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Preparation of 1-Methoxycarbonyl-1-t-Butyldimethylsilyloxy Epoxides. Their Transformation into 3-Hydroxy 2-Acetal-Esters and certain 3-Hydroxy 2-Keto-Esters

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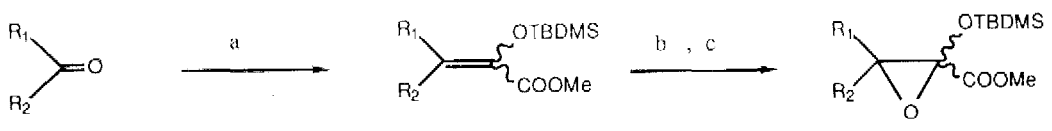
Abstract : The peracid oxidation of methyl 2-(t butyldimethylsilyloxy)-2-alkenoates **2** furnished the corresponding epoxides **3** in good yields.The regiospecific opening of the latter compounds with methanol afforded 3-hydroxy 2-acetal-esters **4**. When alkyl disubstituted in position 3, compounds **3** or **4** could be deprotected to give rise to 3-hydroxy 2-keto-esters **5**.

Since the first report by Rubottom et al. [1], the peracid oxidation of silyl enol ethers has been widely used to prepare α-hydroxy carbonyl compounds . The same conditions applied to silyloxy-keten-acetals, gave α-hydroxy-acids [2] or lactones.[3] Recently the peracid oxidation of 2-methoxycarbonyl silyl enol ethers into 2-hydroxy-3-keto esters has been described.[4] To our knowledge, the same reaction with their isomers,1-methoxycarbonyl enol silyl ethers **2** , has not yet been reported. Since we were interested in these compounds **2** for carbon chain elongation in carbohydrates [5], we decided to examine t: behaviour under the same oxydative conditions. Using a Wittig-Wadsworth-Emmons reaction [6] and starting from commercially available aldehydes or ketones **1** and methyl 2-(t-butyldimethyl)silyloxy-2-(dimethyl phosphono) acetate [7], we first prepared the enol ethers **2a** to **2e** (as a mixture of the diastereoisomers Z and E [8]). When submitted to the action of a slight excess (1.2 eq.) of 3-chloroperoxybenzoic acid in dichloromethane at room temperature overnight, they were transformed into the corresponding epoxides **3** in good to excellent yields.[9]



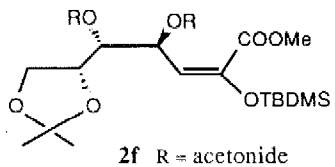
1 **2** **3**

$R_1 = H$	$R_2 = -CH_2-CH_2-CH_3$	**2a** (60%)	**3a** (75%)
$R_1 = H$	$R_2 = -CH_2-(CH_2)_3-CH_3$	**2b** (83%)	**3b** (95%)
$R_1 = H$	$R_2 = -C_6H_5$	**2c** (91%)	**3c** (84%)
$R_1 = CH_3$	$R_2 = -CH_2-CH_2-CH_3$	**2d** (73%)	**3d** (80%)
$R_1 = CH_3$	$R_2 = -CH_2-(CH_2)_2-CH_3$	**2e** (60%)	**3e** (77%)

a $(MeO)_2P(O)-CH(OTBDMS)COOMe$, $LiN(Si(Me)_3)_2$, THF . **b** MCPBA, CH_2Cl_2, 20°C . **c** KF [10]

Thus, in contrast to epoxides resulting from the peracid oxidation of silyl enol ethers or silyloxy keten-acetals, which have been isolated only when non acidic oxidative conditions were used [11], these new epoxides **3**, did not rearrange to 3-trialkylsilyloxy 2-keto-esters either during oxidation or when purified on silica gel. The enhancement of stability is certainly due to the presence of the electron whithdrawing methoxycarbonyl group which destabilized a β-silyl-carbocation .[11a]

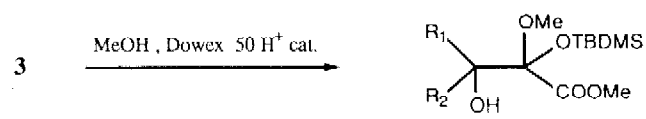
To delimit the scope of this oxidation we then applied the above conditions to functionnalized enol ethers **2f (E)** and **2g (E)** prepared from the corresponding O-protected L-arabinose derivatives. If the compound **2f** furnished the expected epoxide **3f** in good yield (as a mixture ot two diastereoisomers), **2g** was recovered unchanged.[12]



