A convenient synthesis of 2-substituted [1,2,4]triazolo- [1,5-*a*]quinolines and [1,2,4]triazolo[5,1-*a*]isoquinolines

C. N. Hoang,[a,b] Zs. Riedl,[a] G. Timária[§], G. Hajós[*a], and J. G. Schantl[*b]

[a] *Chemical Research Center, Institute of Chemistry, POBox 17, H-1525 Budapest, Hungary*
[b] *Institut für Organische Chemie, Universität Innsbruck, Innrain 52a, A-6020 Innsbruck, Austria*
E-mail: ghajos@cric.chemres.hu; joachim.schantl@uibk.ac.at

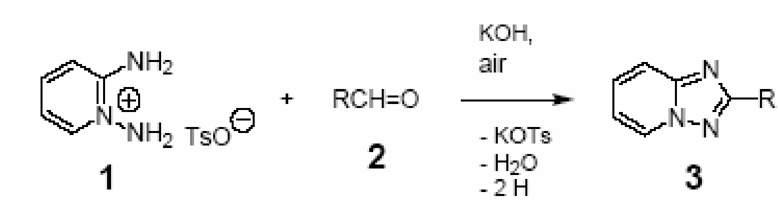
(received 25 Nov 00; accepted 28 Oct 01; published on the web 05 Nov 01)

Abstract
Upon reaction with aqueous potassium hydroxide and aliphatic and aromatic aldehydes **2** the salts 1,2-diaminoquinolinium tosylate **4** and 1,2-diaminoisoquinolinium tosylate **9** were converted into the corresponding 2-substituted [1,2,4]triazolo[1,5-*a*]quinolines **8** and [1,2,4]triazolo[5,1-*a*]isoquinolines **13**, respectively. The formation of the final products requires aerial oxidation.

Key words: Fused [1,2,4]triazoles, 1,2-diaminoquinolinium tosylate, 1,2-diaminoisoquinolinium tosylate, 1-amino-2-iminoquinoline, 2-amino-1-iminoisoquinoline, hydrazone, ring-chain tautomerism, aerial oxidation

Introduction

We have recently reported[1] that 1,2-diaminopyridinium tosylate **1** readily reacts with aldehydes **2** furnishing 2-substituted triazolo[5,1-*a*]pyridines **3** in moderate to good yields (Scheme 1).



Scheme 1

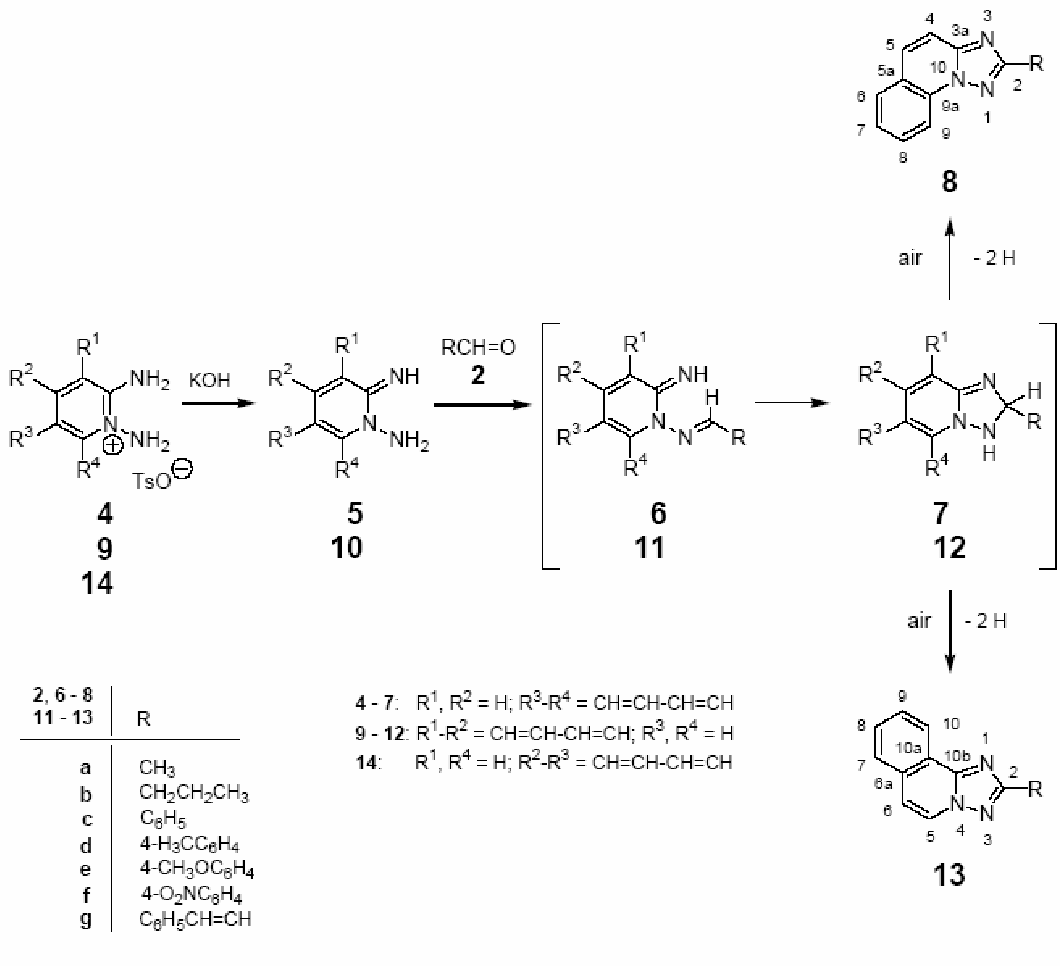
In continuation of this study, and pursuing our continuous interest in the synthesis of polycyclic heteroaromatic compounds we decided to explore if this straightforward ring formation procedure can be extended. In this paper we describe a successful application of this synthetic strategy to prepare 2-substituted angularly fused benzo homologues of **3**, *i.e.* the title ring systems **8** and **13** (Scheme 2).

