Tetrahedron Letters 51 (2010) 2880–2882

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Synthesis of azidochloromethane and azidobromomethane

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ARTICLE INFO

Article history:
Received 15 March 2010
Accepted 22 March 2010
Available online 27 March 2010

Keywords:
Azides
Hazardous compounds
Nucleophilic substitution
Triazoles

ABSTRACT

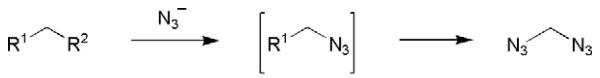
By treatment of tris(azidomethyl)amine with dry hydrogen halide, azidochloromethane and azidobromomethane were prepared. The former product, which is more stable than the latter, was isolated as a colorless liquid. The desired azidohalomethanes are intermediates in the nucleophilic substitution of dihalomethanes to generate diazidomethane but could not be detected in this transformation.

The family of simple azidomethanes was completely characterized starting with the early work on methyl azide published by Dimroth and Wislicenus.[1] Diazidomethane (**3**) and triazidomethane were generated from methylene chloride (**1a**) or bromide (**1b**) and bromoform, respectively (Scheme 1). These transformations were performed by Hassner and co-workers with the help of a polymeric azide reagent.[2] Recently, tetraazidomethane was isolated as a dangerous explosive colorless liquid.[3]

If dichloromethane (**1a**) is used as a solvent in the synthesis of azides, the unwanted formation of hazardous compound **3** is possible.[2,4] Thus, several explosions were reported and attributed to the surprising generation of diazide **3**.[5] Azidochloromethane (**2a**) was included into the corresponding warnings although this compound, like azidobromomethane (**2b**), was never detected or prepared by another method (Scheme 1).[6] However, the equilibrium structure and the force constants of **2a** were calculated in the MNDO approximation.[7] In this Letter, we report the synthesis and characterization of azides **2a**,**b**.

By NMR analysis of the transformation **1a**→**3**, Hassner recognized already that no signal of intermediate **2a** could be registered.[2b] He assumed that the second displacement on **2a** probably proceeded faster than the first chlorine substitution. Thus, we started with the mixed dihalomethane **1c** and hoped that the iodine displacement step **1c**→**2a** would not be significantly slower than the reaction **2a**→**3**. However, we could not detect any trace of **2a**, when treatment of **1c** with a substoichiometric amount of hexadecyltributylphosphonium azide[8] in chloroform was monitored by NMR spectroscopy, which led quantitatively and under mild conditions (18 h at 20 °C) to the diazide **3**.

After this frustration, we thought that the synthesis of **2a** and **2b** can only be successful if the halide is introduced after the formation of the azido group by nucleophilic substitution. Thus, we reacted triazide **4b**[9] (Scheme 2), which is easily accessible from trichloride **4a**,[10] with dry hydrogen chloride in chloroform or hexane (20 min at 20 °C) to obtain a mixture of **2a** and **3** after workup (solid, anhydrous K_2CO_3, and re-condensation). These products could be separated conveniently by preparative gas chromatography (packed column, 1 m, Carbowax, 30 °C) to get **2a** and **3** as explosive colorless liquids (**caution!**).[11] When the mixture of **2a** and **3**, resulting from **4b** and hydrogen chloride, was worked up and then treated with cyclooctyne,[12] the triazoles **8a** (11% based on **4b**), **9**, and **10** were isolated. Cycloaddition product **10** could be prepared quantitatively (based on **3**) if an excess of cyclooctyne was used. All new compounds were characterized by the usual spectroscopic data,[13] and the structure of **8a** was additionally confirmed by single crystal X-ray diffraction analysis (Fig. 1).[14] When **4b** was reacted with an excess of phenylsulfenyl chloride[15] (chloroform, 20 °C) instead of hydrogen chloride, the formation of **2a** (8%), **3** (21%), and **4a** (60%) was observed. Other α-azido amines such as **7**[16,17] could also be utilized to generate mixtures of **2a** and **3**. However, the yield of **2a** (⩽1%) was rather low. Treatment of **4b** with hydrogen bromide in anhydrous tetrachloromethane or



1a $R^1 = R^2 = Cl$
1b $R^1 = R^2 = Br$
1c $R^1 = Cl$, $R^2 = I$

2a $R^1 = Cl$
2b $R^1 = Br$

3

Scheme 1.

