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$AlCl_3$–NaI(NaBr)–*t*-BuOH: mild, chemo- and stereoselective reagents for hydrohalogenation of propiolic derivatives

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ABSTRACT

(*Z*)-β-Iodo-propenamides and -β-iodo-propenoic esters were selectively prepared in high yields, at room temperature, through reaction of 2-propynamides and 2-propynoic esters, respectively, with $AlCl_3$ and NaI in the presence of *t*-BuOH in dichloromethane. These experimental conditions are compatible with the presence of acid sensitive acetal groups. Alternative use of EtOH or H_2O in place of *t*-BuOH was investigated. (*Z*)-Bromo-propenamides and corresponding esters were prepared according to a similar procedure using sodium bromide in refluxing acetonitrile.

1. Introduction

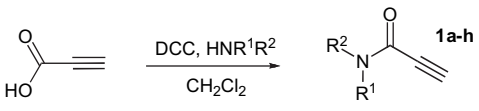
While investigating dialkylzinc-mediated atom transfer radical addition/cyclization process leading to α-alkylidene-γ-lactams,[1] we found out by accident that direct selective hydrohalogenation of 2-propynamides occurred through their reaction with ZnX_2 and *t*-BuX (X=Br, I) at room temperature.[2] However, this methodology was not suitable for substrates bearing acid sensitive groups such as acetals. Direct hydrohalogenation of propynamides had been previously achieved at room temperature in the presence of Ce(III) salts, halotrimethylsilanes and NaI in acetonitrile.[3] Hydroiodination of propynoic acid and its derivatives was also known to proceed with either LiI,[4] or NaI,[5] in acetic acid at 70 °C.

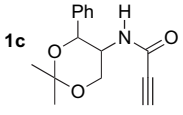
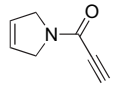
We have investigated whether the methodology of production of these functionalized vinyl halides could be further improved. We report herein a substantial modification of our procedure by using cheaper reagents, i.e., $AlCl_3$ and NaI in the presence *tert*-butanol. The use of water, or ethanol as substitutes for *tert*-butanol was also studied. The protocol, initially developed for hydroiodination of propynamides, was extended to the corresponding esters and ketones.

The association of aluminium trichloride with sodium iodide has widely been used for selective demethylation of aliphatic methyl ethers in the presence of aromatic methyl ethers, either in acetonitrile,[6] or under solvent free conditions.[7] This reagent is known to deprotect some specific esters,[8,6e] and acetals.[9,6e] In close connection with the present report, aluminium trichloride and sodium iodide have also been used in the presence of water, to convert 1,2-allenic sulfoxides into 2-iodoallyl sulfoxides.[10]

2. Results and discussion

Various 2-propynamides (**1a**–**1h**) were prepared from propynoic acid and amines in the presence of DCC (Scheme 1). In our previous studies,[2] we had speculated that *tert*-butyl cation acted as a mild and selective proton donor, according to Scheme 2.[11] The formation of *tert*-butyl cation from reaction of aluminium trichloride with *tert*-butyl alcohol is well known in Friedel and Crafts reactions.[12] Therefore, we have first investigated whether hydroiodination reactions could be carried out in the presence of 1.5 equiv of aluminium trichloride, 2 equiv of sodium iodide in a 1:9 mixture of *t*-BuOH and dichloromethane, at room temperature for 18 h.



1a $R^1 = R^2$ = allyl
1b R^1 = H, $R^2 = CH_2CH(OEt)_2$
1c

1d R^1 = H, R^2 = *m*-$PhNO_2$
1e $R^1 = R^2 = CH_2$*i*-Pr
1f $R^1 = R^2$ = Et
1g

1h R^1 = H, R^2 = allyl

Scheme 1. Synthesis of propynamides **1a**–**h**.

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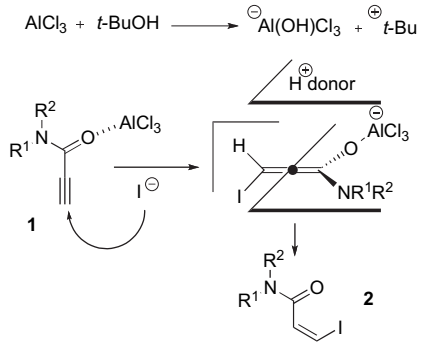
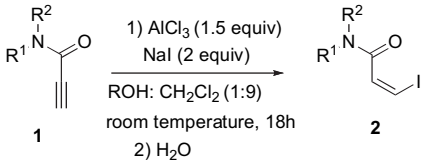


Scheme 2. Mechanism.

