SHORT PAPER

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A one-pot synthesis of β-chloro acetates/benzoates from epoxides

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A variety of epoxides were converted into β-chloroacetates and benzoates by using TMSCl and the corresponding acid anhydride in the presence of a catalytic amount of $Cu(OTf)_2$.

Keywords: β-chloroacetates and benzoates, epoxides

Epoxides are versatile intermediates in organic synthesis and a variety of methods is known for their cleavage.[1] Among the various transformations, conversion of epoxides into chlorohydrin is very common. The hydroxyl group of the chlorohydrin can be converted into acetate or benzoate to provide β-chloroacetates or β-chlorobenzoates. It is useful to synthesise these compounds in one step directly from epoxides and this has been done in several ways. Epoxides have been cleaved into β-chloroesters using $TiCl_4$ and imidazole in EtOAc.[2a] Lanthanoid complexes have also been used to catalyse the opening of epoxides with acyl chlorides into chloroacetates.[2b] Recently, it has been reported that epoxides are cleaved with concomitant acylation using a reagent system composed of organomercury, aluminum metal, and an acyl halide.[2c] In this communication we report that epoxides can be converted into β-chloroacetates and benzoates in one pot by using trimethylsilylchloride (TMSCl) and the corresponding acid anhydride in the presence of a catalytic amount of $Cu(OTf)_2$.[3] We also used this method to synthesise an intermediate for the synthesis of carbovir, an anti-HIV compound.

At the outset, cyclohexene oxide was chosen as a model substrate for the study of the above reaction. Reaction of cyclohexene oxide with acetyl chloride in the presence of 5 mole% of $Cu(OTf)_2$ at room temperature gave chloroacetate in poor yield (34%). Similarly, chlorobenzoate was obtained by the use of benzoyl chloride but again in poor yield (25%). There was no reaction when the acid chloride was replaced by an acid anhydride under the above conditions. In order to study the reaction further, cyclohexene oxide was treated with TMSCl in benzene at room temperature and it was observed that the epoxide opened into the chloro trimethylsilylether in 29% yield. With the hope that the above reaction could be used for preparation of allylic alcohols like Noyori's method,[4] the reaction of cyclohexene oxide with TMSCl was run in the presence of 1 equivalent of DBU and 5 mol% of $Cu(OTf)_2$. Under these conditions, instead of allylic alcohol the same chloro trimethylsilylether was obtained but in high yield (88%) and in much shorter time. In the absence of DBU, the TMS ether was cleaved during the reaction period and a 90% yield of chlorohydrin was obtained. So, it occurred to us that if acetic anhydride was used in the reaction, chloroacetate should be formed in one-pot. Indeed, this was the case. Cyclohexene oxide was treated with TMSCl (1 mmol) and acetic anhydride (2 mmol) in the presence of $Cu(OTf)_2$ (5 mmol %) in benzene (6 ml) at room temperature for 6 h. Usual work-up gave the expected chloroacetate in 89% yield (Table 1, entry 1). Similarly, the chlorobenzoate was obtained when acetic anhydride was replaced by benzoic anhydride (Table 1, entry 2). The reaction took place similarly in other solvents such as toluene, CH_2Cl_2, and ether. Other Lewis acids such as $Sn(OTf)_2$ and $CuCl_2$ gave poor yields (30–45%) of the chloroacetate. The reaction failed when $BF_3.OEt_2$ was used in the above experiment. The epoxide cleavage reaction was extended to a variety of cyclic and acyclic substrates and the results are summarised in Table 1. The *t*-butyldimethylsilyl (TBDMS) group gets converted into acetate during the reaction conditions (Table 1, entry 10).[5] Thus, the compound **9**, which is an intermediate[6] in the synthesis of carbovir, was synthesised in high yield (92 %) in one step.

In conclusion we have developed a one-pot method for the conversion of epoxides into β-chloroacetates and benzoates.

General procedure for conversion of epoxides into chloroacetates/chlorobenzoates: An epoxide (1 mmol) was treated with TMSCl (1 mmol) and acid anhydride (2 mmol) in the presence of $Cu(OTf)_2$ (5 mol %) in dry benzene (6 ml) at room temperature for 6 h. The reaction mixture was diluted with ether and washed with water and brine. The organic layer was dried and concentrated to a crude product, which was purified by column chromatography over silica gel.

