Synlett J. V. Santiago Spotlight

p-Toluenesulfonyl Azide

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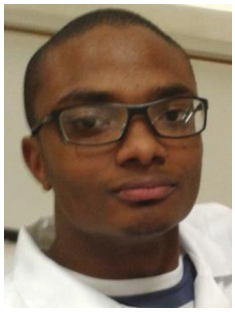
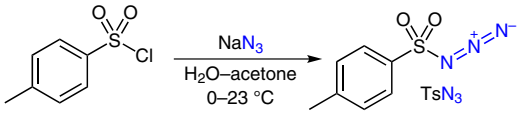


João Victor Santiago was born in 1991 in Brasília, Brazil. He obtained his B.Sc. in Chemistry (2012) and his M.Sc. in Organic Chemistry (2014) from the University of Brasília-UnB. Currently, he works towards his Ph.D. under the guidance of Professor Antonio C. B. Burtoloso. His research focuses on the synthesis of hexahydropyridazines, 1,2-oxazinanes, and substituted cyclohexanes from α,β-unsaturated diazoketones.

Introduction

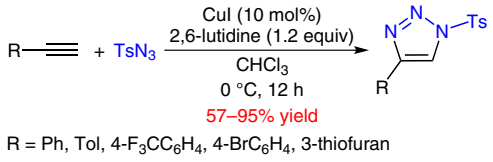
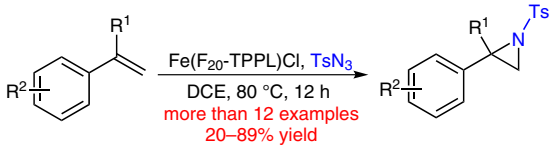
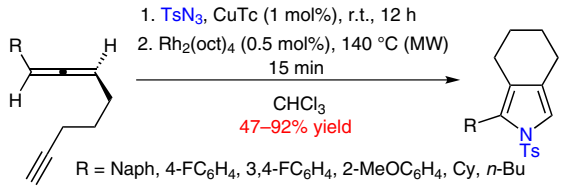
p-Toluenesulfonyl azide (TsN_3, CAS: 941-55-9) can be prepared in good yield from the reaction of *p*-toluenesulfonyl chloride (TsCl) and sodium azide (NaN_3) (Scheme 1).[1] TsN_3 is a colorless oil with a melting point of 21–22 °C and boiling point of 110–115 °C at 0.001mmHg.[2]



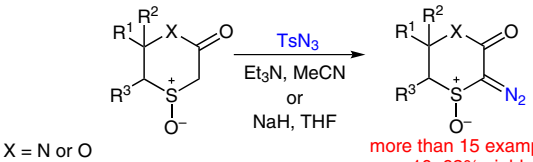
Scheme 1 Classic preparation of *p*-toluenesulfonyl azide

One of the most used applications of TsN_3 is the diazo transfer reaction. One of the first works to describe the concept of diazo transfer was published in 1910 by Dimroth.[3] Since this date, the application of TsN_3 in diazo chemistry is frequently mentioned. Other applications for TsN_3 include cycloaddition reactions, especially the [3+2] cycloaddition with alkynes for the formation of substituted triazoles.[4] Here, some recent examples of reactions employing TsN_3 are presented.

Table 1 Use of TsN_3

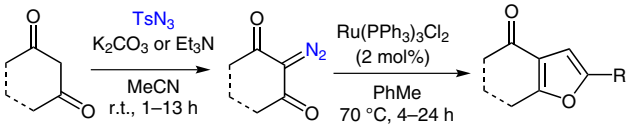
(A) Based on computational and mechanistic studies of copper-catalyzed azide–alkyne cycloaddition (CuAAC), Chang and co-workers[5] have reported the regioselective synthesis of a series of *N*-sulfonyl-1,2,3-triazoles. CuI was employed as catalyst and 2,6-lutidine as an additive. *N*-Sulfonyl-1,2,3-triazoles were synthesized in 57–95% yield.	 R = Ph, Tol, 4-$F_3CC_6H_4$, 4-BrC_6H_4, 3-thiofuran
(B) Zhang and co-workers[6] reported the use of iron porpholactones as catalysts for the aziridination of alkenes and for the amidation of alkanes. In the aziridination of alkenes, mainly styrene derivatives were utilized as substrates. TsN_3 acted as the nitrogen source. The authors synthesized a series of aziridines in 20–89% yield.	 R^1 = H or Me R^2 = 4-Me, 4-*t*-Bu, 4-F, 4-Cl, 4-Br, 4-OMe, 3-OMe, Ph
(C) The application of α-diazo-*N*-sulfonyl-imines as intermediates has often been reported.[7] In 2013, Schultz and Sarpong[8] performed the synthesis of 3,4-fused pyrroles using TsN_3 in the formation of α-Rh-imino-carbenoid as an intermediate by the reaction of α-diazo-*N*-tosyl-imines and a rhodium catalyst. In an one-pot methodology, the authors synthesized a series of 3,4-fused pyrroles in 47–92% yield.	 R = Naph, 4-FC_6H_4, 3,4-FC_6H_4, 2-$MeOC_6H_4$, Cy, *n*-Bu

