SYNTHESIS AND REACTIVITY OF MANNICH BASES. XIV. BASE-CATALYZED CYCLOCONDENSATION OF β–AMINOKETONES TO 1,5-BENZODIAZEPINES AND 1,4-NAPHTHODIAZEPINES

Gheorghe Roman
Department of Chemistry, "Transilvania" University, 29 Eroilor Blvd., Braşov, RO-2200, Romania

Eugenia Comaniță
Department of Organic Chemistry, "Gh. Asachi" Technical University, 71A D. Mangeron Blvd., Iaşi,RO-6600, Romania

Bogdan Comaniță
National Research Council, Institute for Chemical Process and Environmental Technology, Montreal Road Campus, K1A 0R6, Ottawa, Canada

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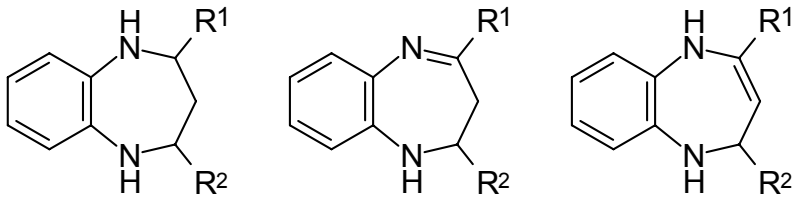
Abstract

Several 2,3-dihydro-1,5-benzodiazepines and 2,3-dihydronaphtho[2,3-*b*]-1,4-diazepines were prepared *via* cyclocondensation of the corresponding *ortho*-arylenediamine with 3-dialkylaminopropiophenone hydrochlorides in ethanol in the presence of anhydrous sodium acetate.

Introduction

The discovery of diazepam followed by many other psychotropic agents sharing a 1,4-benzodiazepine skeleton has also promoted the studies on the isomeric 1,5-benzodiazepine ring system[1] along with the synthetic approaches to mono- and diannelated 1,5-benzodiazepines.[2] Due to their accessibility, easy functionalization and potential pharmacological proprieties, mainly 1,5-benzodiazepinone and 1,5-benzodiazepinedione derivatives have received significant attention. Peripheral cholecystokinin receptor agonists,[3] CCK-B/gastrin receptor antagonists,[4] arginine vasopressin antagonists,[5] CNS depressants,[6,7] antiamoebics[8] and antiproliferative agents[9] derived from 1,5-benzodiazepinones have been reported. Heterofused 1,5-benzodiazepinones have also been evaluated towards benzodiazepine receptor binding[10] or HIV reverse transcriptase inhibition[11] and found to possess anticonvulsant,[12] analgesic or anti-inflammatory,[13] antipsychotic[14] or PAF-induced aggregation inhibitory[15,16] activities.

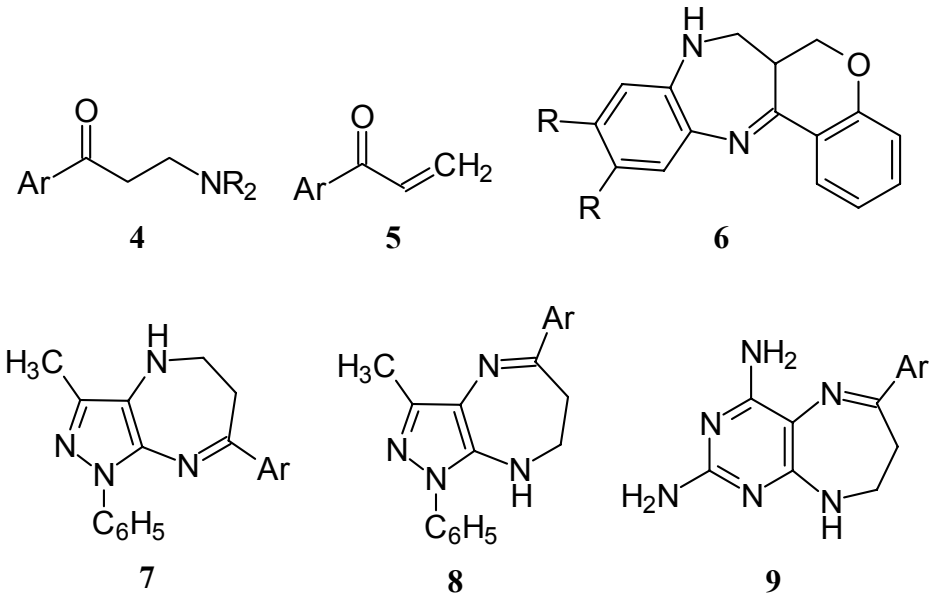
The synthesis of 1,5-benzodiazepine derivatives **1-3**, hydrogenated in the heterocyclic