The results are summarized in Table 1. All three components were necessary for the reaction to proceed. No reaction occurred in the absence of $AlCl_3$, whereas the reaction in the presence of $AlCl_3$ gave **2a** in 90% yield.[13] In the presence of only 0.5 equiv of $AlCl_3$, hydroiodination was slowed down (73% of starting material remained unchanged after 48 h). In the absence of *t*-BuOH, the reaction conducted on diallylpropynamide **1a** produced the corresponding (*Z*)-vinyl iodide **2a** in only 38% yield while starting material was recovered in 33% yield (entry 2). A quantitative yield was reached when *tert*-butanol was used as solvent (entry 3).

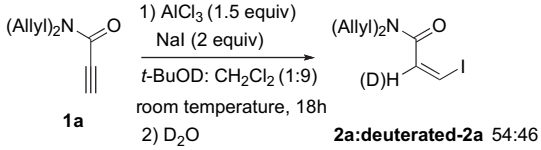
Table 1
Hydroiodination of **1**



Entry	**1a–e**	Alcohol	**2a–e**	Yield (%)
1	**1a**	*t*-BuOH	**2a**	90
2	**1a**	—	**2a**	38[a]
3	**1a**	*t*-BuOH	**2a**	99[b]
4	**1b**	*t*-BuOH	**2b**	87
5	**1c**	*t*-BuOH	**2c**	89
6	**1d**	*t*-BuOH	**2d**	84[c]
7	**1a**	EtOH	**2a**	82
8	**1e**	EtOH	**2e**	100
9	**1f**	EtOH	**2f**	96
10	**1g**	EtOH	**2g**	88
11	**1h**	EtOH	**2h**	80
12	**1a**	H_2O	**2a**	20[c,d]
13	**1a**	H_2O	**2a**	86[c,e]

[a] **1a** was recovered in 33% yield.
[b] In 100% *t*-BuOH.
[c] In CH_3CN.
[d] **1a** was recovered in 79% yield.
[e] Only 1 equiv of H_2O was used.

Since the nature of the proton donor remained hypothetic, the reaction was performed under the following conditions: *t*-BuOD/CH_2Cl_2 1:9 (v/v), followed by work-up with D_2O (Scheme 3). Non-deuterated- and deuterated-**2a** were isolated in 70% yield, in a 54:46 ratio (a similar ratio was obtained upon work-up with H_2O). This result clearly proved the involvement of both *tert*-butyl cation and *t*-BuOD in the protonation and deuteration of the intermediate allenoate.



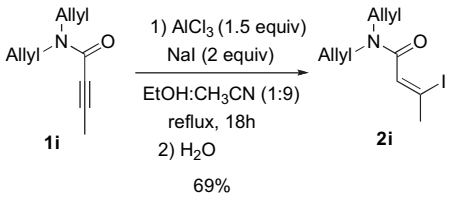
Scheme 3. Deuterium-labelling experiment.

Sensitive acetal groups, known to be deprotected in the presence of $AlCl_3$ and NaI in acetonitrile[9] remained unchanged during the reaction. Propynamides **1b** and **1c**, bearing acyclic and cyclic acetal groups, led to vinyl iodides **2b** and **2c**, in 87% and 89% yields, respectively, (entries 4–5). This is a significant advantage in using the bulky tertiary alcohol. All the reactions described in Table 1 were stereoselective and led exclusively to the formation of (*Z*)-vinyl iodides. No improvement was observed when replacing CH_2Cl_2 with CH_3CN.

Under specific conditions, ethanol and water could be used in place of *t*-BuOH (entries 7–13). It must be noted that, notwithstanding the fact that $AlCl_3$ is reputedly reacting with protic species to form HCl,[12b] no significant hydrochlorination was observed when the reaction was conducted in the absence of NaI whatever the used protic species (*t*-BuOH or EtOH 1:9 (v/v) ratio to CH_2Cl_2, i.e., approximately 6 equiv of alcohol), or H_2O (1 equiv in CH_2Cl_2). As shown in Table 1, reactions carried out in the presence of ethanol were high yielding and stereoselective. However, acetal deprotection occurred with compounds **1b** and **1c**.

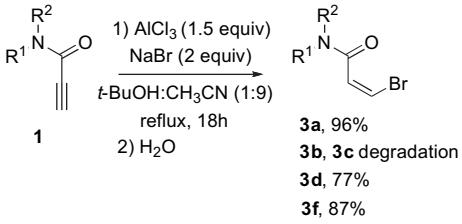
Experiments carried out in the presence of water confirmed the already mentioned observations concerning hydroiodination of allenic sulfoxydes.[10] High yields could only be observed in the presence of 1 equiv of H_2O (entries 12/13). However, it must be noticed that acetals were deprotected under these conditions.

As exemplified in Scheme 4, non-terminal alkynes reacted very slowly at room temperature. Hydroiodination of **1i** led to **2i** in 69% yield after refluxing the reaction mixture for 18 h.



