL) was added, and the resultant mixture was extracted with EtOAc (300 mL). The combined extracts were washed with H_2O (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The obtained amine **10** was used in the next reaction without further purification. The amine **10** (750 mg) was dissolved in CH_2Cl_2 (6 mL), and Fmoc–OSu (1.1 g, 3.40 mmol) was added to the solution. After stirring the reaction mixture at r.t. for 4 h, H_2O (30 mL) was added, and the resultant mixture was extracted with EtOAc (200 mL). The combined extracts were washed with H_2O (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:1) to yield **5f** (820 mg, 59%, 2 steps) as a white solid; mp 179 °C.

IR (KBr): 3061, 2924, 2852, 2760, 1689, 1535, 1464, 1450, 1363, 1317, 1261, 1146 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.22 (1 H, d, *J* = 12.4 Hz), 7.76 (2 H, d, *J* = 8.1 Hz), 7.59 (2 H, d, *J* = 8.1 Hz), 7.40 (2 H, t, *J* = 8.1 Hz), 7.31 (2 H, t, *J* = 8.1 Hz), 5.51 (1 H, br s), 4.76 (1 H, br s), 4.40 (2 H, d, *J* = 7.3 Hz), 4.22 (1 H, t, *J* = 7.3 Hz), 3.19 (2 H, q, *J* = 7.3 Hz), 1.70–1.46 (4 H, m) 1.38–1.22 (20 H, m); δ (minor) = 8.03 (1 H, d, *J* = 2.2 Hz), 7.76 (2 H, d, *J* = 8.1 Hz), 7.59 (2 H, d, *J* = 8.1 Hz), 7.40 (2 H, t, *J* = 8.1 Hz), 7.31 (2 H, t, *J* = 8.1 Hz), 5.10 (1 H, br s), 4.76 (1 H, br s), 4.40 (2 H, d, *J* = 7.3 Hz), 4.22 (1 H, t, *J* = 7.3 Hz), 3.19 (2 H, q, *J* = 7.3 Hz), 1.70–1.46 (4 H, m), 1.38–1.22 (20 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 163.1, 156.3, 143.9, 141.1, 127.4, 126.8, 124.9, 119.7, 66.3, 52.5, 47.1, 40.4, 29.7, 29.6, 29.3, 29.2, 29.0, 28.4, 26.8, 26.5, 23.8, 23.6; δ (minor) = 160.4, 156.3, 143.9, 141.1, 127.4, 126.8, 124.9, 119.7, 66.3, 53.7, 43.5, 40.9, 29.7, 29.6, 29.3, 29.2, 29.0, 28.4, 26.8, 26.5, 23.8, 23.6.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{29}H_{40}N_2O_3$ + Na: 487.2937; found: 487.2940.

Carbamic Acid *N*-(11-Formamino-11-methyldodecyl) 1,1-Dimethylethyl Ester (5g)

Di-*tert*-butyl dicarbonate (2.78 g, 12.7 mmol) was added to a solution of amine **10** (1.40 g) in CH_2Cl_2 (10 mL). After stirring the reaction mixture at r.t. for 18 h, H_2O (30 mL) was added, and the resultant mixture was extracted with EtOAc (200 mL). The combined extracts were washed with sat. aq $NaHCO_3$ (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 2:1) to yield **5g** (389 mg, 20%) as a colorless oil.

IR (neat): 3327, 3292, 2983, 2920, 2852, 2750, 1672, 1545, 1529, 1390, 1365, 1281, 1256, 1167, 1045, 1012 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.23 (1 H, d, *J* = 13 Hz), 5.12 (1 H, br s), 4.50 (1 H, br s), 3.10 (2 H, d, *J* = 6.6 Hz), 1.70–1.40 (13 H, m), 1.33–1.22 (20 H, m); δ (minor) = 8.05 (1 H, d, *J* = 2.2 Hz), 5.52 (1 H, br s), 4.50 (1 H, br s), 3.10 (2 H, d, *J* = 6.6 Hz), 1.70–1.40 (13 H, m), 1.33–1.22 (20 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 163.1, 155.8, 78.5, 52.5, 40.3, 29.7, 29.6, 29.2, 29.1, 28.9, 28.2, 28.2, 26.7, 26.5, 23.7, 23.5; δ (minor) = 160.5, 155.8, 78.5, 53.5, 43.4, 40.3, 29.5, 29.2, 29.2, 28.9, 28.2, 28.2, 26.7, 26.5, 23.7, 23.5.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{19}H_{38}N_2O_3$ + Na: 365.2780; found: 365.2781.

Formic Acid 11-Hydroxy-11-methyldodecyl Ester (11)

Et_3N (1.58 mL, 11.1 mmol) and formic acid (430 μL, 11.1 mmol) were successively added to a solution of 12-bromo-2-methyldodecan-2-ol[11] (1.2 g, 4.3 mmol) in DMF (30 mL). After stirring the reaction mixture at 80 °C for 4 h, brine (50 mL) was added, and the resultant mixture was extracted with EtOAc (150 mL). The combined extracts were washed with aq 3 M HCl (50 mL), sat. aq $NaHCO_3$ (50 mL), and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:3) to yield **12** (355 mg, 38%) as a colorless oil.