1 **2** **3**

Figure 1

ring (Figure 1), has been less investigated. In particular, 2,4-disubstituted 2,3-dihydro-1*H*-1,5-benzodiazepines **2** (R^1, R^2=alkyl, (hetero)aryl) have been synthesized by cyclocondensation of *ortho*-phenylendiamine with ketones,[17] chalcones[18] or via a more recently described three-component one-pot procedure involving a coupling-isomerisation sequence of an electron poor (hetero)aryl halide and a terminal propargyl alcohol, subsequently followed by cyclocondensation with *ortho*-phenylendiamine.[19] When 2,3-dihydro-1*H*-1,5-benzodiazepines substituted only at the position 4 (**2**, R^1=alkyl, (hetero)aryl, R^2=H) represent the preparative target, the cyclocondensation of *ortho*-arylenediamines with Mannich bases **4** (useful synthetic equivalents of the less stable 2-propen-1-ones **5**) seems to be the most reasonable entry. A few older references describing this approach to 1,5-benzodiazepines are available[20] along with a recent one.[21]



4 **5** **6**

7 **8** **9**

Figure 2

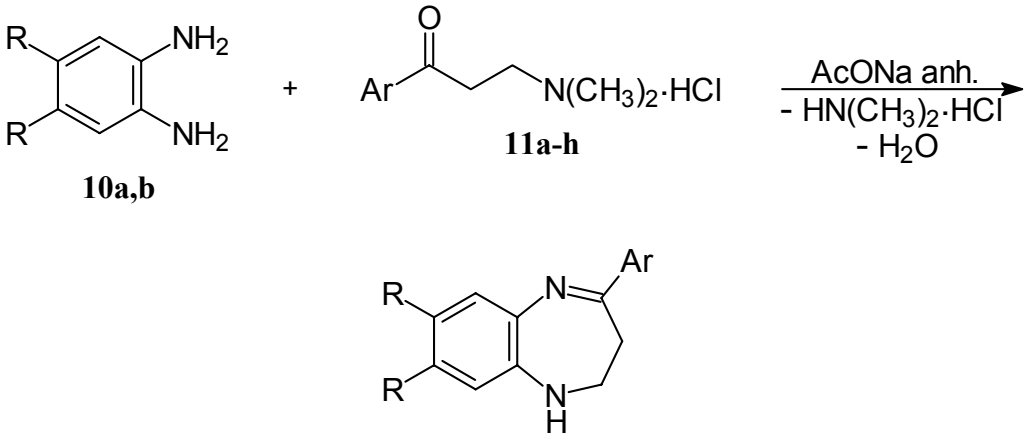
Antileukemic benzopyrano[4,3-*b*]-1,5-benzodiazepine[22] **6** (Figure 2), the heterofused 2,3-dihydropyrazolo[4,3-*b*]diazepines[23] **7** and **8** or 2,3-dihydropyrimidino[4,5-*b*]-1,4-

diazepines[24] **9** (Figure 2) have also been obtained through similar cyclocondensations.

The present paper aims at preparing several simple, but yet unknown 2,3-dihydro-1,5-benzodiazepines through anhydrous sodium acetate-catalyzed cyclocondensation of Mannich bases derived from acetophenones with *ortho*-phenylenediamine. Another series of 2,3-dihydronaphtho[2,3-*b*]-1*H*-1,4-diazepines has been obtained by a similar procedure using 2,3-diaminonaphthalene instead of *ortho*-phenylenediamine.

