A Dehydrohalogenation Methodology for Synthesizing Terminal Olefins under Mild Conditions

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Abstract: A new methodology for preparing terminal olefins in good yield by dehydrohalogenation of primary alkyl iodide with tetrabutylammonium fluoride in dimethyl sulfoxide at room temperature is presented. Optimization of the mild reaction conditions and assays on various alkyl iodides are described.

Key words: alkenes, alkyl halides, elimination, dehydrohalogenation, tetrabutylammonium fluoride

Terminal olefins are widely used in C–C coupling reactions such as Grubbs metathesis[1] and as intermediates in the preparation of typical functional groups such as epoxides, diols or aldehydes. Olefins can be prepared by dehydrohalogenation under many different experimental conditions.[2] Few methods of dehydrohalogenation of primary alkyl halides have, however, been reported to produce terminal olefin as the major compound. Henningsen et al.[3] have developed a nickel-mediated elimination of hydrogen halide from primary alkyl iodide or bromide. The main disadvantage of this method is the production of a mixture of internal olefins contaminating the major terminal olefin product. With this methodology, terminal olefins are generally obtained in good to excellent yields (43–100%). Typical functional groups such as benzyl ether, ketone, ester, hydroxy, olefin and phenyl support the reaction conditions well, but aldehyde and cyanide groups are not compatible. Soderquist et al.[4] used a potassium hydroxide/triisopropylsilanol (KOH/TIPSOH) system as a phase-transfer catalyst for dehydrohalogenation of primary alkyl halides. They quantitatively converted primary alkyl halides to alkenes avoiding both ether and alcohol by-products, but reported only a few examples of application. Terminal olefins can also be obtained using a strong base such as *t*-BuOK,[5] or a hindered base such as DBU,[6] but both have drawbacks. Indeed *t*-BuOK as well as KOH are not well tolerated by all functional groups and by-products are produced, whereas DBU could be applied only for the preparation of conjugated terminal olefins.[7]

Our team was interested in developing a methodology for the synthesis of terminal olefins under mild conditions, for use in cross-metathesis reactions generating inhibitors of 17β-hydroxysteroid dehydrogenase.[8] We knew that tetrabutylammonium fluoride (TBAF) – a reagent widely used for deprotecting silylated alcohol[9] – can also convert an alkyl halide into an alkyl fluoride by nucleophilic substitution.[10] Interestingly, many investigators have observed an alkene by-product under such experimental conditions.[10a,11] We thus decided to optimize the formation of this 'by-product', formed by dehydrohalogenation of alkyl halides by the fluoride ion acting as a base. We designed a series of experiments with the aim of improving the basicity of the fluoride ion over its nucleophilicity. We undertook optimization of the following parameters: nature of the fluoride or ammonium ion, type of solvent, and nature of the dehydrohalogenating reagent. Herein, we report an optimized new methodology for the synthesis of terminal olefins by dehydrohalogenation at room temperature of primary alkyl halides using TBAF as reagent.

Initially we examined the reaction of 11-halogenoundecan-1-ols (compounds **1**) with 1 M TBAF in THF at room temperature. Analysis of the crude material by ^{1}H NMR revealed a low conversion with the chloride, while quantitative conversion was obtained with the iodide and the bromide derivatives (Table 1, entries 1–3). A better dehydrohalogenation/substitution (E/S_N) ratio was however obtained with the iodide. Three sources of TBAF (1 M in THF, hydrated or adsorbed on SiO_2) were next investigated, but no major difference in the E/S_N ratio (entries 1, 4, 5) was evident. 11-Iodoundecan-1-ol was also treated with TBACl, TBABr and TBAI in THF. The results showed that fluoride is a better base than the other halogens, which yielded no olefin products (entries 6–8). Inorganic fluoride salts such as LiF, KF and CsF, were found ineffective as well (entries 9–11). Only the starting material was detected after four hours of reaction. In summary, the reaction of TBAF hydrate with a primary iodide in THF gives the best E/S_N ratio (43/57, entry 4).

We next examined the effect of solvent on the E/S_N ratio. 11-Iodoundecan-1-ol (**1a**) was mixed with four equivalents of TBAF hydrate in various solvents at room temperature. The results obtained by ^{1}H NMR analysis of the crude material are shown in Table 2. Nonpolar solvents such as hexanes and toluene (entries 1, 2) mostly gave the fluoride compound with an E/S_N ratio close to 15:85. A similar E/S_N ratio was observed with 1,4-dioxane, dimethyl sulfide and triethylamine (entries 3–5). Furthermore, a mixture of nucleophilicity and basicity of the fluoride ion is observed with sulfolane, THF, acetonitrile, acetone, pyridine and *N*-methyl-2-pyrrolidinone. The average E/S_N