IR (KBr): 3420 (br), 2966, 2931, 2854, 1730, 1468, 1377, 1180 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.06 (1 H, s), 4.16 (2 H, t, *J* = 7.1 Hz), 1.66 (2 H, t, *J* = 7.1 Hz), 1.48–1.43 (2 H, m), 1.39–1.25 (14 H, m), 1.23–1.18 (7 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 161.2, 71.0, 64.1, 43.9, 32.1, 30.1, 29.5, 29.4, 29.2, 29.1, 28.5, 27.8, 24.3.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{14}H_{28}O_3$ + Na: 267.1936; found: 267.1950.

11-Methyldodecan-1,11-diol (12)

Aq 10% K_2CO_3 (20 mL) was added to a solution of formate **11** (3.45 g, 14.1 mmol) in MeOH (50 mL). After stirring the reaction mixture at r.t. for 6 h, brine (200 mL) was added, and the resultant mixture was extracted with EtOAc (400 mL). The combined extracts were washed with H_2O (100 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by recrystallization from hexane–EtOAc to yield **13** (2.62 g, 86%) as a white solid; mp 53.3–57.3 °C.

IR (KBr): 3390 (br), 2983, 2927, 2848, 2740, 1470, 1381, 1203, 1059 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 3.66–3.72 (2 H, m), 1.61–1.54 (2 H, m), 1.48–1.43 (2 H, m), 1.38–1.19 (22 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 71.0, 62.9, 43.9, 32.7, 30.1, 29.6, 29.5, 29.5, 29.4, 29.2, 25.7, 24.3.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{13}H_{28}O_2$ + Na: 239.1987; found: 239.1989.

Toluene-4-sulfonic Acid 11-Hydroxy-11-methyldodecyl Ester (13)

TsCl (905 mg, 4.75 mmol) was added to a solution of diol **12** (1.06 g, 4.89 mmol) in pyridine (10 mL). After stirring the reaction mixture at r.t. for 16 h, brine (50 mL) was added, and the resultant mixture was extracted with EtOAc (150 mL). The combined extracts were washed with aq 1 M HCl (50 mL), sat. aq $NaHCO_3$ (50 mL), and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced

pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:1) to yield **13** (913 g, 50%) as a colorless oil.

IR (neat): 3354 (br), 3415 (br), 2877, 2754, 1738, 1655, 1599, 1308, 1211, 1120, 1020 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.79 (2 H, d, *J* = 8.5 Hz), 7.34 (2 H, d, *J* = 8.5 Hz), 4.02 (2 H, t, *J* = 6.8 Hz), 2.45 (3 H, s), 1.63 (2 H, quint, *J* = 6.8 Hz), 1.47–1.43 (2 H, m), 1.36–1.19 (21 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 144.5, 133.2, 129.7, 127.8, 70.9, 70.6, 43.9, 30.1, 29.5, 29.3, 29.2, 29.1, 28.8, 28.7, 25.2, 24.2, 21.5.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{20}H_{34}O_4S$ + Na: 393.2075; found: 393.2075.

N-(11-Fluoro-1,1-dimethylundecyl)formamide (5h)

KF (6.20 g, mmol) was added to a solution of tosylate **13** (1.51 g, 4.08 mmol) in ethylene glycol (30 mL). After stirring the reaction mixture at r.t. for 7 d, brine (100 mL) was added, and the resultant mixture was extracted with EtOAc (250 mL). The combined extracts were washed with H_2O (100 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:4) to yield the corresponding alcohol (381 mg, 43%) as a colorless oil. TMSCN (200 μL, 1.62 mmol) and H_2SO_4 (116 μL 1.62 mmol) were successively added to a solution of the above alcohol (381 mg, 1.74 mmol) in AcOH (200 μL) at 0 °C. After stirring the reaction mixture at r.t. for 2 d, aq 10% NaOH (50 mL) was added at 0 °C, and the resultant mixture was extracted with EtOAc (200 mL). The combined extracts were washed with H_2O (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:1) to yield **5h** (212 mg, 89%) as a colorless oil.

IR (neat): 3292 (br), 2924, 2854, 2752, 1684, 1541, 1456, 1387, 1263, 1219, 1049 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.22 (1 H, d, *J* = 12.4 Hz), 5.63 (1 H, br s), 4.44 (2 H, dt, *J* = 47.6, 6.6 Hz), 1.74–1.65 (2 H, m), 1.52–1.22 (22 H, m); δ (minor) = 8.04 (1 H, d, *J* = 2.2 Hz), 5.14 (1 H, br s), 4.44 (2 H, dt, *J* = 47.6, 6.6 Hz), 1.74–1.65 (2 H, m), 1.52–1.22 (22 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 163.1, 83.8 (d, *J* = 163.8 Hz), 62.4, 40.3, 30.0, 29.7, 29.2, 28.9, 26.7, 24.9, 24.8, 23.7, 23.5; δ (minor) = 160.4, 83.8 (d, *J* = 163.8 Hz), 53.5, 43.3, 30.2, 29.6, 29.3, 29.2, 28.2, 24.9, 24.8, 23.7, 23.5.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{14}H_{28}FNO$ + Na: 268.2053; found: 268.2054.

N-(11-Chloro-1,1-dimethylundecyl)formamide (5i)

TsCl (4.50 g, 23.6 mmol) was added to a solution of formamide **9** (2.61 g, 10.7 mmol) in pyridine (8 mL). After stirring the reaction mixture at r.t. for 24 h, brine (30 mL) was added, and the resultant mixture was extracted with EtOAc (300 mL). The combined extracts were washed with aq 1 M HCl (50 mL), sat. aq $NaHCO_3$ (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue (3.1 g) was mixed with 50% AcOH (20 mL), and the reaction mixture was stirred at r.t. for 16 h. Brine (30 mL) was added, and the resultant mixture was extracted with EtOAc (300 mL). The combined extracts were washed with sat. aq $NaHCO_3$ (100 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:2) to yield the **5i** (352 mg, 12%) as a colorless oil.

