SYNLETT Spotlight 422

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

Triflic Acid

Compiled by Nicolas Gigant

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Introduction

Trifluoromethanesulfonic acid (TfOH), more commonly named triflic acid, is one of the strongest Brønsted acids and well known as a ‘super acid’ with a pKₐ of −13.6. The reagent is a colorless liquid and stable towards heating, oxidation and reduction. It was first synthesized in 1954 by Haszeldine and Kidd by oxidation of bis(trifluoromethylthio)mercury with aqueous hydrogen peroxide.¹ It is available on an industrial scale and is produced by electrochemical fluorination. Triflic acid is an effective reagent widely used in organic chemistry and especially as catalyst (historically for esterification and salt formation),² even if more than one equivalent is often used.³ However, its utilization mainly includes addition to α-carbonylated alkynes,⁴ hydrogenation,⁵ Friedel–Crafts reaction,⁶ polymerization,⁷ cycloaddition,⁸ deprotection,⁹ initiation of cyclisation sequences,¹⁰ and as a counterion both for iodonium salts¹¹ and N-heterocyclic carbenes.¹²

Abstracts

(A) TfOH as Catalytic Reagent:
An efficient metal-free diacetoxylation reaction of alkenes catalyzed in the presence of 10 mol% of triflic acid has been described by Gade.²⁵ TfOH plays a double role in this process: it catalyzes the ring-opening of the intermediate epoxide as well as the subsequent acetylation of the hydroxyl group.

(B) Addition to α-Carbonylated Alkynes:
Various vinyl trifluoromethylsulfonates have been recently isolated by the addition of triflic acid to the triple bond of propynoate derivatives.⁴ The stereoselectivity could be controlled by adjusting the reaction conditions. Moreover, the generated vinyl triflates are very reactive intermediates towards metal cross-coupling reactions.¹³

(C) Synthesis of Aryl Triflates:
Another application of triflic acid was illustrated by the synthesis of a potential medicinal agent.¹⁴ After catalytic hydrogenation of the bromine atom, the corresponding naphthylidin was transformed by diazotization of the amine followed by a nucleophilic substitution with TfOH. The resulting aryl triflate was used in a selective Suzuki–Miyaura cross-coupling to give the desired scaffold with good yield.
(D) Catalytic Asymmetric Hydrogenation:
A simple enantioselective hydrogenation catalyzed by an iridium–
diphosphine complex with a catalytic amount of activator was re-
ported by Zhou and co-workers.15 Both the reactivity and enantio-
selectivity were enhanced in the presence of 10 mol% of TfOH. The
complex ‘piperidine-TfOH’ is also efficient.

\[
\begin{align*}
\text{[Ir(COD)Cl]}_2 & \quad \text{PhMe} \\
\text{H}_2 & \quad \text{(700 psi), THF} \\
\text{TfOH (10 mol%)} & \quad >95\% \text{ conversion} \\
\end{align*}
\]

References


(E) Polymerization Catalyzed by TfOH:
Mathers et al. proposed the first polymerization method using hy-
droalkoxylation and hydrocarboxylation reactions catalyzed under
acidic conditions.7 In presence of triflic acid, the conversion, the
weight average, and the molecular weight are improved compared to
the use of H$_2$SO$_4$.

\[
\begin{align*}
\text{Products} & \quad >97\% \text{ conversion} \\
\text{Mn} & \quad 9100 \text{ g/mol} \\
\end{align*}
\]

(F) TfOH as a Deprotecting Agent:
TfOH has been involved in a fast and convenient microwave-assist-
ited N-debenzylation of amides with a benzyl cation as the intermedi-
ate.8 Both secondary and tertiary amides bearing various functional
groups were isolated in good to high yield. Attempts to reduce
the number of equivalents of TfOH, decreased the conversion
dramatically.

\[
\begin{align*}
\text{R1} & \quad \text{Alk, Ar} \\
\text{R2} & \quad \text{Alk, Ar, H} \\
\text{PhMe} & \quad \text{H2 (700 psi), THF} \\
\text{TfOH (4 equiv)} & \quad 17 \text{ examples up to 92% yield} \\
\end{align*}
\]

(G) Domino Reaction:
Gillaizeau and co-worker have demonstrated that triflic acid can be
involved in a domino reaction for the diastereoselective synthesis of
polyfunctionalized nitrogen-fused tetrahydroquinoline frameworks
involved in a domino reaction for the diastereoselective synthesis of
polyfunctionalized nitrogen-fused tetrahydroquinoline frameworks
or 2,3-functionalized enamides.10 The rearrangement and the forma-
tion of the iminium ion intermediate are initiated by triflic acid.
Products were obtained in low yield using a substoichiometric
quantity of TfOH.

\[
\begin{align*}
\text{R1} & \quad \text{Alk, CO2R, halogen, NO2} \\
\text{R2} & \quad \text{H, Me} \\
\text{TfOH (1.2 equiv)} & \quad 15 \text{ examples up to 85% yield} \\
\text{PhMe} & \quad \text{11 examples up to 93% yield} \\
\end{align*}
\]

(H) Counter-ion for Diaryliodonium Triflates:
Triflic acid has been selected for the synthesis of diaryliodonium
salts. Olofsson and co-workers have developed an efficient one-pot
synthesis starting from aryl iodides and amines.11 The aryl iodide
is oxidized by MCPBA to an iodine(III) intermediate. The arene at-
tacks the hypervalent iodine in presence of triflic acid giving the di-
aryliodonium salt. The scope of the reaction includes symmetric and
unsymmetric salts with high yield. These electrophilic species have
recently received considerable attention and are involved in a wide
array of reactions.12

\[
\begin{align*}
\text{R1} & \quad \text{Alk, halogen, NO2} \\
\text{R2} & \quad \text{R2, R3 = H} \\
\text{TfOH (0 equiv)} & \quad 11 \text{ examples up to 100% yield} \\
\text{MCPBA} & \quad \text{Cl2CH2} \\
\end{align*}
\]