Trans-1-acetoxy-2-chlorocyclohexane **(1a)**[2b,7]**:** Yield 89 %; Colourless liquid; R_f: 0.8 (10% EtOAc in petroleum ether); IR (film):1750,1240 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.37 (m, 3H), 1.73 (m, 3H), 2.09 (s, 3H), 2.10 (m, 1H), 2.25 (m, 1H), 3.84 (ddd, *J* = 10.5, 9.0, 4.4 Hz, 1H), 4.81 (ddd, *J* = 9.5, 9.5, 4.6 Hz, 1H).

Trans-1-benzoyloxy-2-chlorocyclohexane **(1b)**[2b]**:** Yield 88 %; solid, mp 40 °C (No lit[2b] value); R_f: 0.6 (5% EtOAc in petroleum ether); IR (KBr):1800, 1300 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.1–1.22 (m, 3H), 1.59 (m, 3H), 2.08 (m, 2H), 3.86 (m, 1H), 4.92 (ddd, *J* = 8.8, 8.8, 4.6 Hz, 1H), 7.27 (m, 2H), 7.38 (m, 1H), 7.94 (d, *J* = 7 Hz, 2H).

Trans-1-acetoxy-2-chlorocyclopentane **(2a)**[2a]**:** Yield 90 %; Colourless liquid; R_f: 0.7 (10% EtOAc in petroleum ether); IR (film): 1760, 1250 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.62 (m, 1H), 1.82 (m, 1H), 1.92 (m, 2H), 2.04 (s, 3H), 2.25 (m, 2H), 4.18 (m, 1H), 5.13 (m, 1H); MS (CI, *m/z*):162 (M^+).

Trans-1-benzoyloxy-2-chlorocyclopentane **(2b):** Yield 85 %; Colourless liquid; R_f: 0.7 (5 % EtOAc in petroleum ether); IR (film): 1780 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.65–1.95 (m, 4H), 2.15–2.35 (m, 2H), 4.25 (m, 1H), 5.31 (m, 1H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.92 (d, *J* = 7.1 Hz, 2H). Anal. calcd for $C_{12}H_{13}O_2Cl$: C, 64.16; H, 5.79; Cl, 15.79; Found: C, 63.78; H, 5.67; Cl, 15.82.

Trans-1-acetoxy-2-chlorocyclo-oct-5-ene **(3a):** Yield 82 %; Colourless liquid; R_f: 0.4 (5% EtOAc in petroleum ether); IR (film): 1740, 1235 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.8 (m, 1H), 2.02 (m, 1H), 2.07 (s, 3H), 2.21 (m, 3H), 2.43 (m, 2H), 2.64 (m, 1H), 4.32 (ddd, *J* = 9.5, 3.9 Hz, 1H), 5.22 (m, 1H), 5.6 (m, 2H). Anal. calcd for $C_{10}H_{15}O_2Cl$: C, 59.27; H, 7.41, Cl, 17.51; Found: C, 59.62; H, 7.46; Cl, 17.58.

Trans-1-benzoyloxy-2-chlorocyclo-oct-5-ene **(3b):** Yield 70 %; Colourless liquid; R_f: 0.8 (5% EtOAc in petroleum ether); IR (film): 1730, 1260 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.8–2.8 (m, 8H), 4.51 (ddd, *J* = 9.5, 3.9 Hz, 1H), 5.46 (ddd, *J* = 9.5, 6.6, 3.4 Hz, 1H), 5.66 (m, 2H), 7.43 (m, 2H), 7.53 (m, 1H), 8.06 (d, *J* = 8 Hz, 2H); MS (FAB, *m/z*): 265 (M^++1). Anal. calcd for $C_{15}H_{17}O_2Cl$: C, 68.07; H, 6.43; Cl, 13.41; Found: C, 68.70; H, 6.28; Cl, 13.52.

