Chapter 2
Preparation of Haloalkynes

Abstract Traditionally, haloalkynes were accessible through the deprotonation of the corresponding terminal alkynes with a strong base, followed by trapping with a halogenating reagent. During the past decades, several mild and convenient methods have been developed, thus increasing the attractiveness of this class of compounds in organic synthesis. Among which, the electrophilic bromination of terminal alkynes with *N*-bromosuccinimide (NBS) and Ag catalyst is one of the most commonly used methods for the preparation of bromoalkynes due to the mild reaction conditions, high efficiency and simple manipulation. In this chapter, we will detailedly describle the general and practical methods to prepare bromoalkynes, chloroalkynes, and iodoalkynes.

Keywords Terminal alkynes · Ag catalyst · Bromoalkyne synthesis · Chloroalkyne synthesis · Iodoalkyne synthesis

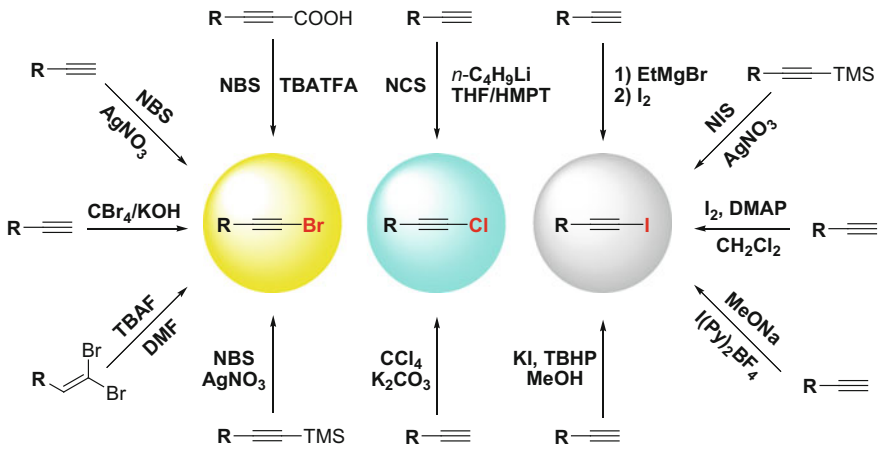
Haloalkynes were traditionally accessible through the deprotonation of the corresponding terminal alkynes with a strong base, followed by trapping with a halogenating reagent. Recently, several mild and convenient methods have been developed (Scheme 2.1), [1] thus increasing the attractiveness of this class of compounds in organic synthesis. Among which, the electrophilic bromination of terminal alkynes with *N*-bromosuccinimide (NBS) and Ag catalyst [2] is one of the most commonly used methods for the preparation of bromoalkynes due to the mild reaction conditions, high efficiency and simple manipulation (Scheme 2.2) [3].

General Procedure for the Synthesis of Bromoalkynes: To a solution of alkyne (1 equiv) in acetone (0.2 mmol/mL) was added NBS (1.1 equiv) and $AgNO_3$ (10 mol%) at room temperature with magnetic stirring. After 2–3 h, the reaction mixture was diluted with hexanes (100 mL) and filtered off the crystals formed. The filtrate was concentrated under reduced pressure and passed through a pad of silica gel using hexanes as an eluent. The filtrate was collected and evaporated under reduced pressure to afford a pure colorless oil of bromoalkyne.

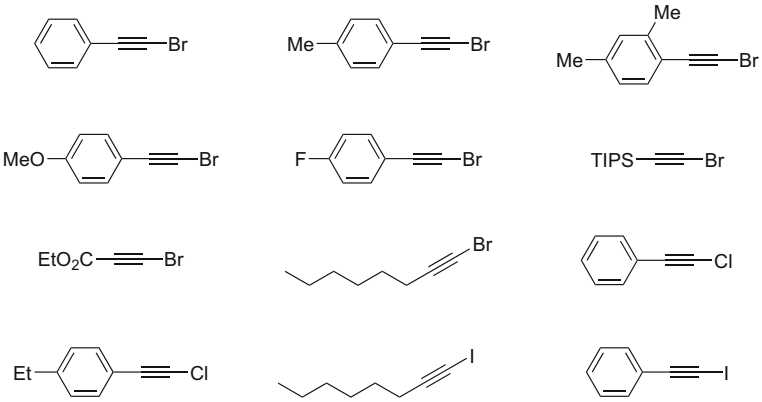
General Procedure for the Synthesis of Chloroalkynes: To a solution of alkyne (1 equiv) in CCl_4 (2 mmol/mL) was added Cs_2CO_3 (1.1 equiv) and Bu_4NCl (5 mol %) at 70 °C with magnetic stirring. After 6–7 h, the reaction mixture was diluted

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Scheme 2.1 Preparation methods for haloalkynes



Scheme 2.2 Representative haloalkynes

with hexanes (100 mL) and filtered off the crystals formed. The filtrate was concentrated under reduced pressure and passed through a pad of silica gel using hexanes as an eluent. The filtrate was collected and evaporated under reduced pressure to afford a pure colorless oil of chloroalkyne.

General Procedure for the Synthesis of Iodoalkynes: To a solution of alkyne (1 equiv) in acetone (0.2 mmol/mL) was added NIS (1.1 equiv) and $AgNO_3$ (10 mol %) at room temperature with magnetic stirring. After 2–3 h, the reaction mixture was diluted with hexanes (100 mL) and filtered off the crystals formed. The filtrate was concentrated under reduced pressure and passed through a pad of silica gel using hexanes as an eluent. The filtrate was collected and evaporated under reduced pressure to afford a pure colorless oil of iodoalkyne.

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Jiang, H.; Zhu, C.; Wu, W.

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