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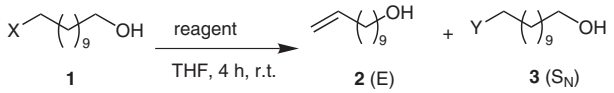
Table 1 Dehydrohalogenation (E) or Nucleophilic Substitution (S_N) of 11-Halogenoundecan-1-ols with Various Fluoride or Ammonium Ions in THF[a]

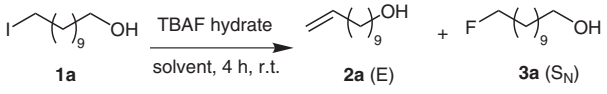


1 **2** (E) **3** (S_N)

Entry	X	Reagents[b]	Conversion (%)[c]	E/S_N[c]	Y
1	I	TBAF 1 M in THF	100	43:57	F
2	Br	TBAF 1 M in THF	100	15:85	F
3	Cl	TBAF 1 M in THF	8	0:100	F
4	**I**	**TBAF hydrate**	**100**	**43:57**	**F**
5	I	TBAF on SiO_2	85	40:60	F
6	I	TBACl	100	0:100	Cl
7	I	TBABr	100	0:100	Br
8	I	TBAI	nd	0:100	I
9	I	LiF	0	nd	F
10	I	KF	0	nd	F
11	I	CsF	0	nd	F

[a] Substrate is dissolved in THF (0.03 M) with the reagent (4 equiv) and stirred for 4 h at r.t.
[b] TBAF: tetrabutylammonium fluoride; TBACl: tetrabutylammonium chloride; TBABr: tetrabutylammonium bromide; TBAI: tetrabutylammonium iodide.
[c] Determined by ^{1}H NMR analysis of the crude material.

Table 2 Dehydrohalogenation (E) or Nucleophilic Substitution (S_N) of 11-Iodoundecan-1-ol (**1a**) with TBAF Hydrate in Various Solvents[a]



1a **2a** (E) **3a** (S_N)

Entry	Solvent	Conversion (%)[b]	E/S_N[b]
1	hexanes	100	16:84
2	toluene	>90	18:82
3	1,4-dioxane	>90	15:85
4	DMS	82	23:77
5	Et_3N	100	18:82
6	sulfolane	75	37:63
7	THF	>90	40:60
8	MeCN	76	43:57
9	acetone	82	35:65
10	pyridine	100	46:54
11	*N*-methyl-2-pyrrolidinone	>90	36:64
12	CH_2Cl_2	0	nd
13	MeOH	0	nd
14	ethylene glycol	0	nd
15	DMF	100	64:36
16	dimethylacetamide	100	66:34
17	**DMSO**	**100**	**72:28**

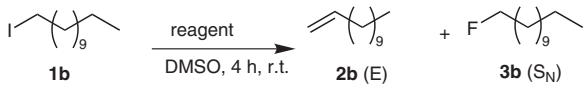
[a] 11-Iodoundecan-1-ol was dissolved in the solvent (0.03 M) with TBAF hydrate (4 equiv) and stirred for 4 h at r.t.
[b] Determined by ^{1}H NMR analysis of the crude material.

ratio with these solvents is around 40:60 (entries 6–11). On the other hand, no reaction was observed with the halogenated solvent dichloromethane or a polar protic solvent such as MeOH and ethylene glycol (entries 12–14). However, the reaction mostly produced the olefin when a polar aprotic solvent was used (entries 15–17), giving a good E/S_N ratio, especially with dimethyl sulfoxide (E/S_N = 72:28). This study of the effect of the nature of the solvent on the E/S_N ratio with TBAF revealed that the fluoride ion has a better nucleophilic activity in nonpolar solvents and that its basicity character is more important in polar aprotic solvents, particularly in dimethyl sulfoxide (entry 17).

After selecting dimethyl sulfoxide as the best solvent for the reaction of elimination, TMAF, TEAF and TBAF were compared as dehydrohalogenating reagents of 1-iodododecane (**1b**) (Table 3). At a concentration of 0.03 M, no major differences were observed between these three reagents, and the E/S_N ratio only ranged from 68:32 to 73:27 (entries 1, 2 and 4). TBAF hydrate was then selected as the reagent because it is more readily available and less expensive than the other ammonium salts. However, it must be noted that the concentration of 1-iodododecane in dimethyl sulfoxide has a significant impact on the E/S_N ratio. Formation of the fluoride compound (S_N) is more important at high concentrations, while the olefin product (E) is more abundant at low concentrations. Thus, the E/S_N ratio varies from 53:47 at 0.3 M to 86:14 at 0.003 M (entries 3–8). A concentration of 0.01 M of alkyl iodide in dimethyl sulfoxide was chosen to continue our optimization, because lower concentrations did not significantly improve the ratio and would involve the use of a large volume of solvent. The quantity of TBAF hydrate needed to complete the reaction was also evaluated. It was found that four equivalents of TBAF hydrate in dimethyl sulfoxide (0.01 M) were needed to rapidly complete the reaction – in less than one hour (data not shown). The optimal temperature was also investigated, but no significant effect was observed on the E/S_N ratio (data not shown).