IR (neat): 3296 (br), 2968, 2929, 2854, 2754, 1740, 1685, 1539, 1466, 1387, 1365, 1311, 1173, 1047, cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.23 (1 H, d, *J* = 13 Hz), 5.60 (1 H, br s), 3.54 (2 H, t, *J* = 7.3 Hz), 1.77 (2 H, quint, *J* = 7.3 Hz), 1.52–1.47 (2 H, m), 1.45–1.38 (2 H, m), 1.36–1.23 (18 H, m); δ (minor) = 8.05 (1 H, s), 5.14 (1 H, br s), 3.54 (2 H, t, *J* = 7.3 Hz), 1.77 (2 H, quint, *J* = 7.3 Hz), 1.52–1.47 (2 H, m), 1.45–1.38 (2 H, m), 1.36–1.23 (18 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 160.4, 52.8, 45.2, 43.8, 40.6, 32.6, 29.8, 29.5, 29.4, 28.8, 28.7, 27.0, 23.8; δ (minor) = 162.9, 54.0, 45.2, 43.8, 40.6, 32.6, 29.9, 29.6, 29.4, 28.8, 28.7, 26.8, 24.0. HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{14}H_{28}ClNO$ + Na: 284.1757; found: 248.1757.

N-(1,1-Dimethyl-10-tosyloxyundecyl)formamide (14)

TsCl (4.50 g, 23.6 mmol) was added to a solution of formamide **9** (2.61 g, 10.7 mmol) in pyridine (8 mL). After stirring the reaction mixture at r.t. for 4 h, brine (30 mL) was added, and the resultant mixture was extracted with EtOAc (300 mL). The combined extracts were washed with aq 1 M HCl (100 mL), sat. aq $NaHCO_3$ (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue (3.1 g) was mixed with 50% AcOH (20 mL) and the reaction mixture was stirred at r.t. for 16 h. Brine (30 mL) was added to the mixture, and the resultant mixture was extracted with EtOAc (300 mL). The combined extracts were washed with sat. aq $NaHCO_3$ (100 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:1) to yield **14** (2.05 g, 48%) as a colorless oil.

IR (neat): 3302 (br), 3053, 2970, 2929, 2854, 2752, 1738, 1689, 1385, 1242, 1047 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.23 (1 H, d, *J* = 12.5 Hz), 7.79 (2 H, d, *J* = 8.1 Hz), 7.35 (2 H, d, *J* = 8.1 Hz), 5.61 (1 H, br s), 4.02 (2 H, t, *J* = 6.6 Hz), 2.45 (3 H, s), 1.71–1.66 (2 H, m), 1.66–1.59 (2 H, m), 1.35–1.19 (20 H, m); δ (minor) = 8.05 (1 H, d, *J* = 1.5 Hz), 7.79 (2 H, d, *J* = 8.1 Hz), 7.35 (2 H, d, *J* = 8.1 Hz), 5.17 (1 H, br s), 4.02 (2 H, t, *J* = 6.6 Hz), 2.45 (3 H, s), 1.71–1.66 (2 H, m), 1.66–1.59 (2 H, m), 1.35–1.19 (20 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 160.4, 144.6, 133.1, 129.7, 127.8, 70.6, 52.7, 43.6, 29.8, 29.4, 29.2, 28.8, 28.7, 28.6, 27.0, 25.2, 23.9, 21.6; δ (minor) = 163.0, 144.6, 133.1, 129.7, 127.8, 70.7, 53.9, 43.6, 29.8, 29.4, 29.2, 28.8, 28.7, 28.6, 27.0, 25.2, 23.9, 21.6.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{21}H_{35}NO_4S$ + Na: 420.2184; found: 420.2183.

N-(11-Iodo-1,1-dimethylundecyl)formamide (5j)

KI (647 mg, 3.90 mmol) was added to a solution of tosylate **14** (502 mg, 1.26 mmol) in MeCN (10 mL). After stirring the reaction mixture under reflux for 72 h, brine (100 mL) was added, and the resultant mixture was extracted with EtOAc (300 mL). The combined extracts were washed with H_2O (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:3) to yield formamide **5j** (404 mg, 91%) as yellow oil.

IR (neat): 3291 (br), 2968, 2927, 2852, 2752, 1740, 1690, 1537, 1466, 1456, 1387, 1365, 1313, 1259, 1240, 1228, 1173, 1088, 1047 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ (major) = 8.23 (1 H, d, *J* = 13 Hz), 5.64 (1 H, br s), 3.19 (2 H, t, *J* = 7.3 Hz), 1.82 (2 H, quint, *J* = 7.3 Hz), 1.70–1.66 (2 H, m), 1.41–1.23 (20 H, m); δ (minor) = 8.05 (1 H, s), 5.15 (1 H, br s), 3.19 (2 H, t, J = 7.3 Hz), 1.82 (2 H, quint, J = 7.3 Hz), 1.70–1.66 (2 H, m), 1.41–1.23 (20 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 160.4, 52.8, 43.8, 33.5, 30.5, 29.9, 29.6, 29.5, 29.3, 28.7, 28.5, 27.0, 24.0, 7.4; δ (minor) =

162.9, 54.0, 40.6, 33.5, 30.5, 29.9, 29.6, 29.5, 29.3, 28.7, 28.5, 27.0, 24.0, 7.4.

