

Synthesis of 4-azido-3-diazo-3*H*-pyrazolo[3,4-*b*]quinoline from 3-amino-4-hydrazino-1*H*-pyrazolo[3,4-*b*]quinoline¹



Wolfgang Stadlbauer* and Gerhard Hojas

Institute of Chemistry, Organic Synthesis Group, Karl-Franzens University of Graz,
Heinrichstrasse 28, A-8010 Graz, Austria

Received (in Cambridge, UK) 13th June 2000, Accepted 25th July 2000

Published on the Web 30th August 2000

The reaction of 3-amino-4-hydrazino-1*H*-pyrazolo[3,4-*b*]quinoline **8** with nitrous acid did not give 2,4-diazoquinoline-3-carbonitrile **5** as reported previously, but afforded in 60% yield 4-azido-3-diazopyrazolo[3,4-*b*]quinoline **10**, which gave by azo coupling with 2-naphthol 4-azido-3-(2-hydroxy-1-naphthylazo)-1*H*-pyrazolo[3,4-*b*]quinoline **11**.

Introduction

In a previous work we studied the reaction of sodium azide with a number of 2,4-dichloroquinolines² and found that depending on the reaction conditions and the substituent in position 3 either 2-azido-, 4-azido- or 2,4-diazoquinolines were formed. For example, 2,4-dichloroquinoline-3-carbonitrile **1** reacted with sodium azide in DMF at 55 °C to give 4-azido-2-chloroquinoline-3-carbonitrile **2**, whereas the reaction in ethanol with methanesulfonic acid at 60 °C gave 2-azido-4-chloroquinoline-3-carbonitrile **3**. Excess of sodium azide in the presence of cryptofix **5** as catalyst in DMF at 0 °C afforded 2,4-diazoquinoline-3-carbonitrile **5**.² The synthesis of azides **2** and **5** was already described,³ however with an irreproducible preparation procedure stated already in ref. 2.

Infrared spectroscopic investigations in potassium bromide pellets and in solvents such as chloroform or trifluoroacetic acid and ¹³C NMR studies gave as the result, that the 4-azido group existed in the azido form of compound **2**. The 2-azido group could be shown *e.g.* by total lack of the azido signal in the infrared spectrum of **3** (also in strong acidic medium) to exist only in the tautomeric tetrazolo form as shown in compounds **4** and **6**.² These findings were supported by ¹³C NMR investigations² and by synthetic reactions: hydrogenation of the tautomer **5/6** with palladium as the catalyst² or reduction with sodium dithionite gave only 5-aminotetrazolo[1,5-*a*]quinoline-4-carbonitrile **9**; the 2-azido/tetrazolo moiety was not attacked. The only method to convert the tetrazolo/azido groups of **3/4** or **5/6** to amines proceeds *via* a Staudinger reaction with phosphazenes as been shown in other heterocyclic systems.^{2,4}

Recently a new method for the synthesis of 2,4-diazoquinoline-3-carbonitrile **5** was published, which started from 2,4-dichloroquinoline-3-carbonitrile **1** *via* the 4-benzylamino compound **7** and the fused 3-amino-4-hydrazino-1*H*-pyrazolo[3,4-*b*]quinoline **8**.⁵ Reaction of **8** with HNO₂ was reported to give *via* nitrosation **5**, which has been claimed to exist exclusively or predominantly in the bis-azido form **5** and not in its tautomeric tetrazolo form **6**.⁵ This unexpected result surprised us because this finding means that **5** has a kind of molecular memory: preparation of **5** *via* nucleophilic attack of azide ions results in the tetrazolo tautomer **6**,² whereas formation of the azido group *via* nitrosation of **8** and subsequent ring opening of the aminopyrazolo moiety gives a stable azido tautomer **5** with no attack of the neighboring quinoline nitrogen.⁵

