# The Conversion of Acetals to Esters by *m*-CPBA Oxidation

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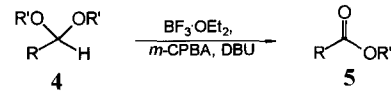
Over the last thirty years, a number of methods for the conversion of aldehydes to esters have appeared in the literature.[1] Baeyer-Villiger oxidation of ketones and aldehydes using peracid is frequently the method of choice due to its easy manipulation and high productivity.[2] The reaction of acyclic acetal derived from a ketone with peracid, however, is known to be sluggish and to provide the orthocarbonate as the result of dual Baeyer-Villiger oxidation.[3] Several methods of direct oxidation of acetal to esters have been reported. Peracetic acid,[4] chromium trioxide,[5] ozone,[6] *tert*-butylhydroperoxide,[7] PDC/*t*-BuOOH,[8] NBS,[9] peroxymonosulfuric acid,[10] and hydrogen peroxide[11] have been used as the oxidizing agent. Since there are a number of methods for the preparation of acetals from the corresponding aldehydes,[12] a method that directly oxidized them to esters would be of great value. Thus, we focused our study on the direct oxidation of acetals to esters using *m*-chloroperoxybenzoic acid (*m*-CPBA).

Recently, we reported a simple one-pot procedure for the conversion of aldehydes to methyl esters **3** *via* dimethyl acetal **1** formation from aldehydes and subsequent oxidation by *m*-CPBA with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).[13] We presumed that the reaction follows the intramolecular hydrogen abstraction through the peroxy intermediate **2** (Scheme 1).

We extend this idea to other alkyl acetals which can be converted to the corresponding alkyl esters. Alkyl acetals were easily prepared by a number of methods from the corresponding aldehydes.[12] The results of the oxidation of alkyl acetals to alkyl esters are summarized in Table 1. As we obtained in the conversion of aldehydes to methyl esters,[13] all of alkyl acetals provided the alkyl esters in excellent yields. From the results of the reaction (Table 1), it suggested that any aldehydes can be converted to the corresponding alkyl esters which can serve as valuable intermediates in synthesis. Especially, the results of entries 10, 11, and 12 imply that this methodology can be applied to the desymmetrization of prochiral diols and diamines.

In conclusion, we have demonstrated an efficient conversion of various alkyl acetals to their corresponding alkyl esters in high yields through the oxidation using *m*-CPBA and DBU. We are currently investigating one-pot procedure of the same reaction from aldehydes and the desymmetrization of *meso*-diol with a chiral Lewis acid or a chiral aldehyde using the same methodology.

**Table 1**. The conversion of alkyl acetals to the corresponding esters by *m*-CPBA with DBU

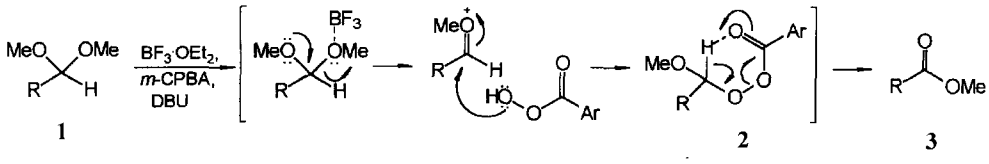



| Entry | Alkyl Acetal | Product | Yield (%)[a] |
|---|---|---|---|
| 1 | $C_6H_5CH(OEt)_2$ (**4a**) | $C_6H_5COOEt$ (**5a**) | 96[b] |
| 2 | *p*-Me-$C_6H_5CH(OEt)_2$ (**4b**) | *p*-Me-$C_6H_5COOEt$ (**5b**) | 97[b] |
| 3 | $C_6H_{13}CH(OEt)_2$ (**4c**) | $C_6H_{13}COOEt$ (**5c**) | 92[b] |
| 4 | $C_6H_5CH(OPr^i)_2$ (**4d**) | $C_6H_5COOPr^i$ (**5d**) | 91 |
| 5 | *p*-MeO-$C_6H_5CH(OPr^i)_2$ (**4e**) | *p*-MeO-$C_6H_5COOPr^i$ (**5e**) | 90 |
| 6 | $C_3H_7CH(OPr^i)_2$ (**4f**) | $C_3H_7COOPr^i$ (**5f**) | 92 |
| 7 | *o*-HO-$C_6H_5CH(OBn)_2$ (**4g**) | *o*-HO-$C_6H_5COOBn$ (**5g**) | 90 |
| 8 | $MeCH(OBn)_2$ (**4h**) | MeCOOBn (**5h**) | 89 |
| 9 | $EtCH(OBn)_2$ (**4i**) | EtCOOBn (**5i**) | 91 |
| 10 | $C_6H_5CH(OCH_2)_2$ (**4j**) | $C_6H_5COOCH_2CH_2OH$ (**5j**) | 73[b] |
| 11 | $C_6H_5CH(OCHMe)_2$ (**4k**) | $C_6H_5COOCHMeCHMeOH$ (**5k**) | 75[c] |
| 12 | $C_6H_5CH(OCH_2CH_2CH_2O)$ (**4l**) | $C_6H_5COOCH_2CH_2CH_2OH$ (**5l**) | 82[c] |