Various synthetic approaches to the tricyclic system of structures **8** and **13** have been reported in the literature. The pyridine and triazole rings of [1,2,4]triazolo[1,5-*a*]quinolines **8** have been prepared by ring closure and cycloaddition reactions: The construction of the pyridine ring by formation of bond 5-C/5a-C bond has been reported in a patent.[2] The triazole ring has resulted from the formation of bonds 1-N/10-N, [3] 2-C/3-N, [4] and 3-N/3a-C. [5] In the course of the [3+2] cycloaddition reaction of 1*H*-[1,2]benzodiazepine with benzonitrile oxide the bonds 1-N/2-C and 3-N/3a-C were formed in one step affording **8c**. [6] Both heterocyclic moieties of **8** were obtained in an obviously geared double condensation reaction forming bonds 3a-C/10-N and 4-C/5-C, [7] and by the intramolecular cycloaddition reaction of an *in situ* generated nitrile imine functionality with a nitrile group providing the 3a-C/10-N and 2-C/3-N bonds. [8] The isomeric [1,2,4]triazolo[5,1-*a*]isoquinolines **13** have been accessed by building up the triazole moiety by either ring closure or [3+2] cycloaddition reactions. The formation of bonds 3-N/4-N, [9] 1-N/10b-C, [5,10,11] and 2-C/3-N[12] has been reported. In a [3+2] cycloaddition reaction of azomethine imines (in situ generated by deprotonation of 2-aminoisoquinolines) with nitriles bonds 1-N/10b-C and 2-C/3-N have been formed concomittantly.[13-16] Some of these compounds, in particular, 2-aryl-substituted [1,2,4]triazolo[5,1-*a*]isoquinolines **13** have received considerable attention because of biological activities; e.g. **13c** or **13** (R = 4-ClC_6H_4, Lotrifen) are nonhormonal antifertility agents.[17, 18]

Results and Discussion

Here we report the formation of the tricyclic structures **8** and **13** in the course of the condensation reaction of 1,2-diaminoquinoline **5** or -isoquinoline **10** with an aldehyde forming two bonds 1-N/2-C and 2-C-3-N of the triazole ring. The starting compounds of this reaction, 1,2-diaminoquinolinium tosylate **4**[19] and 1,2-diaminoisoquinolinium tosylate **9**[19] are readily available from 2-aminoquinoline and 1-aminoisoquinoline by direct N-amination procedure using *O*-tosylhydroxylamine[20] according to our previously published procedure. [21] When a solution of the tosylates **4** or **9** in methanol is mixed with an aliphatic or aromatic aldehyde **2** and treated with aqueous potassium hydroxide at room temperature the respective 2-substituted fused [1,2,4]triazoles **8** and **13** are obtained within a few hours (Scheme 2). In some cases the crystalline products **8** and **13** precipitate from the reaction mixture and are collected by filtration (Method A). Alternatively, the products are isolated upon extraction from the reaction mixture with dichloromethane (Method B). The yields of the tricyclic products **8** (69-95%) and **13** (57-86%) are generally very good. It is interesting to note that these yields are significantly higher than those found for the bicyclic ring system **3**. [1] The higher conversion rates may be due to the enhanced stability of the imino-amino bases **5** and **10** which – in contrast to the quite unstable conjugate base formed from **1** – have been isolated as stable crystalline compounds.

The reaction proceeds *via* the *in situ* generation of the free bases 1-amino-2-iminoquinoline **5**[22] and 2-amino-1-iminoisoquinoline **10**, [23] respectively. This has been proved by separate experiments with these compounds reacting with benzaldehyde **2c** and affording the fused [1,2,4]triazoles **8c** and **13c**, respectively. Thus the free base **5** or **10** reacts with aldehydes **2** to give the condensation products **6** and **11**, respectively. These hydrazones **6** and **11** are presumed to coexist in an equilibrium with ring chain tautomers, the corresponding dihydrotriazole derivatives **7** and **12** which, in turn, upon dehydrogenation induced by air oxidation yield the final heteroaromatic products **8** and **13**, respectively. Oxygen from air is required for this oxidation step. This has been proved by carrying out the reaction of 2-amino-1-iminoisoquinoline **10** with benzaldehyde **2c** under exclusion of air. After 6 h no product 2-phenyl[1,2,4]triazolo[5,1-*a*]isoquinoline **13c** could be detected. When this reaction mixture was stirred and exposed to air the product **13c** was isolated in virtually the same yield as following Procedure A.