Representative primary and secondary iodides and bromides were next subjected to the optimized reaction conditions (Table 4). In all cases, total conversion was

Table 3 Dehydrohalogenation (E) or Nucleophilic Substitution (S_N) of 1-Iodododecane (**1b**) with Ammonium Fluoride Ions in Various Concentrations of DMSO[a]



Entry	Reagents[b]	Concentration DMSO (M)	Conversion (%)[c]	E/S_N[c]
1	TMAF	0.03	100	71:29
2	TEAF	0.03	100	68:32
3	TBAF	0.3	100	53:47
4	TBAF	0.03	100	73:27
5	**TBAF**	**0.01**	**100**	**82:18**
6	TBAF	0.007	100	83:17
7	TBAF	0.005	100	85:15
8	TBAF	0.003	100	86:14

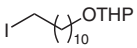
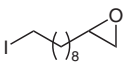
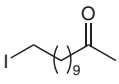
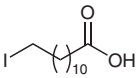
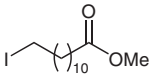
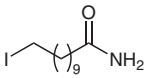
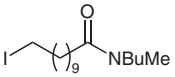
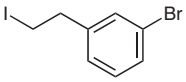
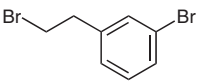
[a] Compound **1b** was dissolved in DMSO with reagent hydrate (4 equiv) and stirred for 4 h at r.t.
[b] TMAF: tetramethylammonium fluoride; TEAF: tetraethylammonium fluoride; TBAF: tetrabutylammonium fluoride.
[c] Determined by ^{1}H NMR analysis of the crude material.

observed by NMR analysis of crude material. Aliphatic alkyl iodides (entries **a**–**i**) with an alcohol, ether, epoxide, ketone, carboxylic acid, ester, primary amide and tertiary amide as functional groups gave excellent E/S_N ratio of 81:19 to 85:15 and good isolated yields of 64–76%. However, an exception was observed for carboxylic acid **1f** with an isolated yield of 20%. Indeed, for carboxylic acids (entry **f**) and phenols (data not shown), the fluoride ion acting as a base produces a carboxylate or a phenolate anion, which can displace the iodide to afford oligomers. Secondary alkyl halides (entries **j**,**k**) and phenethyl halide derivatives (entries **l**,**m**) gave, as expected, only the E product with good isolated yields of 64–77%. The internal olefin was, however, the major product obtained with the secondary alkyl bromides and iodides tested (entries **j**,**k**).

A mixture of olefin and alkyl fluoride generated by our dehydrohalogenation methodology was also tested for the Grubbs olefin metathesis. Using typical reaction conditions previously reported for steroid derivatives,[8,12] the metathesis with 16β-allyl-3-(*tert*-butyldimethylsilyl)-17-(tetrahydro-2*H*-pyranyl)estradiol and **2g/3g** afforded the desired cross-metathesis compound in 85% yield after purification by chromatography. This experiment clearly demonstrated that the small quantity of alkyl fluoride **3g** present with the olefin **2g** is not a problem for the Grubbs reaction.

In conclusion, we have developed a methodology for easily and rapidly preparing terminal olefins by dehydrohalogenation of primary alkyl iodides with TBAF in dimethyl sulfoxide, at room temperature. By optimization of the experimental conditions, we improved the basicity of the fluoride ion over its nucleophilic character, allowing the formation of the expected terminal olefin as the major compound. This one-step easy dehydrohalogenation procedure is a reasonable alternative to other more drastic conditions of olefin synthesis such as pyrolysis and Hofmann elimination. Furthermore, this optimized methodology is a complementary approach to the procedures that exist to prepare terminal olefins by dehydrohalogenation of alkyl halides. Because typical functional groups can

Table 4 Dehydrohalogenation (**2**, E) or Nucleophilic Substitution (**3**, S_N) of Various Substrates with TBAF in DMSO[a]

Entry	Substrate **1**	Conversion (%)[b]	E/S_N[b] **2**:**3**	Yield (%)[c]
a		100	83:17	76
b		100	83:17	71
c		100	83:17	74
d		100	85:15	72
e		100	85:15	64
f		100	82:18	20
g		100	84:16	70
h		100	82:18	76
i		100	81:19	69[d]
j		100	100:0[e]	75
k		100	100:0[f]	64
l		100	100:0	77
m		100	100:0	76

[a] Substrate was dissolved in DMSO (0.01 M) with TBAF hydrate (5 equiv) and stirred for 4 h at r.t.
[b] Determined by ^{1}H NMR analysis of the crude material.
[c] Determined after purification by SiO_2 chromatography, but given only for the major component, olefin **2**, of the mixture obtained.
[d] Obtained as a pure compound after chromatography.
[e] Dodec-1-ene/dodec-2-ene (10:90).
[f] Dodec-1-ene/dodec-2-ene (17:83).

tolerate the reaction conditions (TBAF, DMSO, room temperature) this new methodology could be useful for preparing a variety of terminal olefins under mild conditions.

