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Note

# A mild and selective cleavage of trityl ethers by $CBr_4$–MeOH☆

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**Abstract**

Trityl ethers are selectively deprotected to the corresponding alcohols in high yields by $CBr_4$ in refluxing methanol under neutral reaction conditions. Other hydroxyl protecting groups like isopropylidene, allyl, benzyl, acetyl, benzoyl, methyl, tosyl, prenyl, propargyl, *tert*-butyldiphenylsilyl and *p*-methoxybenzyl ethers are unaffected. 

*Keywords:* Trityl ethers; Carbon tetrabromide; Alcohols

Trityl ethers are widely used protecting groups for primary alcohols, especially in carbohydrate chemistry [1], but procedures for their selective cleavage are scarce. Among various hydroxyl protecting groups, the trityl ether is one of the most commonly used due to its ease of formation/removal and stability towards a variety of reaction conditions. A few methods are reported for its cleavage which include formic acid [2], 80% acetic acid [3], mineral acids [4], zinc bromide [5], trifluoroacetic acid [6], iodine–MeOH [7], ceric ammonium nitrate [8], ferric chloride [9] and $BCl_3$ [10]. In order to avoid the cleavage of the glycosidic bond and the hydrolysis of acetate, some of the methods [11,12] are reported under mild conditions. Most of these methods suffer from the use of strongly acidic conditions, formation of byproducts, cleavage of the glycosidic bond, hydrolysis of acetates, unsatisfactory yields and incompatibility with other functional groups present in the substrate. These limitations prompted us to disclose a new and efficient procedure for selective cleavage of trityl ethers over a wide range of functional groups.

In this communication, we wish to report a facile cleavage of trityl ethers using $CBr_4$ in methanol at reflux temperature. The cleavage proceeds smoothly in high yields by the reaction of trityl ethers with a catalytic amount of $CBr_4$ in refluxing methanol. Trityl and dimethoxytrityl ethers are selectively cleaved without causing any damage to the glycosidic bond and the *O*-isopropylidene group. The more acid-sensitive dimethoxytrityl group is removed more rapidly and at a lower temperature than the trityl group. There are several advantages for the use of $CBr_4$ in methanol, which selectively cleaves trityl ethers leaving other hydroxyl protecting groups intact. Such

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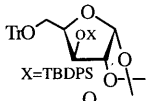
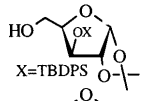
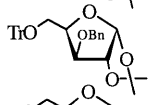
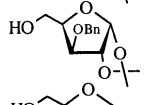
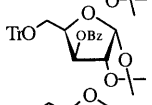
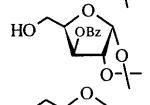
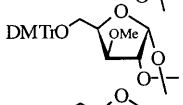
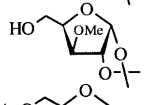
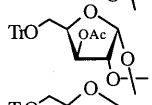
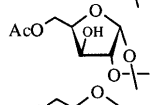
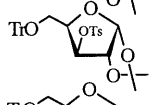
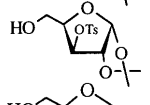
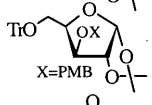
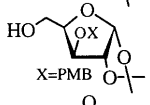
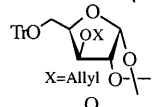
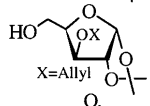
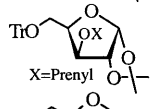
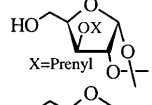
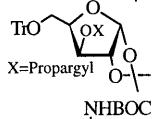
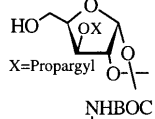
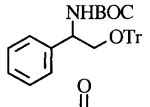
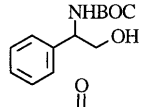
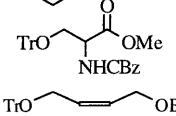
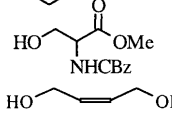
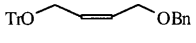
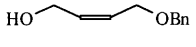
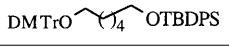
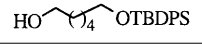
a selectivity is a highly desirable feature in the cleavage of trityl ethers, which offers various beneficial prospects to synthetic organic chemistry. The reaction conditions are compatible with other hydroxyl protecting groups like Bn, Bz, Me, Ac, Ts, allyl, prenyl, propargyl, PMB and TBDPS present in the substrate. Other acid-sensitive protecting groups such as BOC and CBz are also unaffected under these reaction conditions. The trityl group is removed rapidly in high yields with the migration of acetate and the *O*-isopropylidene group left