Scheme 2

The structures of products **8** and **13** were confirmed by ^{1}H and ^{13}C NMR spectra. The assignment of the significant signals is according to a two-dimensional NMR study on

[1,2,4]triazolo[1,5-*f*]phenanthridines, a tetracyclic system that has embedded both tricyclic structures **8** and **13**.[24] The ^{1}H NMR spectra of the quinoline derivatives **8** exhibit the doublet signal of 9-H at lowest field (δ 8.40–8.62). The isoquinoline derivatives **13** show the AB system of 5-H and 6-H at of δ 7.11–7.33 and δ 8.22–8.38, respectively; the signal of 10-H appears in the range of δ 8.53–8.74. On the basis of the NMR data established for [1,2,4]triazolo[1,5-*f*]phenanthridines[24] most of the significant ^{13}C NMR data of compounds **8** and **13** have been assigned.

Further investigation on the application of this triazole ring closure strategy is in progress and is currently extended to 2,3-diaminoisoquinolines **14** (Scheme 2) aiming at the preparation of linearly fused [1,2,4]triazolo[1,5-*b*]isoquinolines.

Experimental Section

General Procedures. Melting points were determined with a Büchi apparatus. IR spectra were recorded with a Nicolet 205 FT spectrometer, NMR spectra were recorded on a Varian VXR-200 (200 MHz ^{1}H NMR) spectrometer, and mass spectra were measured with a MS-902 instrument (70 eV).

1,2-Diaminoquinolinium tosylate (4).[19] To a stirred solution of quinolin-2-ylamine[25] (0.5 g, 3.5 mmol) in dichloromethane (5 mL) was added a solution of *O*-tosylhydroxylamine[20] (0.7 g, 3.9 mmol) in dichloromethane (5 mL) at rt. Within a few minutes a precipitate began to separate. The product was filtered off and recrystallized from methanol to give colorless crystals **4** (0.984 g, 85%); mp 219–222 °C. IR (KBr): 3310, 3240, 3180, 1670, 1640, 1600, 1520, 1500,1450, 1230, 1170, 1120, 1030, 1100, 820, 760, 680 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.27 (s, 3H, CH_3), 6.4 (s, 2H, NH_2), 7.07, 7.12 (AA’, 2H, 3,5-H C_6H_4), 7.16 (d, *J* = 9.4 Hz, 1H, 3-H), 7.45, 7.49 (XX’, 2H, 2,6-H C_6H_4), 7.52 (dd, *J* = 7.6, 8.0 Hz, 1H, 6-H), 7.87 (dd, *J* = 7.6, 8.4 Hz, 1H, 7-H), 7.90 (d, *J* = 8.0 Hz, 1H, 5-H), 8.04 (d, *J* = 8.4 Hz, 1H, 8-H), 8.30 (d, *J* = 9.4 Hz, 1H, 4-H), 9.15 (br s, 2H, NH_2). ^{13}C NMR (DMSO-d_6): δ 20.97, 113.88, 115.99, 121.94, 125.34, 125.65, 128.25, 129.45, 132.70, 137.87, 139.58, 141.24, 155.73. Anal. Calcd. for $C_{17}H_{17}N_3O_3S$ (331.40): C, 57.99; H, 5.17; N, 12.68. Found: C, 57.69; H, 5.05; N, 12.46.

1,2-Diaminoisoquinolinium tosylate (9).[19] Applying the same protocol as described before to isoquinolin-1-ylamine[26] (0.5 g, 3.5 mmol) afforded colorless crystals **9** (1.008 g, 87%); mp 218–220 °C (methanol). IR (KBr): 3300, 3240, 3180, 1670, 1640, 1600, 1510, 1480, 1230, 1170, 1120, 1020, 1000, 800, 670 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.25 (s, 3H, CH_3), 6.8 (s, 2H, NH_2), 7.07, 7.12 (AA’, 2H, 3,5-H C_6H_4), 7.1–7.9 (m, 4H, 5,6,7,8-H), 7.45, 7.49 (XX’, 2H, 2,6-H C_6H_4), 8.55 (d, *J* = 6.4 Hz, 1H, 3-H), 9.25 (br s, 2H, NH_2). ^{13}C NMR (DMSO-d_6): δ 20.76, 110.90 117.81, 125.46, 125.58, 127.62, 128.07, 128.76, 134.13, 134.45, 134.86, 137.71, 145.53, 154.00. Anal. Calcd. for $C_{17}H_{17}N_3O_3S$ (331.40): C, 57.99; H, 5.17; N, 12.68. Found: C, 57.65; H, 5.13; N, 12.57.

General procedures For the Synthesis of Triazoles **8** and **13**.