Results and discussion

The reaction between *ortho*-arylenediamines **10** and Mannich bases **11** is depicted in Scheme 1:



Compound	Ar	R	R
12a	4-methoxyphenyl	H	H
12b	4-bromophenyl	H	H
12c	4-methylphenyl	H	H
12d	2-thienyl	H	H
12e	2-hydroxy-5-methylphenyl	H	H
12f	3-bromo-2-hydroxy-5-methylphenyl	H	H
12g	2-hydroxy-5-methylphenyl	CH=CH-CH=CH	
12h	3-bromo-2-hydroxy-5-methylphenyl	CH=CH-CH=CH	
12i	2-hydroxyphenyl	CH=CH-CH=CH	
12j	2-hydroxy-4-methylphenyl	CH=CH-CH=CH	

Scheme 1. Base-catalyzed **c**yclocondensation of o*rtho*-arylenediamines with ketonic Mannich bases hydrochlorides

The earlier cyclocondensations of *ortho*-phenylenediamines with Mannich bases hydrochlorides carried out by Hideg *et al*[20] or Werner *et al*[22] were conducted in

refluxing apolar solvents (e.g. benzene, toluene, xylene) with water separation as an azeotrope. The work-up in this procedure sometimes comprised, after the filtration of the amine hydrochloride, the distillation *in vacuo* of the solvent prior to the separation of 1,5-benzodiazepine.[22] The present work employs a modification that replaces the highly toxic aromatic hydrocarbons with ethanol as a solvent. This modification ensures a more facile isolation of the reaction product through a simple filtration; the by-products (water and the amine hydrochloride) as well as the unreacted reactants would be removed along with ethanol.

Another difference from the earlier reported procedures refers to the use of anhydrous sodium acetate as a basic catalyst in the cyclocondensation of diamines **10** with Mannich base hydrochlorides **11**, as it has been considered that the addition of a mild base will be beneficial for the condensation between the ketonic group in Mannich bases **11** and the amine group in *ortho*-arylenediamines. While this work was in progress, Insuasty *et al*. reported their own investigations on the reaction of *ortho*-phenylenediamine with 3-(dimethylamino)propiophenones.[21] In their detailed studies, that were also conducted using ethanol as solvent but in the absence of any catalyst, two of the 2,3-dihydro-1,5-benzodiazepines described in this paper (**12a** and **12b**) were presented. As the yields reported by Insuasty *et al* for these two compounds are very similar to those recorded by us, no advantage arises from the use of anhydrous sodium acetate as a catalyst in the investigated reaction.

To produce the fused diazepines **12**, the hydrochloride of the required Mannich base **11** and the diamine **10** were refluxed in ethanol in the presence of anhydrous sodium acetate. A preliminary study conducted for the reaction of 1-(3-bromo-2-hydroxy-5-methylphenyl)-3-dimethylamino-1-propanone hydrobromide **11f** and 1,2-diaminobenzene **10a** has established that a reaction period up to 30 minutes resulted in reasonable yields of benzodiazepines and that refluxing the reaction mixture for longer reaction times lowers the yields of the desired 2,3-dihydro-1,5-benzodiazepines. This is consistent with the findings of Insuasty *et al*[21], which have shown that when Mannich bases hydrochlorides and *ortho*-phenylenediamine were refluxed for 3-4 hrs, complex reaction mixtures comprising derivatives of the initially formed 2,3-dihydro-1,5-benzodiazepines are produced. By applying the established reaction conditions, the

yields in compounds **12** are moderate**,** higher yields of fused diazepines being recorded only in the case of bromine-substituted or naphthalene-fused diazepines, probably due to their lower solubility in ethanol.

As our interest in the chemistry of Mannich bases is mainly directed to β-aminoketones **11** derived from *ortho*-hydroxyacetophenones,[24-28] most of compounds **12** were acquired from this less investigated type of aminomethylated ketones. By using several 3-dialkylamino-1-(2-hydroxy-5-methyl)propiophenone hydrochlorides and 3-(dialkylamino)-1-(3-bromo-2-hydroxy-5-methyl)propiophenone hydrobromides, it has been found out that nor the different amino moieties (dimethylamino, 4-morpholinyl or 1-piperidinyl), neither the nature of the counter ion in these salts could lead to major improvement of the yields.

Only symmetric *ortho*-arylenediamines have been used to generate fused diazepines **12** since the involvement of diamines possessing two non-equivalent amino groups would afford a mixture of regioisomeric cyclocondensation products, whose separation should be performed prior to their characterization.

