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Na_2S mediated synthesis of terminal alkynes from *gem*-dibromoalkenes

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Radhey M. Singh,[a*] Durgesh Nandini,[a,b] Kishor Chandra Bharadwaj,[a] upta[a] and Raj Pal Singh[b]

Na_2S-mediated facile synthesis of terminal alkynes from *gem*-dibromoalkenes, at 20/40 °C under open flask conditions has been developed. Various precursors derived from heteroaromatic/aromatic/aliphatic aldehydes were found compatible. The reaction is proposed to go through the Fritsch-Buttenberg-Wiechell (FBW) rearrangement involving the corresponding vinyl carbene. Mild reaction conditions using inexpensive $Na_2S.9H_2O$ under air, are significant advantages over earlier routes.

Development of new methodology for the synthesis of organic molecules has always been challenging to both organic and medicinal chemists when it is based on cost, reaction conditions and applications. For example, terminal alkynes are useful functional groups and versatile intermediates,[1] widely used in the synthesis of natural products, pharmaceuticals and functional materials.[2,3] They are used as precursors in azide-alkyne cycloaddition reactions,[4] carbon-carbon bond formations,[5] hydroamination,[6] carbohalogenation[7] and oxidative cross coupling reactions.[8] Amongst available methods in the literature[9-13] for alkyne synthesis, *gem*-dibromoalkenes[14a] prepared from aldehydes via one-carbon homologation have been identified as valuable precursors. Corey-Fuchs reactions,[14b] has been a classical method for the synthesis of alkynes using *gem*-dibromoalkenes. However these reactions proceed in the presence of strong and air sensitive bases such as BuLi,[14b,15d] LDA,[15a] Grignard reagents,[15c] *t*-BuOK,[15e] and others.[15b] Further, they require very low temperature and inert atmosphere. Recently, efforts have been directed for alternate methods. Yang has reported synthesis of terminal alkynes[16] using cesium carbonate (Figure 1). Zhang[17a] have used tetra-*n*-butyl ammonium fluoride[17b] and TPP for the same. Ramana utilized DBU for conversion of these precursors to terminal alkyne.[18]

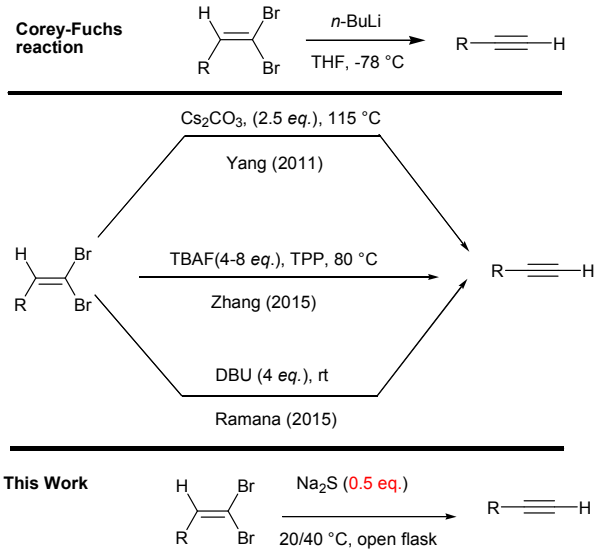

Fig. 1. Access to terminal alkynes from *gem*-dibromo-1-alkenes.

However, these reactions require either excess of base and/or high temperature. Therefore, development of new methodology for terminal alkynes that tolerates some of these drawbacks is highly desirable. Importantly, given the huge importance, application & commercialization of alkynes, a catalytic route for their synthesis would be highly desirable.

As our continued interest in exploring reactivity and synthetic applications of 2-chloroquinyl-3-caboxaldehydes,[19] we recently explored the application of 2-chloro-3(2,2-dibromovinyl)quinoline for the corresponding synthesis of furo (2,3-*b*) quinolines.[20] The reaction was then tried for synthesis of thiophene-fused quinolines from these precursors. Initially, reaction of 2-chloro-3(2,2-dibromovinyl)quinoline, (**1a**) was investigated with 1 *eq*. of $Na_2S.9H_2O$ in 2mL DMSO at 40 °C under air. The reaction afforded thiophene-fused quionline (**2a**) in 55% yield. However, it was interesting to observe the formation of terminal alkyne (**3a**) in 25% yield (Scheme 1).

