

Pyridylcarbene formation by thermal decomposition of 7-bromo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine under pressure

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Dedicated to Professor Joan Bosch on his 60th birthday

Abstract

7-Bromo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine **1** at 1.7 atm and 100°C decompose to form a pyridylcarbene intermediate by nitrogen expulsion. The carbene stabilization give 2-bromo-6-vinylpyridine **2**, 1-(6-bromopyridin-2-yl)ethanol **3**, 1-(6-bromopyridin-2-yl)ethanone **4**, 2-bromo-6-[2-(6-bromopyridin-2-yl)-2-methyl-*trans*-cyclopropyl]pyridine **5**, and 2-bromo-6-[2-(6-bromopyridin-2-yl)-2-methyl-*cis*-cyclopropyl]pyridine **6**.

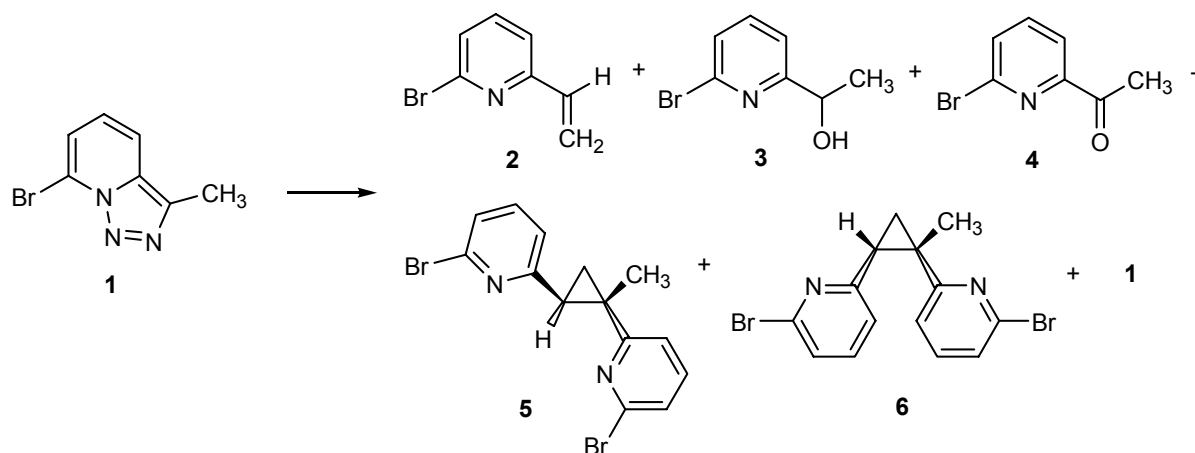
Keywords: Pyridylcarbene, high pressure reaction, triazolopyridines decomposition

Introduction

In the context of our study on the chemistry of [1,2,3]-triazolo[1,5-*a*]pyridines,¹ we had used 7-bromo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine **1**,² as starting material for nucleophilic substitution reactions,^{3,4} and cross-coupling reactions.⁵ Compound **1** is stable under the thermal conditions in which both types of reactions were done at atmospheric pressure. Recently, we are interested in applications of triazolopyridines and derivatives as fluorescent sensors,^{5,6} as cluster formers exhibiting superparamagnetic relaxation,⁷ or as proton sponge.⁸ Our interest now is to obtain new triazolopyridine derivatives as polynitrogenated ligands with the aim to study its potential applications. With this idea in mind, we had interest to do some reactions with **1** at higher pressure, because the pressure affects the molecular environment and the reactions could give new results. First we have investigated the stability of compound **1** at 1.7 atm and 100°C.⁹ The result of this experiment is described in this paper.