The characterization of compounds **12** by IR spectroscopy revealed the typical band for the N-H stretching vibration at 3300-3400 cm^{-1} together with a band at 1610-1640 cm^{-1} due to the >C=N- group. The structure of 2,3-dihydro-1,5-benzodiazepines and 2,3-dihydronaphtho[2,3-*b*]-1,4-diazepines was further assigned by ^{1}H- and ^{13}C-NMR spectroscopy. The representative signal in the ^{1}H-NMR spectra of compounds **12** is the two triplets pattern given by the protons of the neighbouring methylene groups. The signal of the N-H proton mingled with the signals of the 2-CH_2- group,[21,30] whose intensity always corresponds for 2.8-2.9 protons. The peak due to N-H proton could be evidenced only in the case of compound **12d**. The singlet, noticed in the far off-set (above 15 ppm) of the spectra of the cyclocondensation products of Mannich bases derived from *ortho*-hydroxyacetophenones, was attributed to the phenolic proton involved in an intramolecular hydrogen bond with the nitrogen atom. ^{13}C-NMR spectra confirmed the structure of the cyclic reaction products.

Conclusions

Cyclocondensation of ketonic Mannich bases hydrochlorides with *ortho*-arylenediamines proceeds smoothly in ethanol in the presence of anhydrous sodium

acetate and leads to fused diazepines. The use of ethanol instead of aromatic hydrocarbons ensures milder reaction conditions, shorter reaction times and an easy separation of the cyclocondensation products from the reaction mixture. However, the yields of fused diazepines, obtained via a base-catalyzed cyclocondensation, are comparable with those reported when the reaction was carried out without any catalyst. Along with several 1,5-benzodiazepines, a series of naphtho-1,4-diazepines have been prepared starting from 2,3-diaminonaphthalene. The NMR analysis of fused diazepines derived from *ortho*-hydroxyacetophenones revealed the signal for the phenolic proton as a singlet located far in off-set as a result of an intramolecular hydrogen bonding.

Experimental

Melting points were determined using a Boetius hot-stage microscope and are uncorrected. Elemental analyses were performed on a Carlo Erba-1106 analyzer. IR spectra were registered on a SPECORD M80 instrument. ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Gemini 300 NMR spectrometer in $CDCl_3$ (with TMS for ^{1}H- and $CDCl_3$ for ^{13}C-NMR as the internal reference), except for **12j**, whose ^{1}H-NMR spectrum was taken in DMSO-d_6. All commercially available reagents were used without further purification. The Mannich bases hydrochlorides **11** required in this study, namely 1-(4-methoxyphenyl)-3-dimethylamino-1-propanone hydrochloride **11a**,[31] 1-(4-bromophenyl)-3-dimethylamino-1-propanone hydrochloride **11b**,[32] 1-(4-methylphenyl)-3-dimethylamino-1-propanone hydrochloride **11c**,[33] 3-dimethylamino-1-(2-thienyl)-1-propanone hydrochloride **11d**,[34] 1-(2-hydroxy-5-methylphenyl)-3-dimethylamino-1-propanone hydrochloride **11e**,[25] and 1-(3-bromo-2-hydroxy-5-methylphenyl)-3-dimethylamino-1-propanone hydrobromide **11f**,[29] 1-(2-hydroxyphenyl)-3-dimethylamino-1-propanone hydrochloride **11g**,[26] 1-(2-hydroxy-4-methylphenyl)-3-dimethylamino-1-propanone hydrochloride **11h**,[26] were synthesized by described in the literature.

General procedure for the preparation of 4-aryl-2,3-dihydro-1*H*-1,5-benzodiazepines 12a-f. A mixture of *ortho*-phenylenediamine (0.54 g, 5 mmol) and Mannich base hydrochloride **11a-f** (5 mmol) in ethanol (10 mL) were treated with

anhydrous sodium acetate (1.25 g) and refluxed for 30 min, when the color changed from light yellow to deep yellow or reddish. The reaction mixture was cooled to room temperature and then kept in a freezer for several hours. The solids were collected by filtration and washed thoroughly with water to remove the inorganic salts. All 4-aryl-2,3-dihydro-1*H*-1,5-benzodiazepines **12a-f** were recrystallized from ethanol prior to analysis.

