



Tin(II)-chloride (SnCl₂) mediated reduction of α,β -alkynyl carbonyl compounds

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ABSTRACT

An efficient Tin(II)-chloride (SnCl₂) mediated reduction of α,β -alkynyl carbonyl compounds to their corresponding alkanes has been developed and reported. The developed method was optimized by varying parameters such as reaction time, temperature, and the equivalence of SnCl₂ using different solvents. The best reaction condition (80 % yield) involved 2.5 eq. of SnCl₂, at 25 °C for 3 h in ethyl acetate. This method is applicable for the reduction of α,β -alkynyl carbonyl of quinoxaline, pyrimidine, pyrazine and pyridine.

Introduction

Reduction is one of the most important reactions in organic chemistry owing to its significant importance in the synthesis of pharmaceutical drugs and fine chemicals [1]. Over the decades, the important usage of alkenes and alkynes in organic synthesis and natural products chemistry have paved way for the various methods for their reduction [2–4]. Among the reported methods for the hydrogenation of unsaturated hydrocarbons, reduction reaction is one of the most commonly used [5]. Due to its ability to be absorbed onto solid support such as activated carbon, alumina, calcium carbonate or barium sulphate [6], the reduction method that involves the direct addition of molecular hydrogen (H₂) in the presence of nickel (Ni), palladium (Pd), and platinum (Pt) has vastly been explored [7]. Hence, transition metal supported catalysts display excellent activity and selectivity due to their high capability for hydrogen activation [8]. Nevertheless, the use of transition metals has been restricted due to drawbacks such as, high commercial cost and the use of a highly flammable and explosive hydrogen gas [9]. Besides the use of molecular hydrogen, various reagents, such as formic acid [10], ethanol [11], isopropanol [12], 1,4-cyclohexadiene [13], amine borane adducts [14] etc., have been reported as the possible source of hydrogen molecule in the catalytic hydrogenation of alkenes and alkynes. The use of water as the hydrogen donor has also been reported to be highly attractive, since it is cheap, non-toxic, and environmentally friendly [15,16] Other methods for the reduction of unsaturated hydrocarbons that make use of additional

reagents, such as, sodium borohydride (NaBH₄), lithium aluminum hydride (LiAlH₄), di-isobutylaluminum hydride (DIBAL) and triethylsilane (Et₃SiH) have also been adopted for the reduction of alkenes and alkynes [2]. The selective reduction of alkynes into their corresponding alkenes and alkanes using modified borohydrides such as sodium cyano borohydride (NaBH₃CN) and lithium triethylborohydride (LiEt₃BH) have also been reported [17]. Generally, borohydrides are mostly deployed in the reduction of polar functional groups, especially carbonyl-containing groups such as ketones, aldehydes, and esters [18]. Recently, our research group discovered the SnCl₂ mediated reduction of the alkyne functional group of 1-(6-nitroquinoxaline-2-yl)hex-1-yn-3-one (1) to an alkane 3 as shown in Scheme 1. This was evident when SnCl₂ was used as a reducing agent in the reduction of the nitro group (NO₂) of 1-(6-nitroquinoxalin-2-yl)hex-1-yn-3-one. Interestingly, both the nitro and alkyne groups were reduced [19,20]. As a result, we decided to further investigate the use of SnCl₂ as a reducing agent in the reduction of alkynes into alkenes and alkanes. Tin(II)-chloride has been reported to be highly efficient in the synthesis of tertiary and secondary amines via the reductive amination of aliphatic and aromatic carbonyl compounds [21,22]. Although, SnCl₂ has been used in the reduction of nitro group into primary amine, it has not been used in the reduction of alkynes into their corresponding alkenes or alkanes. The attractive properties of SnCl₂ such as, being a stable solid, highly tolerant of water, easily handled, and less corrosive, makes it easier to work with [23]. Due to these properties of SnCl₂ and the adverse side effects of other methods for the reduction of unsaturated hydrocarbons, such as the use of