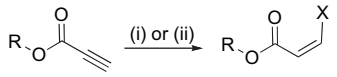
Scheme 4. Hydroiodination of **1i**.

Stereoselective hydrobromination could be achieved by replacing sodium iodide by sodium bromide (Scheme 5). The reactions were slower and the highest yields were reached when the $AlCl_3$–NaBr–*t*-BuOH system was used in refluxing acetonitrile. Again, owing to the higher temperature, substrates containing sensitive acetal moieties (**1b**, **1c**) were degraded in a complex mixture of unidentified products under these conditions.



Scheme 5. Hydrobromination of **1**.

Propynoic esters were also transformed into the corresponding vinyl iodides and bromides in good yields (Scheme 6). No transesterification with ethanol was detected at room temperature. It is worth noting that, although the $AlCl_3$–NaI system is known to cleave benzyl esters and esters derived from aromatic acids,[8,6e] no trace of the corresponding acid was detected, even when performing the reaction on allylic and benzylic esters **4a** and **4b** under refluxing acetonitrile.



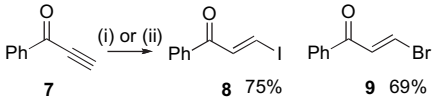
4a, R = Allyl
4b, R = Bn
4c, R = $(CH_2)_3Ph$

5a, (i), X = I, EtOH, 75%
5a, (i), X = I, *t*-BuOH, 71%
5b, (i), X = I, EtOH, 88%
5c, (i), X = I, *t*-BuOH, 93%
6a, (ii), X = Br, 57%
6b, (ii), X = Br, 94%

(i) 1) $AlCl_3$ (1.5 equiv), NaI (2 equiv), alcohol : CH_2Cl_2 (1:9), r.t., 18h, 2) H_2O
(ii) 1) $AlCl_3$ (1.5 equiv), NaBr (2 equiv), *t*-BuOH : CH_3CN (1:9), reflux, 18h, 2) H_2O

Scheme 6. Hydrohalogenation of **4**.

Finally the methodology was shown to apply to phenylpropynone **7** (Scheme 7). Whereas direct hydrohalogenation reactions of similar compounds were reputed to occur in low yield (<50%),[2,4] we were pleased to notice that, under these new experimental conditions, the corresponding vinyl iodide **8** and bromide **9** were isolated in 75 and 69% yields, respectively, as single (*E*)-isomers.[14]



7 **8** 75% **9** 69%

(i) 1) $AlCl_3$ (1.5 equiv), NaI (2 equiv), alcohol : CH_2Cl_2 (1:9), r.t., 18h, 2) H_2O
(ii) 1) $AlCl_3$ (1.5 equiv), NaBr (2 equiv), *t*-BuOH : CH_3CN (1:9), reflux, 18h, 2) H_2O

Scheme 7. Hydrohalogenation of **7**.

3. Conclusion

In conclusion, this paper describes a new and convenient method for the preparation of functionalized vinyl iodides, which are useful building blocks for the synthesis of complex molecules. Hydroiodination of 2-propynamides was improved by using $AlCl_3$–NaI–ROH ternary system in CH_2Cl_2 at room temperature. The reaction is stereoselective and leads to the formation of (*Z*)-iodopropenamides in high yields. It is worth noting that the methodology tolerates acid sensitive acetal groups when using *tert*-butanol, and that ester groups remained unchanged even in the presence of ethanol. NaBr-mediated hydrobromination needed refluxing acetonitrile to give product in moderate to good yield. The methodology was also shown to be suitable to convert propynoic esters into 3-iodo or 3-bromo-propenoates, without concomitant transesterification. Interesting yields were reached with 2-phenylpropynone.

4. Experimental section

4.1. General

NMR spectra were recorded at 300 MHz (^1H) and 75 MHz (^{13}C) using $CDCl_3$ as the solvent. The *J* values are given in Hz. Starting materials **4a**,[15] **4b**,[16] and **4c**[17] were prepared according to known procedures. Spectral data were in accordance with literature.

4.2. General procedure for 2-propynamides synthesis

A solution of propiolic acid (1 equiv) in CH_2Cl_2 (0.4 M) was cooled to −20 °C. Dicyclohexylcarbodiimide (1 equiv) and amine (1 equiv) were added and the reaction was allowed to warm up to room temperature. After one night at room temperature, the solution was filtered through a short pad of silica gel, which was washed with CH_2Cl_2. After concentration in vacuo the resulting oil was purified by FC. Spectral data for 2-propynamides **1a**,[1] **1f**,[18] **1h**[19] were in accordance with literature.