2,3-Dihydro-4-(4-methoxyphenyl)-1*H*-1,5-benzodiazepine (12a). This compound was prepared from *ortho*-phenylenediamine **10a** and Mannich base **11a**, yellow leaflets (0.7 g, 55%), m.p. 152-153 °C (m.p.[21] 155 °C). *Anal*. Calculated for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.05; H, 6.44; N, 11.03. IR (KBr, cm^{-1}): 1628 ($\nu_{C=N}$), 3404 (ν_{NH}). ^{1}H NMR: δ 7.95 (dd, 2H, $J_{1,3}$=2.1 Hz, $J_{1,2}$=6.8 Hz), 7.34 (dd, 1H, $J_{1,3}$=1.8 Hz, $J_{1,2}$=7.6 Hz), 6.91-7.00 (m, 4H), 6.72 (dd, 1H, $J_{1,3}$=1.7 Hz, $J_{1,2}$=7.5 Hz), 3.84 (s, 3H), 3.83 (t, 2H, *J*=5.9 Hz), 2.97 (t, 2H, *J*=5.9 Hz). ^{13}C NMR: δ 168.00, 161.49, 139.75, 138.33, 131.74, 129.44, 128.73, 126.14, 120.82, 119.82, 113.78, 55.39, 53.26, 31.06.

4-(4-Bromophenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (12b). This compound was prepared from *ortho*-phenylenediamine **10a** and Mannich base **11b**, yellow microcrystals (0.74 g, 49%), m.p. 138-139 °C (m.p.[21] 140 °C). *Anal*. Calculated for $C_{15}H_{13}BrN_2$: C, 59.82; H, 4.35; N, 9.30. Found: C, 59.98; H, 4.17; N, 9.09. IR (KBr, cm^{-1}): 1622 ($\nu_{C=N}$), 3410 (ν_{NH}). ^{1}H NMR: δ 7.83 (d, 2H, *J*=8.6 Hz), 7.54 (d, 2H, *J*=8.6 Hz), 7.34 (dd, 1H, $J_{1,3}$=1.4 Hz, $J_{1,2}$=7.7 Hz), 6.88-7.07 (m, 2H), 6.71 (dd, 1H, $J_{1,3}$=1 Hz, $J_{1,2}$=7.8 Hz), 3.80 (t, 2H, *J*=5.7 Hz), 3.00 (t, 2H, *J*=5.6 Hz). ^{13}C NMR: δ 166.26, 140.19, 138.57, 137.52, 131.51, 130.50, 128.47, 126.77, 124.51, 120.66, 119.50, 51.97, 31.95.

2,3-Dihydro-4-(4-methylphenyl)- 1*H*-1,5-benzodiazepine (12c). This compound was prepared from *ortho*-phenylenediamine **10a** and Mannich base **11c**, yellow leaflets (0.49 g, 41%), m.p. 125-126 °C. *Anal*. Calculated for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.85. Found: C, 81.13; H, 6.56; N, 11.94. IR (KBr, cm^{-1}): 1632 ($\nu_{C=N}$), 3405 (ν_{NH}). ^{1}H NMR: δ 7.86 (d, 2H, *J*=7.9 Hz), 7.35-7.21 (m, 3H), 7.01-6.91 (m, 2H), 6.70 (dd, 1H, $J_{1,3}$=1 Hz, $J_{1,2}$=7.9 Hz), 3.82 (t, 2H, *J*=5.7 Hz), 2.98 (t, 2H, *J*=5.7 Hz), 2.39 (s, 3H). ^{13}C NMR: δ

168.04, 140.17, 139.80, 138.44, 136.74, 129.74, 129.07, 126.84, 126.13, 120.65, 119.64, 52.99, 31.34, 21.29.

2,3-Dihydro-4-(2-thienyl)-1*H*-1,5-benzodiazepine (12d). This compound was prepared from *ortho*-phenylenediamine **10a** and Mannich base **11d**, yellow leaflets (0.52 g, 45%), m.p. 109-110 °C. *Anal*. Calculated for $C_{13}H_{12}N_2S$: C, 68.39; H, 5.30; N, 12.27. Found: C, 68.59; H, 5.17; N, 12.37. IR (KBr, cm^{-1}): 1625 ($\nu_{C=N}$), 3405 (ν_{NH}). ^{1}H-NMR: δ 7.41 (d, 1H, *J*=5 Hz), 7.36-7.38 (m, 2H), 7.05 (dd, 1H, *J*=3.8 Hz, *J*=5 Hz), 6.96-7.01 (m, 1H), 6.87-6.92 (m, 1H), 6.67 (d, 1H, *J*=7.8 Hz), 3.85 (bs, 1H), 3.71 (t, 2H, *J*=5.5 Hz), 3.02 (t, 2H, *J*=5.5 Hz). ^{13}C-NMR: δ 162.1, 147.79, 141.39, 136.85, 131.55, 130.42, 128.11, 127.68, 127.14, 120.62, 119.59, 50.52, 33.69.

