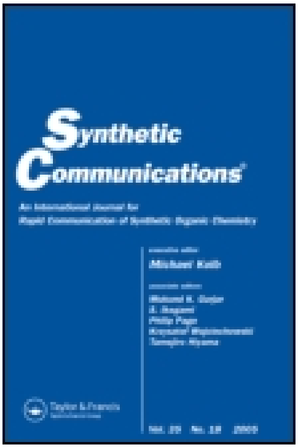

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Facile and Efficient Method for the Prins Reactions of Styrenes and Homoallyl Alcohols to 1,3-Dioxanes and 4-Tetrahydropyranols Using Bismuth(III) Triflate

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To cite this article: B. Sreedhar , V. Swapna , Ch. Sridhar , D. Saileela & A. Sunitha (2005) Facile and Efficient Method for the Prins Reactions of Styrenes and Homoallyl Alcohols to 1,3-Dioxanes and 4-Tetrahydropyranols Using Bismuth(III) Triflate, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 35:9, 1177-1182, DOI: 10.1081/SCC-200054759

To link to this article: http://dx.doi.org/10.1081/SCC-200054759

Synthetic Communications®, 35: 1177–1182, 2005
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ISSN 0039-7911 print/1532-2432 online
DOI: 10.1081/SCC-200054759

Facile and Efficient Method for the Prins Reactions of Styrenes and Homoallyl Alcohols to 1,3-Dioxanes and 4-Tetrahydropyranols Using Bismuth(III) Triflate

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Hyderabad, India

Abstract: Bismuth(III) triflate has been found to be an efficient catalyst for the Prins reactions of styrenes and homoallyl alcohols, the reaction proceeds rapidly and affords the corresponding 1,3-dioxanes and tetrahydropyran-4-ol in good yields. Scope and limitations of the styrenes and homoallyl alcohols are reported.

Keywords: Bismuth(III) triflate, 1,3-dioxanes, homoallyl alcohols, Prins reaction, tetrahydropyran-4-ol

Lewis-acid (LA) catalyzed reactions are of great interest because of their unique reactivity and selectivities and the mild reaction conditions they use.[1] The Prins reaction is a fundamental reaction for carbon–carbon bond formation and is one of the most effective reactions for the synthesis of tetrahydropyrans and dioxanes.[2] There are several types of Prins reactions present in the literature. Some of those are acid-catalyzed olefin–aldehyde condensations to form dioxanes[3] and coupling of homoallyl alcohols with several aldehydes to form tetrahydropyrans.[4] The importance of pyrans is exemplified by its presence in the backbone of various carbohydrates and natural

Received in India December 20, 2004

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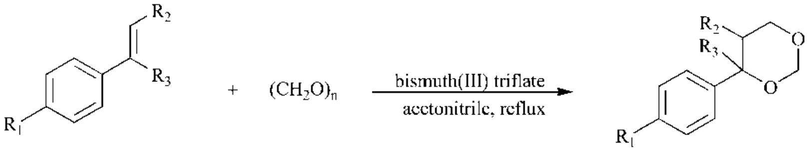
products.[5] The tetrahydropyran ring system is a core unit in a number of natural products. However, the synthesis and application of this important reaction has been underexplored because of the classical conditions of strong acids (e.g., sulfuric acid) and high reaction temperatures, which often generate a range of undesired products. In particular, the polymerization of the olefin that is induced by Lewis or Brønsted acids can severely interfere with desired C-C bond formation. However, many of these classical methods often involve the use of expensive reagents and extended reaction times and generate mixtures of unnecessary products.