HRMS (ESI): *m/z* (M + Na)$^+$ calcd for $C_{14}H_{28}INO$ + Na: 376.1113; found: 376.1114.

Formamides 7; General Procedure

p-TsOH monohydrate (catalytic amount) was added to a solution of the respective aniline (5.0 mmol) in ethyl formate (80 mL) at r.t. After refluxing the reaction mixture for 72 h, EtOAc (200 mL) was added. The organic layer was washed with sat. aq $NaHCO_3$ (50 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel or recrystallization from EtOAc–hexane to yield formamide **7**.

***N*-(2-Benzyloxyphenyl)formamide (7a)**

Yield: 69%; white solid; mp 74–75 °C.

IR (neat): 3305 (br), 3034, 2941, 2902, 2885, 1664, 1595, 1529, 1456, 1379, 1259, 1215, 1003 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 8.42 (1 H, d, *J* = 1.5 Hz), 8.39 (1 H, dd, *J* = 8.1, 1.5 Hz), 7.79 (1 H, br s), 7.45–7.35 (5 H, m), 7.23–7.21 (1 H, m), 7.13–6.94 (3 H, m), 5.11 (2 H, s); δ (minor) = 8.87 (1 H, d, *J* = 11.7 Hz), 8.42 (1 H, d, *J* = 1.5 Hz), 7.79 (1 H, br s), 7.45–7.35 (5 H, m), 7.23–7.21 (1 H, m), 7.13–6.94 (3 H, m), 5.11 (2 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 158.8, 147.0, 136.1, 128.7, 128.3, 127.6, 126.4, 124.1, 120.5, 116.7, 111.4, 70.8; δ (minor) = 161.3, 147.7, 135.8, 128.7, 128.4, 127.9, 127.0, 125.0, 121.3, 116.6, 112.7, 70.7.

HRMS (DART): *m/z* (M + H)$^+$ calcd for $C_{14}H_{14}NO_2$: 228.1025; found: 228.1023.

***N*-(3-Benzyloxyphenyl)formamide (7b)**

Yiel: 82%; white solid; mp 84 °C.

IR (KBr): 3209 (br), 3061, 2918, 2833, 1706, 1610, 1306, 1271, 1157, 1026 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 8.67 (1 H, d, *J* = 11.0 Hz), 7.97–6.67 (11 H, m), 5.06 (2 H, s); δ (minor) = 8.35 (1 H, s), 7.97–6.67 (11 H, m), 5.06 (2 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 162.7, 159.4, 138.1, 136.6, 130.5, 128.5, 128.0, 127.4, 111.2, 111.0, 105.6, 70.0; δ (minor) = 159.7, 159.1, 138.0, 136.4, 129.7, 128.4, 127.9, 127.4, 112.4, 111.1, 106.8, 69.9.

HRMS (DART): *m/z* (M + H)$^+$ calcd for $C_{14}H_{14}NO_2$: 228.1023; found: 228.1036.

***N*-(4-Benzyloxyphenyl)formamide (7c)**

Et_3N (1.93 mL, 13.5 mmol, 1.0 equiv) was added to a solution of 4-benzyloxyaniline [prepared from 4-benzyloxyaniline hydrochloride (3.20 g, 13.5 mmol)] in ethyl formate (80 mL), and the reaction was carried out further as given in the general procedure.

Yield: 68%; white solid; mp 108–109 °C.

IR (KBr): 3403 (br), 3003, 2941, 2872, 2835, 2603, 1593, 1462, 1325, 1232, 1138, 1028 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 8.50 (1 H, d, *J* = 11.0 Hz), 7.87–6.93 (10 H, m), 5.04 (2 H, s); δ (minor) = 8.31 (1 H, s), 7.87–6.93 (10 H, m), 5.05 (2 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 158.8, 155.9, 136.6, 129.7, 128.6, 128.0, 127.4, 121.7, 115.9, 70.3; δ (minor) = 162.9, 156.8, 136.8, 130.1, 128.7, 128.1, 127.4, 121.6, 115.3, 70.4.

HRMS (DART): *m/z* (M + H)$^+$ calcd for $C_{14}H_{14}NO_2$: 228.1023; found: 228.1029.

Ethyl 3-Formaminobenzoate (7e)

Yield: 71%; white solid; mp 106 °C.

IR (KBr): 3350 (br), 3140, 3089, 2983, 2942, 2783, 1713, 1695, 1489, 1306, 1153, 1028 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 10.4 (1 H, s), 8.86 (1 H, d, *J* = 11.0 Hz), 8.35–7.44 (4 H, m), 4.32 (2 H, q, *J* = 6.6 Hz), 1.32 (3 H, t, *J* = 6.6 Hz); δ (minor) = 10.3 (1 H, d, *J* = 11.0 Hz), 8.35–7.44 (5 H, m), 4.32 (2 H, q, *J* = 6.6 Hz), 1.32 (3 H, t, *J* = 6.6 Hz).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 165.5, 159.8, 138.6, 130.5, 129.2, 124.2, 123.6, 119.6, 60.8, 14.1; δ (minor) = 165.3, 162.5, 138.9, 131.1, 129.7, 124.1, 121.6, 118.0, 60.8, 14.1.