Anhyd solvents were purchased from Aldrich and VWR in SureSeal bottles, which were conserved under positive argon pressure. Usual solvents were obtained from Fisher Scientific (Montreal, QC, Canada) and VWR (Ville Mont-Royal, QC, Canada) and were used as received. Reagents and starting material were obtained from Sigma-Aldrich Canada Co. (Oakville, ON, Canada). TLC was performed on 0.25 mm silica gel 60 F_{254} plates from Whatman (distributed by Fisher Scientific) and compounds were visualized by exposure to UV light (254 nm) and/or with a solution of ammonium molybdate/H_2SO_4/H_2O (with heating). Flash chromatography was performed on Silicycle 60 (Québec, QC, Canada) 230–400-mesh silica gel. IR spectra were obtained neat or from a thin film of the solubilized compound on NaCl pellets (usually in CH_2Cl_2). They were recorded on a PerkinElmer series 1600 FT-IR spectrometer (Norwalk, CT, USA). ^{13}C NMR spectra were recorded with a Bruker AC/F 300 spectrometer (Billerica, MA, USA) at 75 MHz and ^1H NMR spectra were recorded with a Bruker AVANCE 400 spectrometer at 400 MHz. The chemical shifts (δ) are expressed in ppm and referenced to $CHCl_3$ (7.26 and 77.0 ppm) or acetone (2.07 and 206.0 ppm) for ^1H and ^{13}C respectively. Low-resolution mass spectra (LRMS) were recorded with an LCQ Finnigan apparatus (San Jose, CA, USA) equipped with an atmospheric pressure chemical ionization (APCI) source on positive or negative mode.

ω-Halo-Substituted Substrates (Table 4)

11-Iodoundecan-1-ol (1a)[13]

11-Bromoundecan-1-ol (5.00 g, 19.9 mmol) was dissolved in acetone (50 mL) and NaI (10.4 g, 69.6 mmol) was added. The mixture was refluxed for 16 h. The product was then extracted with EtOAc and the organic phase was washed with a sat. aq solution of $Na_2S_2O_3$, washed with brine, dried ($MgSO_4$) and evaporated to dryness. Flash chromatography (hexanes–EtOAc, 9:1 to 8:2) afforded **1a** (5.63 g, 95%) as an off-white solid.

IR (film): 3392, 2918, 2850, 1466, 1342, 1260, 1198, 1168, 1050, 1033, 908, 722, 604 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.28 (m, 14 H, 7 × CH_2), 1.47 (br s, 1 H, OH), 1.57 (m, 2 H, C$H_2$$CH_2$OH), 1.82 (m, 2 H, C$H_2$$CH_2$I), 3.19 (t, *J* = 7.0 Hz, 2 H, CH_2I), 3.65 (t, *J* = 6.6 Hz, 2 H, CH_2OH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.3, 25.6, 28.4, 29.2 (2 ×), 29.3, 29.4, 30.3, 32.5, 33.4, 62.6.

LRMS: *m*/*z* [M – H_2O + H]$^+$ calcd for $C_{11}H_{22}I$: 281.1; found: 280.9.

12-Iodododecane (1b)

Commercially available.

2-[(11-Iodoundecyl)oxy]tetrahydro-2*H*-pyran (1c)

2-[(11-Bromoundecyl)oxy]tetrahydro-2*H*-pyran[14] (400 mg, 1.19 mmol) was dissolved in acetone (3 mL) and NaI (626 mg, 4.2 mmol) was added. The mixture was refluxed for 16 h and the product was extracted as described for compound **1a**. Flash chromatography (hexanes–EtOAc, 9:1) afforded **1c** (320 mg, 70%) as a colorless oil. ^1H NMR data are in agreement with those reported.[15]

2-(9-Iodononyl)oxirane (1d)

To a solution of 11-bromoundec-1-ene (420 μL, 2.14 mmol) in anhyd CH_2Cl_2 (40 mL) at 0 °C under argon was added MCPBA (554 mg, 3.2 mmol) and the mixture was stirred for 16 h at 0 °C. The solvent was evaporated and the crude product was extracted with EtOAc. The organic phase was washed with an aq solution of $Na_2S_2O_3$ (10%) and sat. aq solution of $NaHCO_3$, dried ($MgSO_4$) and evaporated to dryness to afford 688 mg of crude 2-(9-bromononyl)oxirane. The crude oxirane (200 mg) was dissolved in acetone (2 mL) and NaI (422 mg, 2.82 mmol) was added. The mixture was refluxed for 16 h and the product was extracted as described for compound **1a**. Flash chromatography (hexanes–EtOAc, 98:2) afforded **1d** (204 mg, 86%) as a colorless oil.