[a]Yields refer to isolated products. [b]Yield refers to the isolated product from corresponding aldehyde. [c]Yield refers to the isolated product from corresponding dimethyl acetal.

## Experimental Section

**General.** All reactions were carried out under an inert atmosphere of argon. Chloroform was freshly distilled from phosphorus pentoxide prior to use. Liquid reagents and solvents used were reagent grade and purified prior to use, if necessary, by methods reported in the literature. Analytical thin layer chromatography was performed on pre-coated Merck silica gel 60 F254 TLC plate. Small and medium-scale purification were performed by flash column chroma-




**Scheme 1**

tography by using Merck 230-400 mesh silica gel. $^1$H NMR spectral data were obtained on a Varian Gemini 400 (400 MHz) or Varian 300 (300 MHz) spectrometer. Infrared spectra were recorded using a BioRad FT-IR spectrophotometer with internal calibration. Mass spectra, elementary analysis, and $^{13}$C NMR spectra were not measured because they were reported on elsewhere. Spectral data of products were compared with those in the Aldrich Library of FT $^1$H NMR and FT-IR spectra books and products were identified.

**General procedure for the preparation of ethyl esters**. To a solution of aldehyde (5 mmol) in dried $CHCl_3$ (15 mL) were added Amberlyst® 15 (wet) ion exchange resin (0.25 g) and triethyl orthoformate (3.3 mL, 20 mmol) under the argon atmosphere at ambient temperature. The mixture was stirred at reflux condition. After being stirred for 3 h, a catalytic amount of $BF_3{\cdot}OEt_2$ and *m*-CPBA (72%, 1.20 g, 5.0 mmol) were added followed by DBU (0.75 mL, 5.0 mmol). The resulting reaction mixture was stirred for 1 h at ambient temperature. The reaction mixture was diluted with $CHCl_3$ (7 mL) and quenched with 0.5 N NaOH solution (15 mL). The organic layer was washed with 0.1 N HCl solution (10 mL) while the organic layer was dried over anhydrous sodium sulfate. The desired ethyl esters were purified by flash column chromatography.

**Ethyl benzoate (5a)**. TLC (EtOAc/*n*-Hexane=1 : 8, v/v), $R_f$=0.5. IR (neat) 1719 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.04 (d, $J$ = 7.8 Hz, 2H), 7.50 (t, $J$ = 7.5 Hz, 1H), 7.39 (t, $J$ = 7.5 Hz, 2H), 4.35 (q, $J$ = 7.4 Hz, 2H), 1.36 (t, $J$ = 7.4 Hz, 3H).

**Ethyl 4-methylbenzoate (5b)**. TLC (EtOAc/*n*-Hexane= 1 : 8, v/v), $R_f$=0.5. IR (neat) 1719 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.92 (d, $J$ = 8.0 Hz, 2H), 7.19 (d, $J$ = 8.4 Hz, 2H), 4.33 (q, $J$ = 7.1 Hz, 2H), 2.36 (s, 3H), 1.36 (t, $J$ = 7.2 Hz, 3H).