HRMS (DART): *m/z* (M + H)$^+$ calcd for $C_{10}H_{12}NO_3$: 194.0817; found: 194.0817.

Ethyl 4-Formaminobenzoate (7f)

Yield: 70%; white solid; mp 110 °C.

IR (KBr): 3305 (br), 2985, 2791, 1736, 1697, 1406, 1257, 1022 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 10.5 (1 H, s), 8.33 (1 H, br s), 8.09–7.25 (4 H, m), 4.27 (2 H, q, *J* = 6.6 Hz), 1.29 (3 H, t, *J* = 6.6 Hz); δ (minor) = 10.4 (1 H, d, *J* = 11.0 Hz), 8.96 (1 H, br s), 8.09–7.25 (4 H, m), 4.27 (2 H, q, *J* = 6.6 Hz), 1.29 (3 H, t, *J* = 6.6 Hz).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 165.2, 160.1, 142.4, 130.3, 124.6, 118.6, 60.4, 14.1; δ (minor) = 165.2, 162.5, 142.9, 130.7, 124.5, 116.4, 60.4, 14.1.

HRMS (DART): *m/z* (M + H)$^+$ calcd for $C_{10}H_{12}NO_3$: 194.0817; found: 194.0826.

***N*-(4-Bromophenyl)formamide (7g)**

Yield: 82%; gray solid; mp 110 °C.

IR (KBr): 3284 (br), 3184, 3115, 3051, 2872, 1680, 1537, 1396, 1251, 1005 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 8.39 (1 H, s), 7.52–7.42 (3 H, m), 7.11 (1 H, br s), 6.97 (2 H, d, *J* = 8.1 Hz); δ (minor) = 8.65 (1 H, d, *J* = 11.0 Hz), 7.52–7.42 (3 H, m), 7.11 (1 H, br s), 6.97 (2 H, d, *J* = 8.1 Hz).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 158.9, 135.9, 132.1, 121.5, 118.3; δ (minor) = 162.3, 135.8, 132.8, 120.3, 118.3.

HRMS (DART): *m/z* (M + H)$^+$ calcd for C_7H_7BrNO: 199.9711; found: 199.9712.

***N*-(2-Methoxy-4-nitrophenyl)formamide (7j)**

Yield: 46%; yellow solid; mp 145 °C.

IR (KBr): 3259 (br), 3107, 3008, 2981, 2914, 1699, 1672, 1520, 1412, 1346, 1281, 1263, 1153, 1028 cm^{-1}.

^{1}H NMR (600 MHz, DMSO-d_6): δ (single isomer) = 10.2 (1 H, br s), 8.47 (1 H, d, *J* = 8.8 Hz), 8.44 (1 H, s), 7.91 (1 H, d, *J* = 8.8 Hz), 7.82 (1 H, d, *J* = 2.2 Hz), 4.00 (3 H, s).

^{13}C NMR (150.8 MHz, DMSO-d_6): δ (single isomer) = 161.0, 148.0, 142.7, 133.5, 118.7, 117.1, 105.9, 56.5.

HRMS (DART): *m/z* (M + H)$^+$ calcd for $C_8H_9N_2O_4$: 197.0562; found: 197.0562.

***N*-(3,5-Dimethoxyphenyl)formamide (7k)**

Yield: 88%; brown solid; mp 84 °C.

IR (KBr): 3452 (br), 3159, 3026, 2945, 2845, 1682, 1599, 1412, 1298, 1159, 1070 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 8.69 (1 H, d, *J* = 11.0 Hz), 8.22 (1 H, br d, *J* = 11.0 Hz), 6.28 (1 H, t, *J* = 2.2 Hz), 6.23 (2 H, d,

J = 2.2 Hz), 3.79 (6 H, s); δ (minor) = 8.34 (1 H, d, J = 1.5 Hz), 7.48 (1 H, br s), 6.78 (2 H, d, J = 2.2 Hz), 6.26 (1 H, t, J = 2.2 Hz), 3.78 (6 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 162.8, 160.8, 138.7, 96.3, 96.6, 55.2; δ (minor) = 161.4, 159.7, 138.6, 96.8, 96.5, 55.1.

HRMS (DART): m/z (M + H)$^+$ calcd for $C_9H_{12}NO_3$: 182.0817; found: 182.0820.

N-(3,4,5-Trimethoxyphenyl)formamide (7l)
Yield: 78%; yellow solid; mp 104 °C.

IR (KBr): 3287 (br), 3085, 2941, 2868, 2775, 1670, 1598, 1415, 1236, 1134 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (major) = 8.36 (1 H, d, J = 1.5 Hz), 7.14 (1 H, br s), 6.84 (2 H, s), 3.87 (6 H, s), 3.83 (3 H, s); δ (minor) = 8.61 (1 H, d, J = 11.0 Hz), 7.59 (1 H, br s), 6.30 (2 H, s), 3.86 (6 H, s), 3.82 (3 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ (major) = 159.4, 152.9, 134.1, 133.4, 97.4, 60.6, 55.7; δ (minor) = 162.7, 152.9, 135.0, 133.4, 97.4, 60.7, 55.7.

HRMS (DART): m/z (M + H)$^+$ calcd for $C_{10}H_{14}NO_4$: 212.0923; found: 212.0933.

