

Scientific paper

Carbonyl-Enamine a New Mode for Azepine Ring Closure: Synthesis and Characterization of Pyrazino[2,3-*c*]azepine, as a New Ring System

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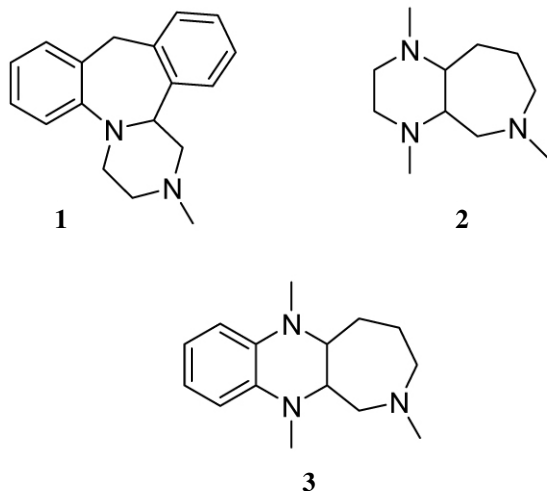
Abstract

Pyrazino[2,3-*c*]azepine and azepino[3,4-*b*]quinoxaline represent new ring systems and were prepared by fusing either of pyrazine ring onto azepine derivative or vice versa. Intramolecular 1,7-carbonyl-enamine cyclization was studied as a new mode for azepine ring closure. Various examples and reaction conditions were studied for this ring closure.

Keywords: Synthesis, Condensation reaction, α -Bromoketone, Carbonyl-Enamine, Mode of ring closure, pyrazine, quinoxaline, pyrazinoazepine, azepinoquinoxaline.

1. Introduction

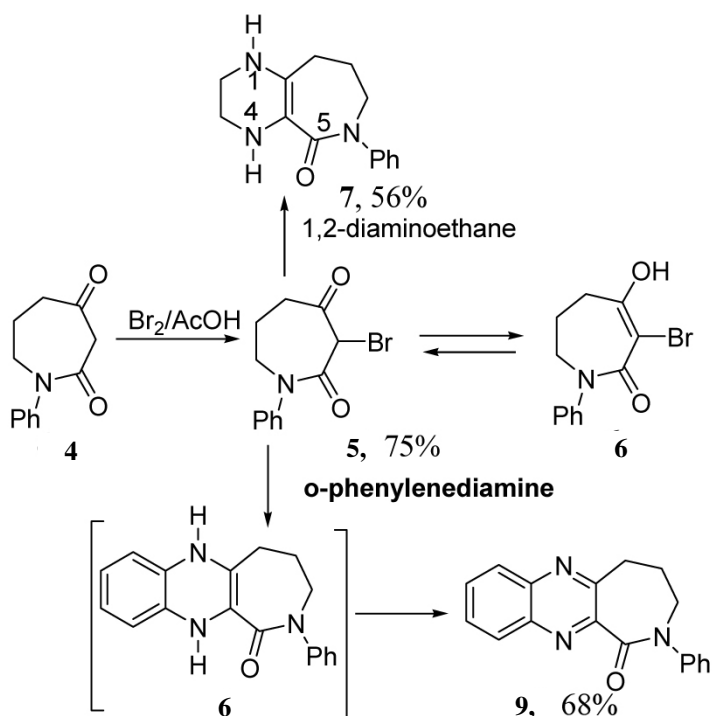
Among a substantial number of bicyclic and tricyclic ring systems that incorporate the azepine ring, pyrazinoazepine and azepino-quinoxaline ring systems are unknown with the exception of **1**, which has a bridged nitrogen atom.¹ As a part of our interest in the azepine chemistry,² new ring systems pyrazino[2,3-*c*]azepine **2** and azepino[3,4-*b*]quinoxaline **3**, have been synthesized as intermediates for the synthesis of new biologically potentially active compounds.