2f R = acetonide
2g R = $-CH_2-C_6H_5$

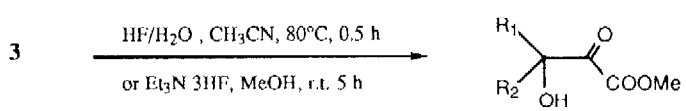
3f (71 %)

In order to obtain interesting 3-hydroxy 2-keto esters **5** [13], the epoxides **3** were then submitted to several deprotecting conditions of the trialkylsilyloxy groups. We first tried the conditions which have been reported to transform silyloxy epoxides into the corresponding 2-hydroxy ketones [11b] and which have been extensively used for the deprotection of TBDMS ethers. [14] When a solution of **3d** in THF was treated with a solution of tetrabutylammonium fluoride in THF (1 eq.), we instantaneously observed the formation of a very polar compound (presumably a complex), which did not evolve, even after several hours of reflux. Then, a methanolic solution of **3d** was treated with a catalytic amount of Dowex 50 H^+.[15] After two hours at room temperature, the starting material was totally transformed into the acetal-ester **4d** in 70 % yield. Compounds **4a** (72 %), **4b** (95 %), **4c** (88 %), and **4e** (76 %), were similarly obtained.



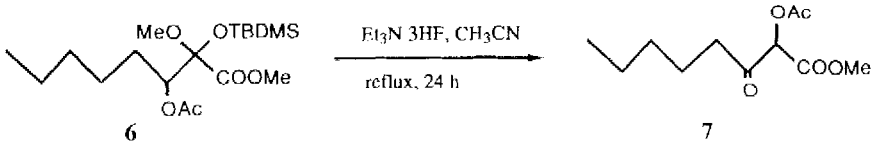
4

Finally, the keto-esters **5d** and **5e** could be obtained by treatment of the epoxides **3d** and **3e** either with aqueous hydrofluoric acid in acetonitrile [16] or triethylamine tris hydrofluoride (Et_3N-3HF [5])in methanol in about the same yields.[17]



5d (80 %) **5e** (70 %)

The above conditions applied to **3b** (or **4b** [17]), led to an unseparable mixture of several products. This is certainly due to the formation of an enolizable 3-hydroxy 2-keto-ester in this case. [18] In contrast, when an acetonitrile solution of the O-protected derivative **6** of **4b** (Pyr, Ac_2O, 87 %) was submitted to the action of a catalytic amount of Et_3N-3HF, it cleanly afforded, after refluxing one day, the rearranged 2-acetoxy-3-keto-ester **7** in 80% yield.



6 **7**

In conclusion, we describe in this note the preparation of a new class of silyloxy epoxides in two steps from aldehydes and ketones. These compounds did not rearrange under acidic conditions into trialkylsilyloxy-keto-esters but are regiospecifically opened with methanol into 3-hydroxy 2-acetal-esters. When the 3 position is dialkylated, deprotection of the latter compounds, or their precursor epoxides, led to the corresponding 3-hydroxy 2-keto-esters. The reactivity of these new epoxides with various nucleophilic reagents is presently being examined in our laboratory.

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8 From aldehydes, we obtained the enol ethers **2 E** as the major isomer (≈ 80-90%). From ketones, both isomers Z and E were formed in about the same quantities.

9 Yields are reported for isolated chromatographically (silica gel) pure products.Their IR, ^1H NMR, ^{13}C NMR and GC/MS (or elemental analysis) spectra were entirely consistent with the assigned structures.

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17 The keto-esters **5d** and **5e** were also obtained from **4d** and **4e** by treatment of an acetonitrile solution of the latter compounds with aqueous hydrofluoric acid but in lower yields (**5d** (65 %) ; **5e** (57 %))

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Typical Procedures :

Epoxides 3 : To a solution of **2b** (**E+Z**) (0.5 g, 1.75 mmol) in dry dichloromethane (10 ml) was added 3-chloroperoxybenzoic acid (0.362 g, 1.2 eq.).The mixture was stirred overnight at room temperature.The 3-chlorobenzoic acid was filtered off and the resultant solution stirred for 4 h with 0.2 g of anhydrous potassium fluoride.[10] The complex thus formed was filtered off, washed with dichloromethane (2x10 ml). After solvent evaporation *in vacuo* the crude product was purified on silica gel (Amicon 35-70 μ ; 40g; eluent ether/pentane 10/90).We thus obtained 0.502 g (95 %) of pure epoxide **3b. IR** (film, cm^{-1}) 2960, 1750, 1150.**^{1}H** NMR (300 MHz, $CHCl_3$,δ ppm, internal reference: TMS): (major isomer formed from **2b** E) : 0.12 (s, 3H), 0.14 (s, 3H), 0.85 (t, J = 7 Hz, 3H), 0.87 (s, 9H), 1.2-1.5 (M, 8H), 3.29 (t, J = 6 Hz, 1H), 3.79 (s, 3H). **^{13}C** NMR (75.47 MHz, multiplicity : DEPT) 167.6 (s), 80.9 (s), 65.1 (d), 52.5 (q), 31.3 (t), 27.5 (t), 25.5 (t), 25.3 (q), 22.4 (t) 17.6 (s), 13.8 (q), 0.3 (q), 0.1 (q).**Anal.** Calcd for $C_{15}H_{30}O_4Si$: C, 59.58 ; H, 9.93 ; Si, 9.27. Found C, 59.60 ; H, 9.96 ; Si, 8.97