Bismuth derivatives are attracting the attention of an increasing number of organic chemists.[6] Over the past few years, bismuth(III) triflate has been reported as a new and efficient catalyst for organic synthesis, which exhibits, in numerous cases, a stronger activity than other known metal triflates, in particular those of transition elements.[7] We are particularly interested in bismuth triflate because it is inexpensive and can be easily prepared in the laboratory from commercially available bismuth(III) oxide and triflic acid.[8]

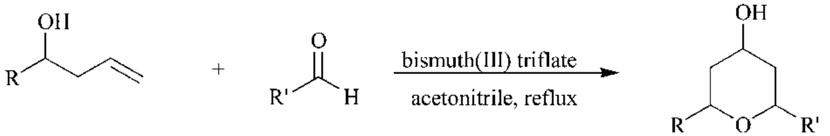
In view of this, we examined the Prins reactions between styrenes and paraformaldehyde (Scheme 1), and homoallyl alcohol and aldehydes (Scheme 2) to produce the corresponding 1,3-dioxanes and tetrahydropyran-4-ols.

Because it was observed that the treatment of styrene with paraformaldehyde in toluene in the presence of bismuth(III) triflate produced 4-phenyl-1,3-dioxane, a search for optimization was first carried out using this catalyst. As a result, the use of a 5 mol% catalyst in acetonitrile at 80 °C for 6 h was revealed to be the condition of choice (Scheme 1) in which the reaction proceeded smoothly to produce 4-phenyl-1,3-dioxane in 90% isolated yield. Solvent has pronounced effect in these reactions. Acetonitrile provided optimum yields, whereas toluene and chloroform offered lower yields. The optimum results were obtained by using 5 mol% catalyst. With 1 mol% catalyst, the reaction was slow and the product yield became low. The controlled Prins reaction conducted under identical conditions and devoid of $Bi(OTf)_3$ gave no products, despite prolonged time.

Subsequently, by controlling the reaction conditions, various tetrahydropyran-4-ols were synthesized via the reaction of homoallylic alcohols and aldehydes using bismuth(III) triflate as the catalyst (Scheme 2).



Scheme 1.



Scheme 2.

The reaction was then applied to a variety of structurally divergent styrenes and homoallyl alcohols to get the corresponding 1,3-dioxanes and tetrahydropyran-4-ols with good yields and the results are summarized in Table 1 and Table 2.

It was clear from Table 1 that styrenes containing electron-donating groups such as 4-methyl styrene (Table 1, entry 2) and 4-metoxy styrene (Table 1, entry 3) react faster and give the corresponding 1,3-dioxanes. When styrenes contain electron-withdrawing functional groups such as 4-chloro (Table 1, entry 4) and 4-acetoxy (Table 1, entry 5), styrene reacts slowly to yield the corresponding 1,3-dioxanes. Here, monmeric formaldehyde might be produced by the decomposition of paraformaldehyde because of the interaction with the bismuth(III) triflate.

It was clear from Table 2 that a variety of homoallyl alcohols were reacted with aldehydes to produce the corresponding tetrahydropyanols. The reactivity for aromatic aldehydes is more when compared to cyclic aldehydes.

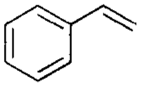
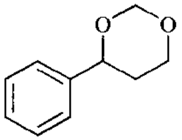
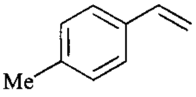
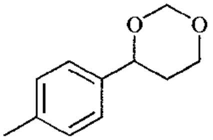
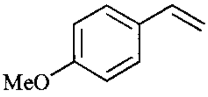
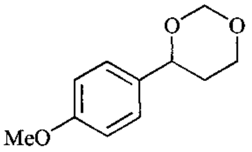
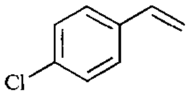
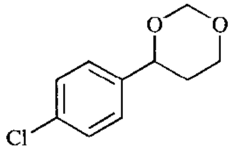
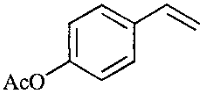
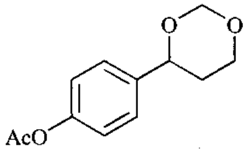
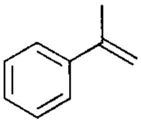
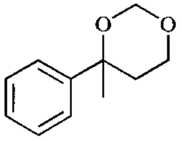
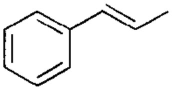
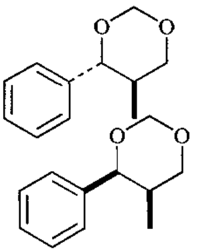
In summary, this work demonstrates a new method for high-yielding, selective synthesis of 1,3-dioxanes and tetrahydropyran-4-ols using bismuth(III) triflate. Advantages of this method include the highly catalytic nature of the reagent, low toxicity and low cost of the Lewis-acid catalyst, fast reaction rates, and insensitivity of the Lewis acid to air and moisture.