Results and discussion

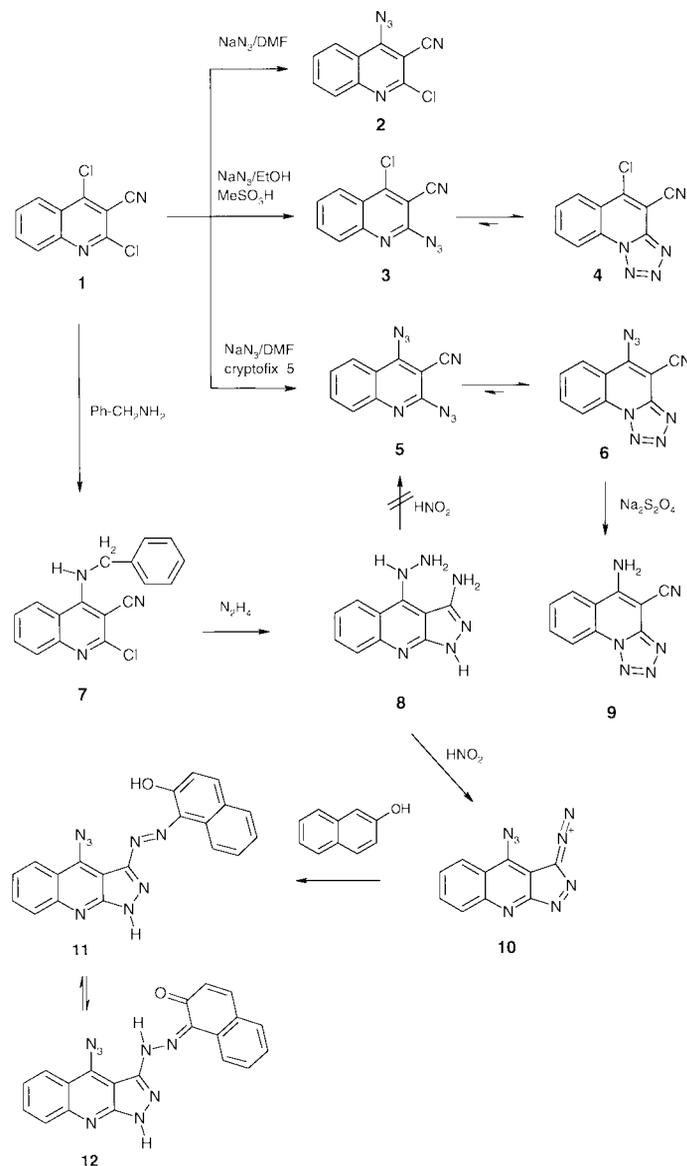
Because no authentic sample of the diazoquinoline **5** obtained from **8** was available,⁶ we tried to prepare it according to the procedure described in ref. 4; however, in our hands, the reaction of 3-amino-4-hydrazino-1*H*-pyrazolo[3,4-*b*]quinoline **8** with HNO₂ gave not 2,4-diazoquinoline-3-carbonitrile **5**, but in 60–70% yield the 4-azido-3-diazo-1*H*-pyrazolo[3,4-*b*]quinoline **10**, as should be expected from textbook chemistry.⁷ The structure of **10** could be elucidated easily because no CN signal in the infrared spectrum was visible at about 2200 cm⁻¹; this fact excluded any nitrile containing structure such as **5** or **6**. The IR signals of the azido and the diazo groups were found at 2123 and 2089 cm⁻¹; microanalysis gave the elemental formula of C₁₀H₄N₈. The structure of **10** was additionally supported by a chemical reaction because azo coupling with 2-naphthol gave in 81% yield the dark blue *ortho*-hydroxy azo compound **11**, a type of compound which is known to exist in an equilibrium with the tautomeric quinoid hydrazone **12** depending on the nature of the solvent.⁸ An attempt to react **5/6** with 2-naphthol gave no product.

The thermal behavior of the azides **6** and **11** was compared with the behavior of the 4-azido-3-diazo compound **10**. The reaction enthalpies of **5** and **11** with –95 and –101 kcal mg⁻¹ were in the average range of azides without reactive *ortho*-groups.⁹ 4-Azido-3-diazo compound **10**, however, showed a strong reaction enthalpy of –348 kcal mg⁻¹, more than three times value of the simple azides **5** and **11**. The thermal decomposition of **10** gave an explosion which destroyed the crucibles of the DSC apparatus (suitable for a pressure of 11 bar) when 1.5 mg of compound was investigated. The data listed in the Experimental were obtained with 0.3 mg of compound **10**. The use of pressure (*e.g.* for KBr pellets) gave no explosions.

