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A Novel Cleavage of Allyl Protection

Biao Yu,* Bing Li, Jianbo Zhang, Yongzheng Hui*

State Key Laboratory of Bio-organic and Natural Products Chemistry,
Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

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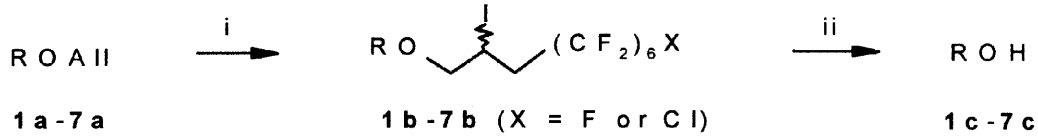
Abstract: A novel, efficient, and mild cleavage of allyl protection is developed employing perfluoroalkylation and subsequent elimination.

The allyl group is one of the most frequently used protecting groups for hydroxyl and carboxyl functions in organic synthesis and more specifically in carbohydrate chemistry.[1] This is due to its ready availability and stability under reasonably strong acidic and basic conditions. The classic procedures for removal of the allyl protection involve a two step sequence in which the allyl function is first isomerized to the corresponding propenyl function with a strong base (*t*-BuOK)[1] or a metal catalyst, such as Pd/C,[2] $(Ph_3P)_3RhCl$,[3] and $[Ir(COD)(PMePh_2)_2]PF_6$ [4] etc, followed by acidic or oxidative cleavage. New methods have been developed for removal of allyl protection under various conditions, these include $SmCl_3/e^-$,[5] Ti(0),[6] $PdCl_2/CuCl/O_2$,[7] Cp_2Zr,[8] NBS/hν,[9] Ti(O-*i*-Pr)$_4$/*n*-BuMgCl,[10] DDQ,[11] $NaBH_4/I_2$,[12] and $TolSO_2H/Pd(PPh_3)_4$ [13] etc. Nonetheless, cleavage of allyl protection is sometimes still capricious in the manipulation of polyfunctional molecules, for example in the cleavage of some anomeric allyl protected acetals in carbohydrates.[14,15] To this end, we developed a novel and efficient procedure for deprotection of the hemiacetal allyl protection in allyl glycosides using a perfluoroalkylation and subsequent elimination sequence.[15] Commonly used protective functions including ether, ester, silyl ether, and ketal all remain intact under these conditions. Further studies disclosed that allyl protection on alcohols and carboxylic acids could also be readily cleaved under this novel procedure. The results are listed in the following scheme and table.

Scheme



i. $I(CF_2)_6X$ (X = F or Cl), $Na_2S_2O_4$, $NaHCO_3$, CH_3CN (or DMF)/H_2O (4/1), rt, 30 min;
ii. Zn powder, NH_4Cl, EtOH, reflux, 15 min.

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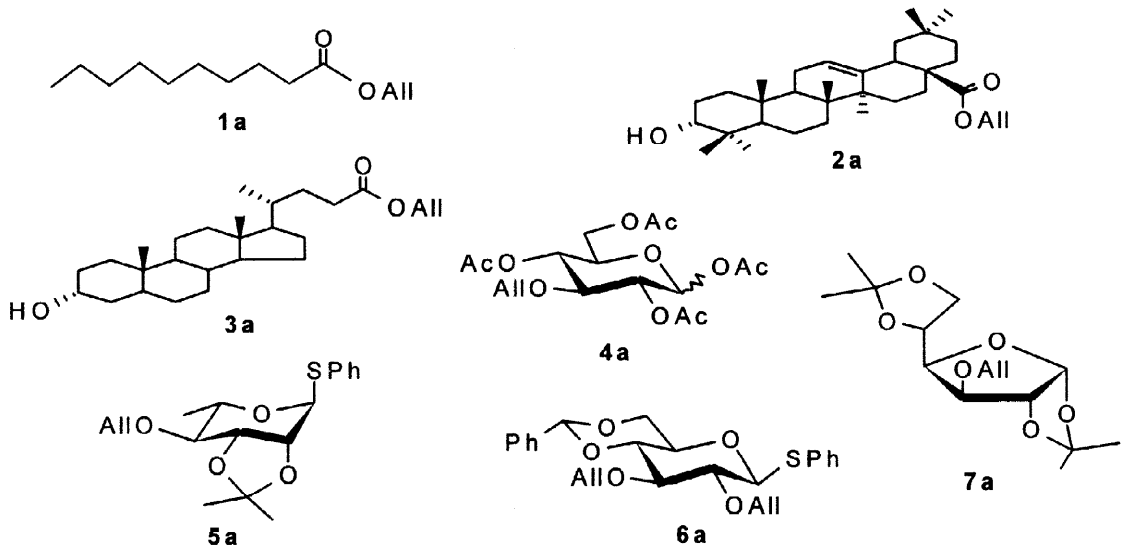

Table. Perfluoroalkylation and subsequent elimination of the allyl protecting group [16]

Entry [a - d]	Substrate	Perfluoroalkylation		Elimination	
		Product [e,f]	Yield (%) [g]	Product [e]	Yield (%) [g]
1 [a, c]	**1a**	**1b**	87	**1c**	92
2 [b, d]	**2a**	**2b**	92	**2c**	90
3 [b, d]	**3a**	**3b**	91	**3c**	93
4 [a, c]	**4a**	**4b**	92	**4c**	79
5 [b, c]	**5a**	**5b**	98	**5c**	90
6 [b, c]	**6a**	**6b**	98	**6c**	87
7 [b, c]	**7a**	**7b**	99	**7c**	93

[a] $I(CF_2)_6Cl$, [b] $I(CF_2)_6F$ was used as a perfluoroalkylation agent. [c] CH_3CN/H_2O (4/1), [d] DMF/H_2O (4/1) was used as solvent in perfluoroalkylation. [e] All new compounds gave satisfactory analytical data,[16,17] including ^1H NMR, ^{19}F NMR, and MS. [f] Each contains stereoisomers due to the new generated stereo center (β-C of the original allyl group). [g] Isolated yield after silica gel column chromatography.