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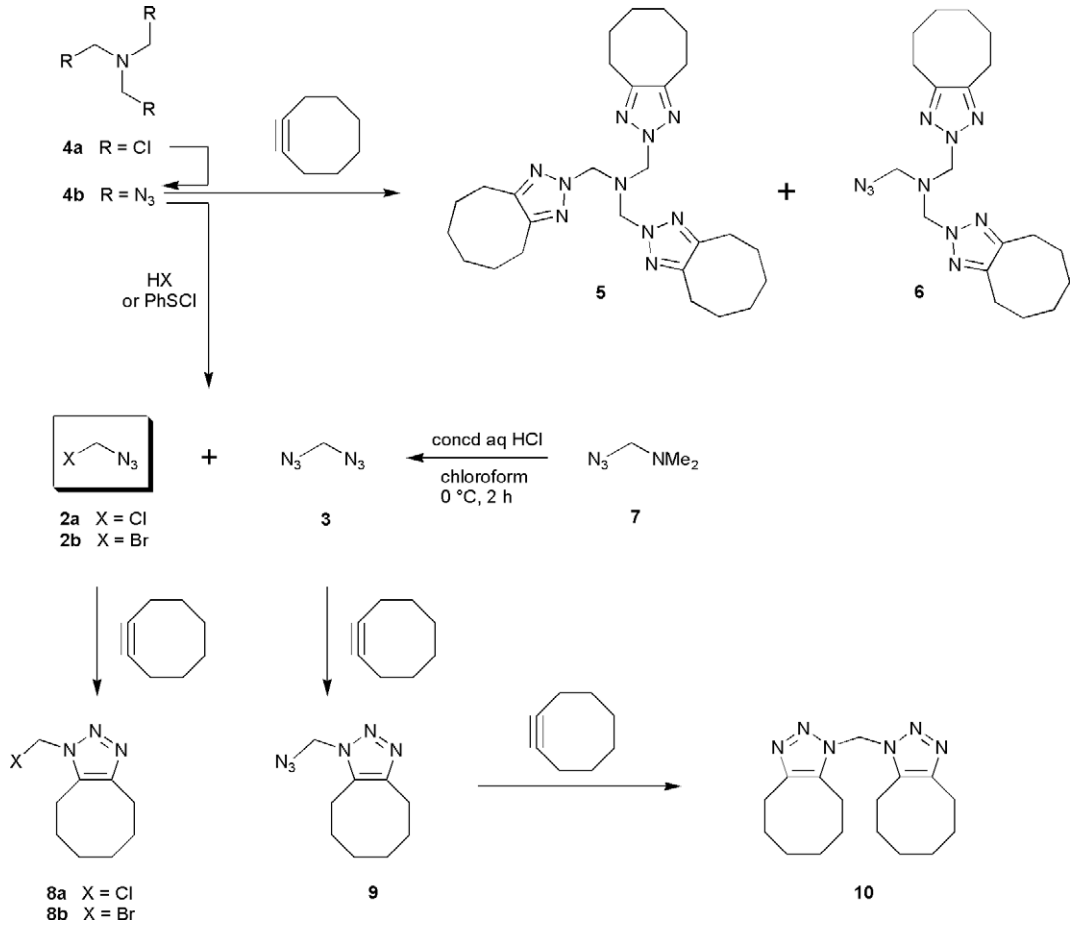
doi:10.1016/j.tetlet.2010.03.094



Scheme 2.

