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TMS Triflate-Catalyzed Cleavage of Prenyl (3-Methylbut-2-enyl) Ester

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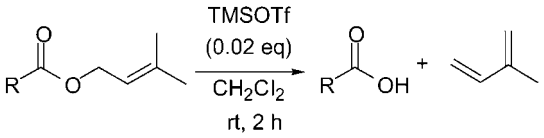
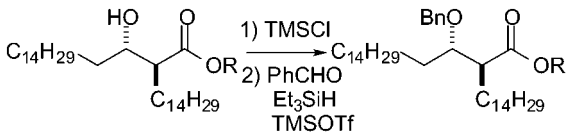
ABSTRACT



Prenyl (3-methylbut-2-enyl) ester is catalytically cleaved by TMS triflate affording carboxylic acid and isoprene in high yield under mild conditions with high chemoselectivity without causing epimerization of the neighboring chiral center.

In 1994 we reported a novel reductive etherification of silyl ether using aldehyde and triethylsilane in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf).[1] When the procedure was applied to β-hydroxy ester **1** that has a chiral center on the α carbon, benzyl ether **2** was obtained in quantitative yield without causing epimerization, dehydration, or retro-aldol reaction.[2,3] During our further synthetic study of trehalose dicorynomycolate, we examined reductive benzylation of prenyl ester alcohol **3** after silylation and found that the prenyl group was cleaved under the reaction conditions to give benzyl ether carboxylic acid **4** in quantitative yield.

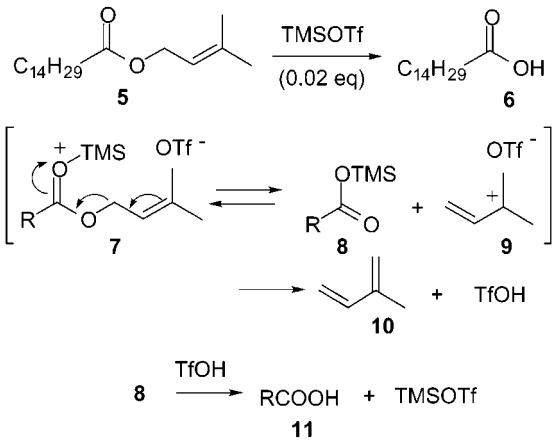


1: R = CH_3
3: R = $CH_2CH{=}C(CH_3)_2$

2: R = CH_3
4: R = H

Throughout the investigation of simple prenyl ester **5**, we found that neither benzaldehyde nor the reducing agent, Et_3SiH, was required for cleavage of the prenyl ester. Only a catalytic amount of TMSOTf was required. The reaction should take place via TMS triflate-catalyzed equilibrium between silylated prenyl ester **7** and TMS ester **8**, and the equilibrium favors the forward reaction, forming isoprene (**10**) (Scheme 1). TMSOTf should be regenerated by the reaction of TMS ester **8** with TfOH (formed in situ), establishing the catalytic cycle. When the reaction was carried

Scheme 1



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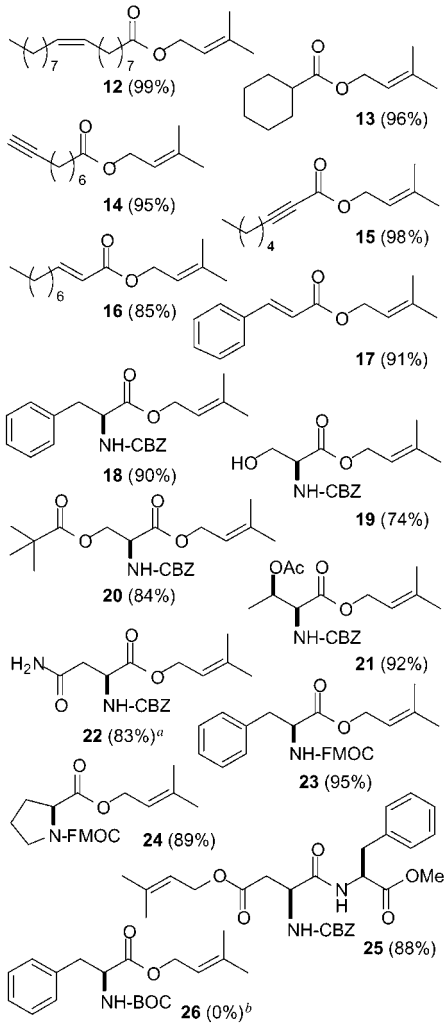
out in an NMR tube using $CDCl_3$ as solvent, appearance of a stoichiometric amount of isoprene (**10**) and carboxylic acid **11** was observed. Therefore, we would like to describe herein mild and neutral cleavage of the prenyl ester by using a catalytic amount of TMSOTf under anhydrous conditions.[4,5] Cleavage of prenyl ester has been conducted by Pd-catalyzed hydrolysis,[2,6,7] fragmentation using I_2,[8] heating with sulfated SnO_2[9] or K-10 clay,[10] and $CeCl_3 \cdot 7H_2O$−NaI-mediated hydrolysis.[11] Recently, Sharma and co-workers reported a similar cleavage of prenyl ethers catalyzed by $Yb(OTf)_3$ and showed an application for the cleavage of prenyl esters.[12] Iodine was also shown to be useful for the cleavage of prenyl ethers.[13]