Employing the well documented and widely applicable perfluoroalkylation method for the terminal carbon carbon double bond with perfluoroalkyl iodide under sodium dithionite ($Na_2S_2O_4$) and sodium bicarbonate ($NaHCO_3$),[18] allyl protective function on either carboxylic acids or alcohols (**1a-7a**) was readily converted into a β-iodide γ-perfluoroalkane substituted derivative (**1b-7b**) in excellent yield. DMF was applied instead of CH_3CN in the aqueous solvent system for the reaction of allyl ester **2a** and **3a** due to their very poor solubility in CH_3CN. The β-iodide γ-perfluoroalkane substituted ether tails in **1b-7b** were easily eliminated under Zn powder and NH_4Cl in refluxing EtOH for 15 min to give the corresponding deallylation product (**1c-7c**) in high yield. Both steps were carried out in almost neutral conditions, other functions presented in the substrates were all untouched, including ester (even the labile anomeric acetyl, entry 4), hydroxyl (entry 2, 3),

ketal (either isopropylidene or benzylidene, entry 5-7), internal carbon carbon double bond (entry 2), as well as thioether (entry 5, 6), which usually cause poisoning to the transition metal species used in deallylation.

Finally, it is worthy noting that, based on the present procedure, allyl group, an "old" protecting group, can be readily derived into a new "secondary" protecting group, which, with a "fluorous" anchor, will find new contributions elsewhere, for example, in the burgeoning field of "fluorous syntheses". [19]

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16. *Typical procedure*: To a stirred solution of **7a** (150 mg, 0.5 mmol) and $I(CF_2)_6F$ (Aldrich, 580 mg, 1.25 mmol) in CH_3CN (12 mL), was added H_2O (3 mL) at rt, the mixture turned to be an emulsion, to which a mixture of $Na_2S_2O_4$ (435 mg, 2.5 mmol) and $NaHCO_3$ (210 mg, 2.5 mmol) was added. After being stirred at rt for 30 min, the mixture was diluted with EtOAc (50 mL), the organic layer was separated, washed with brine twice, dried over anhydrous Na_2SO_4 and concentrated. The residue was chromatographed on a silica gel column to give **7b** (370 mg, 99%). **7b** (200 mg, 0.26 mmol) was treated with Zn powder (86 mg, 1.32 mmol) and NH_4Cl (28 mg, 0.52 mmol) in absolute EtOH. After being refluxed for 15 min, the mixture was cooled to rt, then filtered and concentrated. Flash chromatography of the residue on a silica gel column afforded **7c** (65 mg, 93%). **7b**: ^1H NMR ($CDCl_3$): 5.91, 5.87 (0.5 H each, d each, J = 3.6 Hz, H-1), 4.59, 4.55 (0.5 H each, d each, J = 3.7 Hz, H-2), 4.42-4.24 (2 H, m), 4.16-4.05 (2 H, m), 4.01-3.91 (2 H, m), 3.85 (1 H, d, J = 4.7 Hz), 3.75 (1 H, m), 3.08, 2.70 (1 H each, m each, CH_2R_f), 1.49, 1.31 (3 H each, s each, CH_3), 1.41, 1.40, 1.31, 1.29 (1.5 H each, s each, 2 × CH_3); ^{19}F NMR ($CDCl_3$): -3.57 (3 F, m, CF_3), -34.5 (2 F, m, CF_2CH_2), -42.2, -43.2, -43.8, -46.3 (2 F each, s each, 4×CF_2); EIMS (m/z): 732 (M-CH_3, 14), 487 (65), 101 (100); Anal. Calcd for $C_{21}H_{24}O_6F_{13}I$: C, 33.79%, H, 3.25%, Found: C, 33.63%, H, 2.98%.

17. Selected ^1H NMR data for compound **1b-6b** ($CDCl_3$, 300 MHz). **1b**: 4.48-4.27 (3 H, m), 3.00-2.68 (2 H, m); **2b**: 5.30 (1 H, m), 4.52-4.10 (3 H, m), 3.20 (1 H, dd, J = 5.0, 10.5 Hz), 3.01-2.68 (3 H, m); **3b**: 4.44-4.25 (3 H, m), 3.62 (1 H, m), 3.00-2.68 (2 H, m); **4b**: 6.30 (0.3 H, d, J = 3.5 Hz), 5.63 (0.3 H, dd, J = 1.8, 8.2 Hz), 5.20-5.00 (1.7 H, m), 4.37-3.68 (7.7 H, m), 3.05-2.81 (1 H, m), 2.73-2.50 (1 H, m), 2.18-2.00 (12 H, m); **5b**: 5.11 (1 H, s), 4.40 (1 H, m), 4.16-3.98 (4 H, m), 3.85, 3.76 (0.5 H each, dd each), 3.20-2.95 (2 H, m), 2.72-2.46 (3 H, m); **6b**: 5.55, 5.53 (0.5 H each, s each), 4.69 (1 H, m), 4.48-4.38 (3 H, m), 4.18-3.92 (4 H, m), 3.86-3.61 (3 H, m), 3.50-3.40 (2 H, m), 3.38-2.60 (4 H, m).

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