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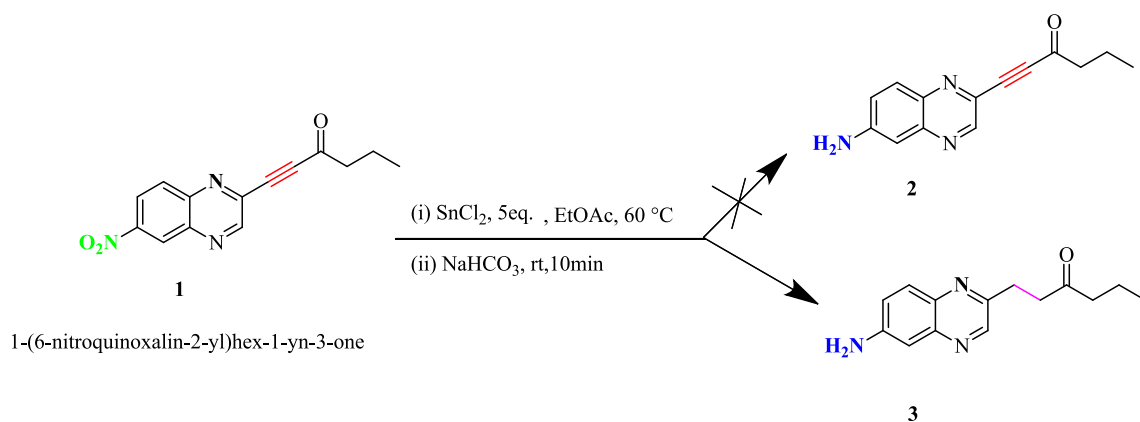
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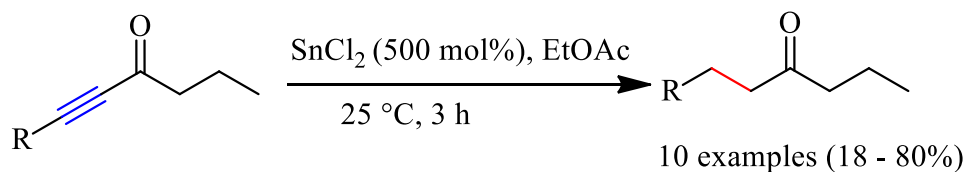
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Scheme 1. The reduction of 1-(6-nitroquinoxalin-2-yl)hex-1-yn-3-one **1** in the presence of SnCl₂ to give the corresponding compound **3**.



Scheme 2. Tin(II)-chloride (SnCl₂) mediated reduction of α, β - alkynyl carbonyl compounds.

hydrogen gas and toxic reagents, we decided to investigate the use of commercially available SnCl₂ as a reagent for the reduction of conjugated α, β -alkynyl carbonyl compounds into their corresponding alkanes. Organic compounds containing the alkynes functional group can undergo further transformation to form their alkene and/ or alkane derivatives. In this regard, quinoxalines, pyridine, pyrazine, and pyrimidine alkynylated derivatives obtained from palladium catalyzed Sonogashira cross-coupling of their halogenated and/ or sulfonated precursors using 1-hexyn-3-ol as coupling partner will constitute valuable substrate for this investigation.

Chemistry

The 1-(6-nitroquinoxalin-2-yl)hex-1-yn-3-ol (**5**) was synthesised from the Sonogashira cross coupling reaction of 6-nitroquinoxalin-3-yl benzenesulfonate (**4**) using 1-hexyn-3-ol as coupling partner. The synthesis and characterization of **4** has previously been reported by our research group [24]. Adopting the literature procedure by Mercier et al., [25], compound **5** (Scheme 2, **5**) was oxidized to afford 1-(6-nitroquinoxalin-2-yl)hex-1-yn-3-one **1** in 66 % with trace amount of starting material being present. In trying to optimize the reaction conditions, we opted for pyridium chlorochromate PCC (5 eq.) as oxidising agent in CH₂Cl₂ (DCM) for 3 h at room temperature. This reaction condition afforded **1** with an improved yield of 76 %.