EXPERIMENTAL

Typical Experimental Procedure for the Prins reaction of Styrenes and Paraformaldehyde

To a mixture of styrene (1 mmol) and paraformaldehyde (10 mmol) in acetonitrile were added bismuth(III) triflate (5 mol%). The mixture was stirred at reflux temperature. The progress of the reaction was monitored by thin layer chromatography. After the completion of the reaction, the reaction was filtered, washed with water, and extracted into ethyl acetate. The combined organic layers were evacuated to obtain 4-phenyl-1,3-dioxane. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.69–1.75 (1H, m), 2.04–2.16 (1H, m),

Table 1. Prins reaction of styrenes with paraformaldehyde using Bi(OTf)$_3$[a]

Entry	Substrate	Product	Time (h)	Yield (%)[b]	Ref.
1			4	90	[9]
2			6	88	[9]
3			7	87	[9]
4			10	82	[9]
5			10	77	[9]
6			6	89	[9]
7			6	85[c]	[10]

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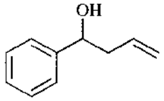
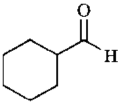
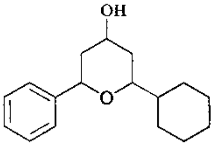
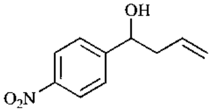
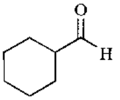
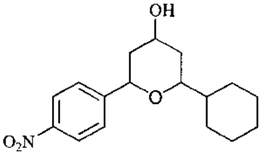
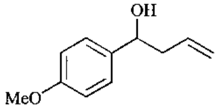
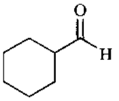
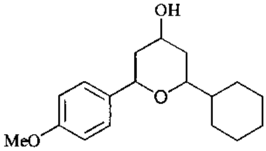
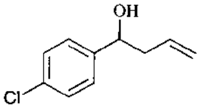
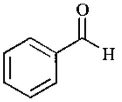
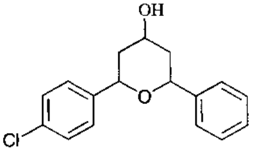
[a] Styrene (1 mmol), paraformaldehyde (10 mmol), acetonitrile (3 mL), Bi(OTf)$_3$ (20 mg).
[b] Based on isolated yields.
[c] Combined yield of two isomers.

Table 2. Prins reaction of aldehydes and homoallyl alcohols with $Bi(OTf)_3$[a]

Entry	Homoallyl alcohol	Aldehyde	Product	Yield (%)[b]
1				73
2				65
3				78
4				82

[a] Homoallyl alcohol (1 mmol), aldehyde (1 mmol), $Bi(OTf)_3$ (5 mol%), acetonitrile (3 mL), reflux.

[b] Based on isolated yields.

3.83–3.92 (1H, m), 4.17–4.24 (m, 1H), 4.65 (1H, dd), 4.90 (1H, d) 5.22 (1H, d), 7.24–7.4 (5H, m). MS m/z: 164, 118, 105 (100), 77.

ACKNOWLEDGMENTS

Ch. Sridhar thanks the Council of Scientific and Industrial Research, India, for a SRF fellowship.

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