Procedure A. An aqueous solution (14 mL) of potassium hydroxyde (2.8 g, 50 mmol) was added to a solution of 1,2-diaminoquinolinium tosylate (**4**) or 1,2-diaminoisoquinolinium tosylate (**9**) (1.66 g, 5 mmol) and aldehyde **2** (7 mmol) in methanol (50 mL). Upon stirring the reaction solution in an open flask at rt for 3-5 min a precipitate appeared. After 1 h the precipitate formed was filtered off and washed with methanol (5 mL). This procedure was repeated in 1 h intervals until no more precipitate was formed and the filtrate remained as a clear solution. The combined crop of solid material was washed with water and dried in a desiccator. Recrystallization from an appropriate solvent provided the pure crystalline products **8** and **13**, respectively.

Procedure B. The reaction mixture of the 1,2-diaminoquinolinium tosylate (**4**) or 1,2-diaminoisoquinolinium tosylate **9** (1.66 g, 5 mmol), the aldehyde **2** (20 mmol) in methanol (50 mL) and an aqueous solution (14 mL) of potassium hydroxyde (2.8 g, 50 mmol) was stirred in an opened flask at rt for 6 h. The reaction solution was then poured into water (100 mL) and extracted with dichloromethane (3 x 50 mL). The combined organic layers were washed until neutral and dried over sodium sulfate. The residue after evaporation of the solvent was purified by column chromatography on silica gel with diethyl ether. Removal of the eluent solvent from the appropriate fractions furnished the solid product on cooling or on standing. Recrystallization from petroleum ether or *n*-hexane gave the pure product.

2-Methyl[1,2,4]triazolo[1,5-*a*]quinoline (8a). Procedure B. Colorless crystals, 0.78 g (85%); mp 77 °C (*n*-hexane). IR (KBr,): 1618 (s), 1561, 1537, 1490, 1486, 1453, 1306 (s), 826, 759, 753 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.67 (s, 3H, CH_3), 7.44–7.84 (m, 5H, 4,5,6,7,8-H), 8.41 (d, J = 8.4 Hz, 1H, 9-H); ^{13}C NMR ($CDCl_3$): δ 14.4 (CH_3), 114.4 (CH), 115.6 (CH), 122.8 (5a-C), 125.1 (CH), 128.5 (CH), 129.9 (CH), 130.2 (CH), 133.4 (9a-C), 149.4 (3a-C), 162.8 (2-C). Anal. Calcd. for $C_{11}H_9N_3$ (183.21): C, 72.11; H, 4.95; N, 22.94. Found: C, 72.38; H, 4.97; N, 22.30.

2-Propyl[1,2,4]triazolo[1,5-*a*]quinoline (8b). Procedure B. Colorless crystals (0.91 g, 86%); mp 47 °C (*n*-hexane). IR (KBr): 2962, 1617 (s), 1538, 1483, 1330, 1312, 815 (s), 760 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.07 (t, J = 7.4 Hz, 3H, CH_3), 1.96 (qt, J = 7.4 Hz, 2H, CH_2CH_3), 2.97 (t, J = 7.4 Hz, 2H, 2-CCH_2), 7.36–7.77 (m, 5H, 4,5,6,7,8-H), 8.40 (d, J = 8.4 Hz, 1H, 9-H); ^{13}C NMR ($CDCl_3$): δ 13.8 (CH_3), 21.7 (CH_2CH_3), 30.6 (2-CH_2), 114.4 (CH), 115.5 (CH), 122.7 (5a-C), 124.9 (CH), 128.3 (CH), 129.7 (CH), 129.9 (CH), 133.3 (9a-C), 149.1 (3a-C), 166.3 (2-C). Anal. Calcd. for $C_{13}H_{13}N_3$ (211.26): C, 73.91; H, 6.20; N, 19.89. Found: C, 74.47; H, 6.37; N, 19.76.

2-Phenyl[1,2,4]triazolo[1,5-*a*]quinoline (8c).[2] Procedure A. Colorless crystals (1.09 g, 89%); mp 142 °C (ethanol/water 4:1; lit.[2] mp 137–139 °C). IR (KBr): 1620, 1561, 1544, 1459, 1453 (s), 1441, 1333, 834, 767, 750, 718, 717, 699, 686 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.45–7.86 (m, 8H_{arom}), 8.36 (dd, J = 8.2, 2.0 Hz, 2H, 2,6-H C_6H_5), 8.57 (dd, J = 8.4, 0.6 Hz, 1H, 9-H); ^{13}C NMR ($CDCl_3$): δ 114.8 (CH), 116.0 (CH), 123.1 (5a-C), 125.5 (CH), 127.1 (2,6-C or 3,5-C C_6H_5), 128.6 (3C, 1-C, 2,6-C or 3,5-C C_6H_5), 129.8 (CH), 130.1 (CH), 130.7 (CH), 130.9 (4-C C_6H_5), 133.7 (9a-C), 149.8 (3a-C), 163.2 (2-C). Anal. Calcd. for $C_{16}H_{11}N_3$ (245.28): C, 78.35; H, 4.52; N, 17.13. Found: C, 78.25; H, 4.62; N, 17.03. Following Procedure A and using 1-amino-2-

iminoquinoline (**5**)[22] (0.80 g, 5 mmol) and water (11 mL, instead of an aqueous potassium hydroxide solution) afforded after 6 h **8c** (0.90 g, 73%).