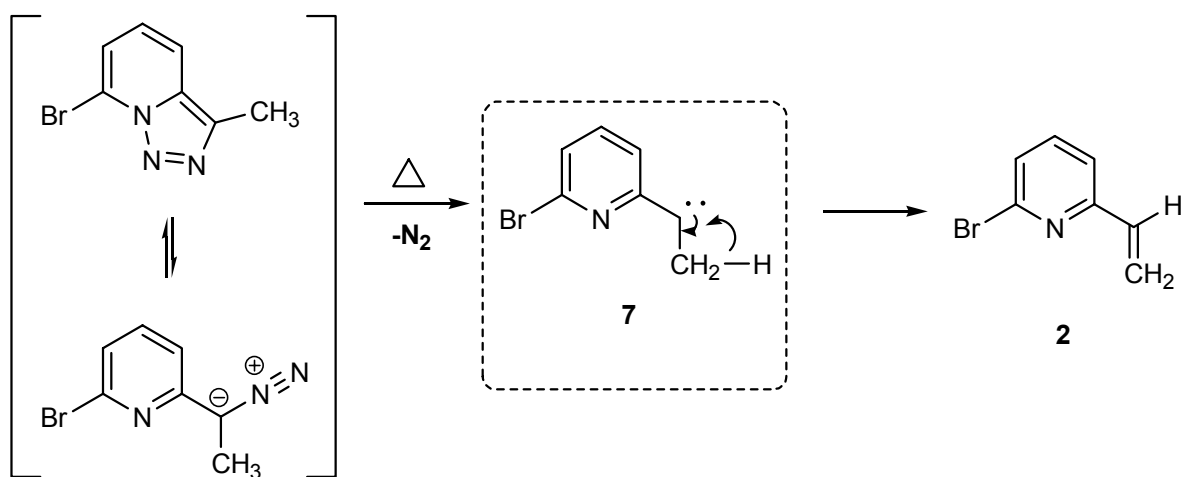
Results and Discussion

A solution of 7-bromo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine **1** in acetonitrile (75 mL) was poured into a steel reactor that was hermetically closed. Then, the reactor was heated at 100°C for 5 days. After that a mixture, difficult to manipulate, was formed, however it could be purified by chromatotron and we have isolated and characterized five compounds, in small yield, together with some starting material and a big amount of an unidentified polymer (Scheme 1). The first compound eluting showed a molecular ion with isotope abundance correlating with a bromine atom at m/z 182.9671/184.9660 corresponding to a molecular formula of C_7H_6BrN . The 1H NMR shows an ABC system in the aromatic region with $J_1=J_2=7.7\text{Hz}$ and an ABX alkene system with $J_{\text{trans}}=17.3\text{Hz}$, $J_{\text{cis}}=10.5\text{Hz}$ and $J_{\text{gem}}=1.1\text{Hz}$ corresponding with the structure of the novel 2-bromo-6-vinylpyridine **2**. The 1-(6-bromopyridin-2-yl)-ethanol **3** was also identified by HRMS, isotopic masses for a bromine atom at m/z 200.9764/202.9786, and by its spectra.¹⁰ The ketone **4** is readily shown by its analytical and spectral properties.¹¹ Two new different compounds with very similar spectra were also isolated and characterized. The m/z values for M^+ in EI HRMS spectrum was 369.9318/367.9346/365.9360 for compound **5**, and $(M+1)^+$ in the FAB HRMS spectrum was 370.9425/368.9441/366.9451 for compound **6** corresponding to a molecular formula of $C_{14}H_{12}Br_2N_2$. A carefully 1H NMR study shows in both compounds the presence of two 2,6-disubstituted pyridines, three different deshielded aliphatic protons as AMX system, and one methyl group. By ^{13}C NMR analysis we saw that in the aliphatic zone were four different carbons, C, CH, CH_2 , CH_3 groups. GHSQC experiments correlate the ^{13}C NMR signal at $\delta 22.8$ (CH_2) in compound **5** with the protons at $\delta 1.84$ and $\delta 1.72$, and the ^{13}C NMR signal at $\delta 20.1$ (CH_2) in compound **6** with the protons at $\delta 2.18$ and $\delta 1.29$. All these data lead us to assign to them the structure of two diastereomeric 1,3-disubstituted cyclopropanes linking two 6-bromo-2-pyridyl radicals (*cis/trans*). A NOESY spectrum of compound **5** shows cross signals at 1.28 (3H) and 1.72 (1H) from the methyl protons which are close to only one cyclopropanic proton. This means that compound **5** is the *trans* isomer.