The reaction was carried out simply as follows. A solution of the prenyl ester (1 mmol) and TMSOTf (0.02−0.03 mmol) in dichloromethane (3 mL) was stirred at room temperature for 1 to 5 h. After evaporation of volatile materials under vacuum, the residue was purified directly by crystallization or column chromatography on silica gel, providing pure carboxylic acid in the yield shown in Table 1. As in the case of **12**, the isolated double bond was not affected and the corresponding carboxylic acid was obtained in nearly quantitative yield. The isolated triple bond of **14** was unaffected as well. The conjugated triple bond of **15** and the conjugated double bonds of **16** or **17** also do not interfere in the reaction and afford carboxylic acids in 98% and 85% yield, respectively. The method was particularly useful for amino acid derivatives. The CBZ-protected prenyl ester of L-phenylalanine **18** afforded carboxylic acid in 90% yield without any change in the CBZ group and the optical purity. The hydroxyl group of **19**, pivaloyl group of **20**, and acetyl group of **21** also did not participate in the reaction, affording the corresponding carboxylic acids in reasonable yields. The amide moiety of **22** was also stable under the reaction conditions but required 0.06 equiv of catalyst to complete the reaction. The FMOC protecting groups of **23** and proline **24** were also entirely inert under the reaction conditions and afforded FMOC amino acids in 95% and 89% yield, respectively. The peptide bond and the methyl ester of **25** were also inert, giving the corresponding CBZ-protected aspartame in 88% yield. On the other hand, BOC-protected L-phenylalanine **26** did not afford a carboxylic acid, and the BOC group was cleaved in a stoichiometric amount to the catalyst prior to cleavage of the prenyl group, affording phenylalanine prenyl ester.

Table 1. TMSOTf-Catalyzed Cleavage of Prenyl Ester (Yield)



[a] TMSOTf (0.06 equiv) was employed. [b] TMSOTf (0.1 equiv) was employed, and phenylalanine prenyl ester was formed in ca. 10% yield.

FMOC protected L-tyrosine derivative **27** afforded carboxylic acid **28** in only 15% yield, and the major product was the new amino acid **29** in 70% yield, formed by incorporating the isoprene unit (Scheme 2).[14]

Therefore, the present procedure to cleave the prenyl ester proceeds under very mild conditions and is characteristic in its high chemoselectivity and operational simplicity without

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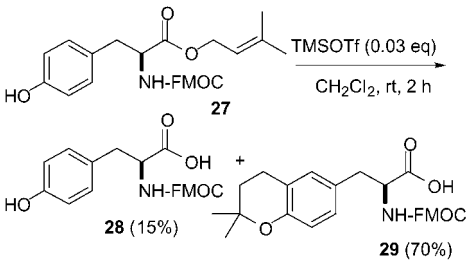
(14) ^{1}H NMR (600 MHz in $CDCl_3$) δ 1.28 (3H, s), 1.28 (3H, s), 1.72 (2H, t, J = 6.59 Hz), 2.70 (2H, t, J = 6.59 Hz), 3.01 (1H, dd, J = 14.01, 6.32 Hz), 3.11 (1H, dd, J = 14.01, 4.95 Hz), 4.18 (1H, t, J = 7.14 Hz), 4.32 (1H, dd, J = 10.71, 7.14 Hz), 4.40 (1H, dd, J = 10.71, 7.42 Hz), 4.65 (1H, m), 5.33 (1H, d, J = 7.80 Hz), 6.70 (1H, d, J = 8.80 Hz), 6.85 (1H, m), 6.84 (1H, m), 7.27 (2H, t, J = 7.41 Hz), 7.37 (2H, t, J = 7.41 Hz), 7.52 (1H, d, J = 7.41 Hz), 7.55 (1H, d, J = 7.41 Hz), 7.73 (2H, d, J = 7.41 Hz). ^{13}C NMR (150 MHz, in $CDCl_3$) δ 22.33 t, 26.75 q, 26.81 q, 32.56 t, 36.85 t, 47.02 d, 54.70 d, 67.04 t, 74.17 s, 117.32 d, 119.89 d, 120.98 s, 125.00 d, 126.31 s, 127.00 d, 127.63 d, 128.15 d, 130.23 d, 141.18 s, 143.61 s, 143.68 s, 153.11 s, 155.81 s, 176.03 s. FT−IR ν 3315 (br), 3064, 1718, 1486 cm^{-1}. High-resolution ms m/z 471.2034 (calcd for $C_{29}H_{29}O_5N$ 471.2046). $[\alpha]^{25}_D$ +31.27° (c 1.05, $CHCl_3$).

Scheme 2



causing epimerization of the neighboring chiral center. It is noteworthy that the process is not a hydrolysis but a novel catalytic fragmentation under nonaqueous conditions. Although cleavage of the *tert*-butyl ester has been carried out by using a stoichiometric amount of TMSOTf/triethylamine,[15] we have already found that the present procedure can be applied to catalytic cleavage of the *tert*-butyl ester, and the details will be described elsewhere.

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