*4.2.1. Propynoic acid (2,2-diethoxy-ethyl)-amide (**1b**).* Reacting propiolic acid (1 mL), DCC (3.34 g) and 2,2-diethoxyethanamine (2.35 mL), according to the general procedure, led to **1b** (2.14 g) isolated in 71% yield after purification (FC, pentane/ether, 80:20). ^1H NMR ($CDCl_3$, 300 MHz): δ 1.21 (t, *J*=7.0, 6H), 2.83 (s, 1H), 3.43 (dd, *J*=5.1 and 6.1, 2H), 3.54 (dq, *J*=9.4 and 7.0, 2H), 3.70 (dq, *J*=9.4 and 7.0, 2H), 4.52 (t, *J*=5.1, 1H), 6.22 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 15.6 ($CH_3\times2$), 42.5 (CH_2), 63.4 ($CH_2\times2$), 73.9 (C≡), 77.6 (≡CH), 100.6 (CH), 152.6 (C=O). HRMS for $C_9H_{15}NO_3$, $[MH]^+$ calcd: 186.1125; found: 186.1122.

*4.2.2. Propynoic acid (2,2-dimethyl-4-phenyl-1,3-dioxinan-5-yl)-amide (**1c**).* Reacting propiolic acid (0.5 mL), DCC (1.67 g) and 2,2-dimethyl-4-phenyl-1,3-dioxan-5-amine (1.68 g), according to the general procedure, led to **1c** (1.83 g) isolated in 87% yield after purification (FC, pentane/ether, 80:20). ^1H NMR ($CDCl_3$, 300 MHz): δ 1.59 (s, 3H), 1.60 (s, 3H), 2.73 (s, 1H), 3.88–3.95 (m, 1H), 4.24–4.32 (m, 2H), 5.22 (d, *J*=1.5, 1H), 6.44 (br d, *J*=8.5, 1H), 7.26–7.42 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.9 (CH_3), 30.1 (CH_3), 47.8 (CH), 64.7 (CH_2), 72.2 (CH), 74.0 (C≡), 77.3 (≡CH), 100.2 (C), 125.7 (=CH), 128.2 (=CH), 128.8 (=CH), 138.1 (=C), 151.9 (C=O). HRMS for $C_{15}H_{17}NO_3$, $[MH]^+$ calcd: 260.1281; found: 260.1281.

*4.2.3. Propynoic acid (3-nitro-phenyl)-amide (**1d**).* Reacting propiolic acid (0.5 mL), DCC (1.67 g) and 3-nitrobenzenamine (1.11 g), according to the general procedure, led to **1d** (710 mg) isolated in 46% yield after purification (FC, pentane/AcOEt, 80:20). ^1H NMR (DMSO-d_6, 300 MHz): δ 4.54 (s, 1H), 7.63 (t, *J*=8.3, 1H), 7.94 (td, *J*=2.4 and 8.3, 1H), 7.96 (td, *J*=2.2 and 8.3, 1H), 8.58 (t, *J*=2.1, 1H), 11.3 (s, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 78.2 (≡CH), 78.5 (C≡), 114.3 (=CH), 119.1 (=CH), 125.9 (=CH), 130.7 (=CH), 139.6 (=C), 148.3 (=C), 150.4 (C=O).

*4.2.4. Propynoic acid diisobutylamide (**1e**).* Reacting propiolic acid (1.8 mL), DCC (6 g) and diisobutylamine (2.7 mL), according to the general procedure, led to **1e** (3.6 g) isolated in 68% yield after purification (FC, pentane/ether, 90:10). ^1H NMR ($CDCl_3$, 300 MHz): δ 0.88 (d, *J*=6.6, 6H), 0.92 (d, *J*=6.6, 6H), 1.91–2.06 (m, 2H), 3.10 (s, 1H), 3.20 (d, *J*=7.7, 2H), 3.38 (d, *J*=7.6, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.3 ($2\times CH_3$), 20.5 ($2\times CH_3$), 26.7 (CH), 27.7 (CH), 52.1 (CH_2), 56.7 (CH_2), 76.9 (≡CH), 79.2 (C≡), 154.3 (C=O). HRMS for $C_{10}H_{17}NO$, $[MH]^+$ calcd: 182.1539; found: 182.1539.

*4.2.5. 1-(2,5-Dihydro-pyrrol-1-yl)-propynone (**1g**).* Reacting propiolic acid (1 mL), DCC (3.34 g) and 2,5-dihydro-1*H*-pyrrole (1.23 mL), according to the general procedure, led to **1g** (1.43 g) isolated in 72% yield after purification (FC, pentane/ether, 60:40). ^1H NMR ($CDCl_3$, 300 MHz): δ 3.08 (s, 1H), 4.22–4.28 (m, 2H), 4.41–4.47 (m, 2H), 5.80–5.88 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 52.8 (CH_2), 55.1 (CH_2), 76.8 (≡CH), 78.0 (C≡), 125.3 (=CH), 125.9 (=CH), 151.8 (C=O).