In our research group, SnCl₂ mediated reduction of nitro group into their corresponding amine has previously been reported [24]. Upon developing the reduction method, we decided to investigate the effect of time, temperature, solvent and the equivalence of SnCl₂ on the reaction yield. The results obtained from the optimised reaction conditions are represented in Table 1 below.

Adopting this literature precedent, 1-(6-nitroquinoxalin-2-yl)hex-1-yn-3-one **1** was reacted with 5 eq. of SnCl₂ in ethyl acetate, at 60 °C for 3 h (Scheme 2, **1**) to afford the corresponding 1-(6-aminoquinoxaline-2-yl)hexane-3-one **3** in 18 % yield (Table 1, entry 1), with both the nitro and alkyne groups reduced to their corresponding amino and alkane functionality, respectively. Reducing the temperature to 25 °C resulted in an increase in the yield (Table 1, entry 4).

However, optimizing the reaction conditions (Table 1, entries 5–11)

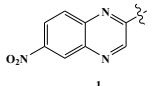
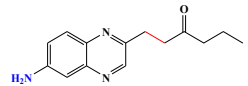
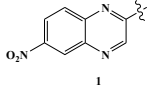
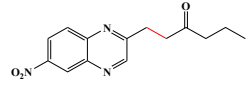
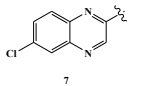
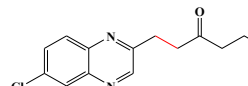

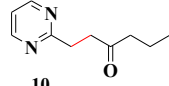

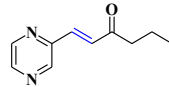
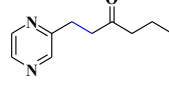

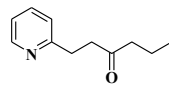

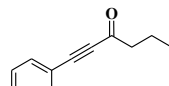
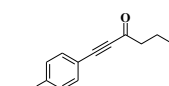
resulted in the reduction of only the alkyne group with good to excellent yield ranging from 45–80 % (Table 1, entries 5–11). The optimal condition for the reduction reaction was the use of 2.5 eq. of SnCl₂ at 25 °C as it gave a higher yield of 80 % compared to other conditions (Table 1, entries 5–11). This reduction is presumably due to the inductive and resonance effect between the conjugated pi system of the alkyne and carbonyl groups. Conversely, we noted that when the carbonyl group is replaced with the hydroxyl (OH) group, the reduction of the alkyne functionality does not occur. This could probably be due to the stability of the triple bond by the electron-donating OH group.

The replacement of the nitro group in compound **1** with a chlorine atom was also investigated using similar reduction reaction conditions. With 2.5 eq. of SnCl₂ at 25 °C for 3 h, 55 % of **8** was isolated (Table 1, entry 12). But with 5 eq. SnCl₂ under same reaction conditions, 73 % yield (Table 1, entry 13) was isolated. The presence of the chlorine atom gave a less yield as compared to the nitro group.

The optimised reaction conditions for the SnCl₂ mediated reduction of the α, β alkynylated pyrazine, pyrimidine, pyridine, and benzene derivatives containing the carbonyl group was also investigated and reported Table 1. The use of 2 eq. of SnCl₂ at 25 °C for 3 h, afforded 51 % yield (Table 1, entry 14) with 49 % of the starting material recovered. However, a complete reduction of **9** was obtained in 80 % yield when the equivalence of SnCl₂ was increased to 5 eq. (Table 1, entry 15). On the other hand, the reduction of compound **11** using 2 eq. SnCl₂ at 25 for 3 h, afforded a mixture of products **12** (alkene) and **13** (alkane) in 38 % and 48 % yields (Table 1 entry 16), respectively. Nevertheless, increasing the equivalence of SnCl₂ to 5 eq. gave a complete reduction of **13** with an excellent yield of 95 % (Table 1, entry 17). With the alkynylated pyridine **14**, no reduction took place using 2 eq. of SnCl₂ at 25 °C and 60 °C (Table 1, entry 18). However, 60 % yield of the reduced product (Table 1, entry 19) was isolated when the equivalence of SnCl₂ was increased to 5 eq. The reduction of the alkynylated benzene derivatives on the other hand, did not occur under any reaction condition as the starting materials were recovered in all cases (Table 1, entries 20–23).