Table 1
Selective cleavage of trityl ethers by $CBr_4$–MeOH

| Entry | Trityl ether **1** | Alcohol [a] **2** | Reaction time (h) | Yield [b] (%) |
|---|---|---|---|---|
| a. |  |  | 2.5 | 88 |
| b. |  |  | 3.0 | 93 [d] |
| c. |  |  | 3.5 | 90 [d] |
| d. |  |  | 1.5 | 94 |
| e. |  |  | 2.0 | 87 [c,d] |
| f. |  |  | 3.5 | 90 |
| g. |  |  | 3.0 | 92 [e] |
| h. |  |  | 3.5 | 90 |
| i. |  |  | 1.5 | 88 |
| j. |  |  | 2.5 | 91 |
| k. |  |  | 4.5 | 90 [f] |
| l. |  |  | 4.0 | 85 |
| m. |  |  | 5.0 | 92 |
| n. |  |  | 1.5 | 88 [f] |

[a] All products were characterized by $^1H$ NMR and IR spectra and also by comparison with authentic samples. The spectroscopic data was identical with the data reported in the literature.
[b] Isolated yields after purification.
[c] Acetate migration was observed.
[d] For spectroscopic data see [15].
[e] For spectroscopic data see [14].
[f] For spectroscopic data see [13].

intact (Table 1, entry c). Among various solvents studied, methanol was found to be more effective for this cleavage. The occurrence of this cleavage may be attributed to the formation of HBr in situ itself by the reaction of $CBr_4$ with MeOH. To confirm the effect of solvent, the reactions were also carried out in refluxing acetonitrile in the presence of 10% $CBr_4$, which resulted in moderate yields (45–65%) of cleavage products after a long reaction time (8–12 h). Even though the deprotection is slow by $CBr_4$ in refluxing acetonitrile, various functional groups like acetates, THP ethers and epoxides are unaffected. Most of the starting materials and the products were known in literature, and their characterization was easily achieved from $^1$H NMR spectra. The starting materials showed triphenyl proton signals, while the products showed an upfield shift of H-5 and H-5′ and the disappearance of trityl signals. The spectroscopic data of the products was identical with the data reported in the literature. No racemization was observed under the present reaction conditions, which was confirmed by the comparison of optical rotation of compound **2b** {$[\alpha]_D$ −58.5° (*c* 7.5, $CHCl_3$)} with an authentic sample [9] {$[\alpha]_D$ −58.7° (*c* 7.5, $CHCl_3$)}. The results summarized in Table 1 reveal the scope and selectivity of the reaction with respect to various functionalized ethers.

In summary, this communication describes a mild and efficient procedure for chemoselective removal of the trityl group by $CBr_4$ in refluxing methanol. The method offers several advantages like mild reaction conditions, simple experimental/workup procedures, high yields of detritylated products, inexpensive reagents and compatibility with other acid-sensitive functional groups. This method will extend the scope of applicability of the trityl group by obviating the difficulty often encountered in its cleavage.

## 1. Experimental

*General methods.*—$^1$H and $^{13}$C NMR spectra were recorded on a Varian Gemini-200 spectrometer. The samples were dissolved in $CDCl_3$ using $Me_4Si$ as the internal standard, and chemical shifts are reported as $\delta$ values. IR spectra were recorded on a Nicolet 740 FTIR spectrophotometer. Optical rotations were recorded on Jasco DIP 360 digital polarimeter. Thin-layer chromatography (TLC) was checked on 0.25 μm E. Merck precoated Silica Gel 60 $F_{254}$ plates with detection by charring with 30% (v/v) $H_2SO_4$ in MeOH. The solvents MeOH and MeCN were distilled over magnesium cake and $P_2O_5$, respectively.

