Synthesis of Functionalised Vinyl Triflates from Terminal Alkynes

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The preparation of vinyl trifluoromethanesulfonates (triflates) containing a halide or triflate leaving group by the addition of triflic acid to terminal alkynes is described. The subsequent displacement of the halide or triflate leaving group by benzylamine was investigated.

Vinyl triflates are versatile intermediates for the synthesis of a wide variety of organic molecules. Originally used as precursors for vinyl cations and alkylidene carbenes they have been used most recently for a range of palladium-catalysed coupling reactions.[1]

The two most common routes to vinyl triflates involve trapping of an enol or enolate with an appropriate triflating agent or by the addition of triflic acid to an alkyne.[2] For highly functionalised organic substrates, the trapping of an enol or enolate is usually the preferred method since triflic acid is not compatible with many organic functional groups. As part of our program on the synthesis of lactones and lactams by intramolecular carbonylative couplings of hydroxy[3] and amino vinyl triflates, we have explored the synthesis of vinyl triflates from the addition of triflic acid to functionalised terminal alkynes.

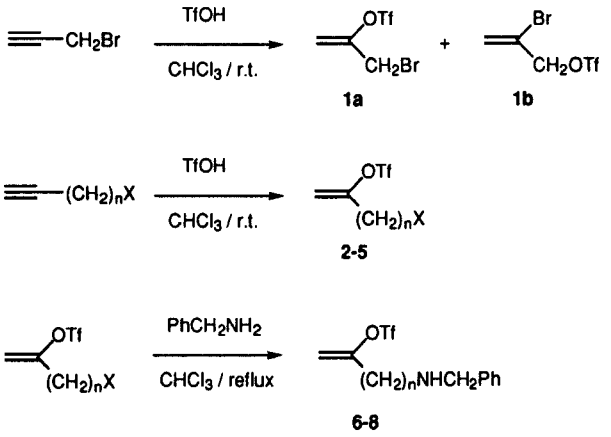
The addition of triflic acid to propargyl bromide gave a mixture of regioisomers **1a** and **1b**. These regioisomers could not be separated by distillation or column chromatogrphy but a simple method for their separation involved the addition of pyridine to the crude reaction mixture which resulted in the displacement of the allylic trifloxy group from **1b** and subsequent formation of a water soluble pyridinium salt. The allyl triflate is formed from an intermediate bromonium ion which reacts with the triflate anion to give **1b** whereas **1a** is presumably formed from the triflate anion reacting with the vinyl cation. The more electronegative chlorine atom should be less able to stabilise a vinyl cation and indeed addition of triflic acid to propargyl chloride gave none of the unwanted isomer and **2** was isolated in 68% yield. However, for the longer chain 5-chloropent-1-yne, the addition of triflic acid gave a mixture of regioisomers, but after the addition of pyridine and an aqueous workup pure **3** could be obtained in 39% yield (Table 1).

In order to avoid the formation of the unwanted regioisomer, triflic acid was added to the corresponding alkynyl triflates. The resulting vinyl triflate **4** was formed in moderate yield and could not be stored at room temperature without decomposition, whereas **5** was formed in good yield and could be stored for short periods at room temperature. For reactions carried out on larger scales it was occasionally necessary to add more triflic acid if ^{1}H-NMR analysis of the mixture indicated that no further conversion of the alkyne was taking place.

Table 1.

Compound	n	X	bp (°C)/Torr or mp (°C)	Yield (%)
1a			100/15	17
2[a]	1	Cl	r.t./0.05	68
3[a]	3	Cl	r.t./0.15	39
4	2	OTf	90–100/0.04	46
5[a]	3	OTf	90–100/0.03	71
6[a]	1		100–102	55
7[a]	2		100–110/0.02	68
8[a]	3		110–120/0.02	67

[a] C, H (and N where appropriate) analysis ±0.25%.



Benzylamine was reacted with compounds **1a–5** in order to investigate the ease with which the leaving group underwent nucleophilic substitution. The allylic bromide of **1a** was readily displaced by benzylamine, however, the chloride of **2** or **3** could not be displaced under a variety of conditions. Changing the solvent, base or temperature gave either starting material or decomposition. In contrast to this lack of reactivity, the alkyl trifloxy group of **4** and **5** could be readily displaced by benzylamine at room temperature or reflux to give the corresponding amino vinyl triflates **7** and **8** in good yield.

1-Bromo-2-[(trifluoromethanesulfonyl)oxy]prop-2-ene (1a):
Triflic acid (2.32 mL, 26.23 mmol) was added dropwise under N_2 over 10 min to a stirred solution of propargyl bromide (2.0 mL, 26.23 mmol) in $CHCl_3$ (30 mL) at 0°C. The ice bath was removed and the dark solution was stirred at r.t. for 60 min, followed by the addition of pyridine (5 mL). The solution was washed with water (50 mL) and dil. hydrochloric acid (2 × 50 mL). The organic phase was dried and the solvent evaporated. The residue was purified by Kugelrohr distillation to yield **1a** as a colorless liquid.

