Nickel-catalyzed cycloaddition of methyleneaziridines with diynes to synthesize fused anilines

Xiaodong Lu †, Bin Pan †, Fan Wu, Xiaoyi Xin *, Boshun Wan *

Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, China

A R T I C L E   I N F O

Article history:
Received 25 May 2015
Revised 12 June 2015
Accepted 16 June 2015
Available online 20 June 2015

Keywords:
Methyleneaziridines
Diynes
Anilines
Nickel
Cycloaddition

A B S T R A C T

Methyleneaziridines reacted with diynes to generate fused anilines. This reaction involved a C2–C3 bond cleavage of methyleneaziridine. This work provides a new reaction pattern of methyleneaziridine.

© 2015 Elsevier Ltd. All rights reserved.

Three-membered rings are versatile building blocks in the synthesis of a large variety of chemical compounds due to their ring strains. 1 Methyleneaziridines, a kind of three-membered ring bearing an exocyclic double bond, are easy to handle in spite of their ring strain. The ring-opening and ring expansion reactions of methyleneaziridines have been extensively studied. 3–6 On the terms of the formation of heterocycles and carbocycles from methyleneaziridines, 4–6 there are three bond-cleavage pathways (Scheme 1): (1) N–C2 bond cleavage. 4 In 1987, Alper and coworker reported the synthesis of lactams from methyleneaziridines and carbon monoxide (Scheme 1, Eq. 1). 4a Yamamoto and coworkers reported a reaction of methyleneaziridines with acetylpyridines to synthesize pyridinylpyrroles (Scheme 1, Eq. 2). 4b Nakamura et al also reported the generation of pyrroles from methyleneaziridines and 1,3-diketones (Scheme 1, Eq. 3). 4c Shipman and coworkers reported intramolecular radical rearrangement reactions of methyleneaziridines to synthesize substituted pipiperidines (Scheme 1, Eq. 4). 4d,4e (2) N–C3 bond cleavage. 5 Cleavage of the N–C3 bonds of methyleneaziridines and then reacted with unsaturated bonds to generate β-lactams (Scheme 1, Eq. 5). 5a imidazolidin-2-ones (Scheme 1, Eq. 6) 5b and cyclopentanamines (Scheme 1, Eq. 7). 5c Shipman and coworkers reported a Lewis acid-catalyzed intramolecular [4+3] cycloaddition of methyleneaziridines with dienes to give seven-membered rings (Scheme 1, Eq. 8). 5d Shipman and coworkers also reported an intramolecular ring opening of indole functionalised methyleneaziridines with alcohols to generate tetrahydro-β-carbolines (Scheme 1, Eq. 9). 5e (3) C2–C3 bond cleavage. In 2013, we reported a transition metal-catalyzed cycloaddition of methyleneaziridines with diynes to afford functionalized pyrroles via C2–C3 bond cleavage. 6 Meanwhile, it is noteworthy that the nitrogen atoms of methyleneaziridines were usually incorporated into the heterocyclic and carbocyclic ring cores in most of these reactions, 4,5a,5b,5e,6 there are only two examples that the nitrogen atom of methyleneaziridine was not incorporated into the product ring cores (Scheme 1, Eqs. 7 and 8). 5c,5d among heterocycle and carbocycle synthesis. Herein, we report a nickel-catalyzed synthesis of fused anilines from methyleneaziridines and diynes via C2–C3 bond cleavage of the methyleneaziridines (Scheme 1, Eq. 11). The nitrogen atom of methyleneaziridine serves as amine functional group of the product.

In the course of our continuous studies on the chemistry of methyleneaziridines and diynes, 7 we unexpectedly found that fused anilines 3aa was obtained from the reaction between methyleneaziridine 1a and diyne 2a catalyzed by Ni(COD)/IPr (Table 1). The structure of 3aa was unambiguously confirmed by single crystal X-ray diffraction analysis. 8 When equimolar amounts of 1a and 2a were reacted in the presence of 10 mol % of Ni(COD) and 10 mol % of IPr using THF as solvent at 45 °C, the desired 3aa was generated in 37% GC yield (Table 1, entry 1). Switching the solvent from THF to 1,4-dioxane gave a higher yield (Table 1, entry 2).
Increasing the amount of IPr to 15 mol % did not improve the efficiency (Table 1, entry 3). However, to ensure the coordination of the nickel catalyst, we still use 15 mol % of IPr to investigate the influence of temperature to the yield (Table 1, entries 4–6). Neither slight lowering of the reaction temperature to 40 °C (Table 1, entry 4) nor elevating the temperature to 60 °C (Table 1, entry 5) distinctly resulted in higher yields. When the reaction temperature was elevated to 80 °C, 3aa was formed in 67% GC yield (Table 1, entry 6). Increasing the proportion of 1a:2a to 2:1 did not improve the efficiency (Table 1, entry 7). Employing 15 mol % of SIPr as ligand did not give a better result (Table 1, entry 8), too. When the reaction was carried out at 100 °C in toluene, 3aa was obtained in 70% GC yield (Table 1, entry 9).

The scope and limitations of this reaction were then investigated and the results described in Table 2. Ph(Me)CH-substituted methyleneaziridine (1a) could react with malonate-, tosylamide-, and oxygen-linked diynes (2a, 2b, and 2c, respectively), providing...
the desired products in low to moderate yields (Table 2, entries 1–3). However, the reaction of 1a with CH2-lit diyne 2d gave a very complicated mixture, the desired product was not successfully purified (Table 2, entry 4). Benzyl-substituted methyleneaziridine (1b) could react with 2a, 2c, and 2d, and the yields were also low to moderate (Table 2, entries 5, 7 and 8). Tosylamide-linked diyne (2b) was not compatible with 1b, and the desired product 3bb was not obtained (Table 2, entry 6). 4-MeOC6H4CH2-substituted methyleneaziridine (1c) was not compatible with 2b and 2d (Table 2, entries 10 and 12). Interestingly, compared with the benzyl-substituted 1b, 1c reacted with 2a gave a lower yield than that of 1b (15% vs 53%, entry 9 vs entry 5). In contrast, 1c reacted with 2c gave a higher yield than that of 1b (45% vs 15%, entry 11 vs entry 7). The aliphatic Cy-substituted methyleneaziridine (1d) was also tolerated in these transformations (Table 2, entries 13, 15 and 16). Unfortunately, similar to 1b and 1c, tosylamide-linked diyne 2b was not also compatible with 1d, and the desired products were not generated, too (Table 2, entry 14).

A plausible reaction mechanism is depicted in Scheme 2. Initially, the oxidative addition of nickel(0) with diyne 2 gives nickelacycloptadiene intermediate A. Coordination of the alkene moiety of methyleneaziridine 1 and insertion into the Ni(II)-carbon bond generates nickelacycloheptadiene intermediate B. Then reductive elimination of B affords intermediate C and regenerates the Ni(0) catalyst. Finally, intermediate C aromatizes to product 3.

In summary, we have developed a nickel-catalyzed synthesis of anilines from methyleneaziridines and diyynes. The structure of the product indicated that the C2–C3 bond of methyleneaziridine cleavage occurred, and the nitrogen atom of methyleneaziridine was not incorporated into the benzene but served as amine functional group, which is a new reaction pattern of methyleneaziridine. We expect these results will find new insights into the methyleneaziridine chemistry.

Acknowledgment

We are grateful to the National Natural Science Foundation of China (21372219 and 21172218) for financial support.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.06.045.

References and notes

6. (a) CCDC 1400557 contains the supplementary crystallographic data for 3aa in this paper. These data can be obtained via www.ccdc.cam.ac.uk/data_request/cif.