*Detritylation procedure.*—A mixture of trityl ether (5 mmol) and $CBr_4$ (0.5 mmol) in freshly distilled MeOH (15 mL) was refluxed for an appropriate time as required to complete the reaction. On completion, as indicated by TLC, the reaction mass was cooled to rt, diluted with water, and extracted twice with EtOAc (2 × 15 mL). The combined organic layers were washed with brine, dried over anhyd $Na_2SO_4$ and concentrated in vacuo. The resulting product was purified by column chromatography on silica gel (E. Merck, 100–200 mesh, 2:8 EtOAc–hexane) to afford the pure alcohol.

The $^1$H NMR data of some compounds are as follows.

**1a**: $^1$H NMR ($CDCl_3$): $\delta$ 7.70 (m, 2 H), 7.45–7.25 (m, 23 H), 5.85 (d, 1 H, *J* 4.0 Hz), 4.30 (d, 1 H, *J* 3.7 Hz), 4.20 (d, 1 H, *J* 4.0 Hz), 4.15 (m, 1 H), 3.60 (dd, 1 H, *J* 3.8 and 7.8 Hz), 3.15 (dd, 1 H, *J* 3.8 and 7.8 Hz), 1.45 (s, 3 H), 1.20 (s, 3 H), 0.9 (s, 9 H). **2a**: $\delta$ 7.65 (m, 4 H), 7.40 (m, 6 H), 5.90 (d, 1 H, *J* 4.1 Hz), 4.30 (d, 1 H, *J* 3.8 Hz), 4.25 (d, 1 H, *J* 4.1 Hz), 4.15 (m, 1 H), 3.85 (dd, 1 H, *J* 4.0 and 8.0 Hz), 3.65 (dd, 1 H, *J* 4.0 and 8.0 Hz), 1.75 (brs, 1 H, OH), 1.40 (s, 3 H) 1.20 (s, 3 H), 1.05 (s, 9H). **1b**: $\delta$ 7.50–7.30 (m, 20 H), 5.90 (d, 1 H, *J* 4.2 Hz), 4.58 (d, 1 H, *J* 4.2 Hz), 4.60, 4.45 (2 d, 2 H, *J* 12.8 Hz), 4.35 (m, 1 H), 4.05 (d, 1 H, *J* 3.7 Hz), 3.50 (dd, 1 H, *J* 4.2 and 8.7 Hz), 3.35 (dd, 1 H, *J* 4.2 and 8.7 Hz), 1.50, (s, 3 H), 1.30 (s, 3 H). **2b**: $\delta$ 7.45–7.35 (m, 5 H), 5.90 (d, 1 H, *J* 4.2 Hz), 4.58 (d, 1 H, *J* 4.2 Hz), 4.65–4.45 (2 d, 2 H, *J* 12.8 Hz), 4.25 (m, 1 H), 4.05 (d, 1 H, *J* 3.7 Hz), 3.95–3.85 (m, 2 H), 2.15 (brs, 1 H, OH), 1.55 (s, 3 H), 1.35 (s, 3 H). **1c**: $\delta$ 8.25 (m, 6 H), 7.75 (m, 3 H), 7.55 (m, 7 H), 7.35 (m, 2 H), 7.15 (m, 2 H), 5.90 (d, 1 H, *J* 4.0 Hz), 5.55 (dd, 1 H, *J* 3.7 Hz), 5.30 (d, 1 H, *J* 4.0 Hz), 4.60 (m, 1 H), 3.55 (dd, 1 H, *J* 4.0 and 8.2 Hz), 3.35 (dd, 1 H, *J* 4.0 and