IR (neat): 3044, 2926, 2853, 1716, 1456, 1428, 1362, 1258, 1221, 1190, 1167, 914, 832, 720 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.50 (m, 12 H, 6 × CH_2), 1.51 (m, 2 H, CH_2CO), 1.81 (m, 2 H, C$H_2$$CH_2$I), 2.45 (dd, *J* = 5.0, 2.8 Hz, 1 H, CH_2O), 2.74 (dd, *J* = 5.0, 4.1 Hz, 1 H, CH_2O), 2.90 (m, 1 H, CHO), 3.18 (t, *J* = 7.0 Hz, 2 H, CH_2I).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.3, 25.9, 28.4, 29.3, 29.4 (2 ×), 30.4, 32.4, 33.5, 47.1, 52.4.

LRMS: *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{22}IO$: 297.1; found: 296.9.

12-Iodododecan-2-one (1e)

To a solution of 11-bromoundecanoic acid (1.01 g, 3.8 mmol) in THF (25 mL) under argon was slowly added MeLi (4.69 mL, 7.5 mmol) at –78 °C and the reaction was kept at 0 °C for 1 h. An aq solution of NH_4Cl was then added and the product extracted with Et_2O. The organic phase was dried ($MgSO_4$) and evaporated to dryness (963 mg). A portion of the crude ketone (713 mg) was dissolved in acetone (13.5 mL) and NaI (1.6 g, 10.84 mmol) was added. The mixture was refluxed for 24 h and the product was extracted as described for compound **1a**. Flash chromatography (hexanes–EtOAc, 95:5) afforded **1e** (598 mg, 69%) as a white solid.

IR (film): 2926, 2852, 1716, 1462, 1425, 1359, 1161 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.25 to 1.70 (m, 14 H, 7 × CH_2), 1.82 (m, 2 H, C$H_2$$CH_2$I), 2.14 (s, 3 H, $COCH_3$), 2.42 (t, *J* = 7.4 Hz, 2 H, CH_2CO), 3.19 (t, *J* = 7.0 Hz, 2 H, CH_2I).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.3, 23.8, 28.5, 29.1, 29.3 (3 ×), 29.8, 30.4, 33.5, 43.8, 209.3.

LRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{24}IO$: 311.1; found: 310.9.

12-Iodododecanoic Acid (1f)

12-Bromododecanoic acid (1.00 g, 3.58 mmol) was dissolved in acetone (18 mL) and NaI (2.15 g, 14.3 mmol) was added. The mixture was refluxed for 16 h. The mixture was cooled down to r.t. and the crude product was extracted with Et_2O. The organic phase was washed with sat. aq solution of $Na_2S_2O_3$. The product was next extracted with NaOH (10% in H_2O). The aqueous phase was acidified with HCl (10% in H_2O) and the product was extracted with Et_2O. The last organic phase was washed with brine, dried ($MgSO_4$) and evaporated to dryness to afford **1f** (788 mg, 68%) as a white solid. ^1H NMR data are in agreement with those reported.[16]

^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.4, 24.6, 28.5, 29.0, 29.2, 29.3 (2 ×), 29.4, 30.5, 33.5, 34.0, 179.6.

Methyl 12-Iodododecanoate (1g)

To a solution of **1f** (350 mg, 1.07 mmol) in anhyd MeOH (10 mL) at 0 °C under argon was added $TMSCHN_2$ (2.0 M in hexanes) (3.2 mL, 6.43 mmol). After 15 min., the solvent was evaporated to dryness. The crude product was purified by flash chromatography (hexanes–EtOAc, 95:5) to afford **1g** [232 mg, 64% (non-optimized yield)] as a colorless oil.

IR (neat): 2925, 2853, 1740, 1461, 1437, 1361, 1249, 1196, 1167, 1120 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.25 to 1.40 (m, 14 H, 7 × CH_2), 1.61 (m, 2 H, C$H_2$$CH_2$CO), 1.81 (m, 2 H, C$H_2$$CH_2$I), 2.30 (t, *J* = 7.5 Hz, 2 H, CH_2CO), 3.19 (t, *J* = 7.0 Hz, 2 H, CH_2I), 3.66 (s, 3 H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.4, 24.9, 28.4, 29.1, 29.2, 29.3 (2 ×), 29.4, 30.4, 33.5, 34.0, 51.4, 174.3.

LRMS: *m*/*z* [M – H_2O + H]$^+$ calcd for $C_{13}H_{26}IO_2$: 341.1; found: 340.9.

11-Iodoundecanamide (1h)

To a solution of 11-bromoundodecanoic acid (1.02 g, 3.9 mmol) in anhyd CH_2Cl_2 (25 mL) were added oxalyl chloride (0.5 mL) and DMF (1 mL). After 1 h at 0 °C, the solvent was evaporated and the crude acid chloride was dissolved in anhyd benzene under argon and reacted with 28% NH_4OH (3 mL). After 15 min, H_2O was added, the aqueous phase extracted with CH_2Cl_2 and the organic phase dried ($MgSO_4$) and evaporated under vacuum (952 mg). A portion of the crude amide (707 mg) was dissolved in acetone (13.4 mL) and NaI (1.6 g, 10.84 mmol) was added. The mixture was refluxed for 24 h and the product was extracted as described for compound **1a**. Flash chromatography (hexanes–acetone, 60:40) afforded **1h** (680 mg, 82%) as a white solid.