*4.2.6. But-2-ynoic acid diallylamide (**1i**).* Reacting butynoic acid (1.36 g), DCC (3.34 g) and diallylamine (2 mL), according to the general procedure, led to **1g** (1.42 g) isolated in 54% yield after purification (FC, pentane/ether, 85:15). ^1H NMR ($CDCl_3$, 300 MHz): δ 1.95 (s, 3H), 3.92–4.13 (m, 4H), 5.05–5.21 (m, 4H), 5.61–5.81 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 4.3 (CH_3), 46.5 (CH_2), 51.0 (CH_2),

73.6 (≡C), 89.2 (C≡), 118.1 (=CH_2), 118.2 (=CH_2), 132.6 (=CH), 133.3 (=CH), 154.9 (C=O). HRMS for $C_{10}H_{13}NO$, $[MH]^+$ calcd: 164.1070; found: 164.1066.

4.3. General procedure for hydroiodination reaction

To a solution of substrate (1 equiv) in dichloromethane (or acetonitrile)/ROH (0.2 M, 9:1, v/v), $AlCl_3$ (1.5 equiv) and sodium iodide (2 equiv) were added at room temperature under inert atmosphere. After 18 h, water was added and the reaction was extracted twice with dichloromethane. The organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Flash chromatography on silica gel afforded the corresponding vinyl iodide.

*4.3.1. (Z)-N,N-Diallyl-3-iodo-acrylamide (**2a** and deuterated-**2a**).* Hydroiodination of **1a** (50 mg) in the presence of $AlCl_3$ (67 mg) and NaI (100 mg) in dichloromethane (1.5 mL) and *t*-BuOH (0.17 mL) afforded **2a** (84 mg) isolated in 90% yield after flash chromatography (100% pentane then 100% Et_2O). Spectral data were in accordance with literature.[2] Hydroiodination of **1a** (50 mg) in the presence of $AlCl_3$ (67 mg) and NaI (100 mg) in dichloromethane (1.5 mL) and *t*-BuOD (0.17 mL) afforded **2a** and ***d*-2a** (64 mg, 70%, ratio: 54:46) after treatment with D_2O and flash chromatography (100% pentane then 100% Et_2O). ^1H NMR for ***d*-2a** ($CDCl_3$, 300 MHz): δ 3.85 (br d, 5.1 Hz, 2H), 4.05 (br d, 5.9 Hz, 2H), 5.11–5.28 (m, 4H), 5.68–5.89 (m, 2H), 6.88–6.91 (br m, 1H). ^{13}C NMR (75 MHz): δ 47.4 (CH_2), 49.9 (CH_2), 87.6 (=CHI), 117.9 (=CH_2), 118.4 (=CH_2), 132.9 (=CH), 133.1 (=CH), 134.5 (=CD, t (1:1:1), *J*=25), 167.1 (C=O).

*4.3.2. (Z)-N-(2,2-Diethoxy-ethyl)-3-iodo-acrylamide (**2b**).* Hydroiodination of **1b** (50 mg) in the presence $AlCl_3$ (54 mg) and NaI (82 mg) in dichloromethane (1.2 mL) and *t*-BuOH (0.14 mL) afforded **2b** (74 mg) isolated in 87% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ 1.22 (t, *J*=7.0, 6H), 3.49 (t, *J*=5.7, 2H), 3.57 (dq, *J*=9.4 and 7.0, 2H), 3.72 (dq, *J*=9.4 and 7.0, 2H), 4.57 (t, *J*=5.1, 1H), 6.16 (br s, 1H), 6.87 (d, *J*=8.9, 1H), 7.06 (d, *J*=8.9, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 15.7 (CH_3×2), 42.2 (CH_2), 63.4 (CH_2×2), 88.5 (=CHI), 100.9 (CH), 133.3 (=CH), 164.9 (C=O). HRMS for $C_9H_{16}INO_3$, $[MH]^+$ calcd: 314.0248; found: 314.0248.