[a] *Department of Chemistry, Institute of Science, Banaras Hindu University, Varanasi, India. Email: rmohan@bhu.ac.in*
[b] *Centre for Fire Explosive and Environment Safety, Defence Research Development Organization, Delhi, India.*

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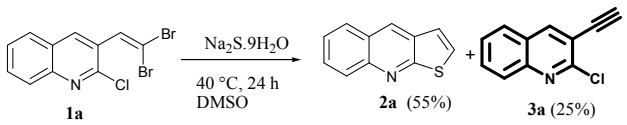
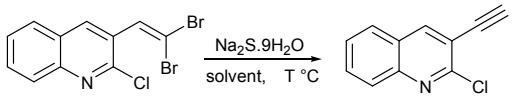


Scheme 1. Reaction of 2-chloro-3(2,2-dibromovinyl)quionline (**1a**) with Na_2S.

This result was enthralling because it led to synthesis of alkyne under ambient conditions using $Na_2S.9H_2O$ as a cheap, commercial and stable reagent. Thus we focused our attention for the development of this method. We report herein a base-free, efficient synthesis of terminal alkynes at rt under open flask conditions in good yields.

Systematic study began for exclusive synthesis of terminal alkyne. Results are summarized in table 1. Further increase of the temperature to 50 °C lead to reduced yield (entry 2). Interestingly when reaction temperature was lowered to 20 °C, reaction was completed in 2h affording alkyne as single product in 72% yield. Further lowering of temperature to 0 °C didn't afford reaction. After establishment of 20 °C as reaction temperature for synthesis of terminal alkyne, optimization of reaction was performed by screening mole variations of $Na_2S.9H_2O$ and solvents. When 0.5 *eq*. of Na_2S was used, we were delighted to observe a complete reaction in 2h with an yield of 75% (entry 5). This was intriguing, as it suggested reaction to proceed in catalytic pathway. Further decrease of mole equivalent of reagent to 0.25 *eq*. lead to reduced yield of 62%. Similarly, screening of various solvents like DMF, CH_3OH, CH_3CN, DCM and benzene (entries 7-11) gave inferior results. Thus, a combination of substrate **1a** (1 mmol) and $Na_2S.9H_2O$ (0.5 *eq*.) in 2mL DMSO at 20 °C under open flask, was identified as best reaction condition (entry 5, table 1). Having an optimized condition in hand the scope of the reaction was investigated with substituted 2-chloro-3-(2,2-dibromovinyl) quinolines.

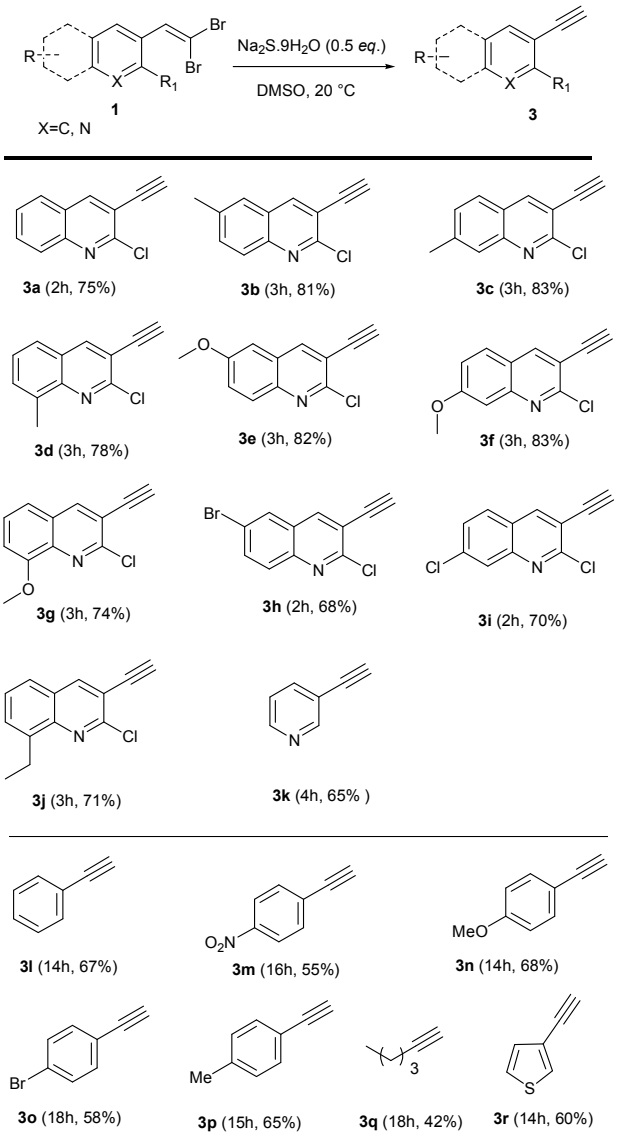
Table 1. Optimization of the reaction conditions.



