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LiCl-mediated, easy and low-cost removal of the trityl group from protected alcohols and diols

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Dedicated to Professor Joaquín Plumet on occasion of his retirement

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Abstract: The reaction of primary, secondary, phenyl, allyl and benzyl trityl ethers with lithium chloride in methanol at reflux led to deprotection of the trityl group affording the corresponding alcohol in good to excellent yields under mild reaction conditions.

The trityl (triphenylmethyl) group is often employed for the selective protection of primary alcohols and amines in carbohydrate,[1] peptide[2] and nucleotide[3] chemistry, due to its high steric demand. On the other hand, the cleavage of trityl ethers is involved in the manufacture of a number of pharmaceuticals, drugs and other fine chemicals.[4]

In the search for useful methods for the selective deprotection of trityl protected alcohols or phenols,[5] various conditions for reductive cleavage of the trityl-oxygen bond have been reported including triethylsilane,[6] or low-valent titanium reagents.[7] Catalytic cerium(IV) ammonium nitrate adsorbed onto silica gel can efficiently oxidatively cleave the trityl-oxygen bond in nucleosides and nucleotides.[8] This protecting group can be also easily removed using Brønsted[9] and Lewis acids[10] or bases,[11] electrolytically,[12] and by catalytic hydrogenation[13] or reduction with sodium in liquid ammonia;[14] however most of these procedures are incompatible with reducible functionalities, including multiple bonds.

In the last few years, our group has been interested in the deprotection of several functional groups using naphthalene-catalyzed lithiation,[15] including trityl ethers,[16] trityl amines,[17] silylated alcohols, amines and thiols,[18] Alloc- or Cbz- or Boc-protected alcohols, amines or thiols,[19] esters, amides and thioesters,[20] and *N*-pivaloyltetrazoles.[15l] Other metals, such as indium[21] or zinc[22] under protic conditions (MeOH), have been used for the deprotection of *N*-tritylated tetrazoles.