IR (film): 3346, 3184, 2916, 2848, 1634, 1468, 1410, 1325, 1297, 1265, 1232, 1199, 1162, 1140 cm^{-1}.

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.25–1.45 (m, 12 H, 6 × CH_2), 1.59 (m, 2 H, CH_2), 1.83 (m, 2 H, CH_2CH$_2$I), 2.16 (t, *J* = 7.5 Hz, 2 H, CH_2CO), 3.30 (t, *J* = 7.0 Hz, 2 H, CH_2I), 6.0 and 6.7 (2 br s, 2 H, $CONH_2$).

^{13}C NMR (75 MHz, acetone-d_6): δ = 7.9, 26.2, ~30 (5 ×, under solvent peaks), 31.1, 34.4, 36.1, 174.9.

LRMS: *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{23}INO$: 312.1; found: 312.0.

11-Iodoundecanoic Acid Butylmethylamide (1i)

N-Butyl-*N*-methyl-11-bromoundecanamide[17] (400 mg, 1.196 mmol) was dissolved in acetone (3 mL) and NaI (627 mg, 4.2 mmol) was added. The mixture was refluxed for 16 h and the product was extracted as described for compound **1a**. Flash chromatography (hexanes–EtOAc, 5:5) provided **1i** (365 mg, 80%) as a yellow viscous solid.

IR (film): 2926, 2853, 1648, 1458, 1296, 1260, 1210, 1079, 726 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (m, 3 H, CH_2CH_3), 1.25–1.40 (m, 16 H, 8 × CH_2), 1.50 (m, 2 H, CH_2CH$_2$N), 1.61 (m, 2 H, CH_2CH$_2$CO), 1.80 (m, 2 H, CH_2CH$_2$I), 2.28 (m, 2 H, CH_2CO), 2.90 and 2.96 (2 s, 3 H, NCH_3), 3.17 (t, *J* = 7.0 Hz, 2 H, CH_2I), 3.24 and 3.35 (2 t, *J* = 7.4 Hz, 2 H, CH_2N).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.4, 13.8, 20.0, 25.1 (25.5), 28.5, 29.3 (5 ×), 29.4 (30.6), 30.4, 32.9 (33.3), 33.5 (35.3), 47.4 (49.8), 172.9.

LRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{33}INO$: 382.2; found: 382.1.

2-Iodododecane (1j)

To a solution of **1k** (400 mg, 1.60 mmol) in acetone (8 mL) was added NaI (962 mg, 6.42 mmol). The mixture was refluxed for 16 h and the product was extracted as described for compound **1a**. Flash chromatography (hexanes–EtOAc, 95:5) afforded **1j** (430 mg, 91%) as a yellowish oil. ^{1}H NMR data are in agreement with those reported.[18]

2-Bromododecane (1k)

Commercially available.

1-Bromo-3-(2′-iodoethyl)benzene (1l)

To a solution of **1m** (260 mg, 0.985 mmol) in acetone (5 mL) was added NaI (738 mg, 4.92 mmol). The reaction mixture was refluxed for 16 h and the product was extracted as described for compound **1a**. Flash chromatography (hexanes–EtOAc, 95:5) afforded **1l** (230 mg, 75%) as a yellowish oil.

IR (neat): 3058, 2957, 1682, 1596, 1568, 1472, 1427, 1256, 1235, 1199, 1171, 1071, 997, 883, 846, 783, 689, 668, 630 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.15 (t, *J* = 7.7 Hz, 2 H, CH_2CH$_2$I), 3.33 (t, *J* = 7.9 Hz, 2 H, CH_2I), 7.13 (d, *J* = 7.6 Hz, 1 H, 4-CH), 7.20 (t, *J* = 7.7 Hz, 1 H, 5-CH), 7.35 (d, *J* = 1.6 Hz, 1 H, 2-CH), 7.40 (dd, *J* = 7.9, 1.1 Hz, 1 H, 6-CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 4.9, 39.6, 122.6, 127.0, 129.9, 130.1, 131.3, 142.6.

1-Bromo-3-(2′-bromoethyl)benzene (1m)

To a solution of 3-bromophenethyl alcohol (688 mg, 3.42 mmol) in anhyd CH_2Cl_2 (43 mL) at 0 °C under argon was added Ph_3P (1.79 g, 6.84 mmol) and CBr_4 (2.27 g, 6.84 mmol). The mixture was stirred at r.t. After 2 h, the mixture was quenched with a sat. aq solution of $NaHCO_3$. The product was extracted with CH_2Cl_2. The organic phase was washed with brine, dried ($MgSO_4$) and evaporated to dryness. Purification by flash chromatography (hexanes–EtOAc, 99:1 to 95:5) provided **1m** (528 mg, 58%) as a colorless oil.