N-[3-(Benzyloxy)-2-pyridinyl]formamide (7m)
Ac_2O (3.3 mL, 29.8 mmol) was added to a solution of 2-amino-3-benzyloxypyridine (1.99 g, 9.94 mmol) in formic acid (10 mL). After stirring the reaction mixture at r.t. for 72 h, MeOH (4 mL) and sat. aq $NaHCO_3$ (5 mL) were successively added at 0 °C. After stirring the mixture at 0 °C for 15 min, brine (30 mL) was added, and the resultant mixture was extracted with EtOAc (300 mL). The combined extracts were washed with sat. aq $NaHCO_3$ (100 mL) and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:1) to yield **7m** (609 mg, 27%) as a white solid; mp 76 °C.

IR (KBr): 3237 (br), 3107, 3051, 3026, 2908, 2872, 1689, 1597, 1255, 1176 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ (single isomer) = 9.48 (1 H, d, J = 11.0 Hz), 8.08 (1 H, br s), 7.86 (1 H, d, J = 5.1 Hz), 7.44–7.36 (5 H, m), 7.19 (1 H, d, J = 8.0 Hz), 6.98 (1 H, dd, J = 8.0, 5.1 Hz), 5.10 (2 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 161.7, 141.6, 141.4, 139.3, 135.1, 128.9, 128.8, 127.8, 119.4, 118.9, 70.8.

HRMS (DART): m/z (M + H)$^+$ calcd for $C_{13}H_{13}N_2O_2$: 229.0977; found: 229.0993.

Isocyanides 4, 6, and 8; General Procedure
$PhOPOCl_2$ (127 mg, 0.6 mmol) or $EtOPOCl_2$ (98 mg, 0.6 mmol) was added to a solution of the appropriate formamide (0.5 mmol) in Et_3N (1.0 mL) or to a 1:1 mixture of Et_3N and CH_2Cl_2 (1.0 mL). After stirring the reaction mixture at r.t. for 1 or 2 h, brine (30 mL) was added, and the resultant mixture was extracted with EtOAc (150 mL). The combined extracts were washed with 1 M HCl (50 mL), sat. aq $NaHCO_3$ (50 mL), and brine (50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc–hexane) to yield the corresponding isocyanide (Tables 3 and 4).

4-Heptylisocyanobenzene (4)
Green oil.

IR (neat): 2956, 2927, 2856, 2123, 1506, 1466, 843, 822 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.27 (2 H, t, J = 8.1 Hz), 7.18 (2 H, d, J = 8.1 Hz), 2.61 (2 H, t, J = 8.1 Hz), 1.59 (2 H, quint, J = 7.3 Hz), 1.30 (8 H, m), 0.88 (3 H, t, J = 7.2 Hz).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 163.2, 144.6, 129.2, 126.1, 124.1 (t, J = 11.2 Hz), 35.6, 31.6, 31.0, 29.0, 29.0, 22.5, 14.0.

HRMS (DART): m/z (M + H)$^+$ calcd for $C_{14}H_{20}N$: 202.1596; found: 202.1593.

11-Isocyano-11-methyldodecyl Formate (6b)
Colorless oil.

IR (neat): 2735, 2688, 2131, 1724, 1468, 1390, 1371, 1306, 1281, 1174 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.06 (1 H, s), 4.17 (2 H, t, J = 6.6 Hz), 1.66 (2 H, quint, J = 7.3 Hz), 1.58–1.52 (2 H, m), 1.48–1.25 (20 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 161.1, 152.7 (t, J = 5.0 Hz), 64.0, 57.3 (t, J = 5.0 Hz), 42.3, 29.4, 29.3, 29.3, 29.0, 28.9, 28.4, 25.7, 24.0.

HRMS (ESI): m/z (M + Na)$^+$ calcd for $C_{15}H_{27}NO_2$ + Na: 276.1939; found: 276.1939.

11-Isocyano-1-methoxy-11-methyldodecane (6c)
Colorless oil.

IR (neat): 2981, 2933, 2854, 2131, 1468, 1390, 1371, 1223, 1120 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.37 (2 H, t, J = 6.6 Hz), 3.33 (3 H, s), 1.63–1.52 (4 H, m), 1.48–1.18 (20 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 152.7 (t, J = 5.0 Hz), 72.9, 58.5, 57.3 (t, J = 5.0 Hz), 42.4, 29.6, 29.5, 29.4, 29.4, 29.4, 28.9, 26.0, 24.0.

HRMS (ESI): m/z (M + Na)$^+$ calcd for $C_{15}H_{29}NO$ + Na: 262.2147; found: 262.2147.

1-*tert*-Butyldimethylsilyloxy-11-isocyano-11-methyldodecane (6e)
Colorless oil.

IR (neat): 2981, 2929, 2856, 2133, 1471, 1254, 1099 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.60 (2 H, t, J = 7.3 Hz), 1.58–1.36 (10 H, m), 1.34–1.24 (14 H, m), 0.90 (9 H, s), 0.05 (6 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 153.0 (t, J = 5.0 Hz), 63.1, 57.2 (t, J = 5.0 Hz), 42.4, 32.7, 29.5, 29.4, 29.4, 29.3, 29.3, 28.9, 25.9, 25.7, 24.0, 18.2, –5.4.

HRMS (ESI): m/z (M + Na)$^+$ calcd for $C_{20}H_{41}NOSi$ + Na: 362.2855; found: 362.2851.

Carbamic Acid N-(11-Isocyano-11-methyldodecyl) (9*H*-Fluoren-9-yl)methyl Ester (6f)
White solid; mp 156 °C.