*4.3.3. (Z)-N-(2,2-Dimethyl-4-phenyl-1,3-dioxinan-5-yl)-3-iodo-acrylamide (**2c**).* Hydroiodination of **1c** (100 mg) in the presence of $AlCl_3$ (77 mg) and NaI (114 mg) in dichloromethane (1.8 mL) and *t*-BuOH (0.2 mL) afforded **2c** (133 mg) isolated in 89% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ 1.57 (s, 3H), 1.60 (s, 3H), 3.97 (dd, *J*=12.1 and 1.7, 1H), 4.28 (dd, *J*=12.1 and 1.9, 1H), 4.37 (dq, *J*=9.0 and 1.9, 1H), 5.25 (d, *J*=1.9, 1H), 6.50 (br d, *J*=9.0, 1H), 6.68 (d, *J*=9.1, 1H), 6.92 (d, *J*=9.1, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.9 (CH_3), 30.0 (CH_3), 47.1 (CH), 64.7 (CH_2), 72.0 (CH), 88.0 (=CHI), 100.0 (C), 125.6 (=CH), 127.9 (=CH), 128.6 (=CH), 133.2 (=CH), 138.3 (=C), 164.1 (C=O). HRMS for $C_{15}H_{18}INO_3$, $[MH]^+$ calcd: 388.0404; found: 388.0402.

*4.3.4. (Z)-3-Iodo-N-(3-nitro-phenyl)-acrylamide (**2d**).* Hydroiodination of **1d** (50 mg) in the presence of $AlCl_3$ (52 mg) and NaI (79 mg) in acetonitrile (1.2 mL) and *t*-BuOH (0.13 mL) afforded **2d** (70 mg) isolated in 84% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR (DMSO-d_6, 300 MHz): δ 7.20 (d, *J*=8.7, 1H), 7.57 (d, *J*=8.7, 1H), 7.61 (t, *J*=8.3, 1H), 7.92–7.94 (m, 2H), 8.69 (br t, *J*=1.5, 1H), 10.7 (s, 1H). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 94.2 (=CHI), 113.7 (=CH), 118.5 (=CH), 125.5 (=CH), 130.6 (=CH), 132.1 (=CH), 140.3 (=C), 148.3 (=C), 163.3 (C=O). HRMS for $C_9H_7IN_2O_3$, $[MH]^+$ calcd: 318.9574; found: 318.9573.

*4.3.5. (Z)-3-Iodo-N,N-diisobutyl-acrylamide (**2e**).* Hydroiodination of **1e** (50 mg) in the presence of $AlCl_3$ (55 mg) and NaI (83 mg) in dichloromethane (1.3 mL) and EtOH (0.14 mL) afforded **2e** (91 mg) isolated in 100% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ 1.88 (d, *J*=6.6, 6H), 0.95 (d, *J*=6.6, 6H), 1.90 (nonet, *J*=6.8, 1H), 2.10 (nonet, *J*=6.8, 1H), 3.12 (d, *J*=7.6, 2H), 3.24 (d, *J*=7.6, 2H), 6.79 (d, *J*=8.9, 1H), 7.13 (d, *J*=8.9, 1H). ^{13}C NMR (75 MHz): δ 20.4 (2×CH_3), 20.9 (2×CH_3), 26.8 (CH), 27.8 (CH), 52.6 (CH_2), 56.1 (CH_2), 86.1 (=CHI), 135.6 (=CH), 167.7 (C=O). HRMS for $C_{11}H_{20}INO$, $[MH]^+$ calcd: 310.0662; found: 310.0661.

*4.3.6. (Z)-3-Iodo-N,N-diethyl-acrylamide (**2f**).* Hydroiodination of **1f** (50 mg) in the presence of $AlCl_3$ (80 mg) and NaI (120 mg) in dichloromethane (1.8 mL) and EtOH (0.2 mL) afforded **2f** (97 mg) isolated in 96% yield after flash chromatography (100% pentane then 100% Et_2O). Spectral data for **2f** were in accordance with literature.[3]

*4.3.7. (Z)-1-(2,5-Dihydro-pyrrol-1-yl)-3-iodo-propenone (**2g**).* Hydroiodination of **1g** (50 mg) in the presence of $AlCl_3$ (83 mg) and NaI (124 mg) in dichloromethane (1.8 mL) and EtOH (0.2 mL) afforded **2g** (91 mg) isolated in 88% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ 4.22–4.36 (m, 4H), 5.78–5.84 (m, 1H), 5.87–5.94 (m, 1H), 7.03 (d, *J*=8.9, 1H), 7.11 (d, *J*=8.9, 1H). ^{13}C NMR (75 MHz): δ 53.2 (CH_2), 53.7 (CH_2), 88.8 (=CHI), 125.1 (=CH), 126.5 (=CH), 133.1 (=CH), 164.6 (C=O). HRMS for C_7H_8INO, $[MH]^+$ calcd: 249.9723; found: 249.9729.