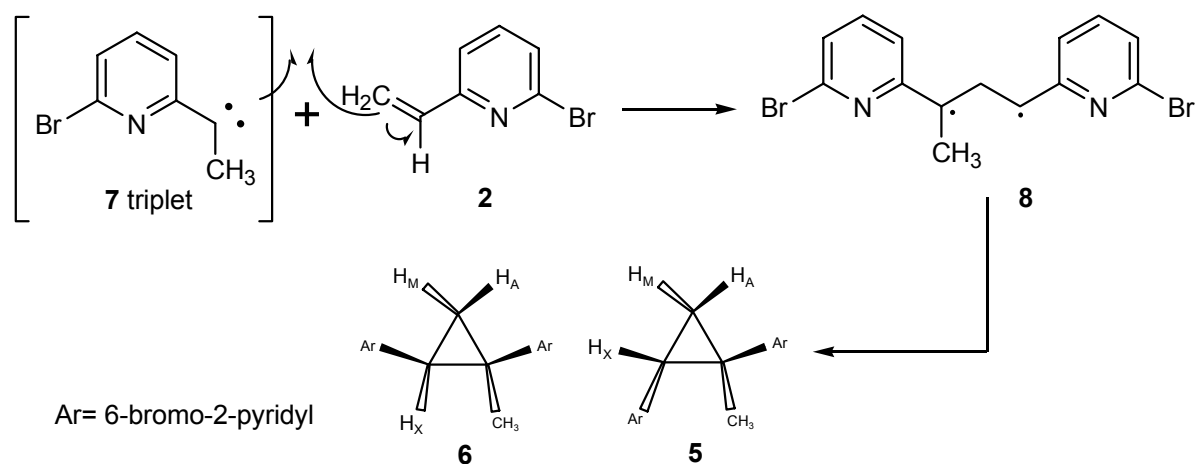


Scheme 1

To explain the formation of all these compounds we propose that 7-bromo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine **1** could form a pyridyl carbene **7** by extrusion of nitrogen (scheme 2), as Wentrup suggested for 3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine on flash vacuum pyrolysis conditions.¹² The different stabilization of this carbene could explain the formation of all isolated compounds. A concerted shift of the H, with its two electrons, to the empty orbital in the singlet carbene rapidly stabilizes the system to give 2-bromo-6-vinylpyridine **2** (scheme 2). The addition of **7** to the double bond of vinylpyridine **2**, could form the diradical **8**, and explain the formation of the diastereomeric mixture of cyclopropane derivatives **5** and **6** (scheme 3). Cyclopropane formation is the most interesting reaction of a carbene with an olefin.^{13,14}