As result of this short contribution it can be stated that 2,4-diazoquinoline-3-carbonitrile **5** was not obtained from **8** by the method described in ref. 5. The synthesis of its tetrazolo tautomer **6** can be performed easily and reproducibly using a nucleophilic halogen exchange as described in ref. 2.

Experimental

Mps were obtained on a Gallenkamp Melting Point Apparatus, Mod. MFB-595 in open capillary tubes. Microanalyses were performed on a Fisons elemental analyzer, Mod. EA 1108.



Scheme 1

IR (KBr) spectra were taken on a Perkin-Elmer 298 or a Galaxy Series FTIR 7000. ^1H NMR spectra (at 200 or 360 MHz) were obtained on a Varian Gemini 200 or a Bruker AM 360 instrument in $[\text{D}_6]$ dimethyl sulfoxide as solvent. Chemical shifts are reported in ppm from internal tetramethylsilane and are given in δ -units. J -Values are given in Hz. DSC (differential scanning calorimetry) data were obtained on a Rheometric Scientific DSC-Plus instrument with the DSC software V5.42. The DSC plots were recorded between 25 and 500 $^\circ\text{C}$, with a heating rate of 2–10 $^\circ\text{C min}^{-1}$, and 0.3–2.5 mg of compound in sealed aluminium crucibles (11 bar). Analytical TLC was carried out on 0.2 mm silica gel F254 (Merck) plates using UV light (254 and 366 nm) for detection.

CAUTION: Compound **10** is an explosive. A detonation occurs on heating to more than 110 $^\circ\text{C}$.

2,4-Dichloroquinoline-3-carbonitrile **1**

Prepared from 4-hydroxyquinoline-3-carbonitrile¹⁰ and phosphoryl chloride according to our previously reported method.²

4-Azido-2-chloroquinoline-3-carbonitrile **2**

Prepared from **1** and sodium azide in DMF at 55 $^\circ\text{C}$ according to our previously reported method.²

5-Chlorotetrazolo[1,5-*a*]quinoline-4-carbonitrile **4**

Prepared from **1** and sodium azide in ethanol and methanesulfonic acid at 60 $^\circ\text{C}$ according to our previously reported method.²

5-Azidotetrazolo[1,5-*a*]quinoline-4-carbonitrile **6**

Prepared from **1** and excess sodium azide in DMF at 0 $^\circ\text{C}$ using cryptofix 5 as catalyst according to our previously reported method.² The yield was 85%, mp 175–178 $^\circ\text{C}$ (decomp.) (ethanol) (lit. mp 185² and 190³ $^\circ\text{C}$). Differential scanning calorimetric data: 170.1 $^\circ\text{C}$ (onset), 176.9 $^\circ\text{C}$ (reaction peak), $\Delta H = -95 \text{ kcal mg}^{-1}$ (reaction enthalpy), 218.2 $^\circ\text{C}$ (onset), 257.8 $^\circ\text{C}$ (decomp. peak), -61 kcal mg^{-1} (reaction enthalpy); no mp.

4-Benzylamino-2-chloroquinoline-3-carbonitrile **7**

Prepared from **1** and benzylamine according to ref. 5.

3-Amino-4-hydrazino-1*H*-pyrazolo[3,4-*b*]quinoline **8**

Prepared from **7** and hydrazine according to ref. 5.