IR (neat): 3059, 2963, 2876, 1593, 1568, 1474, 1428, 1258, 1216, 1072, 997, 889, 849, 779, 697, 667, 651, 548 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.14 (t, *J* = 7.4 Hz, 2 H, CH_2CH$_2$Br), 3.55 (t, *J* = 7.5 Hz, 2 H, CH_2Br), 7.18 (m, 2 H, 4-CH and 5-CH), 7.39 (m, 2 H, 2-CH and 6-CH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.3, 38.7, 122.5, 127.3, 130.0, 130.1, 131.7, 141.0.

Dehydrohalogenation of ω-Halo-Substituted Substrates; Undec-10-en-1-ol (2a); Typical Procedure

11-Iodoundecan-1-ol (200 mg, 0.67 mmol) was dissolved in DMSO (70 mL). TBAF hydrate (876 mg, 3.35 mmol) was added and the mixture was stirred for 4 h at r.t. The reaction was then quenched with H_2O and the product was extracted with EtOAc. The organic phase was washed with H_2O (to remove traces of DMSO), washed with brine, dried ($MgSO_4$) and evaporated to dryness. The crude product was purified by silica gel chromatography with 10–30% EtOAc in hexanes to afford a mixture of **2a**[19] (87 mg, 76%) and 11-fluoroundecan-1-ol (**3a**); ratio **2a**/**3a** = 83:17. In Table 4, yield of **2** was calculated based on ^{1}H NMR ratio. The peaks corresponding specifically to the minor product **3** are written between brackets in order to simplify the description of the ^{1}H NMR spectra (Table 4).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.40 (m, 10 H, 5 × CH_2), 1.46 (m, 2 H, CH_2CH$_2$CH=), 1.56 (m, 2 H, CH_2CH$_2$OH), [1.68 (m, 2 H, CH_2CH$_2$F)], 2.04 (m, 2 H, CH_2CH=), 3.64 (t, *J* = 6.6 Hz, 2 H, CH_2OH), [4.44 (dt, *J* = 47.4, 6.2 Hz, 2 H, CH_2F)], 4.96 (m, 2 H, CH=CH_2), 5.81 (m, 1 H, C*H*=CH_2).

Dodec-1-ene (2b)[19]

Ratio **2b**/**3b** = 83:17.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.8 Hz, CH_3), 1.20–1.35 (m, 14 H, 7 × CH_2), 1.37 (t, *J* = 6.9 Hz, 2 H, CH_2CH$_2$CH=), [1.68 (m, 2 H, CH_2CH$_2$F)], 2.04 (m, 2 H, CH_2CH=), [4.44 (dt, *J* = 47.4, 6.2 Hz, 2 H, CH_2F)], 4.97 (m, 2 H, CH=CH_2), 5.82 (m, 1 H, C*H*=CH_2).

11-(Tetrahydropyran-2′-yloxy)undec-1-ene (2c)[20]

Ratio **2c**/**3c** = 83:17.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.30 (m, 10 H, 5 × CH_2), 1.35 (m, 2 H, CH_2CH$_2$CH=), 1.50–1.75 (m, 8 H, CH_2CH$_2$OTHP and 3 × CH_2 of THP), 2.03 (m, 2 H, CH_2CH=), 3.38 and 3.72 (2 m, 2 H, CH_2OTHP), 3.51 and 3.87 (2 m, 2 H, CH_2O of THP), [4.43 (dt, *J* = 47.4, 6.2 Hz, 2 H, CH_2F)], 4.58 (m, 1 H, OCH of THP), 4.96 (m, 2 H, CH=CH_2), 5.81 (m, 1 H, C*H*=CH_2).

2-(Non-8-enyl)oxirane (2d)[21]
Ratio **2d/3d** = 85:15.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.50 (m, 10 H, 5 × CH_2), 1.52 (m, 2 H, CH_2CHO), [1.68 (m, 2 H, CH_2CH$_2$F)], 2.04 (m, 2 H, CH_2CH=), 2.46 (dd, *J* = 5.0, 2.8 Hz, 1 H, CH_2O), 2.75 (dd, *J* = 4.9, 4.2 Hz, 1 H, CH_2O), 2.88 (m, 1 H, CHO), [4.44 (dt, *J* = 47.4, 6.2 Hz, 2 H, CH_2F)], 4.96 (m, 2 H, CH=CH_2), 5.81 (m, 1 H, C*H*=CH_2).