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

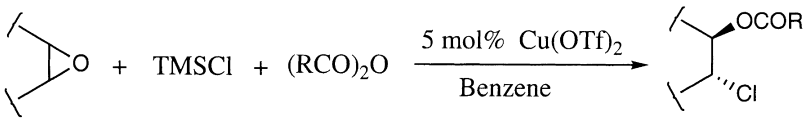
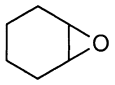
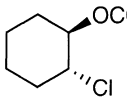
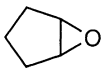
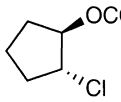
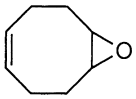
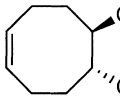
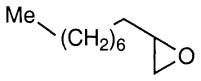
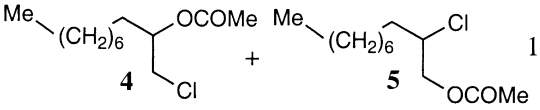
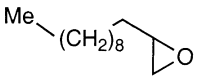
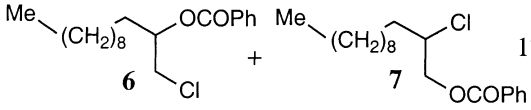
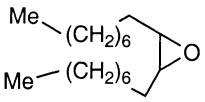
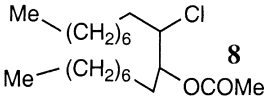
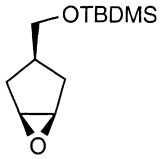
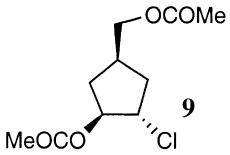
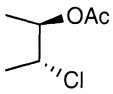
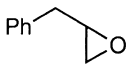
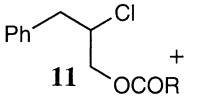
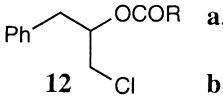


Table 1 An efficient one pot method for the conversion of expoxides in to β-chloroacetates and benzoates[a]

Sample no.	Epoxides	Chloro acetates/benzoates	Time/h	Yield/%
1.		 **1a**; R = Me	06	89
2.		**1b**; R = Ph	12	88
3.		 **2a**; R = Me	08	90
4.		**2b**; R = Ph	12	85
5.		 **3a**; R = Me	10	82
6.		**3b**; R = Ph	16	70
7.		 **4** + **5**	10	71[b]
8.		 **6** + **7**	17	71[c]
9.		 **8**	10	73
10.		 **9**	06	92
11.		 **10**	06	89
12.		 **11** +  **12** **a**, R = Me	16	67[d]
13.		**b**, R = Ph	22	61[e]

[a]The *trans* stereochemistry in the products was confirmed by coupling constant data. [b]Ratio of **4** and **5** is 56:44. [c]Ratio of **6** and **7** is 62.38. [d]Ratio of **11a** and **12a** is 71:29. [e]Ratio of **11b** and **12b** is 82:18.

1-Acetoxy-2-chlorodecane (**4**) and *2-acetoxy-1-chlorodecane* (**5**)[8]**:** Yield 71%; Colourless liquid; IR(film):1760 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, *J* = 7.3 Hz, 3H), 1.26 (bs, 12H), 1.63–1.83 (bm, 2H), 2.08 (s, 1.32H), 2.1 (s, 1.68H), 3.6 (dABq, *J* = 11.7, 5.7 Hz, –C<u>H</u>$_2$–Cl, 56 %), 4.04 (m, –C<u>H</u>–Cl, 44 %), 4.21 (m, –C<u>H</u>$_2$–OAc, 44 %), 5.02 (m, –CH–OAc, 56 %).

1-Benzoyloxy-2-chloro-dodecane (**6**) and *2-benzoyloxy-1-chloro dodecane* (**7**): Yield 71%; Colourless liquid; R_f: 0.7 (2% EtOAc in petroleum ether); IR (film): 1740, 1250 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.87 (t, *J* = 7.3 Hz, 3H), 1.25 (bs, 16H), 1.83 (m, 2H), 3.72 (dABq, *J* = 4.6 Hz, 11.7 Hz, –C<u>H</u>$_2$Cl, 38%), 4.18 (m, –C<u>H</u>Cl, 62%), 4.46 (dABq, *J* = 5.3 Hz, 11.9 Hz, –C<u>H</u>$_2$OBz, 62%), 5.29 (m, –C<u>H</u>OBz, 38%), 7.44 (m, 2H), 7.56 (m, 1H), 8.06 (d, *J* = 8 Hz, 1H); MS (FAB, *m/z*): 325 (M^++1), 289. Anal. calcd for $C_{19}H_{29}O_2Cl$: C, 70.27; H, 8.94; Cl, 10.93; Found: C, 70.62; H, 9.02; Cl, 10.98.