5-Aminotetrazolo[1,5-*a*]quinoline-4-carbonitrile **9**

Sodium dithionite (0.44 g, 2.5 mmol) was added in portions to a stirred suspension of 5-azidotetrazolo[1,5-*a*]quinoline-4-

carbonitrile **6** (0.20 g, 0.8 mmol) in a mixture of methanol (10 mL) and water (5 mL). Stirring was maintained at 50–60 °C for 5 h. After cooling to 20 °C, water (100 mL) was added and the resulting solid product was filtered by suction, washed with water (50 mL), dried and recrystallized from ethyl acetate to give compound **9** as yellowish prisms (0.13 g, 75%), mp 307–309 °C (decomp.) (lit.³ mp 320 °C) (Found: C, 57.35; H, 2.86; N, 39.60. C₁₀H₆N₆ requires C, 57.14; H, 2.88; N, 39.98%); $\nu_{\max}/\text{cm}^{-1}$ 3460 m, 3315 m, 3215 m (NH₂), 2205 s (CN), 1655 sh, 1650 s, 1615 sh, 1610 s (C=C); δ 7.74 (t, *J* 7, 1 H, ArH), 7.97 (t, *J* 7, 1 H, ArH), 8.40 (m, 3 H, -NH₂, ArH), 8.51 (dd, *J* 1.5 and 7, 1 H, ArH).

4-Azido-3-diazo-3*H*-pyrazolo[3,4-*b*]quinoline **10**

A solution of NaNO₂ (0.19 g, 2.8 mmol) in water (1.0 mL) was added dropwise to a solution of 3-amino-4-hydrazino-1*H*-pyrazolo[3,4-*b*]quinoline **8** (0.20 g, 0.9 mmol) in H₂SO₄ (5 mL, 70%) cooled in ice–salt to –10 °C, while the temperature of the reaction mixture was maintained at –10 to –5 °C. The reaction mixture was kept at –5 °C for 1 h and then poured into ice–water (50 mL). The resulting precipitate was collected by filtration, washed with water (100 mL), dried and recrystallized from toluene to give the brownish needles of the diazo compound **10** (0.14 g, 60%), mp 138–140 °C (explosive decomp.). Differential scanning calorimetric data: 132.7 °C (onset), 139.1 °C (reaction peak), $\Delta H = -348$ kcal mg⁻¹ (reaction enthalpy); no mp (Found C, 51.15; H, 1.86; N, 47.05. C₁₀H₄N₈ requires C, 50.85; H, 1.71; N, 47.44%); $\nu_{\max}/\text{cm}^{-1}$ 2123 s (N₃, N₂), 2089 sh, 1598 s (C=C); δ 7.75 (t, *J* 7, 1 H, ArH), 7.94 (t, *J* 7, 1 H, ArH), 8.18 (d, *J* 7, 1 H, ArH), 8.31 (dd, *J* 1.5 and 7, 1 H, ArH).

4-Azido-3-(2-hydroxy-1-naphthylazo)-1*H*-pyrazolo[3,4-*b*]quinoline **11**/4-azido-3-(2-oxo-1,2-dihydro-1-naphthylidenehydrazino)-1*H*-pyrazolo[3,4-*b*]quinoline **12**

A solution of 4-azido-3-diazo-3*H*-pyrazolo[3,4-*b*]quinoline **10** (0.10 g, 0.42 mmol) in half-concentrated H₂SO₄ (1.0 mL) was cooled to 5–10 °C and treated with a solution of 2-hydroxynaphthalene (0.06 g, 0.42 mmol) in 2 M NaOH (3 mL).

The reaction mixture was stirred for 15 min at 20 °C to give a dark blue reaction mixture. The mixture was made alkaline with 2 M NaOH; the precipitate was filtered by suction and washed with water (100 mL) to afford the dye **11/12** as dark blue prisms (0.13 g, 81%), mp 136–138 °C (decomp.). Differential scanning calorimetric data: 126.5 °C (onset), 136.5 °C (reaction peak), $\Delta H = -101$ kcal mg⁻¹ (reaction enthalpy); no mp (Found C, 63.42; H, 3.34; N, 29.07. C₂₀H₁₂N₈O requires C, 63.15; H, 3.18; N, 29.46%); $\nu_{\max}/\text{cm}^{-1}$ 3030 m, br, (OH), 2120 s (N₃), 1610 s (C=N), 1575 sh, 1560 m (N=N).

Acknowledgements

This work was supported by the “Österreichischer Fonds zur Förderung der wissenschaftlichen Forschung”, project No. P 10785-CHE.

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