**Ethyl heptanoate (5c)**. TLC (EtOAc/*n*-Hexane=1 : 8, v/v), $R_f$=0.4. IR (neat) 1739 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 4.04 (q, $J$ = 7.2 Hz, 2H), 2.20 (t, $J$ = 7.6 Hz, 2H), 1.54 (quintet, $J$ = 7.2 Hz, 2H), 1.19-1.27 (m, 6H), 1.17 (t, $J$ = 7.2 Hz, 3H), 0.81 (t, $J$ = 7.2 Hz, 3H).

**General procedure for the preparation of diisopropyl acetals and dibenzyl acetals**. To a stirred solution of aldehyde (5 mmol) and 2-propanol (0.92 mL, 12 mmol) (or benzyl alcohol (1.24 mL, 12 mmol)) in benzene (20 mL) were added *p*-toluenesulfonic acid monohydrate (0.50 g, 2.6 mmol), and anhydrous $CaCl_2$ (2.0 g). The mixture was heated under reflux condition using a Dean-Stark trap for water separation. The acetal formation was monitored by TLC (EtOAc/*n*-Hexane=1 : 8, v/v). Upon completion of the reaction, the mixture was filtered and the residue was washed with benzene. The solvent was evaporated and the product was purified by column chromatography.

**General procedure for the preparation of isopropyl esters and benzyl esters**. To a solution of diisopropyl acetal (or dibenzyl acetal) (5 mmol) in dried $CHCl_3$ (15 mL) were added $BF_3{\cdot}OEt_2$ (0.063 mL, 0.50 mmol) and *m*-CPBA (72%, 1.20 g, 5.0 mmol), followed by DBU (0.75 mL, 5.0 mmol) under argon atmosphere at ambient temperature. The reaction mixture was stirred for 3 h and then diluted with $CHCl_3$ (7 mL). The reaction was quenched with 0.5 N NaOH solution (15 mL) and the organic layer was washed with 0.1 N HCl solution (10 mL). The organic layer was dried over anhydrous sodium sulfate, then the filtrate was concentrated. The corresponding desired isopropyl ester (or benzyl ester) was purified by a flash column chromatography.

**Isopropyl benzoate (5d)**. TLC (EtOAc/*n*-Hexane=1 : 8, v/v), $R_f$=0.45. IR (neat) 1717 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 8.04 (d, $J$ = 7.1 Hz, 2H), 7.48 (t, $J$ = 7.4 Hz, 1H), 7.38 (t, $J$ = 7.4 Hz, 2H), 5.24 (septet, $J$ = 6.3 Hz, 1H), 1.34 (d, $J$ = 6.4 Hz, 6H).

**Isopropyl 4-methoxybenzoate (5e)**. TLC (EtOAc/*n*-Hexane = 1 : 8, v/v), $R_f$=0.38. IR (neat) 1711 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.99 (d, $J$ = 7.0 Hz, 2H), 6.89 (d, $J$ = 7.0 Hz, 2H), 5.22 (septet, $J$ = 6.0 Hz, 1H), 3.85 (s, 3H), 1.37 (d, $J$ = 6.1 Hz, 6H).

**Isopropyl butyrate (5f)**. TLC (EtOAc/*n*-Hexane=1 : 8, v/v), $R_f$=0.50. IR (neat) 1734 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 5.00 (septet, $J$ = 6.3 Hz, 1H), 2.23 (t, $J$ = 7.3 Hz, 2H), 1.64 (sextet, $J$ = 7.4 Hz, 2H), 1.22 (d, $J$ = 6.3 Hz, 6H), 0.94 (t, $J$ = 7.4 Hz, 3H).

**Benzyl 2-hydroxybenzoate (5g)**. TLC (EtOAc/*n*-Hexane =1 : 8, v/v), $R_f$=0.35. IR (neat) 3419, 1721 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 10.7 (s, 1H), 7.25-7.45 (m, 9H), 5.39 (s, 2H).

**Benzyl acetate (5h)**. TLC (EtOAc/*n*-Hexane=1 : 8, v/v), $R_f$=0.55. IR (neat) 1740 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.34-7.36 (m, 5H), 5.11 (s, 2H), 2.10 (s, 3H).

**Benzyl propionate (5i)**. TLC (EtOAc/*n*-Hexane=1 : 8, v/v), $R_f$=0.50. IR (neat) 1739 cm$^{-1}$. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 7.34-7.36 (m, 5H), 5.11 (s, 2H), 2.38 (q, $J$ = 7.5 Hz, 2H), 1.16 (t, $J$ = 7.5 Hz, 3H).

