SYNLETT
Spotlight 42

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Thallium Trinitrate (TTN)

Compiled by Tiago Oliveira Vieira

Tiago O. Vieira was born in Salvador, Brazil in 1977. He studied chemistry at the University of São Paulo where he received his BSc degree in 2000. He joint the group of Prof. Helena M. C. Ferraz in 1996 as an undergraduate researcher and is currently working toward his PhD under her supervision at the University of São Paulo. He is recipient of a FAPESP scholarship and his research involves the ring contraction reactions mediated by thallium(III) salts and its application to the total synthesis of bakkanes.

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Introduction

Thallium(III) salts have proved to be very versatile reagents to oxidize a great variety of organic functionalities, as attested by the several review articles in the field.[1,2] They are highly toxic and must be handled with care. However, they are not cumulative, since they are excreted in urine. The three most common salts are the thallium triacetate (TTA), thallium *tris*-trifluoroacetate (TTFA) and thallium trinitrate (TTN), the latter having the broader application.

TTN was firstly employed in organic synthesis, during the 70's, in the oxidation of olefins and ketones, leading, respectively, to aldehydes and carboxylic acid derivatives, as reviewed by McKillop.[3] TTN is highly ionic and shows great solubility either in inorganic or in organic solvents. TTN can also be supported on clays, such as Montmorillonite K-10. The thallium(I) nitrate formed in the end of the reactions is insoluble in almost all common solvents. Thus, the reaction can often be monitored by the formation of a precipitate, which can be easily separated from the product by filtration.

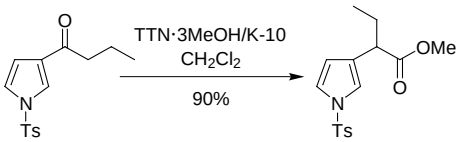
Another important aspect is the poor nucleophilicity of the nitrate ion. In this way, it is rarely incorporated into the final product.

Preparation

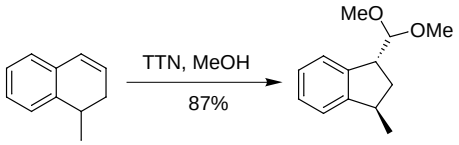
TTN·$3H_2O$ is commercially available as a crystalline and stable solid. However, this salt can be prepared from thallium(III) oxide, whose price is significantly lower, and concentrated nitric acid.[4]

Abstracts

The very first use of TTN by organic chemists was in the rearrangement of ketones, making possible, direct access to carboxylic esters.[3] An application of such a rearrangement was the preparation of pyrrole monomers, by using TTN supported on Montmorillonite clay K-10, as recently reported.[5]



A convenient application of TTN in organic synthesis is the oxidative rearrangement of olefins. In this fashion, cyclohexene is classically converted into a cyclopentane moiety.[3] Such a reaction has been recently used to obtain the indan ring system in a highly diastereoselective manner, starting from a readily available 1,2-dihydronaphtalene.[6]



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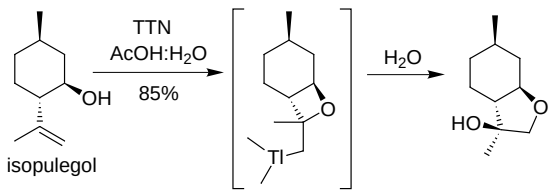
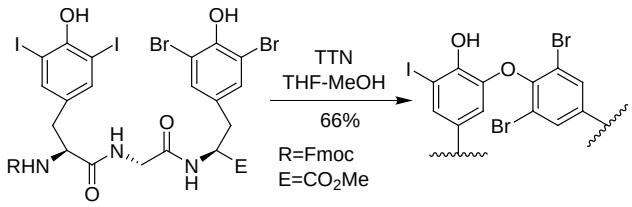
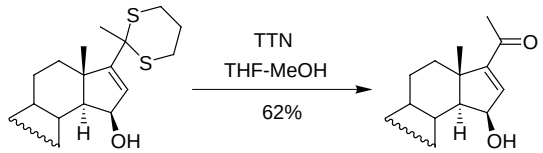
Electrophilic cyclization of unsaturated substrates bearing an internal nucleophile mediated by TTN and other thallium(III) salts is an useful transformation, known since the pioneer work of Bartlett[7] in the 80's. The special feature of this kind of reactions is the fact that thallium, contrary to all other electrophiles, is not incorporated in the final product, owing to an additional step of solvolysis of the oxythallated adduct. A very interesting example of such a transformation is the cyclization of monoterpenic alkenols, such as isopulegol.[8] This protocol was employed in the synthesis of monoterpene (–)-mintlactone.[9]



Since the early 80's, Yamamura[10] and Evans[11] have been using TTN to perform phenolic oxidative couplings in aromatic systems, towards the synthesis of natural products, such as vancomycin. In these macrocyclizations, halogens at both ortho-positions are required for the S_NA reaction to occur. Excess of oxidant is usually required.[12]



Hydrolysis of dithianes is probably the least known, but not the least important application of TTN. This reaction was firstly demonstrated by Smith and Hannah.[13] The last use of this reaction was during the construction of xestobergsterol skeleton, when all classic methods failed.[14]



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