^{1}H NMR: δ = 4.00 (s, 2H, CH_2Br), 5.32 (d, 1H, J_{gem} = 3.9 Hz), 5.36 (d, 1H, J_{gem} = 3.8 Hz).

^{13}C NMR: δ = 27.9, 108.6, 118.5 (J_{CF} = 320.0 Hz), 150.8.

IR (neat): ν = 1660, 1425, 1250, 1210, 1140, 1120, 1060, 965, 890, 780, 715, 670, 610 cm^{-1}.

MS: m/z (%) = 270/268 (M^+, 1), 189 (60), 137/135 (5), 121/119 (15), 93 (29), 69 (25), 59 (47), 39 (100).

HRMS (C_4H_4 $^{79}BrF_3O_3S$): calc., 267.9017; found, 267.9004.

Without the addition of pyridine, varied amounts of regioisomer **1b** were obtained.

^1H NMR: δ = 4.07 (s, 2 H), 5.38 (d, 1 H, J_{gem} = 4.00 Hz), 5.44 (d, 1 H, J_{gem} = 3.90 Hz).

1-Chloro-2-[(trifluoromethanesulfonyl)oxy]prop-2-ene (2):
Prepared as described for **1a** from triflic acid (5.94 mL, 67.1 mmol) and propargyl chloride (2.5 g, 33.6 mmol). The residue was purified by Kugelrohr distillation to yield **2** as a colorless liquid.

^1H NMR: δ = 4.16 (s, 2 H, CH_2Cl), 5.39 (br m, 2 H, CH_2=C).

^{13}C NMR: δ = 42.1, 108.6, 118.4 (q, J_{CF} = 319.87 Hz), 150.6.

IR (neat): ν = 3020, 1665, 1425, 1260, 1225, 1145, 970, 920, 980s, 785, 740, 695, 615 cm^{-1}.

MS: m/z (%) = 226/224 (M^+, 5), 191/189 (5), 125 (52), 69 (100).

1-Chloro-4-[(trifluoromethanesulfonyl)oxy]pent-4-ene (3):
Prepared as described for **1a** from triflic acid (1.55 mL, 17.50 mmol) and 5-chloro-1-pentyne (2.0 g, 19.50 mmol). The residue was purified by Kugelrohr distillation to yield **3** as a clear liquid.

^1H NMR: δ = 2.03 (m, 2 H), 2.56 (t, 2 H, J = 7.21 Hz), 3.60 (t, 2 H, CH_2Cl, J = 6.11 Hz), 5.03 (d, 1 H, J_{gem} = 3.50 Hz), 5.18 (d, 1 H, J_{gem} = 3.59 Hz).

^{13}C NMR: δ = 28.5, 31.0, 43.1, 105.4, 118.4 (q, J_{CF} = 319.9 Hz), 155.0.

IR (neat): ν = 2965, 1670, 1415, 1250, 1215, 1145, 1040, 980, 910, 855, 795, 735, 705, 610 cm^{-1}.

MS: m/z (%) = 254/252 (M^+, 1), 219/217 (1), 121/119 (5), 103 (2), 69 (100).

Without the addition of pyridine the unwanted regioisomer (3:2) was obtained.

^1H NMR: δ = 2.12 (m, 2 H), 2.53 (t, 2 H, J = 7.75 Hz), 4.58 (t, 2 H, CH_2OTf, J = 6.06 Hz), 5.24 (d, 1 H, J_{gem} = 1.19 Hz), 5.27 (d, 1 H, J_{gem} = 1.45 Hz).

3-[(Trifluoromethanesulfonyl)oxy]-3-butenyl Trifluoromethanesulfonate (4):
Triflic acid (0.66 mL, 7.44 mol) was added dropwise over 10 min to a stirred solution of 3-butynyl trifluoromethanesulfonate[4] (0.43 g, 2.13 mmol) in $CHCl_3$ (30 mL) at r. t. The yellow solution was stirred for 60 min and added slowly to water (30 mL). The organic phase was partitioned, dried, and the solvent removed to give a dark-red oil which was purified by Kugelrohr distillation to yield **3** as an r. t. unstable, colorless oil.

^1H NMR: δ = 2.89 (t, 2 H, J = 5.98 Hz), 4.69 (t, 2 H, CH_2OTf, J = 6.04 Hz), 5.20 (d, 1 H, J_{gem} = 3.96 Hz), 5.37 (d, 1 H, J_{gem} = 4.14 Hz).

^{13}C NMR: δ = 34.4, 71.3, 108.7, 118.4 (q, J_{CF} = 318.39 Hz), 118.5 (q, J_{CF} = 319.80 Hz), 149.6.

IR (neat): ν = 2985, 1670, 1420, 1250, 1220, 1145, 1060, 935, 845, 790, 740, 705, 615 cm^{-1}.

MS: m/z (%) = 289 (22), 202 (51), 201 (58), 138 (64), 133 (55), 112 (53), 69 (100).

HRMS ($C_6H_6F_6O_6S_2$, [M−TfOH]$^+$: calc., 201.99115; found 201.99236.