*4.3.8. (Z)-N-Allyl-3-iodo-acrylamide (**2h**).* Hydroiodination of **1h** (50 mg) in the presence of $AlCl_3$ (92 mg) and NaI (138 mg) in dichloromethane (1.8 mL) and EtOH (0.2 mL) afforded **2h** (87 mg) isolated in 80% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ 3.97 (tt, *J*=5.9 and 1.5, 2H), 5.16 (dq, *J*=10.2 and 1.5, 1H), 5.24 (dq, *J*=17.2 and 1.5, 1H), 5.85 (ddt, *J*=17.2, 10.2 and 5.9, 1H), 6.3 (br s, 1H), 6.91 (d, *J*=8.9, 1H), 7.05 (d, *J*=8.9, 1H). ^{13}C NMR (75 MHz): δ 42.3 (CH_2), 88.6 (=CHI), 117.3 (=CH_2), 133.3 (=CH), 134.0 (=CH), 164.8 (C=O). HRMS for C_6H_8INO, $[MH]^+$ calcd: 237.9723; found: 237.9728.

*4.3.9. (Z)-3-Iodo-but-2-enoic acid diallylamide (**2i**).* Hydroiodination of **1i** (50 mg) in the presence of $AlCl_3$ (65 mg) and NaI (92 mg) in acetonitrile (1.5 mL) and EtOH (0.15 mL) afforded **2i** (62 mg) isolated in 69% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ 2.62 (d, *J*=1.5, 3H), 3.87–3.94 (m, 2H), 4.00–4.08 (m, 2H), 5.11–5.30 (m, 4H), 5.68–5.90 (m, 4H), 6.44 (q, *J*=1.5, 1H). ^{13}C NMR (75 MHz): δ 33.5 (CH_3), 45.9 (CH_2), 48.7 (CH_2), 104.1 (=CI), 116.5 (=CH_2), 116.8 (=CH_2), 129.0 (=CH), 131.6 (=CH), 131.8 (=CH), 166.3 (C=O). HRMS for $C_{10}H_{14}NOI$, $[MH]^+$ calcd: 292.0193; found: 292.0193.

*4.3.10. (Z)-3-Iodo-acrylic acid allyl ester (**5a**).* Hydroiodination of **4a** (50 mg) in the presence of $AlCl_3$ (93 mg) and NaI (139 mg) in dichloromethane (2.1 mL) and EtOH (0.2 mL) afforded **5a** (82 mg) isolated in 75% yield after flash chromatography (100% pentane then 100% Et_2O). Spectral data for **5a** were in accordance with literature.[4b]

*4.3.11. (Z)-3-Iodo-acrylic acid benzyl ester (**5b**).* Hydroiodination of **4b** (50 mg) in the presence of $AlCl_3$ (62 mg) and NaI (94 mg) in dichloromethane (1.4 mL) and EtOH (0.15 mL) afforded **5b** (79 mg) isolated in 88% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ 5.26 (s, 2H), 6.97 (d, *J*=9.1, 1H), 7.35–7.45 (m, 5H), 7.51 (d, *J*=9.1, 1H). ^{13}C NMR (75 MHz): δ 67.0 (CH_2), 96.0 (=CHI), 128.8 (=CH), 128.9 (=CH), 129.0 (=CH),

130.0 (=CH), 135.9 (=C), 164.8 (C=O). HRMS for $C_{10}H_9IO_2$, $[MH]^+$ calcd: 288.9720; found: 288.9725.

*4.3.12. (Z)-3-Iodo-acrylic acid 3-phenyl-propyl ester (**5c**).* Hydroiodination of **4c** (50 mg) in the presence of $AlCl_3$ (53 mg) and NaI (80 mg) in dichloromethane (1.2 mL) and *t*-BuOH (0.10 mL) afforded **5c** (78 mg) isolated in 93% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ 2.05 (tt, J=7.6 and 6.6, 2H), 2.76 (t, J=7.6, 2H), 4.25 (t, J=6.6, 2H), 6.94 (d, J=8.9, 1H), 7.13–7.35 (m, 5H), 7.48 (d, J=8.9, 1H). ^{13}C NMR (75 MHz): δ 30.6 (CH_2), 32.6 (CH_2), 64.6 (CH_2), 95.2 (=CHI), 126.5 (=CH), 128.8 (=CH), 128.9 (=CH), 130.3 (=CH), 141.5 (=C), 165.0 (C=O). HRMS for $C_{12}H_{13}IO_2$, $[MH]^+$ calcd: 317.0033; found: 317.0034.

*4.3.13. (E)-3-Iodo-1-phenyl-propenone (**8**).* Hydroiodination of phenylpropynone **7** (50 mg) in the presene of $AlCl_3$ (77 mg) and NaI (115 mg) in dichloromethane (1.8 mL) and EtOH (0.2 mL) afforded **8** (74 mg) isolated in 75% yield after flash chromatography (100% pentane then 100% Et_2O). Spectral data for **7** were in accordance with literature.[4b]

4.4. General procedure for hydrobromination reaction

To a solution of substrate (1 equiv) in acetonitrile/*t*-BuOH (0.2 M, 9:1, v/v) $AlCl_3$ (1.5 equiv) and sodium bromide (2 equiv) were added at room temperature under inert atmosphere. After 18 h stirring at reflux, water was added and the reaction was extracted twice with ether. The organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Flash chromatography on silica gel afforded the corresponding vinyl bromide.