2. Results and Discussion

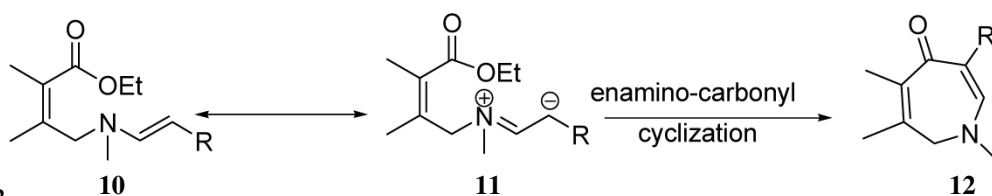
Two obvious strategies for the synthesis of molecules of type **2** and **3** include construction of a pyrazine ring onto a pre-formed azepine derivative or elaboration of an azepine ring onto a suitably substituted pyrazine.

For the first strategy, the α -bromoazepandione **5** was prepared by bromination of 2,4-azepandione derivative **4**² with bromine in glacial acetic acid. The product **5**, however predominantly exists in its enol form **6**. On the other hand, bromination with $\text{Br}_2/\text{CHCl}_3$ failed to give bromoazepandione **5**, and the starting material was recovered. The ¹H NMR spectra for compound **5** showed an exchangeable enolic hydroxyl proton at δ 12.3 ppm, while the solid IR spectrum reflects the ketone character for this compound and gave the carbonyl absorptions at 1732 cm^{-1} (CO, ketone) and 1680 cm^{-1} (CO, amide). Condensation of ethylenediamine or *o*-phenylenediamine with the compound **5** gave the pyrazinoazepine **7** and azepinoquinoxaline **9** derivatives, respectively (Scheme 1). Both values of 1-NH and 4-NH in the ¹H NMR spectra for compound **7** were upfield chemical shielded from the typical values of secondary aliphatic amines. Proton at 1-NH appears at δ 7.5 ppm, due to its enamine properties, and 4-NH appears at δ 8.2 ppm due to the effect of the neighboring group on the β position (C-5 carbonyl group). Azepinoquinoxaline **9** did not show any exchangeable NH protons in its ¹H NMR spectrum. This evidence supports air oxidation of the azepinoquinoxaline intermediate **8** to give compound **9**.³



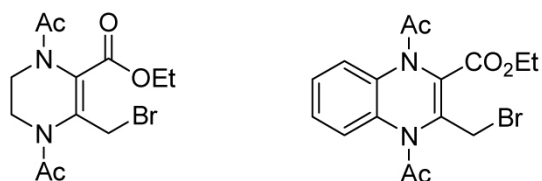
Shema 1

For an example of the second strategy we report a new 1,7-carbonyl-enamine azepine ring closure, as a new mode for ring closure. The stereoselective azepine ring formation through the thermal 1,7-imino-ene and 1,7-carbonyl-ene reactions has been reported.⁴ The present work describes a successful new extension of the azepine ring formation leading to functionalized heterocyclic fused azepine ring systems. The resonance forms **10** and **11** have structural features characteristic of tertiary enamines,⁵ and likewise could cyclize via favoured 7-exo-trig,⁶ forming the azepine ring derivative **12** in a new mode for ring closure (Scheme 3).



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For the syntheses of pyrazine and quinoxaline derivatives having the enamine-ester structure **10**, the bromopyrazine derivatives **13**⁷ and bromoquinoxaline **14** were selected. Compound **14** was synthesized via the synthetic procedure of compound **13**.⁷