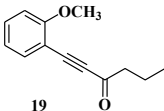
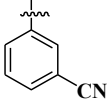
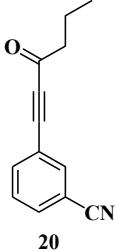
From Table 1, 1-(pyrimidine-2-yl)hex-1-yn-3-one **9** was considered to have best conditions after optimization with 5 eq. of SnCl₂ at 25 °C for 3 h (Scheme 3). It was further selected to investigate the effect of various

Table 1
Optimized conditions for the SnCl₂-catalysed reduction of alkynes.

R-group	Entry	SnCl ₂ (eq.)	Temp (°C)	Time (h)	%Yield	Products	
 1	1	5	60	3	18	 3	
	2	5	60	18	29		
	3	5	60	1	35		
	4	5	25	3	47		
 1	5	2.5	25	3	80	 6	
	6	1	25	3	45		
	7	1.5	25	3	60		
	8	2	25	1	57		
	9	2	25	1:30	70		
	10	2	25	3	74		
	11	2	60	3	80		
 7	12	2.5	25	3	55	 8	
	13	5	25	3	73		
 9	14	2	25	3	51	 10	
	15	5	25	3	80		
 11	16	2	25	3	38	 12	
					48		 13
	17	5	25	3	95		
 14	18	2	60	3	0	 15	
	19	5	60	3	60		
 16	20	5	60	3	0	 16	
 17	21	5	60	3	0	 18	

(continued on next page)

Table 1 (continued)

R-group	Entry	SnCl ₂ (eq.)	Temp (°C)	Time (h)	%Yield	Products
	22	5	60	3	0	
	23	5	60	3	0	

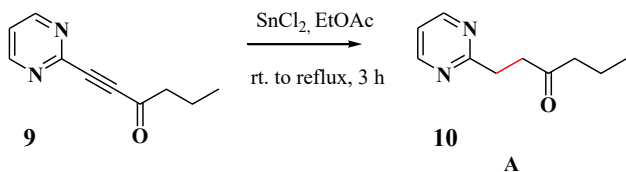
Scheme 3. Optimized reaction conditions on 1-(pyrimidine-2-yl)hex-1-yn-3-one **9**.

Table 2

The effect of various organic solvents such as ethanol, methanol, THF, dioxane, diethyl ether, DCM, and water on the reduction of triple bond using 5 eq. of SnCl₂ on 1-(pyrimidine-2-yl)hex-1-yn-3-one **9**.

entry	solvents	Temperature	Yield (%) A
1	Ethanol	25	0
		60	0
		reflux	0
2	Methanol	25	0
		60	0
		reflux	0
3	THF	25	0
		60	0
		reflux	0
4	Dioxane	25	0
		60	0
		reflux	0
5	Diethyl ether	25	75
		reflux	75
6	DCM	25	0
		60	0
		reflux	0
7	H ₂ O	25	0
		60	0
		reflux	0

solvents such as ethanol, methanol, THF, dioxane, diethyl ether, DCM, and water on the reduction of triple bond using SnCl₂. Under the optimized reaction conditions, using 5 eq. SnCl₂, the use of diethyl ether in the reduction of the 1-(pyrimidine-2-yl)hex-1-yn-3-one **9** afforded 75 % yield of **10** with the recovery of the starting material as shown in Table 2.