2,3-Dihydro-4-(2-hydroxy-5-methylphenyl)-1*H*-1,5-benzodiazepine (12e). This compound was prepared from *ortho*-phenylenediamine **10a** and Mannich base **11e**, orange crystals (0.77 g, 61%), m.p. 112-113 °C. *Anal*. Calculated for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.38; H, 6.48; N, 10.97. IR (KBr, cm^{-1}): 1610 ($\nu_{C=N}$), 3307 (ν_{NH}). ^{1}H NMR: δ 15.55 (s, 1H), 7.34 (bs, 1H), 7.24-7.31 (m, 1H), 7.14 (d, 1H, *J*=8.4 Hz), 6.99-7.09 (m, 1H), 6.87-6.97 (m, 2H), 6.71 (d, 1H, *J*=7.9 Hz), 3.81 (t, 2H, *J*=5.3 Hz), 3.09 (t, 2H, *J*=5.4 Hz), 2.30 (s, 3H). ^{13}C NMR: δ 171.58, 160.42, 140.63, 133.62, 133.57, 129.31, 127.87, 127.27, 126.69, 120.40, 119.45, 118.78, 118.10, 51.02, 30.90, 20.68.

4-(3-Bromo-2-hydroxy-5-methylphenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (12f). This compound was prepared from *ortho*-phenylenediamine **10a** and Mannich base **11f**, orange-reddish crystals (1.23 g, 74%), m.p. 192-193 °C. *Anal*. Calculated for $C_{16}H_{15}BrN_2O$: C, 58.02; H, 4.56; N, 8.46. Found: C, 57.81; H, 4.68; N, 8.36. IR (KBr, cm^{-1}): 1613 ($\nu_{C=N}$), 3321 (ν_{NH}). ^{1}H NMR: δ 7.44 (d, 1H, *J*=1.6 Hz), 7.29 -7.34 (m, 2H), 7.03-7.07 (m, 1H), 6.85-6.89 (m, 1H), 6.71-6.73 (m, 1H), 3.74 (t, 2H, *J*=5.4 Hz), 3.15 (t, 2H, *J*=5.2 Hz), 2.28 (s, 3H). ^{13}C NMR: δ 170.17, 158.45, 141.55, 136.72, 131.08, 129.56, 128.04, 127.30, 126.85, 120.18, 119.18, 112.54, 94.36, 48.86, 31.96, 20.49.

General procedure for the preparation of 4-aryl-2,3-dihydro-1*H*-naphtho[2,3-*b*]-1,4-diazepines 12g-j. 2,3-Diaminonaphthalene (1.1 g, 7 mmol) was dissolved in ethanol (35 mL) and then treated with the Mannich base hydrochloride **11e-h** (7 mmol) and anhydrous sodium acetate (1.75g). The reaction mixture was refluxed for 30 min. and afterwards cooled in a freezer. The solids were collected by filtration, washed with plenty of water and air-dried. Recrystallization from ethanol afforded 4-aryl-2,3-dihydronaphtho[2,3-*b*]-1*H*-1,4-diazepines **12g-j**.

2,3-Dihydro-4-(2-hydroxy-5-methylphenyl)-1*H*-naphtho[2,3-*b*]-1,4-diazepine (12g). This compound was prepared from 2,3-diaminonaphthalene **10b** and Mannich base **11e**, yellow-greenish crystals (1.16 g, 55%), m.p. 182-183 °C. *Anal*. Calculated for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.63; H, 6.14; N, 9.05. IR (KBr, cm^{-1}): 1639 ($\nu_{C=N}$), 3404 (ν_{NH}). ^{1}H NMR: δ 15.13 (s, 1H), 7.70-7.75 (m, 2H), 7.61 (d, 1H, *J*=8 Hz), 7.24-7.39 (m, 3H), 7.15-7.17 (m, 2H), 6.95 (d, 1H, *J*=8.4 Hz), 3.87 (t, 2H, *J*=6.1 Hz), 3.08 (t, 2H, *J*=6.1 Hz), 2.32 (s, 3H). ^{13}C NMR: δ 173.15, 160.57, 139.44, 137.53, 134.10, 132.84, 129.78, 128.02, 127.69, 127.01, 126.18, 126.07, 125.64, 124.11, 118.51, 118.28, 115.58, 52.06, 29.44, 20.74.