2-(4-Methylphenyl)[1,2,4]triazolo[1,5-*a*]quinoline (8d). Procedure A. Colorless crystals, 1.02 g (78%); mp 191 °C (ethanol). IR (KBr): 1618 (s), 1560, 1542, 1459 (s), 1330, 1316, 1176, 1126, 826, 819 (s), 739 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.42 (s, 3H, CH_3), 7.29, 7.33 (AA', 2H, 3,5-C C_6H_4), 7.48 (t, *J* = 7.6 Hz, 1H, 7-H), 7.63 (d, *J* = 9.4 Hz, 1H, 4-H), 7.66–7.82 (m, 3H, 5,6,8-H), 8.22, 8.26 (XX', 2H, 2,6-H C_6H_4), 8.54 (d, *J* = 8.6 Hz, 1H, 9-H); ^{13}C NMR ($CDCl_3$): δ 21.4 (CH_3), 114.7 (CH), 115.9 (CH), 123.1 (5a-C), 125.4 (CH), 127.0 (3,5-C or 2,6-C C_6H_4), 128.2 (1-C C_6H_4), 128.6 (CH), 129.3 (3,5-C or 2,6-C C_6H_4), 130.0 (CH), 130.5 (CH), 133.6 (9a-C), 139.8 (4-C C_6H_4), 149.8 (3a-C), 163.4 (2-C). Anal. Calcd. for $C_{17}H_{13}N_3$ (259.31): C, 78.74; H, 5.05; N, 16.20. Found: C, 78.54; H, 5.09; N, 16.13.

2-(4-Methoxyphenyl)[1,2,4]triazolo[1,5-*a*]quinoline (8e). Procedure A. Colorless crystals, 0.96 g (69%); mp 146 °C (ethanol/water 3:1). IR (KBr): 1617, 1543, 1464 (s), 1459 (s), 1440, 1288, 1253 (s), 1170, 1034, 832, 804 (s), 744 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.88 (s, 3H, CH_3), 7.01, 7.05 (AA', 2H, 3,5-H C_6H_4), 7.50 (td, *J* = 7.6, 1.2 Hz, 1H, 7-H), 7.64 (d, *J* = 9.4 Hz, 1H, 4-H), 7.70-7.86 (m, 3H, 5,6,8-H), 8.27, 8.31 (XX', 2H, 2,6-H C_6H_4), 8.56 (d, *J* = 8.4 Hz, 1H, 9-H); ^{13}C NMR ($CDCl_3$): δ 55.3 (CH_3O), 114.0 (3,5-C C_6H_4), 114.7 (CH), 115.9 (CH), 123.1 (1-C C_6H_4), 123.7 (5a-C), 125.3 (CH), 128.6 (CH and 2,6-C C_6H_4), 130.0 (CH), 130.5 (CH), 133.7 (9a-C), 149.8 (3a-C), 161.0 (4-C C_6H_4), 163.3 (2-C). Anal. Calcd. for $C_{17}H_{13}N_3O$ (275.30): C, 74.17; H, 4.76; N, 15.26. Found: C, 74.13; H, 4.59; N, 15.18.

2-(4-Nitrophenyl)[1,2,4]triazolo[1,5-*a*]quinoline (8f). Procedure A. Yellowish needles, 1.38 g (95%); mp 279 °C (DMF). IR (KBr): 1618, 1541, 1517 (s), 1453, 1341 (s), 1306, 1105, 861, 818, 755, 723 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.58–7.96 (m, 5H, 4,5,6,7,8-H), 8.35, 8.39 (AA', 2H, 3,5-H C_6H_4), 8.52, 8.57 (BB', 2H, 2,6-H C_6H_4), 8.62 (d, *J* = 7.6 Hz, 1H, 9-H). Anal. Calcd. for $C_{16}H_{10}N_4O_2$ (290.28): C, 66.20; H, 3.47; N, 19.30. Found: C, 66.32; H, 3.34; N, 19.11.

2-Styryl[1,2,4]triazolo[1,5-*a*]quinoline (8g). Procedure A. Yellowish needles, 1.11 g (81%); mp 175 °C (ethanol). IR (KBr): 1613 (s), 1497, 1474, 1461, 1445, 1311, 963, 832, 754 (s), 687 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.26-7.90 (m, 12H, H_{arom} and CH=CH), 8.45 (d, *J* = 8.4 Hz, 1H, 9-H); ^{13}C NMR ($CDCl_3$): δ 114.5 (CH), 115.7 (CH), 117.7 (CH), 123.0 (5a-C), 125.4 (CH), 127.1 (2C, C_6H_5), 128.55 (CH), 128.59 (CH), 128.7 (2C, C_6H_5), 130.1 (4-C C_6H_5), 130.8 (CH), 133.5 (9a-C), 135.7 (CH), 136.2 (1-C C_6H_5), 149.5 (3a-C), 162.8 (2-C). Anal. Calcd. for $C_{18}H_{13}N_3$ (271.32): C, 79.68; H, 4.83; N, 15.49. Found: C, 79.66; H, 4.69; N, 15.40.