IR (KBr): 3342 (br), 2983, 2921, 2852, 2131, 1693, 1533, 1450, 1263, 1146 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.75 (2 H, d, J = 8.1 Hz), 7.59 (2 H, d, J = 8.1 Hz), 7.38 (2 H, t, J = 8.1 Hz), 7.30 (2 H, t, J = 8.1 Hz), 4.84 (1 H, br s), 4.47–4.34 (2 H, m), 4.20 (1 H, t, J = 6.6 Hz), 3.23–3.03 (2 H, m), 1.55–1.21 (24 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 156.3, 152.7 (br), 143.9, 141.2, 127.5, 126.9, 125.0, 119.9, 66.4, 57.3 (t, J = 5.0 Hz), 47.2, 42.4, 41.0, 29.9, 29.4, 29.4, 29.3, 29.3, 29.1, 28.9, 26.6, 24.0.

HRMS (ESI): m/z (M + Na)$^+$ calcd for $C_{29}H_{38}N_2O_2$ + Na: 469.2831; found: 469.2821.

Carbamic Acid N-(11-Isocyano-11-methyldodecyl) 1,1-Dimethylethyl Ester (6g)
Colorless oil.

IR (neat): 3327 (br), 2980, 2929, 2856, 2131, 1693, 1524, 1248, 1173 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 4.48 (1 H, br s), 3.11 (2 H, q, *J* = 6.6 Hz), 1.58–1.53 (4 H, m), 1.49–1.41 (13 H, m), 1.41–1.38 (6 H, m), 1.35–1.25 (12 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 155.8, 152.8 (br), 78.6, 57.1 (t, *J* = 5.0 Hz), 42.3, 40.4, 29.9, 29.2, 29.2, 29.2, 29.2, 29.0, 28.7, 28.2, 26.5, 23.9.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{19}H_{38}N_2O_3$ + Na: 365.2780; found: 365.2781.

1-Fluoro-11-isocyano-11-methyldodecane (6h)
Colorless oil.

IR (neat): 2980, 2937, 2854, 2131, 1468, 1390, 1371, 1225, 1043, 1007 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 4.44 (2 H, dt, *J* = 47.4, 6.2 Hz), 1.74–1.63 (2 H, m), 1.58–1.25 (22 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 152.8 (t, *J* = 4.7 Hz), 84.2 (d, *J* = 163.8 Hz), 57.4 (t, *J* = 4.7 Hz), 42.4, 30.4, 30.3, 29.4, 29.4, 29.4, 29.2, 28.9, 25.1, 25.1, 24.1.

HRMS (DART): *m*/*z* $(M + H)^+$ calcd for $C_{14}H_{27}FN$: 228.2128; found: 228.2123.

1-Chloro-11-isocyano-11-methyldodecane (6i)
Colorless oil.

IR (neat): 2983, 2926, 2854, 2131, 1466, 1369, 1225, 1176, 1086 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 3.54 (2 H, t, *J* = 7.3 Hz), 1.77 (2 H, quint, *J* = 7.3 Hz), 1.58–1.52 (2 H, m), 1.48–1.37 (10 H, m), 1.35–1.25 (10 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 152.8 (t, *J* = 5.0 Hz), 57.4 (t, *J* = 5.0 Hz), 45.1, 42.4, 32.6, 29.4, 29.4, 28.9, 28.8, 26.8, 24.1.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{14}H_{26}ClN$ + Na: 266.1651; found: 266.1655.

1-Bromo-11-isocyano-11-methyldodecane (6j)
Colorless oil.

IR (neat): 2983, 2931, 2854, 2131, 1468, 1369, 1227, 1176, 1088 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 3.41 (2 H, t, *J* = 7.3 Hz), 1.86 (2 H, quint, *J* = 7.3 Hz), 1.59–1.51 (2 H, m), 1.48–1.36 (10 H, m), 1.35–1.24 (10 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 152.8 (t, *J* = 5.0 Hz), 57.4 (t, *J* = 5.0 Hz), 42.5, 34.0, 32.8, 29.5, 29.4, 29.4, 29.0, 28.7, 28.1, 24.1.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{14}H_{26}BrN$ + Na: 310.1146; found: 310.1150.

1-Iodo-11-isocyano-11-methyldodecane (6k)
Yellow oil.

IR (neat): 2981, 2929, 2854, 2131, 1468, 1225, 1174, 1084 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 3.19 (2 H, d, *J* = 7.3 Hz), 1.82 (2 H, quint, *J* = 7.3 Hz), 1.57–1.25 (24 H, m).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 152.8 (t, *J* = 5.0 Hz), 57.4 (t, *J* = 5.0 Hz), 42.5, 33.5, 30.5, 29.5, 29.4, 29.3, 29.0, 28.5, 24.1, 7.3.

HRMS (ESI): *m*/*z* $(M + Na)^+$ calcd for $C_{14}H_{26}IN$ + Na: 358.1008; found: 358.1013.

2-Benzyloxyphenyl Isocyanide (8a)
Yellow solid; mp 51 °C.

IR (KBr): 3107, 3072, 3035, 2933, 2125, 1591, 1491, 1286, 1003 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.46–6.91 (9 H, m), 5.17 (2 H, d, *J* = 8.1 Hz).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 167.6, 154.0, 135.9, 130.3, 128.6, 128.1, 127.7, 126.9, 120.8, 116.7 (t, *J* = 11.0 Hz), 113.4, 70.5.