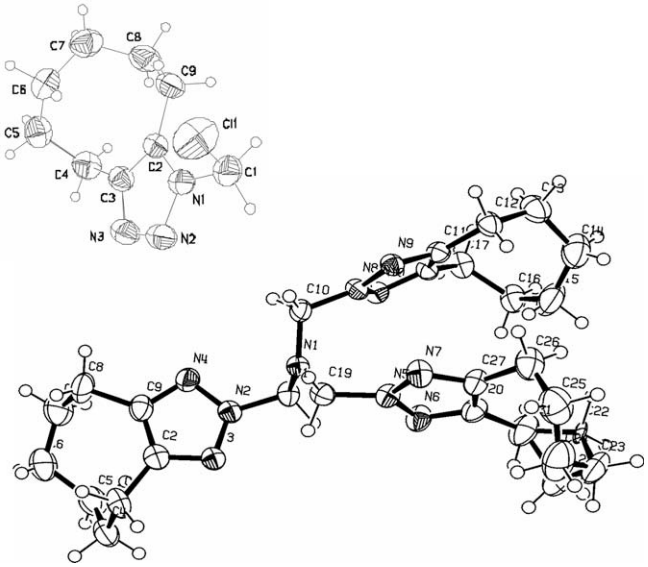


Figure 1. ORTEP diagrams (50% probability level) of the molecular structures of **8a** (above) and **5** (below). For **5**, disordered atoms have been omitted for clarity.

chloroform (4 °C, 30 min) led to the bromo compound **2b**, which was less stable than **2a** and could only be characterized in solution.[13] Cycloadduct **8b** was isolated in 14% yield, when **4b** was reacted with hydrogen bromide followed by conversion with cyclooctyne. NMR data[13] of the heterocycles **8a**, **8b**, **9**, and **10** indicated unambiguously the structures of 1*H*-1,2,3-triazoles. In contrast to this, cycloaddition of **4b** at cyclooctyne is accompanied by a rapid rearrangement reaction leading to the 2*H*-1,2,3-triazoles **5** (17% yield) and **6** (25%). The molecular structure of **5** was confirmed by single crystal X-ray diffraction analysis (Fig. 1).[14]

In conclusion, we have shown that azidochloromethane (**2a**) and azidobromomethane (**2b**) can be synthesized from triazide **4b**. Possibly, these products are able to enrich the multifarious chemistry of organic azides.[18]