(D) Collins et al.[9] reported the application of TsN_3 as a reagent in the synthesis of α-diazo-β-oxo-sulfoxides by a diazo-transfer reaction. In this work, the authors utilized sulfoxides containing monocyclic, bicyclic, or acyclic lactones and lactams. A series of α-diazo-β-oxo-sulfoxides were synthesized in 10–62% yield.

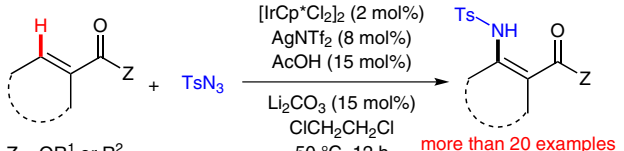


X = N or O
$R^3 = R^1$= -$(CH_2)_3$-, -$(CH_2)_4$-, -$(CH_2)_5$-, Me, Ph;
R^2 = H or Me

(E) Lee and Xia[10] have reported the regioselective synthesis of a series of functionalized furans from the reaction of terminal alkynes and cyclic or acyclic diazocarbonyl compounds. The authors utilized TsN_3 in a diazo-transfer reaction, furnishing diazocarbonyl compounds in 86–94% yield.[11] The products were utilized in the synthesis of functionalized furans in 29–89% yield by a ruthenium-catalyzed [3+2] cycloaddition.

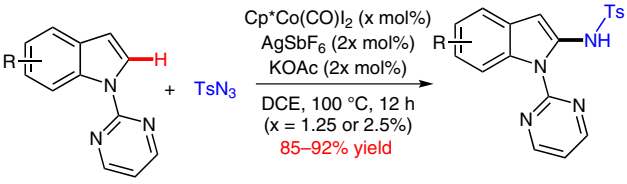


(F) C–H bond activation is versatility and has been widely applied in organic synthesis for the formation of functionalized bonds. In 2014, Chang and Kim[12] reported the iridium-catalyzed amidation of C–H bonds in α-aryl or α,β-unsaturated carbonyl compounds (esters or ketones). The authors propose that TsN_3 allows the formation of the C–N bond by insertion of the amide group, followed by the extrusion of molecular nitrogen. In this work, more than 20 products of C–H insertion were synthesized in 51–99% yield.



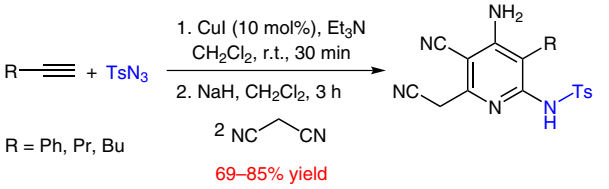
Z = OR^1 or R^2

(G) Kanai and co-workers[13] reported the directed selective amidation of C-2 carbons on an indole nucleus by C–H bond activation. The authors utilized an in situ generated cobalt catalyst for the transformation. TsN_3 was employed as the reagent for the insertion of *N*-tosyl into the C-2 carbon, furnishing the products in 85–92% yield.



R = H, 4-Br, 5-Me, 5-OMe, 5-CO_2Me,
5-F, 5-Cl, 5-Br, 6-Me, 6-OMe

(H) Yavari and co-workers[14] synthesized a series of pentasubstituted pyridines by copper catalysis using a tandem process. Sulfonyl compounds, including TsN_3, were utilized for the formation of sulfonoketenimides as key intermediates, which in one step furnished pentasubstituted pyridines with good yields (69–85%).



R = Ph, Pr, Bu

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