4-[(Trifluoromethanesulfonyl)oxy]-4-pentenyl Trifluoromethanesulfonate (5):
Prepared as described for **4** from triflic acid (0.51 mL, 5.78 mmol) and 4-pentynyl trifluoromethanesulfonate[5] (0.50 g, 2.31 mmol). The resultant dark-brown oil was purified by Kugelrohr distillation to yield **5** as a clear oil.

^1H NMR: δ = 2.11 (m, 2 H), 2.54 (t, 2 H, J = 7.45 Hz), 4.60 (t, 2 H, CH_2OTf, J = 5.99 Hz), 5.07 (d, 1 H, J_{gem} = 3.70 Hz), 5.24 (d, 1 H, J_{gem} = 3.80 Hz).

^{13}C NMR: δ = 25.7, 29.8, 75.1, 106.2, 118.4 (q, J_{CP} = 320.17 Hz), 118.6 (q, J_{CF} = 319.34 Hz).

IR (neat): ν = 3005, 2980, 1670, 1420, 1250, 1210, 1140, 1080, 995, 935, 830, 740, 705 cm^{-1}.

MS: m/z (%) = 280 (7), 216 (35), 189 (28), 151 (19), 126 (30), 86 (100).

***N*-Benzyl-2-[(trifluoromethanesulfonyl)oxy]-2-propenylamine (6):**
A solution of benzylamine (81 µL, 0.74 mmol) in $CHCl_3$ (4 mL) was added dropwise to a mixture of **1a** and Et_3N (0.1 mL, 0.74 mmol) in $CHCl_3$ (4 mL) at 0 °C. The solution was then heated at reflux for 15 h. The mixture was washed with water (10 mL), the organic extracts were dried and the solvent was evaporated. The residue was purified by flash chromatography (hexanes–EtOAc, 9:1) to yield **6** as a pale-yellow solid.

^1H NMR: δ = 3.45 (s, 2 H, C=C–CH_2), 3.81 (s, 2 H, CH_2Ph), 5.21 (d, 1 H, J_{gem} = 3.34 Hz), 5.25 (d, 1 H, J_{gem} = 3.40 Hz).

^{13}C NMR: δ = 52.5, 54.5, 105.6, 119.9 (q, J_{CF} = 322.14 Hz), 127.3, 128.8, 128.9, 129.1, 133.3.

IR (Nujol): ν = 3400, 1670, 1500, 1425, 1325, 1250, 1210, 1180, 1135, 1090, 1010, 935, 800, 745, 700, 605 cm^{-1}.

MS: m/z (%) = 296 ([M + 1]$^+$, 1), 295 (M^+, 1), 294 (2), 238 (3), 218 (1), 204 (4), 162 (20), 91 (100).

***N*-Benzyl-3-[(trifluoromethanesulfonyl)oxy]-3-butenylamine (7):**
Prepared as described for **6** from benzylamine (31 µL, 0.28 mmol), **3** (0.050 g, 0.14 mmol), and Et_3N (40 µL, 0.28 mmol) but stirring at r. t. for 15 h. The residue was purified by flash chromatography (hexanes–EtOAc acetate, 4:1) to yield **7** as a clear yellow oil.

^1H NMR: δ = 2.55 (t, 2 H, J = 6.75 Hz), 2.85 (t, 2 H, J = 6.76 Hz), 3.81 (s, 2 H, CH_2Ph), 5.02 (d, 1 H, J_{gem} = 3.45 Hz), 5.16 (d, 1 H, J_{gem} = 3.62 Hz), 7.26–7.36 (m, 5 H, Ph).

^{13}C NMR: δ = 34.4, 44.9, 53.5, 105.4, 118.4 (q, J_{CF} = 319.95 Hz), 127.0, 128.0, 128.3, 139.7, 154.6.

IR (neat): ν = 3305, 3030, 1670, 1500, 1455, 1420, 1250, 1210, 1140, 1030, 935, 845, 740 cm^{-1}.

MS: m/z (%) = 310 ([M + 1]$^+$, 12), 235 (4), 121 (65), 91 (100).

***N*-Benzyl-4-[(trifluoromethanesulfonyl)oxy]-4-pentenylamine (8):**
Prepared as described for **7**. Flash chromatography (hexanes–EtOAc, 7:3) gave **8** as a clear oil that discolored quickly during storage.

^1H NMR: δ = 1.75 (m, 2 H, J = 7.06 Hz), 2.43 (t, 2 H, J = 7.51 Hz), 2.9 (t, 2 H, J = 6.97 Hz), 3.79 (s, 2 H, CH_2Ph), 4.94 (d, 1 H, J_{gem} = 3.49 Hz), 5.09 (d, 1 H, J_{gem} = 3.55 Hz), 7.26–7.36 (m, 5 H, Ph).

^{13}C NMR: δ = 26.4, 31.6, 47.8, 104.3, 118.4 (q, J_{CF} = 319.87 Hz), 127.0, 127.6, 128.2, 140.1, 156.5.

IR (neat): ν = 3330, 3025, 2930, 1670, 1605, 1495, 1455, 1420, 1250, 1220, 1140, 1030, 945, 790, 735, 700 cm^{-1}.

MS: m/z (%) = 324 ([M + 1]$^+$, 1), 322 (1), 190 (15), 120 (20), 91 (100).

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