SHORT PAPER

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Ene-type chlorination of functionalised olefins using sulfuryl chloride in the absence of a base†

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Treatment of functionalised olefins with sulfuryl chloride in cyclohexane without the use of a base resulted in the formation of the rearranged allylic chlorides in moderate yields.

Keywords: ene-type chlorination, olefins, sulfuryl chloride

Ene-type chlorination of olefins provides the rearranged allylic chlorides as valuable intermediates in organic synthesis. A number of reagents have been reported for this chlorination, including *N*-chlorosuccinimide with arylselenenyl chlorides or aryl diselenides as catalysts,[1] chlorine oxide (Cl_2O),[2] *t*-butyl hypochlorite with[3a,3b] or without[4a,4b] the use of silica gel, hypochlorous acid,[5] calcium hypochlorite and acetic acid,[6] sulfuryl chloride and sodium carbonate,[7] and a Vilsmeier-type reagent in the presence of hydrogen peroxide.[8] Electrochemical methods using sodium chloride as halogen source were also developed for the ene-type chlorination of a variety of isoprenoids.[9]

In the course of our synthesis of the pentahalogenated monoterpene halomon[10] and its analogues as potential antitumor therapeutic agents, we required the preparation of the intermediate allylic chloride **1b** from the corresponding functionalised olefin **1a** through an ene-type chlorination using sulfuryl chloride. Initially, treatment of **1a** with one equivalent of sulfuryl chloride in CH_2Cl_2 at 0°C gave the desired allylic chloride **1b** in 60% yield together with a small amount of the pentahalogenated ester **1c**[11] (8% yield). Sodium carbonate or other bases were not used because of the presence of base-sensitive groups such as halogens and ester in **1a**. Formation of the byproduct **1c** presumably resulted from further chlorination of the desired product **1b** with sulfuryl chloride. We observed that these two compounds were not readily separated by column chromatography on silica gel. Moreover, the formation of the byproduct **1c** could not be avoided even using only 0.5 equivalent of sulfuryl chloride in CH_2Cl_2.

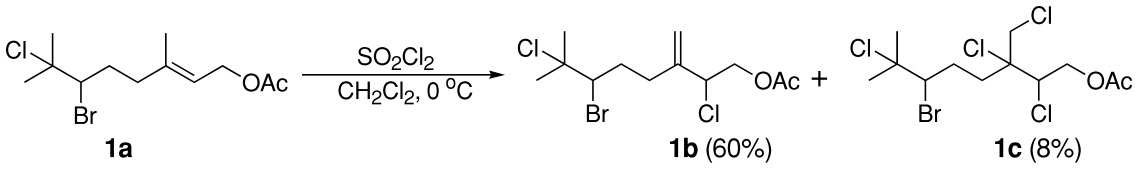
We next tested a nonpolar solvent cyclohexane in the hope of decreasing the reactivity of sulfuryl chloride to some extent and inhibiting further chlorination of the product **1b**. As expected, treatment of **1a** with sulfuryl chloride (1 equiv) in cyclohexane at 0°C indeed gave the allylic chloride **1b** as a colourless oil in better yield (80%) without the byproduct **1c** being detected. Similarly, reaction of other olefins (**2a**–**6a**) with sulfuryl chloride in cyclohexane afforded the respective products **2b**–**6b** in moderate yields. The results are summarised in Table 1. All products exhibited ^1H and ^{13}C NMR spectral data in accord with the assigned structures. In the case of geranyl acetate, geraniol, and geranyl bromide (entries 4–6), selective ene-type chlorination at the more reactive C_6-C_7 double bond was achieved by using one equivalent of sulfuryl chloride. The allylic hydroxyl group in **5a** was also simultaneously replaced by chlorine, probably owing to the leaving tendency of the hydroxyl group being favoured by the acidity of the reaction mixture (entry 5). In contrast, this hydroxyl group was reported to remain intact when the reaction was carried out in the presence of sodium carbonate (4.2 equiv).[7]

Table 1 ene-type chlorination of functionalised olefins with SO_2Cl_2 (1 eq) in cyclohexane at 0°C

Entry	Substrate	Product	Yield/%[a]
1	**1a**	**1b**	80
2	**2a**	**2b**	68
3	**3a**	**3b**	54
4	**4a**	**4b**	39
5	**5a**	**5b**	65
6	**6a**	**6b**	45

[a]The yield of isolated product.