4-(3-Bromo-2-hydroxy-5-methylphenyl)-2,3-dihydro-1*H*-naphtho[2,3-*b*]-1,4-diazepine (12h). This compound was prepared from 2,3-diaminonaphthalene **10b** and Mannich base **11f**, brick-reddish crystals (2.16 g, 81%), m.p. 237-239 °C. *Anal*. Calculated for $C_{20}H_{17}BrN_2O$: C, 63.00; H, 4.49; N, 7.35. Found: C, 63.17; H, 4.61; N, 7.22. IR (KBr, cm^{-1}): 1644 ($\nu_{C=N}$), 3358 (ν_{NH}). ^{1}H NMR: δ 7.16-7.80 (m, 8H), 3.84 (t, 2H, *J*=5.8 Hz), 3.16 (t, 2H, *J*=6 Hz), 2.31 (s, 3H).

2,3-Dihydro-4-(2-hydroxyphenyl)-1*H*-naphtho[2,3-*b*]-1,4-diazepine (12i). This compound was prepared from 2,3-diaminonaphthalene **10b** and Mannich base **11g**, greenish crystals (1.17 g, 58%), m.p. 176-177 °C. *Anal*. Calculated for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.72. Found: C, 79.33; H, 5.68; N, 9.57. IR (KBr, cm^{-1}): 1627 ($\nu_{C=N}$), 3397 (ν_{NH}). ^{1}H NMR: δ 15.44 (s, 1H), 7.72-7.75 (m, 2H), 7.60 (d, 2H, *J*=8 Hz), 7.30-7.39 (m, 3H), 7.13 (s, 1H), 7.05 (d, 1H, *J*=8.2 Hz), 6.87 (t, 1H, *J*=8 Hz), 3.84 (t, 2H, *J*=6

Hz), 3.07 (t, 2H, *J*=6 Hz). ^{13}C NMR: δ 173.13, 162.83, 139.47, 137.20, 133.17, 132.87, 129.71, 128.03, 127.68, 126.24, 126.17, 125.64, 124.11, 118.89, 118.53, 118.10, 115.54, 51.81, 29.60.

2,3-Dihydro-4-(2-hydroxy-4-methylphenyl)-1*H*-naphtho[2,3-*b*]-1,4-diazepine (12j). This compound was prepared from 2,3-diaminonaphthalene **10b** and Mannich base **11h**, greenish crystals (1.31 g, 62%), m.p. 180-181 °C. *Anal*. Calculated for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.34; H, 6.11; N, 9.36. IR (KBr, cm^{-1}): 1632 ($\nu_{C=N}$), 3407 (ν_{NH}). ^{1}H NMR: δ 15.42 (s, 1H), 7.70-7.75 (m, 2H), 7.61 (d, 1H, *J*=7.9 Hz), 7.48 (d, 1H, *J*=8.1 Hz), 7.24-7.38 (m, 2H), 7.14 (bs, 1H), 6.85 (bs, 1H), 6.68 (d, 1H, *J*=8.1 Hz), 3.84 (t, 2H, *J*=5.6 Hz), 3.06 (t, 2H, *J*=5.7 Hz), 2.35 (s, 3H). ^{13}C NMR: δ 173.05, 162.91, 144.25, 139.47, 137.42, 132.78, 129.78, 127.89, 127.65, 126.12, 125.94, 125.63, 124.09, 119.35, 118.79, 116.47, 115.53, 52.03, 29.07, 21.56.

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Povzetek

Opisana je enostavna enostopenjska sinteza 4-substituiranih 2,3-dihidro-1H-1,5-benzodiazepinov in 2,3-dihidro-1H-nafto[2,3-*b*]-1,4-diazepinov. Avtorji so izhajali iz β-dialkilaminopropiofenonov (Mannichovih baz) in orto-arilendiaminov, pretvorbe pa so potekale v etanolu pod refluksom v prisotnosti brezvodnega natrijevega acetata. Produkti, benzodiazepini **12a–f** in naftodiazepini **12g–j**, so bili v večini primerov izolirani v zmernih izkoristkih (41–81%).