9-Acetoxy-10-chloroctadecane (**8**)**:** Yield 73%; Colourless liquid; R_f: 0.5 (5% EtOAc in petroleum ether); IR (film): 1735, 1240 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, *J* = 6.8 Hz, 6H), 1.27 (bs, 24H), 1.54–1.75 (m, 3H), 2.09 (s, 3H), 2.39 (t, *J* = 7.6 Hz, 1H), 3.93 (m, 1H), 5.05 (m, 1H). Anal. calcd for $C_{20}H_{39}O_2Cl$: C, 69.27; H, 11.26; Cl, 10.23; Found: C, 69.62; H, 11.36; Cl, 10.30.

1-Acetoxy-4-(acetoxymethyl)-2-chlorocyclopentane (**9**)[6]**:** Yield 92%; Colourless liquid; R_f: 0.4 (10% EtOAc in petroleum ether); IR (film): 1710, 1260 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.7 (m, 1H), 1.83 (m, 1H), 1.95 (m, 1H), 2.01 (s, 6H), 2.45 (m, 2H), 4.0 (m, 2H), 4.11 (m, 1H), 5.06 (m, 1H).

2-Acetoxy-3-chlorobutane **(10):** Yield 89%; Colourless liquid; R_f: 0.7 (5% EtOAc in petroleum ether); IR (film): 1740, 1240 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.3 (d, *J* = 6.3 Hz, 3H), 1.47 (d, *J* = 6.8 Hz, 3H), 2.08 (s, 3H), 4.03 (m, 1H), 5.03 (m, 1H). Anal. calcd for $C_6H_{11}O_2Cl$: C, 47.86; H, 7.31; Cl, 23.56; Found: C, 47.76; H, 7.18; Cl, 23.70.

1-Acetoxy-2-chloro-3-phenylpropane **(11a)** and *2-acetoxy-1-chloro-3-phenylpropane* **(12a):** Yield 67 %; Colourless liquid; R_f: 0.8 (5% EtOAc in petroleum ether); IR (film): 1730, 1240 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.03 (s, 2.11H), 2.07 (s, 0.89H), 2.97 (d, *J* = 6.8 Hz, 2H), 3.01 (dABq, *J* = 5.6 Hz, 14 Hz, -C<u>H</u>$_2$Cl, 29.6%), 3.56 (dABq, *J* = 4.8 Hz, 11.8 Hz, -C<u>H</u>$_2$OAc, 70.4%), 4.23 (m, -C<u>H</u>Cl, 70.4%), 5.22 (m, -C<u>H</u>OAc, 29.6%), 7.25 (m, 5H, aromatics); MS(FAB, *m*/*z*): 213 (M^++1), 155. Anal. calcd for $C_{11}H_{13}O_2Cl$: C, 62.13; H, 6.12; Cl, 16.69; Found: C, 61.98; H, 6.20; Cl, 16.80.

1-Benzoyloxy-2-chloro-3-phenylpropane **(11b)** and *2-benzoyloxy-1-chloro-3-phenylpropane* **(12b):** Yield 61 %; Colourless liquid; R_f: 0.7 (5% EtOAc in petroleum ether); IR (film):1740, 1250 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.12 (dd, *J* = 2.3 Hz, 6.8 Hz, 2H), 3.19 (m, –C<u>H</u>$_2$Cl, 18%), 3.66 (dABq, *J* = 4.6 Hz, 11.8 Hz, –C<u>H</u>$_2$OBz, 82%), 4.46 (m, –C<u>H</u>Cl, 82%), 5.46 (m, –C<u>H</u>OBz, 18%), 7.28 (m, 5H, aromatics), 7.44 (m, 2H), 7.55 (m, 1H), 8.05 (m, 2H); MS (FAB, *m*/*z*): 275 (M^++1), 153. Anal. calcd for $C_{16}H_{15}O_2Cl$: C, 69.96; H, 5.47; Cl, 12.92; Found: C, 69.83; H, 5.29; Cl, 12.98.

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