2-Methyl[1,2,4]triazolo[5,1-*a*]isoquinoline (13a).[27, 28] Procedure B. Colorless crystals, 0.52 g (57%); mp 84 °C (*n*-hexane; lit.[27] mp 88–89 °C; lit.[28] mp 86.5–88 °C). IR (KBr): 1639, 1524 (s), 1490, 1474, 1368, 1345, 1248, 810, 752, 710 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 2.66 (s, 3H, CH_3), 7.17 (d, *J* = 7.4 Hz, 1H, 6-H), 7.63–7.81 (m, 3H, 7,8,9-H), 8.23 (d, *J* = 7.4 Hz, 1H, 5-H), 8.53-8.61 (m, 1H, 10-H); ^{13}C NMR ($CDCl_3$): δ 14.3 (CH_3), 113.3 (CH), 121.8 (6a-C), 124.0 (CH), 124.2 (CH), 127.0 (CH), 128.2 (CH), 129.7 (CH), 131.2 (10a-C), 149.7 (10b-C), 162.5 (2-C). Anal. Calcd. for $C_{11}H_9N_3$ (183.21): C, 72.11; H, 4.95; N, 22.94. Found: C, 72.80; H, 5.08; N, 22.41.

2-Propyl[1,2,4]triazolo[5,1-*a*]isoquinoline (13b). Procedure B. Colorless crystals, 0.91 g

(86%); mp 58 °C (petroleum ether). IR (KBr): 2936, 1638, 1530, 1527, 1471, 1434, 1373, 1285, 800 (s), 752, 706 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.06 (t, *J* = 7.4 Hz, 3H, CH_3), 1.95 (qt, *J* = 7.4 Hz, 2H, C*H*$_2$CH$_3$), 2.96 (t, *J* = 7.4 Hz, 2H, 2-CCH$_2$), 7.11 (d, *J* = 7.4 Hz, 1H, 6-H), 7.60–7.75 (m, 3H, 7,8,9-H), 8.22 (d, *J* = 7.2 Hz, 1H, 5-H), 8.55–8.60 (m, 1H, 9-H); ^{13}C NMR ($CDCl_3$): δ 13.8 (CH_3), 21.8 (*C*H$_2$CH$_3$), 30.6 (2-CH$_2$), 113.1 (CH), 121.7 (6a-C), 123.9 (CH), 124.1 (CH), 126.8 (CH), 128.0 (CH), 129.4 (CH), 131.0 (10a-C), 149.4 (10b-C), 166.0 (2-C). Anal. Calcd. for $C_{13}H_{13}N_3$ (211.26): C, 73.91; H, 6.20; N, 19.89. Found: C, 74.53; H, 6.22; N, 19.77.

2-Phenyl[1,2,4]triazolo[5,1-*a*]isoquinoline (13c).[27] Procedure A. Colorless needles, 1.03 g (84%); mp 160 °C (ethanol/water 4:1; lit.[27] mp 157–158 °C). IR (KBr): 1638, 1518, 1461, 1450, 1440, 1421, 1364, 1355, 1250, 1126, 816, 749, 719 (s), 685 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.17 (d, *J* = 7.2 Hz, 1H, 6-H), 7.41–7.78 (m, 6H, 7,8,9-H and 3,4,5-H C_6H_5), 8.30 (d, *J* = 7.8 Hz, 1H, 5-H), 8.34 (dd, *J* = 7.8 Hz, 1.8 Hz, 2H, 2,6-H C_6H_5), 8.65-8.70 (m, 1H, 10-H); ^{13}C NMR ($CDCl_3$): δ 113.8 (CH), 122.2 (6a-C), 124.3 (CH), 124.5 (CH), 127.1 (3C), 128.3 (CH), 128.6 (2C), 129.7 (CH), 129.8 (CH), 131.0 (1-C C_6H_5), 131.2 (10a-C), 150.1 (10b-C), 163.2 (2-C). Anal. Calcd. for $C_{16}H_{11}N_3$ (245.28): C, 78.35; H, 4.52; N, 17.13. Found: C, 79.44; H, 4.53; N, 17.22. Following Procedure A and using 1-amino-2-iminoquinoline **(10)**[23] (0.80 g, 5 mmol; instead of the tosylate **8**) and water (11 mL; instead of an aqueous potassium hydroxide solution) after 6 h afforded **13c** (0.98 g, 80%). When this reaction was carried out under exclusion of air in a closed reaction flask no product precipitated after 6 h. After opening the flask and continued stirring **13c** precipitated within 2 h and was isolated by filtration (0.97 g, 79%).