8.2 Hz), 1.45 (s, 3 H), 1.25 (s, 3 H). **2c**: $\delta$ 8.15 (m, 2 H), 7.60 (m, 1 H), 7.45 (m, 2 H), 6.0 (d, 1 H, *J* 4.1 Hz), 5.45 (d, 1 H, *J* 3.8 Hz), 4.65 (d, 1 H, *J* 4.1 Hz), 4.50 (m, 1 H), 3.85 (dd, 1 H *J* 4.0 and 8.2 Hz), 3.70 (dd, 1 H, *J* 4.0 and 8.2 Hz), 1.45 (s, 3 H), 1.25 (s, 3 H). **1d**: $\delta$ 7.50 (m, 4 H), 7.30 (m, 9H), 5.85 (d, 1 H, *J* 4.0 Hz), 4.55 (d, 1 H, *J* 4.0 Hz), 4.35 (m, 1 H), 3.90 (s, 6 H), 3.78 (d, 1 H, *J* 3.7 Hz), 3.45 (dd, 1 H, *J* 3.0 and 7.5 Hz), 3.35 (s, 3 H), 3.25 (dd, 1 H, *J* 3.0 and 7.5 Hz), 1.55 (s, 3 H), 1.35 (s, 3 H). **2d**: $\delta$ 5.87 (d, 1 H, *J* 4.0 Hz), 4.55 (d, 1 H, *J* 4.0 Hz), 4.25 (m, 1 H), 3.80 (m, 2 H), 3.75 (d, 1 H, *J* 3.7 Hz), 3.40 (s, 3 H), 2.30 (brs, 1 H, OH), 1.50 (s, 3 H), 1.30 (s, 3 H). **1f**: $\delta$ 7.75–7.55 (m, 19 H), 5.85 (d, 1 H, *J* 4.0 Hz), 4.80 (d, 1 H, *J* 3.8 Hz), 4.45 (d, 1 H, *J* 4.0 Hz), 4.25 (m, 1 H), 3.55 (dd, 1 H, *J* 3.7 and 8.7 Hz), 3.15 (dd, 1 H, *J* 3.7 and 8.7 Hz), 2.45 (s, 3 H), 1.45 (s, 3 H), 1.25 (s, 3 H). **2f**: $\delta$ 7.85 (d, 2 H, *J* 8.7 Hz), 7.45 (d, 2 H, *J* 8.7 Hz), 5.90 (d, 1 H, *J* 4.0 Hz), 4.85 (d, 1 H, *J* 3.7 Hz), 4.50 (d, 1 H, *J* 4.0 Hz), 4.25 (m, 1 H), 3.75 (dd, 1 H, *J* 3.7 and 8.7 Hz), 3.60 (dd, 1 H, *J* 3.7 and 8.7 Hz), 2.40 (s, 3 H), 1.45 (s, 3 H), 1.25 (s, 3 H). **1h**: $\delta$ 7.45 (m, 6 H), 7.25 (m, 9H), 5.85 (d, 1 H, *J* 4.1 Hz), 4.75 (m, 1 H), 5.18 (m, 2 H), 4.48 (d, 1 H, *J* 4.1 Hz), 4.30 (m, 1 H), 4.05 (m, 1 H), 3.90 (d, 1 H, *J* 3.8 Hz), 3.85 (m, 1 H), 3.45 (dd, 1 H, *J* 2.7 and 8.0 Hz), 3.24 (dd, 1 H, *J* 2.7 and 8.0 Hz), 1.48 (s, 3 H), 1.30, (s, 3 H). **2h**: $\delta$ 5.92 (d, 1 H, *J* 4.0 Hz), 5.85 (m, 1 H), 5.25 (m, 2 H), 4.55 (d, 1 H, *J* 4.0 Hz), 4.25 (m, 1 H), 4.15 (m, 1 H), 4.05 (m, 1 H), 3.95 (d, 1 H, *J* 3.7 Hz), 3.85 (m, 2 H), 1.45 (s, 6 H), 1.25 (s, 3 H). **1i**: $\delta$ 7.45 (m, 6 H), 7.20 (m, 9 H), 5.80 (d, 1 H, *J* 4.0 Hz), 5.25 (m, 1 H), 4.45 (d, 1 H, *J* 4.0 Hz), 4.25 (m, 1 H), 4.10 (m, 1 H), 4.05 (m, 1 H), 3.90 (d, 1 H, *J* 3.7 Hz), 3.40 (dd, 1 H, *J* 3.7 and 7.8 Hz), 3.20 (dd, 1 H, *J* 3.7 and 7.8 Hz), 1.75 (s, 3 H), 1.65 (s, 3 H), 1.45 (s, 3 H), 1.25 (s, 3 H). **2i**: $\delta$ 5.90 (d, 1 H, *J* 4.0 Hz), 5.30 (m, 1 H), 4.50 (d, 1 H, *J* 4.0 Hz), 4.25 (m, 1 H), 4.15 (m, 1 H), 4.05 (m, 1 H), 3.87 (d, 1 H, *J* 3.8 Hz), 3.80 (m, 2 H), 2.50 (brs, 1 H, OH), 1.75 (s, 3 H), 1.70 (s, 3 H), 1.45 (s, 3 H), 1.30 (s, 3 H). **1j**: $\delta$ 7.40 (m, 6 H), 7.20 (m, 9H), 5.85 (d, 1 H, *J* 4.2 Hz), 4.45 (d, 1 H, *J* 4.2 Hz), 4.25 (m, 1 H), 4.05 (m, 1 H), 3.95 (d, 1 H, *J* 3.8 Hz), 3.88 (m, 1 H), 3.40 (dd, 1 H, *J* 3.8 and 8.0 Hz), 3.20 (dd, 1 H *J* 3.8 and 8.0 Hz), 1.8 (m, 1 H), 1.45 (s, 3 H), 1.25 (s, 3 H). **2j**: $\delta$ 5.90 (d, 1 H, *J* 4.1 Hz), 4.50 (d, 1 H, *J* 4.1 Hz), 4.30 (m, 1 H), 4.15 (m, 1 H), 4.05 (m, 1 H), 3.95 (d, 1 H, *J* 3.8 Hz), 3.85 (m, 2 H), 1.80 (m, 1 H), 1.40 (s, 3 H), 1.25 (s, 3 H). **1l**: $\delta$ 7.45 (m, 5 H), 7.35–7.15 (m, 15 H), 5.75 (brs, 1 H, NH), 5.15 (s, 2 H), 4.45 (m, 1 H), 3.85 (s, 3 H), 3.45 (m, 2 H). **2l**: 7.45 (m, 5 H), 5.85 (brs, 1 H, NH), 5.20 (s, 2 H), 4.50 (m, 1 H), 3.95 (m, 2 H), 2.20 (brs, 1 H, OH). **1m**: $\delta$ 7.35–7.25 (m, 20 H), 5.75 (m, 2 H), 4.45 (s, 2 H), 3.65 (d, 2 H *J* 6.8 Hz), 3.90 (d, 2 H, *J* 6.8 Hz). **2m**: $\delta$ 7.30 (m, 5 H), 5.80 (m, 2 H), 4.50 (s, 2 H), 4.10 (d, 2 H, *J* 6.8 Hz), 4.05 (d, 2 H, *J* 6.8 Hz), 2.50 (brs, 1 H, OH).