We further investigated the effect of the reducing ability of SnCl₂ on non *N*-heterocyclic compounds consisting of two aromatic rings connected by a three-carbon α,β -unsaturated carbonyl system. In this investigation, a solution (*E*)-1-(phenyl)-3-phenylprop-2-en-1-one **21** in ethyl acetate was treated with 5 eq. of SnCl₂ for 3 h (Scheme 4). The reaction was conducted both at room temperature as well as under reflux. In both reaction conditions, compound **22** was not produced, instead the starting material was fully recovered as shown in Scheme 4 below.

To strengthen our point on the importance of the carbonyl functionality as well as the reduction method been applicable only on compounds containing α,β -alkynyl carbonyl groups, we decided to adopt the reduction approach using substrates with alkyl and aryl substituents on the alkyne terminus. The SnCl₂ mediated reduction of these substrates with alkyl and aryl substituents on the alkyne terminus under various reaction conditions (Scheme 5) resulted in the recovery of the starting material without the formation of any form of the reduced product after 3 h.

In our quest to investigate the source of hydrogen atoms on the SnCl₂ mediated reduction of α,β -alkynyl carbonyl compounds, we opted on conducting the reduction of 1-(pyrimidine-2-yl)hex-1-yn-3-one **9** using an anhydrous SnCl₂. A stirred solution of 1-(pyrimidine-2-yl)hex-1-yn-3-one **9** in ethyl acetate was treated with anhydrous SnCl₂ using various reaction conditions as stated in Table 1. No reduction took place as 100 % of the starting material was recovered in all reaction conditions. However, spiking the reaction mixture with few drops of deuterium oxide resulted in the formation of trace amount of 1-(pyrimidin-2-yl)hexan-3-one **10**, in 10 % yield. Increasing the quantity of water with a decrease in the equivalence of SnCl₂, resulted in a general decrease in the yield of the product obtained. With this, it could be concluded that the source of hydrogen atoms in the SnCl₂ mediated reduction of α,β -alkynyl carbonyl compounds is partially from the moisture in the SnCl₂.

The reaction mechanism depicted in Fig. 1, illustrates the reduction of an α,β -alkynyl carbonyl compound via a stepwise electron transfer and protonation process. The reaction proceeds from the nucleophilic attack at the carbonyl carbon, leading to the formation of a negatively charged intermediate, which undergoes protonation, stabilizing the structure by forming a hydroxyl functional group. This is followed by an