Hydroxy-acetal-esters 4 : To a solution of **3b** (0.500 g, 1.65 mmol) in dry methanol (10 ml) was added 0.05 g of Dowex H^+ and the mixture was stirred at room temperature for 2 h. After filtration and concentration a column chromatography (SiO_2 : 40 g, eluent ether/pentane : 30/70) of the crude product, furnished 0.524 g (95 %) of pure acetal-ester **4b IR** (film, cm^{-1}) 2500, 2960, 1750, 1120, 1090. **^{1}H** (major isomer) 0.14 (s, 3H), 0.15 (s, 3H), 0.91 (t, J = 7 Hz, 3H), 0.91 (s, 9H), 1.2-1.6 (M, 8H), 2.1 (OH), 3.32 (s, 3H), 3.72 (m, 1H), 3.76 (s, 3H). **^{13}C** 170.1 (s), 100.7 (s), 75.3 (d), 52.0 (q), 51.3 (q) 31.5 (t), 30 (t), 25.7 (q), 25.5 (t), 22.4 (t), 18.7 (s), 13.8 (q).0.3 (q), 0.1 (q). **Anal.** Calcd for $C_{16}H_{34}O_5Si$: C, 57.48 ; H, 10.17 ; Si, 8.38. Found C, 57.42 ; H, 10.20 ; Si, 8.00

Hydroxy-keto-esters 5 : .To a solution of 1.5 mmol of **3d** (0.432 g) or **4d** (0.480 g), in 10 ml of dry acetonitrile was added 2.5 ml of a 50% aqueous solution of hydrofluoric acid.The mixture was refluxed for 0.5 h then diluted with dichloromethane (40 ml) and washed two times with water (10 ml) and then dried (Na_2SO_4) and concentrated.The crude product was purified by silica gel (50 g) column chromatography (eluent : ether/pentane : 40/60) furnishing 0.209 g (80 %, from **3d**) or 0.170 g (65 % , from **4d**) of pure **5d IR** (film, cm^{-1}) 3500, 2945, 1740, 1720, 1285, 1025. **^{1}H** NMR 0.89 (t, J = 7 Hz, 3H), 1-1.5 (M, 2H), 1.5 (s, 3H) 1.6-2.0 (M, 2H), 3.15 (OH) 3.89 (s, 3H). **^{13}C** 198.9 (s), 162.7 (s). 78.9 (s), 52.8 (q), 41.3 (t), 24.7 (q), 16.7 (t), 14.2 (q). **GC-MS** : 175 (M^+ +1; 7.5%) , 157 (23%), 146 (1.5%), 87 (78 %).

Acetoxy-keto-ester 7 : To a solution of 0.5 g (1.33 mmol) of **6** in acetonitrile (10 ml) was added three drops of Et_3N 3HF (Fluka) and the mixture was refluxed for 24 h.After dilution with diethylether (50 ml), the organic layer was washed with water (2 x 10 ml) and dried (Na_2SO_4). The crude product obtained after concentration was column chromatographed (SiO_2 : 40 g ; eluent : ether/pentane : 50/50) furnishing 0.245 g (80 %) of pure compound **7. IR** (film, cm^{-1}) 2960, 1750, 1740, 1220.**^{1}H** 0.83 (t, J = 7 Hz, 3H), 1.23 (m, 4H), 1.55 (m, 2H), 2.17 (s, 3H), 2.60 (t, J = 7 Hz, 2H) 3.76 (s, 3H), 5.46 (s, 1H). **^{13}C** 199.8 (s) 169.3 (s) 165.1 (s), 77.3 (d), 52.9 (q), 39.5 (t), 30.9 (t), 22.5 (t), 22.2 (t), 20.2 (q), 13.7 (q), **GC-MS** 199 (M^+-31 ; 1.5 %), 188 (4.5 %), 132 (6 %), 99 (62 %), 71 (37 %), 43 (100 %).

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