HRMS (DART): *m*/*z* $(M + H)^+$ calcd for $C_{14}H_{12}NO$: 210.0904; found: 210.0919.

3-Benzyloxyphenyl Isocyanide (8b)
Yellow solid; mp 40 °C.

IR (KBr): 3088, 3034, 2933, 2916, 2123, 1595, 1489, 1387, 1146, 1018 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.40–6.96 (9 H, m), 5.05 (2 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 163.8, 159.1, 135.9, 132.2, 128.7, 128.3, 127.4, 127.3 (t, *J* = 11.2 Hz), 118.9, 116.4, 112.8, 70.3.

HRMS (DART): *m*/*z* $(M + H)^+$ calcd for $C_{14}H_{12}NO$: 210.0904; found: 210.0910.

4-Benzyloxyphenyl Isocyanide (8c)
Yellow solid; mp 81–82 °C.

IR (KBr): 3057, 3039, 2904, 2123, 1606, 1504, 1460, 1385, 1257, 1028 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.40–6.96 (9 H, m), 5.05 (2 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 162.7, 159.0, 136.0, 128.7, 128.3, 127.7, 127.4, 119.7 (t, *J* = 14.0 Hz), 115.5, 70.3.

HRMS (DART): *m*/*z* calcd for $C_{14}H_{12}NO$: 210.0904 $(M + H)^+$; found: 210.0907.

Ethyl 3-Isocyanobenzoate (8e)
Yellow solid; mp 65 °C.

IR (KBr): 3066, 2985, 2933, 2908, 2129, 1720, 1439, 1288, 1186, 1101, 1024 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.06 (1 H, dt, *J* = 8.1, 1.5 Hz), 8.05 (1 H, t, *J* = 2.2 Hz), 7.56 (1 H, dt, *J* = 8.1, 1.5 Hz), 7.50 (1 H, t, *J* = 8.1 Hz), 4.41 (2 H, q, *J* = 7.3 Hz), 1.41 (3 H, t, *J* = 7.3 Hz).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 165.5 (br), 164.8, 132.2, 130.3, 130.3, 129.6, 126.9, 126.8 (t, *J* = 12.4 Hz), 61.7, 14.3.

HRMS (DART): *m*/*z* $(M + H)^+$calcd for $C_{10}H_{10}NO_2$: 176.0712; found: 176.0734.

4-Iodophenyl Isocyanide (8h)
White solid; mp 102 °C.

IR (KBr): 3467 (br), 3412, 3005, 2131, 1620, 1477, 1394, 1053 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.73 (2 H, t, *J* = 8.8 Hz), 7.25 (2 H, t, *J* = 8.8 Hz).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 166.1, 138.7, 127.9, 126.1 (t, *J* = 11.0 Hz), 95.0.

HRMS (DART): *m*/*z* $(M + H)^+$ calcd for C_7H_5IN: 229.9467; found: 229.9467.

1-Isocyano-2-methoxy-4-nitrobenzene (8j)
Yellow solid; mp 89 °C.

IR (KBr): 3089, 3059, 2993, 2949, 2133, 1539, 1493, 1352, 1090, 1022 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.88–7.84 (2 H, m), 7.52 (1 H, d, *J* = 8.1 Hz), 4.07 (3 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 172.8, 155.4, 148.3, 128.0, 121.0 (t, *J* = 11.0 Hz), 115.8, 107.1, 56.8.

HRMS (DART): *m*/*z* (M + H)$^+$ calcd for $C_8H_7N_2O_3$: 179.0457; found: 179.0438.

3,5-Dimethoxyphenyl Isocyanide (8k)
Yellow solid; mp 81–82 °C.

IR (KBr): 3095, 2980, 2950, 2135, 1614, 1464, 1194, 1067 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.51 (2 H, s), 6.48 (1 H, dd, *J* = 3.5, 2.2 Hz), 3.79 (6 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 163.5, 160.9, 127.6 (t, *J* = 11.0 Hz), 104.7, 102.0, 55.5.

HRMS (DART): *m*/*z* (M + H)$^+$ calcd for $C_9H_{10}NO_2$: 164.0712; found: 164.0711.

3,4,5-Trimethoxyphenyl Isocyanide (8l)
Brown solid; mp 68 °C.

IR (KBr): 3098, 3008, 2972, 2939, 2131, 1593, 1502, 1331, 1234, 1001 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.61 (2 H, s), 3.86 (9 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 163.3, 153.5, 139.2, 121.9 (t, *J* = 11.0 Hz), 104.1, 61.0, 56.4.

HRMS (DART): *m*/*z* (M + H)$^+$ calcd for $C_{10}H_{12}NO_3$: 194.0817; found: 194.0822.

3-Benzyloxy-2-isocyanopyridine (8m)
Yellow solid; mp 56 °C.

IR (KBr): 3072, 3032, 3008, 2945, 2881, 2127, 1570, 1439, 1389, 1286, 1126 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.06 (1 H, dd, *J* = 8.1, 2.2 Hz), 7.46–7.27 (7 H, m), 5.24 (2 H, s).

^{13}C NMR (150.8 MHz, $CDCl_3$): δ = 168.3, 150.2, 140.6, 135.0, 128.9, 128.6, 127.8, 125.3, 121.5, 70.9.

HRMS (DART): *m*/*z* (M + H)$^+$ calcd for $C_{13}H_{11}N_2O$: 211.0871; found: 211.0861.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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