2-(4-Methylphenyl)[1,2,4]triazolo[5,1-*a*]isoquinoline (13d). Procedure A. Colorless crystals, 1.11 g (85%); mp 204 °C (ethanol/water 4:1). IR (KBr): 1637, 1517, 1457 (s), 1438, 1410, 1363, 1346, 1251, 1181, 1125, 898, 826, 819, 742 (s), 708 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.42 (s, 3H, CH_3), 7.18 (d, *J* = 7.4 Hz, 1H, 6-H), 7.29, 7.33 (AA', 2H, 3,5-H C_6H_4), 7.62–7.80 (m, 3H, 7,8,9-H), 8.21, 8.25 (XX', 2H, 2,6-H C_6H_4), 8.31 (d, *J* = 7.4 Hz, 1H, 5-H), 8.66-8.71 (m, 1H, 10-H); ^{13}C NMR ($CDCl_3$): δ 21.4 (CH_3), 113.7 (CH), 122.2 (6-C), 124.4 (CH), 124.5 (CH), 127.1 (3,5-C C_6H_4, CH), 128.3 (CH), 129.4 (2,6-C C_6H_4), 129.7 (CH), 131.3 (10a-C), 139.8 (4-C C_6H_4, 150.1 (10b-C), 163.4 (2-C). Anal. Calcd. for $C_{17}H_{13}N_3$ (259.31): C, 78.74; H, 5.05; N, 16.20. Found: C, 78.94; H, 4.96; N, 16.14.

2-(4-Methoxyphenyl)[1,2,4]triazolo[5,1-*a*]isoquinoline (13e). Procedure A. Colorless crystals, 0.99 g (72%); mp 162 °C (ethanol/water 4:1). IR (KBr): 1613, 1519, 1457 (s), 1436, 1363, 1252 (s), 1171, 1034, 837, 749 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.85 (s, 3H, CH_3), 6.99, 7.04 (AA', 2H, 3,5-H C_6H_4), 7.14 (d, *J* = 7.4 Hz, 1H, 6-H), 7.62–7.67 (m, 2H, 7-H, 8- or 9-H), 7.70–7.77 (m, 1H, 8- or 9-H), 8.24, 8.29 (XX', 2H, 2,6-H C_6H_4), 8.27 (d, *J* = 7.2 Hz, 1H, 5-H), 8.63–8.68 (m, 1H, 10-H); ^{13}C NMR ($CDCl_3$): δ 55.2 (CH_3O), 113.5 (CH), 114.0 (3,5-C C_6H_4), 122.1 (6-C), 123.6 (1-C C_6H_4), 124.3 (CH), 124.4 (CH), 127.1 (CH), 128.1 (CH), 128.5 (2,6-C, C_6H_4), 129.6 (CH), 131.2 (10a-C), 150.0 (10ba-C), 160.9 (4-C C_6H_4), 163.1 (2-C). Anal. Calcd. for $C_{17}H_{13}N_3O$ (275.30): C, 74.17; H, 4.76; N, 15.26. Found: C, 74.33; H, 4.62; N, 15.26.

2-(4-Nitrophenyl)[1,2,4]triazolo[5,1-*a*]isoquinoline (13f). Procedure A. Yellowish crystals, 1.20 g (83%); mp 282 °C (DMF). IR (KBr): 1639, 1604, 1527 (s), 1519 (s), 1456, 1440, 1368, 1341 (s), 1307, 1105, 862, 854, 800, 755, 723 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.33 (d, *J* = 7.4 Hz, 1H, 6-H), 7.75–7.20 (m, 2H, 7-H, 8- or 9-H), 7.84–7.91 (m, 1H, 8- or 9-H), 8.34, 8.37 (AA', 2H, 3,5-H C_6H_4), 8.38 (d, *J* = 7.2 Hz, 1H, 5-H), 8.51, 8.55 (BB', 2H, 2,6-H C_6H_4), 8.69-8.74 (m, 1H, 10-H); MS (EI) *m/z* (%): 290 (100, $M^{+\cdot}$), 244 (33, M $-NO_2$), 128 (19, C_9H_6N). Anal. Calcd. for $C_{16}H_{10}N_4O_2$ (290.28): C, 66.20; H, 3.47; N, 19.30. Found: C, 66.84; H, 3.38; N, 19.21.

2-Styryl[1,2,4]triazolo[5,1-*a*]isoquinoline (13g). Procedure A. Yellowish crystals, 1.14 g (84%); mp 156 °C (ethanol/water 4:1). IR (KBr): 1524, 1500, 1461, 1437, 1373, 982, 970, 792 (s), 783, 759, 754, 695 (s), 686 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.15 (d, *J* = 7.2 Hz, 1H, 6-H), 7.27 (d, *J* = 16.4 Hz, 1H, =C*H*C_6H_5), 7.26–7.43 (m, 3H, H_{arom}), 7.60–7.78 (m, 5H, H_{arom}), 7.89 (d, *J* = 16.4 Hz, 1H, 2-CH=), 8.24 (d, *J* = 7.2 Hz, 1H, 5-H), 8.61-8.66 (m, 1H, 10-H); ^{13}C NMR ($CDCl_3$): δ 113.8 (CH), 117.7 (CH), 121.9 (6a-C), 124.3 (CH), 124.2, 127.1 ($2CH_{Ph}$), 127.1 (CH), 128.3 (CH), 128.5 (CH), 128.7 (CH_{Ph}), 129.8 (CH), 131.3 (10a-C), 135.7 (CH), 136.3 (C_{Ph}), 149.8 (10b-C), 162.6 (2-C). Anal. Calcd. for $C_{18}H_{13}N_3$ (271.32): C, 79.68; H, 4.83; N, 15.49. Found: C, 80.33; H, 4.82; N, 15.52.