Dodec-11-en-2-one (2e)[22]
Ratio **2e/3e** = 85:15.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20–1.50 (m, 10 H, 5 × CH_2), 1.56 (m, 2 H, CH_2CH$_2$CH=), [1.70 (m, 2 H, CH_2CH$_2$F)], 2.03 (m, 2 H, CH_2CH=), 2.13 (s, 3 H, $COCH_3$), 2.42 (t, *J* = 7.4 Hz, 2 H, CH_2CO), [4.44 (dt, *J* = 47.3, 6.2 Hz, 2 H, CH_2F)], 4.96 (m, 2 H, CH=CH_2), 5.81 (m, 1 H, C*H*=CH_2).

Dodec-11-enoic Acid (2f)[23]
Ratio **2f/3f** = 82:18.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.40 (m, 12 H, 6 × CH_2), 1.63 (m, 2 H, CH_2CH$_2$CO), [1.66 (m, 2 H, CH_2CH$_2$F)], 2.03 (m, 2 H, CH_2CH=), 2.34 (t, *J* = 7.5 Hz, 2 H, CH_2CO), [4.44 (dt, *J* = 47.4, 6.2 Hz, 2 H, CH_2F)], 4.96 (m, 2 H, CH=CH_2), 5.80 (m, 1 H, C*H*=CH_2).

Methyl Dodec-11-enoate (2g)[24]
Ratio **2g/3g** = 84:16.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.30 (m, 10 H, 5 × CH_2), 1.36 (m, 2 H, CH_2CH$_2$CH=), 1.59 (m, 2 H, CH_2CH$_2$CO), [1.66 (m, 2 H, CH_2CH$_2$F)], 2.03 (m, 2 H, CH_2CH=), 2.30 (t, *J* = 7.5 Hz, 2 H, CH_2CO), 3.66 (s, 3 H, CH_3), [4.44 (dt, *J* = 47.4, 6.2 Hz, 2 H, CH_2F)], 4.96 (m, 2 H, CH=CH_2), 5.81 (m, 1 H, C*H*=CH_2).

Undec-10-enamide (2h)[25]
Ratio **2h/3h** = 82:18.

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.25–1.50 (m, 10 H, 5 × CH_2), 1.59 (m, 2 H, CH_2CH$_2$CH=), [1.65 (m, 2 H, CH_2CH$_2$F)], 2.03 (m, 2 H, CH_2CH=), 2.17 (t, *J* = 7.4 Hz, 2 H, CH_2CO), [4.44 (dt, *J* = 47.6, 6.1 Hz, 2 H, CH_2F)], 4.96 (m, 2 H, CH=CH_2), 5.82 (m, 1 H, C*H*=CH_2), 6.0 and 6.7 (2 br s, 2 H, $CONH_2$).

Undec-10-enoic Acid Butylmethylamide (2i)
Compound **2i** was obtained as a pure product after purification.

IR (film): 2926, 2854, 1648, 1466, 1400, 1298, 1266, 1210, 1141, 1113, 1085, 997 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (m, 3 H, CH_2CH_3), 1.25 to 1.40 (m, 12 H, 6 × CH_2), 1.50 (m, 2 H, CH_2CH$_2$N), 1.62 (m, 2 H, CH_2CH$_2$CO), 2.02 (m, 2 H, CH_2CH=), 2.29 (t, *J* = 7.5 Hz, 2 H, CH_2CO), 2.91 and 2.96 (2 s, 3 H, NCH_3), 3.25 and 3.36 (2 t, *J* = 7.2 Hz, 2 H, CH_2N), 4.96 (m, 2 H, CH=CH_2), 5.81 (m, 1 H, C*H*=CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 20.0, 25.1 (25.5), 28.9, 29.1, 29.4 (4 ×), 29.5 (30.6), 33.0 (33.6), 33.8 (35.3), 47.4 (49.8), 114.1, 139.2, 173.0.

LRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{32}NO$: 254.3; found: 254.2.

Dodec-2-ene[26]/Dodec-1-ene[19] (2j: 90:10/ 2k: 83:17)
Peaks corresponding specifically to the minor product dodec-1-ene are given between brackets.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.8 Hz, CH_3), 1.20–1.40 (m, 14 H, 7 × CH_2), 1.64 (m, 3 H, CH_3CH=), 1.95 (m, 2 H, CH_2CH=), [2.03 (m, 2 H, CH_2CH=)], [4.97 (m, 2 H, CH=CH_2)], 5.42 (m, 2 H, CH=CH), [5.82 (m, 1 H, C*H*=CH_2)].

3-Bromostyrene (2l and 2m)[19]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.30 (d, *J* = 10.9 Hz, 1 H, CH_2=CH), 5.76 (d, *J* = 17.5 Hz, 1 H, CH_2=CH), 6.64 (dd, *J* = 17.5, 10.9 Hz, 2 H, C*H*=CH_2), 7.20 (t, *J* = 7.8 Hz, 1 H, 5-CH), 7.32 (d, *J* = 7.8 Hz, 1 H, 6-CH), 7.38 (dd, *J* = 7.8, 1.7 Hz, 1 H, 4-CH), 7.56 (t, *J* = 1.7 Hz, 2-CH).

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