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11. Caution should be exercised during isolation of explosive azides. Especially, **2a**, **2b**, and **3** are dangerous compounds, which should be handled in solution.
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13. *Azidochloromethane* (**2a**): Colorless liquid. IR ($CDCl_3$): $\tilde{\nu}$ = 2095 cm^{-1} (N_3), 1235 (N_3). ^1H NMR ($CDCl_3$): δ = 5.00 (s, 2H). ^{13}C NMR ($CDCl_3$): δ = 61.43 (t, $^1J_{CH}$ = 171.2 Hz).
Azidobromomethane (**2b**): IR ($CDCl_3$): $\tilde{\nu}$ = 2138 cm^{-1} (N_3). ^1H NMR ($CDCl_3$): δ = 4.99 (s, 2H). ^{13}C NMR ($CDCl_3$): δ = 50.05 (t, $^1J_{CH}$ = 173.5 Hz).
Tris-[(4,5,6,7,8,9-hexahydro-2H-cycloocta-1,2,3-triazol-2-yl)methyl]amine (**5**): white solid. Mp: 86–89 °C. IR ($CDCl_3$): $\tilde{\nu}$ = 2935 cm^{-1}, 2856, 2238. ^1H NMR ($CDCl_3$): δ = 1.43 (m, 12H), 1.69 (br. m, 12H), 2.73 (m, 12H), 5.54 (s, 6H). ^{13}C NMR ($CDCl_3$): δ = 23.63 (t), 25.39 (t), 28.47 (t), 69.26 (tquin, $^1J_{CH}$ = 152.9 Hz, $^3J_{CH}$ = 4.6 Hz), 146.32 (s). MS (ESI) *m/z* (%) = 545.4 (100) $[M+K]^+$. $C_{27}H_{42}N_{10}$ (506.70) calcd: C, 64.00; H, 8.35; N, 27.64; found: C, 63.80; H, 8.32; N, 27.09.
Azidomethyl-{bis-[(4,5,6,7,8,9-hexahydro-2H-cycloocta-1,2,3-triazol-2-yl)methyl]} amine (**6**): yellow liquid. IR ($CDCl_3$): $\tilde{\nu}$ = 2935 cm^{-1}, 2857, 2106 (N_3). ^1H NMR ($CDCl_3$): δ = 1.40 (m, 8H), 1.67 (m, 8H), 2.75 (m, 8H), 4.44 (s, 2H), 5.37 (s, 4H). ^{13}C NMR ($CDCl_3$): δ = 23.49 (t), 25.25 (t), 28.46 (t), 68.16 (t), 68.91 (t), 146.94 (s).
1-Chloromethyl-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (**8a**): Colorless crystals. Mp: 63 °C. IR ($CDCl_3$): $\tilde{\nu}$ = 3118 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.41–1.56 (m, 4H), 1.70–1.78 (m, 2H), 1.84–1.92 (m, 2H), 2.83–2.92 (m, 4H), 5.94 (s, 2H). ^{13}C NMR ($CDCl_3$): δ = 21.46 (t), 24.32 (t), 24.59 (t), 25.83 (t), 25.87 (t), 27.78 (t), 52.82 (t, $^1J_{CH}$ = 167.2 Hz), 133.81 (s), 145.73 (s). MS (ESI) *m/z* (%) = 200.1 (18) $[M+H]^+$, 363.2 (100) $[2\,M - Cl]^+$. $C_9H_{14}N_3Cl$ (199.69) calcd: C, 54.14; H, 7.07; N, 21.04; found: C, 54.77; H, 7.16; N, 20.54.
1-Bromomethyl-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (**8b**): Colorless oil. IR ($CDCl_3$): $\tilde{\nu}$ = 2935 cm^{-1}, 2858. ^1H NMR ($CDCl_3$): δ = 1.38–1.44 (m, 2H), 1.48–1.53 (m, 2H), 1.68–1.75 (m, 2H), 1.85–1.91 (m, 2H), 2.80–2.83 (m, 2H), 2.85–2.89 (m, 2H), 5.93 (s, 2H). ^{13}C NMR ($CDCl_3$): δ = 21.59 (t), 24.26 (t), 24.49 (t), 25.55 (t), 25.86 (t), 27.65 (t), 38.60 (t, $^1J_{CH}$ = 169.8 Hz), 133.78 (s), 145.67 (s). MS (ESI) *m/z* (%) = 244.1 (100) $[M+H, {}^{79}Br]^+$, 246.1 (90) $[M+H, {}^{81}Br]^+$. HR MS (ESI) *m/z* = 244.0496 [calcd $C_9H_{14}BrN_3$ 244.0444].
1-Azidomethyl-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (**9**): Colorless liquid. IR ($CDCl_3$): $\tilde{\nu}$ = 2101 cm^{-1} (N_3), 1234 (N_3). ^1H NMR ($CDCl_3$): δ = 1.43–1.56 (m, 4H), 1.73–1.81 (m, 2H), 1.81–1.87 (m, 2H), 2.79–2.83 (m, 2H), 2.90–2.94 (m, 2H), 5.50 (s, 2H). ^{13}C NMR ($CDCl_3$): δ = 21.39 (t), 24.43 (t), 24.73 (t), 25.85 (t), 26.28 (t), 28.04 (t), 61.05 (t, $^1J_{CH}$ = 158.0 Hz), 133.46 (s), 145.69 (s).
Bis-(4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazol-1-yl)methane (**10**): Colorless crystals. Mp: 149–152 °C. IR ($CDCl_3$): $\tilde{\nu}$ = 2934 cm^{-1}, 2858, 2236. ^1H NMR ($CDCl_3$): δ = 1.32–1.41 (m, 8H), 1.55–1.63 (m, 4H), 1.67–1.75 (m, 4H), 2.83–2.87 (m, 4H), 2.93–2.97 (m, 4H), 6.61 (s, 2H). ^{13}C NMR ($CDCl_3$): δ = 21.29 (t), 24.35 (t), 24.78 (t), 25.65 (t), 26.21 (t), 27.97 (t), 57.71 (t, $^1J_{CH}$ = 155.2 Hz), 134.44 (s), 145.92 (s). MS (ESI) *m/z* (%) = 315.2 (100) $[M+H]^+$. $C_{17}H_{26}N_6$ (314.44) calcd: C, 64.94; H, 8.33; N, 26.73; found: C, 64.76; H, 8.42; N, 25.87.
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