Acknowledgements

Grant OTKA T26476 is gratefully acknowledged. The present research has been carried out in the frame of the bilateral intergovernmental S&T cooperation between the Hungarian Ministry of Education and the Austrian Bundesministerium für Auswärtige Angelegenheiten (*via* ÖAD), Projekt A27/98.

References

[§] Present address: CHINOIN Pharm. and Chem. Works Co. Ltd, PO Box 110, H-1325 Budapest, Hungary.

1. Hajós, G.; Timari, G.; Messmer, A.; Zagyva, A.; Miskolczi, I.; Schantl, J. G. *Monatsh. Chem.* **1995**, *126*, 1213.
2. Winters G.; Odasso, G.; Galliani, G.; Lerner, L. J. *Ger. Offen.* DE 2551879, 1976; *Chem. Abstr.* **1976**, *85*, 94369.
3. Cusmano, G.; Macaluso, G.; Gruttadauria, M. *Heterocycles* **1993**, *36*, 1577.
4. Talukdar, P. B.; Sengupta, S. K.; Datta, A. K. *Indian J. Chem.* **1976**, *14B*, 176.
5. Batori, S.; Sandor, P.; Messmer, A. *Heterocycles* **1990**, *31*, 289.
6. Beltrame, P.; Cadoni, E.; Carnasciali, M. M.; Gelli, G.; Mugnoli, A. *Heterocycles* **1996**, *43*, 2179.
7. Evdokimoff, V. *Bull. Chim. Farm.* **1970**, *109*, 240; *Chem. Abstr.* **1970**, *73*, 77155.
8. Bruche, L.; Garanti, L.; Zecchi, G. *J. Chem. Soc., Perkin Trans. 1* **1983**, 539.

9. Reimlinger, H.; Billiau, F.; Lingier, W. R. F. *Chem. Ber.* **1976**, *109*, 118.
10. Omodei-Sale, A.; Consonni, P.; Lerner, L. *U.S. Pat.* 4075341, 1978; *Chem. Abstr.* **1978**, *89*, 24316.
11. Omodei-Sale, A.; Consonni, P.; Lerner, L. J. *Ger. Offen.* 1978, DE 2707272 *Chem. Abstr.* **1979**, *90*, 23059.
12. Deady, L. W.; Loria, P. M.; Quazi, N. H. *Aust. J. Chem.* **1996**, *49*, 485.
13. Favara, D.; Omodei-Sale, A. *Ger. Offen.* DE 2942196, 1980; *Chem. Abstr.* **1980**, *93*, 186357.
14. Guzzi, U.; Omodei-Sale, A.; Galliani, G. *Ger. Offen.* DE 2943286 1980; *Chem. Abstr.* **1980**, *93*, 186360.
15. Batori, S.; Hajos, G.; Sandor, P.; Messmer, A. *J. Org. Chem.* **1989**, *54*, 3062.
16. Hu, Y.; He, B.; Cao, Y. *Zhejiang Yike Daxue Xuebao* **1992**, *21*, 17; *Chem. Abstr.* **1992**, *117*, 150942.
17. Toja, E.; Omodei-Sale, A.; Favara, D.; Cattaneo, C.; Gallico, L.; Galliani, G. *Arzneim. Forsch.* **1983**, *33*, 1222.
18. Omodei-Sale, A.; Consonni, P.; Galliani, G. *J. Med. Chem.* **1983**, *26*, 1187.
19. Messmer, A.; Benkó, P.; Giegler, G.; Gyertyán, I.; Hajós, Gy.; Hegedús, M.; Juhász-Riedl, Zs.; Pallos, L.; Petócz, L.; Szirt-Kiszely, E. *Ger. Pat*. DE 3,833.615; *Chem. Abstr.* **1989**, *111*, 174136.
20. Glover, E. E.; Rowbottom, K. T. *J. Chem. Soc., Perkin Trans 1* **1976**, 367.
21. Messmer, A.; Hajós G. *J. Org. Chem.* **1981**, 46, 843.
22. Hajós, G.; Riedl, Zs; Messmer, A. *Act. Chim. Hung., Models Chem.* **1994**, *131*, 397; *Chem. Abstr*. **1995**, *123*, 169579.
23. Hajós, G.; Riedl, Zs; Messmer, A. *Act. Chem. Scand.* **1993**, *47*, 296.
24. Cirrincione, G.; Dattolo, G.; Almerico, A. M.; Aiello, E.; Cusmano, G.; Macaluso, G.; Ruccia, M.; Hinz W. *J. Heterocycl. Chem.* **1986**, *23*, 1273.
25. Korodi, F. *Synth. Commun.* **1991**, *21*, 1841.
26. Commercially available from Sigma-Aldrich.
27. Reimlinger, H.; Lingier, W. R. F.; Vandewalle, J. J. M.; Merenyi, R. *Chem. Ber.* **1971**, *104*, 3965.
28. Hoogzand, C. *Recl. Trav. Chim. Pays-Bas* **1971**, *90*, 1225; *Chem. Abstr.* **1972**, *76*, 3763.