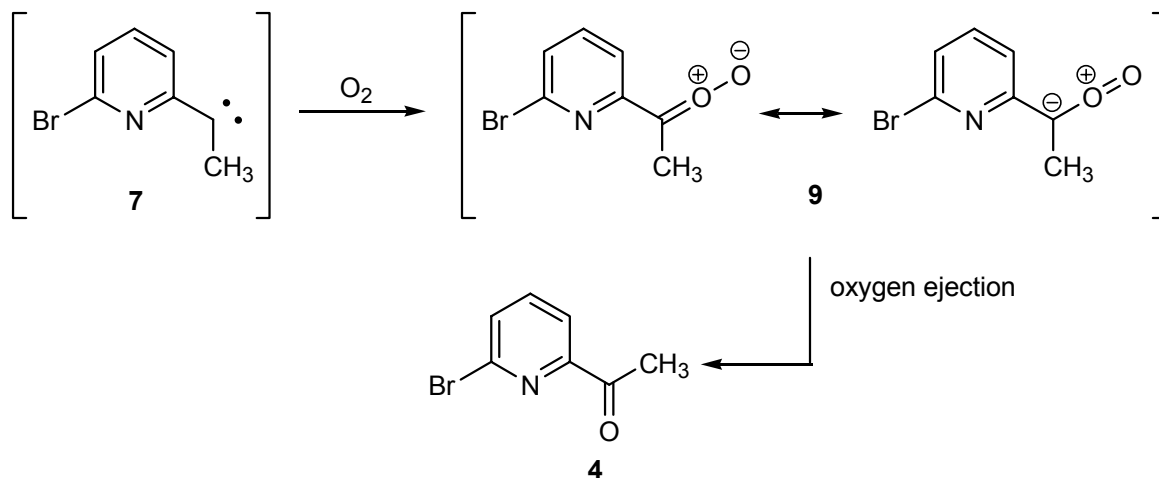
Scheme 2



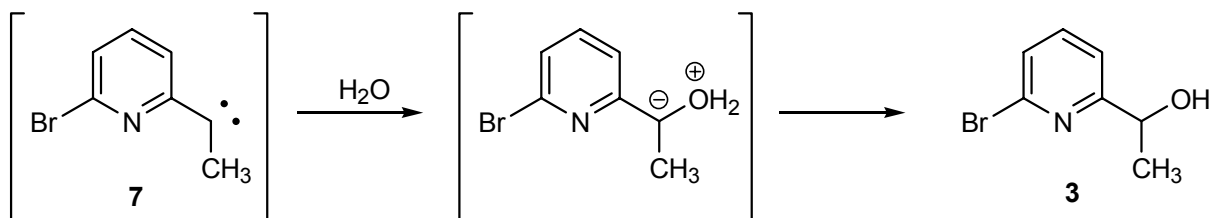
Scheme 3

On the other hand, triplet carbenes can combine with oxygen to form carbonyl oxides,¹⁵ that can fragment by an unimolecular oxygen atom ejection to produce the corresponding carbonyl

compound.^{15,16} In this way it is possible to explain the formation of **4** through the carbonyl oxide **9** (scheme 4). Because carbenes react with water,¹⁷ traces of water in the reaction medium could justify the formation of the alcohol **3** (scheme 5).



Scheme 4



Scheme 5

Finally we have tested that the parent compound 3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine is stable under the conditions in which 7-bromo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine **1** decompose. Probably the presence of bromine in compound **1** favours the equilibrium to the diazo form,¹⁸ (scheme 2), which activation energy for decomposition to the carbene must be lower than for the corresponding diazo form of the parent compound.

Experimental Section

General Procedures. Melting points were determined on a Kofler heated stage and are uncorrected. 1H NMR spectra (300 or 400 MHz) and ^{13}C NMR spectra (75.4 or 100 MHz) were recorded on a Bruker AC300MHz or on a JEOL Lambda 400 MHz spectrometers. Chemical shifts (δ) are given from TMS (0 ppm) as internal standard for 1H NMR and $CDCl_3$ (77.0 ppm) for ^{13}C NMR. Mass spectra and high resolution mass spectra (EI and FAB) determinations were

made using a VG Autospec Trio 1000 (Fisons). Chromatography was performed on a Chromatotron, using 2 cm plates of silica Merck Pf254.

Thermal decomposition under pressure of 7-bromo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine

A solution of 7-bromo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine **1** (300mg, 1.42mmol) in dry acetonitrile (75 mL) was poured in a test tube into a steel reactor that was hermetically closed. The reactor was heated at 100°C during 5 days. Then, it was cooled to reach room temperature. An intractable solid was formed that was filtered. The filtrate was dried and a complex mixture was obtained (190mg). The mixture was purified by chromatography on a chromatotron using ethyl acetate/hexane with an increasing proportion of ethyl acetate as eluent. The following compounds, by elution order, were isolated and characterized.

2-Bromo-6-vinylpyridine (2). Colourless oil. Yield 1%. HRMS found M^+ 184.9660 / 182.9671; C_7H_6BrN requires 184.9663 / 182.9683. 1H NMR δ 7.43 (dd, $J_1=J_2=7.7$ Hz, 1H), 7.27 (d, $J=7.70$ Hz, 1H), 7.20 (d, $J=7.7$ Hz, 1H), 6.66 (dd, $J_1=17.3$ Hz, $J_2=10.5$ Hz, 1H), 6.17 (dd, $J_1=17.3$ Hz, $J_2=1.1$ Hz, 1H), 5.46 (dd, $J_1=10.5$ Hz, $J_2=1.1$ Hz, 1H). ^{13}C NMR δ 157.41 (C), 142.39 (C), 139.12 (CH), 135.78 (CH), 127.04 (CH), 120.39 (CH), 120.28 (CH₂). MS m/z 185, 183, 159, 157, 104, 77, 57, 51.