*4.4.1. (Z)-N,N-Diallyl-3-bromo-acrylamide (**3a**).* Hydrobromination of **1a** (50 mg), in the presence of $AlCl_3$ (67 mg) and NaBr (69 mg) in acetonitrile (1.5 mL) and *t*-BuOH (0.17 mL) afforded **3a** (74 mg) isolated in 96% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ 3.86 (br d, J=5.9, 2H), 4.01 (br d, J=5.9, 2H), 5.06–5.24 (m, 4H), 5.64–5.83 (m, 2H), 6.58 (d, J=8.1, 1H), 6.76 (d, J=8.1, 1H). ^{13}C NMR (75 MHz): δ 47.1 (CH_2), 50.0 (CH_2), 113.5 (=CH), 117.9 (=CH_2), 118.2 (=CH_2), 128.7 (=CH), 132.8 (=CH), 133.1 (=CH), 165.9 (C=O). HRMS for $C_9H_{12}BrNO$, $[MH]^+$ calcd: 230.0175; found: 230.0180.

*4.4.2. (Z)-3-Bromo-N-(3-nitro-phenyl)-acrylamide (**3d**).* Hydrobromination of **1d** (70 mg), in the presence of $AlCl_3$ (73 mg) and NaBr (76 mg) in acetonitrile (1.7 mL) and *t*-BuOH (0.18 mL), afforded **3d** (77 mg) isolated in 77% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ 6.83 (d, J=8.5, 1H), 6.95 (d, J=8.5, 1H), 7.52 (t, J=8.1, 1H), 7.97–8.07 (m, 2H), 8.48 (br t, J=2.1, 1H), 8.53 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 115.2 (=CH), 117.6 (=CH), 119.7 (=CH), 126.2 (=CH), 128.1 (=CH), 130.3 (=CH), 139.0 (=C), 148.9 (=C), 162.6 (C=O). HRMS for $C_9H_7BrN_2O_3$, $[MH]^+$ calcd: 270.9713; found: 270.9717.

*4.4.3. (Z)-3-Bromo-N,N-diethyl-acrylamide (**3f**).* Hydrobromination of **1f** (50 mg), in the presence of $AlCl_3$ (80 mg) and NaBr (82 mg) in acetonitrile (1.8 mL) and *t*-BuOH (0.2 mL), afforded **3f** (72 mg) isolated in 87% yield after flash chromatography (100% pentane then 100% Et_2O). Spectral data for **3f** were in accordance with literature.[3]

*4.4.4. (Z)-3-Bromo-acrylic acid allyl ester (**6a**).* Hydrobromination of **4a** (50 mg), in the presence of $AlCl_3$ (93 mg) and NaBr (96 mg) in acetonitrile (2.1 mL) and *t*-BuOH (0.2 mL), afforded **6a** (50 mg) isolated in 57% yield after flash chromatography (100% pentane then 100% Et_2O). Spectral data for **6a** were in accordance with literature.[4b]

*4.4.5. (Z)-3-Bromo-acrylic acid benzyl ester (**6b**).* Hydrobromination of **4b** (50 mg), in the presence of $AlCl_3$ (62 mg) and NaBr (64 mg) in acetonitrile (1.4 mL) and *t*-BuOH (0.15 mL), afforded **5b** (71 mg) isolated in 94% yield after flash chromatography (100% pentane then 100% Et_2O). ^1H NMR ($CDCl_3$, 300 MHz): δ 5.25 (s, 2H), 6.69 (d, J=8.3, 1H), 7.04 (d, J=8.3, 1H), 7.32–7.47 (m, 5H). ^{13}C NMR (75 MHz): δ 67.0 (CH_2), 122.3 (=CH), 124.6 (=CH), 128.8 (=CH), 128.9 (=CH), 129.0 (=CH), 135.9 (=C), 164.1 (C=O). HRMS for $C_{10}H_9BrO_2$, $[MH]^+$ calcd: 240.9859; found: 240.9859.

*4.4.6. (E)-3-Bromo-1-phenyl-propenone (**9**).* Hydrobromination of phenylpropynone **7** (50 mg), in the presence of $AlCl_3$ (77 mg) and NaBr (78 mg) in acetonitrile (1.8 mL) and *t*-BuOH (0.2 mL), afforded **9** (55 mg) isolated in 69% yield after flash chromatography (100% pentane then 100% Et_2O). Spectral data for **9** were in accordance with literature.[4b]

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