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## References

[1] (a) T.W. Greene, P.G.M. Wuts, *Protective Groups in Organic Synthesis*, 3rd ed., Wiley, New York, 1999. (b) P.J. Kocienski, *Protecting Groups* Georg Thieme Verlag, Stuttgart 1994.
[2] M. Bessodes, D. Komiotis, K. Antonakis, *Tetrahedron Lett.*, 27 (1986) 579–582.
[3] F. Micheel, *Ber. Dtsch. Chem. Ges.*, 65 (1932) 262–265.
[4] (a) Y.M. Choy, A.M. Unrau, *Carbohydr. Res.*, 17 (1971) 439–443. (b) N.C. Yung, J.J. Fox, *J. Am. Chem. Soc.*, 83 (1961) 3060–3066.
[5] H. Koster, N.D. Sinha, *Tetrahedron Lett.*, 23 (1982) 2641–2644.
[6] M. MacCoss, D.J. Cameron, *Carbohydr. Res.*, 60 (1978) 206–209.
[7] J.L. Wahlstrom, R.C. Konald, *J. Org. Chem.*, 63 (1998) 6021–6022.
[8] J.R. Hwu, M.L. Jain, S.C. Tsay, G.H. Hakimelahi, *Chem. Commun. (Cambridge)*, (1996) 545–546.
[9] X. Ding, W. Wang, F. Kong, *Carbohydr. Res.*, 303 (1997) 445–448.
[10] G.B. Jones, G. Hynd, J.M. Wright, A. Sharma, *J. Org. Chem.*, 65 (2000) 263–265.
[11] J. Lehrfeld, *J. Org. Chem.*, 32 (1967) 2544–2546.
[12] J. Fuentes, T. Cuevas, M.A. Pradera, *Synth. Commun.*, 24 (1994) 2237–2245.
[13] J.S. Yadav, H.M. Meshram, G.S. Reddy, G. Sumithra, *Tetrahedron Lett.*, 39 (1998) 3043–3046.
[14] A. Bouzige, G. Sauve, *Tetrahedron Lett.*, 40 (1999) 2883–2886.
[15] Y. Ishido, N. Sabuiri, M. Sekiga, N. Nakazaki, *Carbohydr. Res.*, 97 (1981) 51–79.