2-Bromo-6-[2-(6-bromopyridin-2-yl)-2-methyl-*trans*-cyclopropyl]pyridine (5). White solid. Mp 105°C. Yield 8%. (EI) HRMS found M^+ 369.9318 / 367.9346 / 365.9360; $C_{14}H_{12}Br_2N_2$ requires 369.9326 / 367.9347 / 365.9367. 1H NMR δ 7.37 (dd, $J_1=J_2=7.7$ Hz, 1H), 7.35 (dd, $J_1=J_2=7.7$ Hz, 1H), 7.22 (dd, $J_1=7.7$ Hz, $J_2=0.75$ Hz, 1H), 7.21 (dd, $J_1=7.9$ Hz, $J_2=0.75$ Hz, 1H), 7.15 (d, $J=7.7$ Hz, 1H), 7.12 (d, $J=7.7$ Hz, 1H), 2.80 (dd, $J_1=8.7$ Hz, $J_2=6.6$ Hz, 1H), 1.84 (dd, $J_1=8.7$ Hz, $J_2=4.1$ Hz, 1H), 1.72 (dd, $J_1=6.6$ Hz, $J_2=4.1$ Hz, 1H), 1.28 (s, 3H). ^{13}C NMR δ 166.11 (C), 160.73 (C), 142.03 (C), 141.59 (C), 138.67 (CH), 138.45 (CH), 125.54 (CH), 125.06 (CH), 123.56 (CH), 118.91 (CH), 35.56 (CH), 29.72 (C), 22.78 (CH₂), 15.61 (CH₃). MS m/z 369, 368, 367, 288, 287, 275, 274, 273.

1-(6-Bromopyridin-2-yl)-ethanone (4).¹¹ Colourless oil. Yield 4%. HRMS found M^+ 200.9605 / 198.9621; C_7H_6BrNO requires 200.9612 / 198.9633. 1H NMR δ 7.92 (d, $J=6.8$ Hz, 1H), 7.63 (m, 2H), 2.64 (s, 3H). ^{13}C NMR δ 190.0 (CO), 154.7 (C), 141.7 (C), 139.5 (CH), 132.9 (CH), 26.2 (CH₃). MS m/z 201, 199, 173, 172, 159, 78, 61, 50.

2-Bromo-6-[2-(6-bromopyridin-2-yl)-2-methyl-*cis*-cyclopropyl]pyridine (6). White solid. Mp 72-73°C. Yield 15%. (FAB) HRMS found $(M+1)^+$ 370.9425 / 368.9441 / 366.9451; $C_{14}H_{13}Br_2N_2$ requires 370.9405 / 368.9426 / 366.9445. 1H NMR δ 7.26 (dd, $J_1=J_2=7.7$ Hz, 1H), 7.17 (dd, $J_1=J_2=7.7$ Hz, 1H), 7.08 (d, $J=7.7$ Hz, 2H), 6.99 (dd, $J_1=7.9$ Hz, $J_2=0.75$ Hz, 1H), 6.85 (dd, $J_1=7.9$ Hz, $J_2=0.75$ Hz, 1H), 2.41 (dd, $J_1=8.3$ Hz, $J_2=6.2$ Hz, 1H), 2.18 (dd, $J_1=8.3$ Hz, $J_2=5.1$ Hz, 1H), 1.58 (s, 3H), 1.29 (dd, $J_1=6.2$ Hz, $J_2=5.1$ Hz, 1H). ^{13}C NMR δ 162.49 (C), 160.29 (C), 140.90 (C), 140.87 (C), 138.40 (CH), 138.02 (CH), 125.62 (CH), 124.95 (CH), 123.24 (CH), 121.86 (CH), 34.26 (CH), 33.48 (C), 26.28 (CH₃), 20.14 (CH₂). MS m/z 369, 368, 367, 288, 287, 275, 274, 273.

1-(6-Bromopyridin-2-yl)-ethanol (3).¹⁰ Colourless oil. Yield 2%. HRMS found M^+ 202.9786 / 200.9764; C_7H_8BrNO requires 202.9768 / 200.9764. 1H NMR δ 7.49 (t, $J=7.5$ Hz, 1H), 7.32 (d, $J=7.5$ Hz, 1H), 7.22 (d, $J=7.5$ Hz, 1H), 4.81 (m, 1H), 3.34 (brs, 1H, OH), 1.44 (d, $J=6.8$ Hz, 3H, CH_3). MS m/z 203, 202, 201, 188, 186, 158, 106, 78.

7-Bromo-3-methyl-[1,2,3]triazolo[1,5-*a*]pyridine (1). Recovered 30%.

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