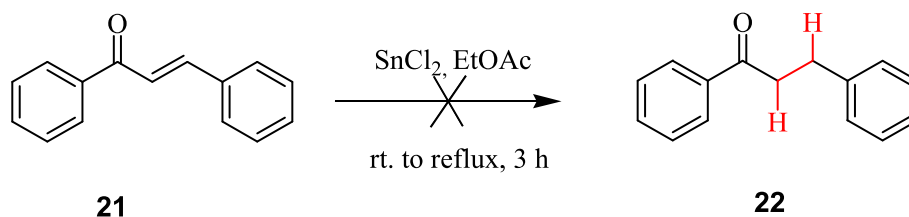
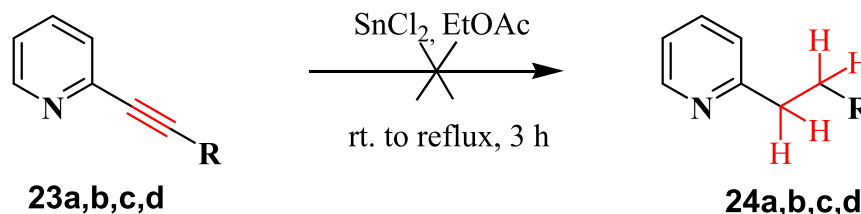
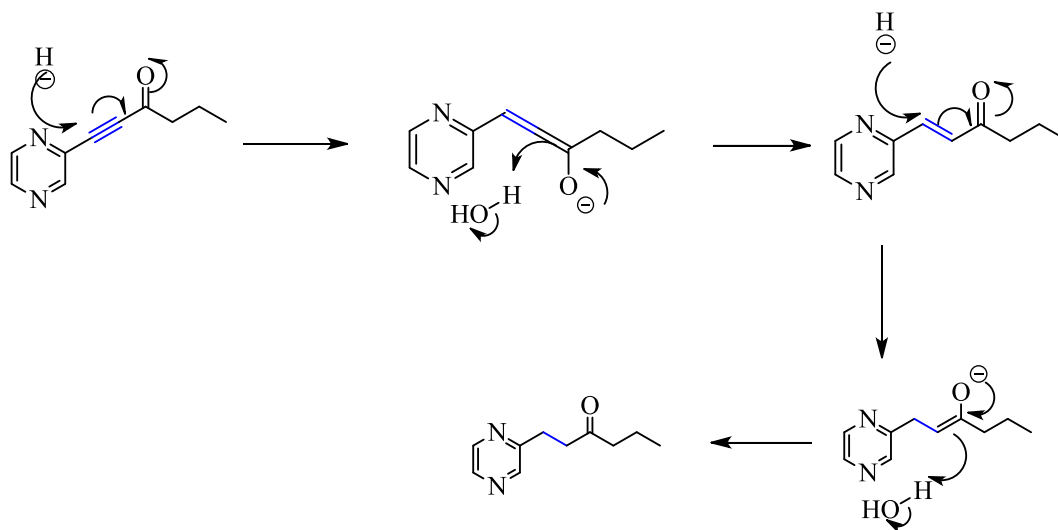
Scheme 4. SnCl₂ mediated reduction of (*E*)-1-(phenyl)-3-phenylprop-2-en-1-one **21**.Scheme 5. SnCl₂ mediated reduction of alkyl and aryl substituents on the alkyne terminus.

Fig. 1. Plausible mechanism for the reduction reaction.

electron rearrangement that facilitates the addition of another proton, ultimately yielding the final reduced product where the alkyne functionality has been transformed into a saturated alkyl chain, with the carbonyl group now in a stable ketone or alcohol form. The process follows a concerted mechanism, possibly involving a metal-catalysed or radical-mediated pathway.

Conclusion

An efficient method for the reduction of selected *N*-heterocyclic compounds with α,β -alkynyl carbonyl frameworks using SnCl₂ as a reducing agent has been developed. The reduction proceeded successfully in moderate to good yields, with spectroscopic data confirming the proposed structures. The reaction's selectivity is influenced by the proximity of the nitrogen and carbonyl groups to the alkyne functionality, while non-*N*-heterocyclic analogs or absence of these functionalities led to recovery of starting materials. Reduction was effective below 2.5 equivalents of SnCl₂, selectively targeting alkynes over other reducible groups like carbonyls or nitro groups, and moisture in SnCl₂

appeared critical for the reaction. This method is simple, safe, cost-effective, and scalable, offering a valuable tool in organic synthesis.

Author contributions

Conceptualize and design of the project: W.N, Synthesis, purification and characterization: R.U, K.L and E.N.A. Writing and editing of the manuscript: All authors wrote and proofread the manuscript.

CRediT authorship contribution statement

U. Ralepelle: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation. **E.N. Agbo:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation. **K. Lekgau:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation. **H. Chauke:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Formal analysis, Data curation. **I. Cukrowski:** Writing – original draft, Supervision, Project administration, Formal

analysis, Data curation. **W. Nxumalo:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Funding acquisition, Formal analysis, Conceptualization.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Winston Nxumalo reports financial support was provided by University of Limpopo. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.tetlet.2025.155481>.

Data availability

Data will be made available on request.

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