1a **3a**

Entry	Na_2S (*eq*.)	Solvent	Temperature (°C)	Time (h)	Yield[a] (%)
1	1.0	DMSO	40	24	25
2[b]	1.0	DMSO	50	24	20
3	1.0	DMSO	20	2	72
4	1.0	DMSO	0	2	-
5	**0.5**	**DMSO**	**20**	**2**	**75**
6	0.25	DMSO	20	6	62
7	0.5	DMF	20	3	70
8	0.5	CH_3OH	20	3.5	68
9	0.5	CH_3CN	20	5	55
10	0.5	DCM	20	8	SM
11	0.5	Benzene	20	8	SM

[a]Isolated yield.[b] 60% of **2a** was observed.



Scheme 2. Substrate scope for terminal alkyne synthesis.[a]

[a]For **3l-3r**, reaction were carried out at 40 °C

Results of corresponding terminal alkynes **3b-3j** are listed in scheme 2. Substrates with electron-donating groups at 6 and 7 positions led to enhance yields of terminal alkynes relative to substrates with electron withdrawing groups. However, lower yields were observed with electron donating groups at position 8. The reaction was extendable to pyridine framework **3k**. We were able to get single crystal structure for one of the alkyne (**3b**) which further confirmed the structure (Figure 2).[21] We were also able to carry out reaction of **1f** on 1.122 g (3 mmol) scale to obtain **3f** in 79% yield. To broaden the scope of the reaction, *gem*-dibromovinyl derivatives of aromatic/other hetroaromatic and aliphatic analogues were also evaluated under the optimized conditions. Results are summarized in scheme 2. The reaction of these *gem*-dibromovinyl derivatives

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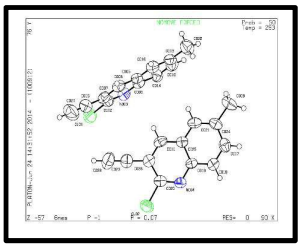
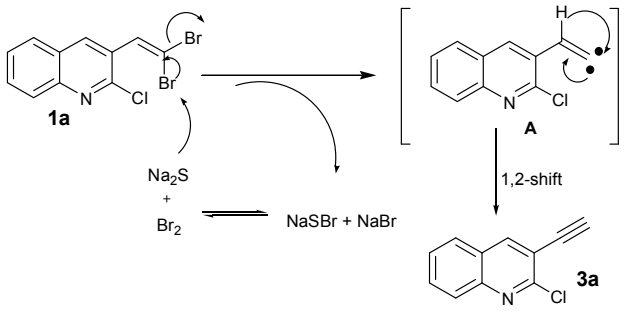


Fig. 2. ORTEP diagram of **3b**.

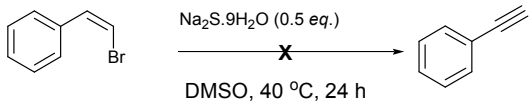


Scheme 3. Plausible Mechanism.

were less reactive than hetero aromatic analogues and proceeded at 40 °C in 14-18h affording terminal alkynes **3l-3r**[17a,22] in 42-68% respectively. Phenyl ring bearing electron-donating groups were relatively more reactive than those with electron-withdrawing groups and afforded better yields of terminal alkynes.

A plausible mechanism based on FBW rearrangement is as depicted in scheme 3.[23,24] Initially, sodium sulphide anion attacks as nucleophile on one of bromine atom of *gem*-dibromoalkenes **1** followed by cleavage of another C-Br bond to afford vinylene carbene **A**. The carbene **A** subsequently undergoes rearrangement leading to terminal alkyne. NaSBr and NaBr react together to regenerate Na_2S along with formation of bromine which can exist in equilibrium. To rule out the possibility of Na_2S acting as a base, the reaction of (*Z*)2-bromovinylbenzene[25] was examined for the synthesis of terminal alkyne under optimized reaction condition (Scheme 4). However reaction failed to proceed and starting material was recovered. This further ruled out Na_2S acting as base.

In summary, we have developed a catalytic route for the synthesis of terminal alkynes from *gem*-dibromoalkenes. This route is superior over other methods because of cheap and commercial availability of reagent. The reactions proceeds without base at 20/40 °C under open atmosphere in good yields. Different heteroaromatic, aromatic and aliphatic *gem*-dibromoalkenes afforded corresponding terminal alkynes from this method.



Scheme 4. Reaction of 1-bromovinylbenzene with $Na_2S.9H_2O$.

Reaction opens up gateways for the development of catalytic and mild routes for the synthesis of terminal alkynes. Further work in this direction is under progress.

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Conflicts of interest

There are no conflicts to declare.

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