**Preparation of 2-hydroxyethyl benzoate (5j)**. To a stirred solution of benzaldehyde (0.51 mL, 5 mmol) and ethylene glycol (0.67 mL, 12 mmol) in benzene (20 mL) were added *p*-toluenesulfonic acid monohydrate (0.5 g, 2.6 mmol), and anhydrous $CaCl_2$ (2.0 g). The mixture was heated under reflux condition using a Dean-Stark trap for water separation. The acetal formation was monitored by TLC (EtOAc/*n*-Hexane= 1 : 8, v/v). Upon completion of the reaction, the reaction solution was filtered. To filtrate a catalytic amount of $BF_3{\cdot}OEt_2$ and *m*-CPBA (72%, 1.20 g, 5.0 mmol) were added. The resulting reaction mixture was stirred for 1 h at ambient temperature. The reaction mixture was diluted with benzene (7 mL) and quenched with 0.5 N NaOH solution (15 mL). The organic layer was washed with 0.1 N HCl solution (10 mL) while the organic layer was dried over anhydrous sodium sulfate. The desired 2-hydroxyethyl benzoate was purified by flash column chromatography. TLC (EtOAc/*n*-Hexane=1 : 10, v/v), $R_f$=0.20. IR (neat) 3426, 1720 cm$^{-1}$. $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.06 (d, $J$ = 7.2 Hz, 2H), 7.57 (t, $J$ = 7.6 Hz, 1H), 7.44 (t, $J$ = 7.6 Hz, 2H), 4.46 (t, AB type, 2H), 3.96 (t, AB type, 2H), 2.45 (br s, 1H).

**General procedure for the preparation of *rac*-1,2-dimethyl-2-hydroxyethyl benzoate (5k) and 3-hydroxypropyl benzoate (5l)**. To a solution of benzaldehyde dimethyl acetal (0.75 mL, 5 mmol) in benzene (15 mL) were added Amberlyst® 15 (wet) ion exchange resin (0.25 g) and *meso*-2,3-butane-

diol (1.08 g, 12 mmol) (or 1,3-propanediol (0.87 mL, 12 mmol)) under the argon atmosphere at reflux temperature. After being stirred for 5 h, a catalytic amount of $BF_3 \cdot OEt_2$ and *m*-CPBA (72%, 1.20 g, 5.0 mmol) were added to the reaction mixture. The resulting reaction mixture was stirred for 1 h at ambient temperature. The reaction mixture was diluted with benzene (7 mL) and quenched with 0.5 N NaOH solution (15 mL). The organic layer was washed with 0.1 N HCl solution (10 mL) while the organic layer was dried over anhydrous sodium sulfate. The desired esters were purified by flash column chromatography.

***rac*-1,2-Dimethyl-2-hydroxyethyl benzoate (5k).** TLC (EtOAc/*n*-Hexane=1 : 10, v/v), $R_f$=0.25. IR (neat) 3425, 1719 $cm^{-1}$. $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.98 (d, $J$ = 6.9 Hz, 2H), 7.51 (t, $J$ = 7.4 Hz, 1H), 7.38 (t, $J$ = 7.7 Hz, 2H), 5.07 (qd, $J$ = 6.4, 3.3 Hz, 1H), 3.96 (qd, $J$ = 6.5, 3.3 Hz, 1H), 1.57 (br s, 1H), 1.28 (d, $J$ = 6.6 Hz, 3H), 1.19 (d, $J$ = 6.3 Hz, 3H).

**3-Hydroxypropyl benzoate (5l).** TLC (EtOAc/*n*-Hexane =1 : 10, v/v), $R_f$=0.25. IR (neat) 3425, 1720 $cm^{-1}$. $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.02 (d, $J$ = 7.3 Hz, 2H), 7.53 (t, $J$ = 7.3 Hz, 1H), 7.41 (t, $J$ = 7.5 Hz, 2H), 4.45 (t, $J$ = 6.3 Hz, 2H), 3.77 (t, $J$ = 6.1 Hz, 2H), 3.15 (br s, 1H), 2.00 (quintet, $J$ = 6.2 Hz, 2H).

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