In summary, we have demonstrated that ene-type chlorination of functionalised olefins was accomplished by treatment with sulfuryl chloride in cyclohexane without the use of a base. This approach is useful especially for the preparation of allylic chlorides from olefins bearing base-sensitive groups.



1a **1b** (60%) **1c** (8%)

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Experimental

Geranyl acetate (**4a**), geraniol (**5a**), and geranyl bromide (**6a**) were obtained from Aldrich. 7-Chloro-3,7-dimethyl-2-octenyl acetate (**2a**) was prepared in 66% yield from geranyl acetate according to the procedure reported by Julia and Roy.[12]

6-Bromo-7-chloro-3,7-dimethyl-2-octenyl acetate (**1a**) was prepared in 91% yield by treatment of geranyl acetate with 4.4 M bromine chloride (BrCl) solution in CH_2Cl_2 at –78ºC. Data for **1a**: ^{1}H NMR ($CDCl_3$) δ 5.43–5.38 (m, 1 H), 4.57 (d, *J* = 7.1 Hz, 2 H), 3.97–3.94 (m, 1 H), 2.45–2.34 (m, 2 H), 2.22–2.10 (m, 2 H), 2.03 (s, 3 H), 1.76 (s, 3 H), 1.70 (s, 3 H), 1.64 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 171.6, 140.7, 120.4, 72.5, 65.3, 61.7, 38.2, 33.8, 32.7, 27.7, 21.6, 16.9; IR (neat) 2983, 2935, 1741, 1370, 1024 cm^{-1}; Anal. Calcd for $C_{12}H_{20}BrClO_2$: C, 46.25; H, 6.47; Found: C, 46.44; H, 6.47.

6-Bromo-3,7-dimethyl-2-octenyl acetate (**3a**) was prepared by selective epoxidation of geranyl acetate with *m*-chloroperoxybenzoic acid, followed by epoxide ring opening with sodium cyanoborohydride in the presence of boron trifluoride diethyl etherate and reaction with triphenylphosphine and carbon tetrabromide. Data for **3a**: ^{1}H NMR ($CDCl_3$) δ 5.37 (t, *J* = 6.1 Hz, 1 H), 4.56 (d, *J* = 7.1 Hz, 2 H), 3.93 (dt, *J* = 9.1, 4.0 Hz, 1 H), 2.31–2.26 (m, 1 H), 2.17-2.07 (m, 1 H), 2.03 (s, 3 H), 1.96–1.78 (m, 3 H), 1.69 (s, 3 H), 1.07 (d, *J* = 6.7 Hz, 3 H), 0.96 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 177.6, 141.3, 119.8, 66.5, 61.7, 38.3, 35.1, 34.9, 21.5, 21.4, 18.1, 17.0.*

General procedure for the ene-type chlorination of functionalised olefins: To a stirred solution of olefins (1 mmol) in cyclohexane (10 ml) at 0ºC was added sulfuryl chloride (1 mmol) dropwise. The mixture was stirred at 0–5ºC. The progress of the reaction was monitored by TLC (hexanes-ethyl acetate, 15:1) and GC analyses. Upon completion, the mixture was diluted with diethyl ether (25 ml), and the organic layer was washed with cold water and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexanes-ethyl acetate, 15:1) to afford the products shown in Table 1.

1b: ^{1}H NMR ($CDCl_3$) δ 5.28 (d, *J* = 7.0 Hz, 1 H), 5.18 (s, 1 H), 4.61-4.57 (m, 1 H), 4.35 (d, *J* = 9.1 Hz, 1 H), 4.33 (d, *J* = 9.8 Hz, 1 H), 4.05 (t, *J* = 11.0 Hz, 1 H), 2.70–2.42 (m, 3 H), 2.38–2.18 (m, 1 H), 2.08 (s, 3 H), 1.80 (s, 3 H), 1.69 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 170.8, 144.1, 116.3, 72.7, 72.3, 66.5, 65.5, 33.6, 33.1, 29.8, 27.7, 21.8; IR (neat) 2983, 2936, 1746, 1371, 1228, 1011 cm^{-1}; Anal. Calcd for $C_{12}H_{19}BrCl_2O_2$: C, 41.65; H, 5.53; Found: C, 41.78; H, 5.50.

2b: ^{1}H NMR ($CDCl_3$) δ 5.21 (s, 1 H), 5.04 (s, 1 H), 4.53 (t, *J* = 7.1 Hz, 1 H), 4.29–4.22 (m, 2 H), 2.13 (t, *J* = 6.0 Hz, 2 H), 2.04 (s, 3 H), 1.60–1.56 (m, 4 H), 1.50 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 171.2, 144.7, 116.1, 64.4, 61.8, 35.4, 35.2, 21.5, 21.4, 18.7, 16.8; Anal. Calcd for $C_{12}H_{20}Cl_2O_2$: C, 53.94; H, 7.54; Cl, 26.54; Found: C, 54.14; H, 7.60; Cl, 26.68.

3b: ^{1}H NMR ($CDCl_3$) δ 5.21 (s, 1 H), 5.04 (s, 1 H), 4.54 (t, *J* = 7.1 Hz, 1 H), 4.28–4.22 (m, 2 H), 3.89 (m, 1 H), 2.60–2.56 (m, 1 H), 2.04 (s, 3 H), 2.08–1.69 (m, 4 H), 1.09 (d, *J* = 6.6 Hz, 3 H), 0.96 (d, *J* = 6.4 Hz,, 3 H); ^{13}C NMR ($CDCl_3$) δ 170.8, 144.8, 116.6, 66.4, 66.2, 61.7, 35.4, 35.2, 31.0, 21.5, 21.4, 18.7; IR (neat) 2965, 1746, 1654, 1446, 1369, 1232, 1041, 912 cm^{-1}.*

4b:[2,3a,5,7,9a] ^{1}H NMR ($CDCl_3$) δ 5.31 (t, 1 H), 5.02 (s, 1 H), 4.89 (s, 1 H), 4.65–4.60 (m, 2 H), 4.12 (t, *J* = 7.1 Hz, 1 H), 2.01 (s, 3 H), 1.98–1.91 (m, 2 H), 1.82 (s, 3 H), 1.78 (s, 3 H), 1.75–1.69 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 171.0, 147.4, 139.1, 120.2, 109.5, 63.2, 62.7, 37.2, 35.2, 18.5, 17.8, 16.7.

5b: ^{1}H NMR ($CDCl_3$) δ 5.41 (t, 1 H), 5.01 (s, 1 H), 4.87 (s, 1 H), 4.14 (t, *J* = 7.1 Hz, 1 H), 4.10 (d, *J* = 7.2 Hz, 2 H), 2.01–1.97 (m, 2 H), 1.83 (s, 3 H), 1.76 (s, 3 H), 1.79–1.74 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 147.2, 141.2, 119.2, 108.8, 62.7, 41.2, 36.7, 30.8, 18.4, 16.9. Anal. Calcd for $C_{10}H_{16}Cl_2$: C, 57.98; H, 7.79; Cl, 34.23; Found: C, 58.09; H, 7.75; Cl, 34.16.

6b: ^{1}H NMR ($CDCl_3$) δ 5.42 (t, 1 H), 5.02 (s, 1 H), 4.89 (s, 1 H), 4.15 (t, *J* = 7.2 Hz, 1 H), 3.95 (d, *J* = 7.2 Hz, 2 H), 1.99–1.95 (m, 2 H), 1.80 (s, 3 H), 1.79 (s, 3 H), 1.75-1.71 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 147.3, 142.8, 118.2, 107.8, 62.6, 39.2, 38.7, 30.2, 18.5, 16.7.*

*In the absence of anlaytical data the structures and purity of **3a**, **3b** and **6b** must be regarded formally as tentative but the spectroscopic data are consistent with the structural formulae.

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11 Data for **1c**: ^{1}H NMR ($CDCl_3$) δ 4.81–4.72 (m, 2 H), 4.58–4.51 (m, 1 H), 4.34–4.22 (m, 2 H), 4.06–3.96 (m, 1 H), 2.58–1.86 (m, 4 H), 2.08 (s, 3 H), 1.76 (s, 3 H), 1.65 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 170.8, 72.5, 72.3, 66.0, 65.1, 61.7, 43.7, 33.8, 30.6, 27.7, 26.7, 21.3; Anal. Calcd for $C_{12}H_{19}BrCl_4O_2$: C, 34.56; H, 4.59; Found: C, 34.82, H, 4.55.
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