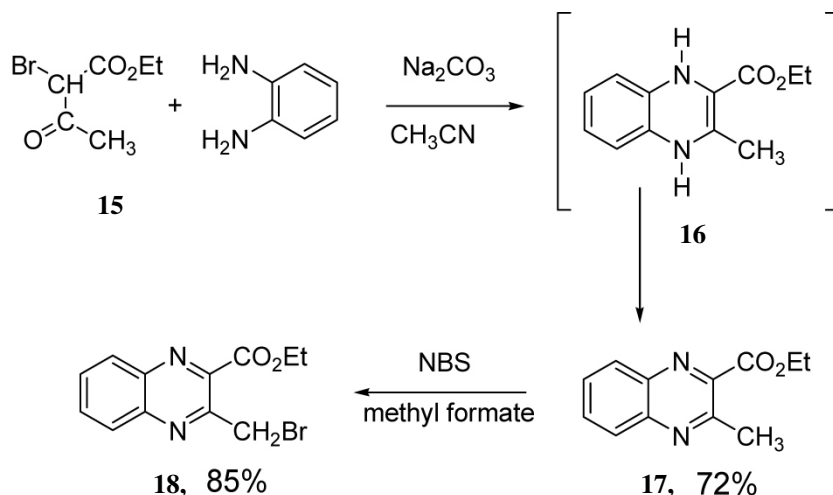


Condensation of *o*-phenylenediamine with ethyl bromoacetoacetate (**15**)⁸ gives rise to a fully aromatized quinoxaline derivative **17**, instead of 1,4-dihydroquinoxaline derivative **16**. This evidence supports air oxidation of the 1,4-dihydroquinoxaline derivative **16** to give compound **17** (Scheme 3).³ This reaction has to be initially carried out at low temperature, as elevated temperatures at the beginning of the reaction lead to black mass, which is insoluble in organic solvents.

In the ¹H NMR spectrum for compound **17** no exchangeable protons were observed, but C-3 methyl protons were characterized by a signal at δ 1.75 ppm. Compound

17 was efficiently brominated with *N*-bromosuccinimide⁹ to give the bromomethylquinoxaline derivative **18** (Scheme 3). Methyl formate was used as a solvent for this bromination reaction since carbon tetrachloride did not dissolve compound **17**.

The synthesis of an enamine-ester such as **20**, by the reaction of the bromopiperazine derivative **13** with the preformed *N*-benzylvinylamine **19** in the presence of polar aprotic solvents (THF, acetonitrile or DMF) was unsuccessful. However, in absolute ethanol and with anhydrous sodium carbonate, the reaction affords a product consistent with the structure **22**, rather than the enamine-



Shema 3

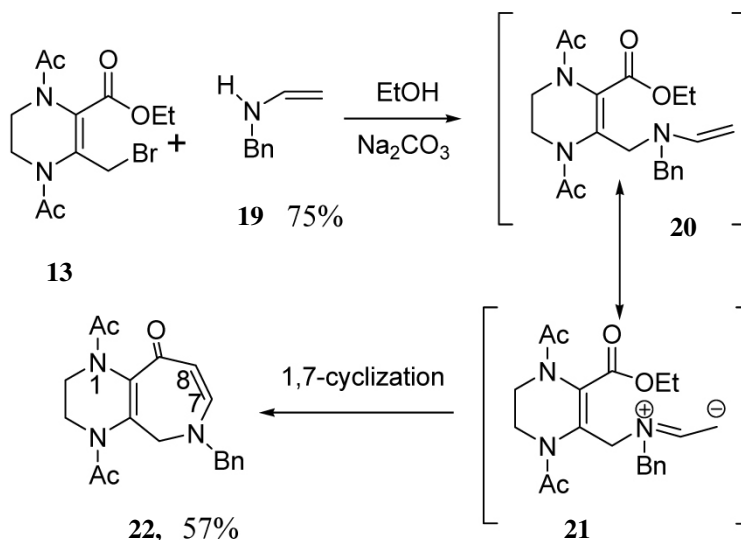
ester **20** (Scheme 4). TLC test during the reaction has shown instant appearance of an intermediate which disappeared by time.

The IR spectrum of **22** has shown three absorption bands due to three different carbonyl groups. Two of them are at 1660, 1665 cm^{-1} for two different acetyl groups in 4-NCOCH₃ and 1-NCOCH₃, respectively. The third peak is at 1689 cm^{-1} , which can be attributed to an α,β -unsaturated ketone at 9-C. The ¹H NMR spectrum of compound **22** has shown two vinyl protons, for 8-CH and 7-CH at δ 5.20 and 5.90 ppm, respectively, characteristic for the enamine moiety. The ¹³C NMR spectrum of **22** showed an upfield chemical shift for 7-C at δ 171.3 ppm but downfield chemical shift for 8-C at δ 144.5 ppm. The proposed route for this new mode of ring closure may include the formation of an enamine-ester intermediate **20**, which could form quaternary iminium ion **21**. Based on the previous evidence, the reaction could proceed by 1,7-cyclization of **20** and formed the piperazinoazepine **22**.

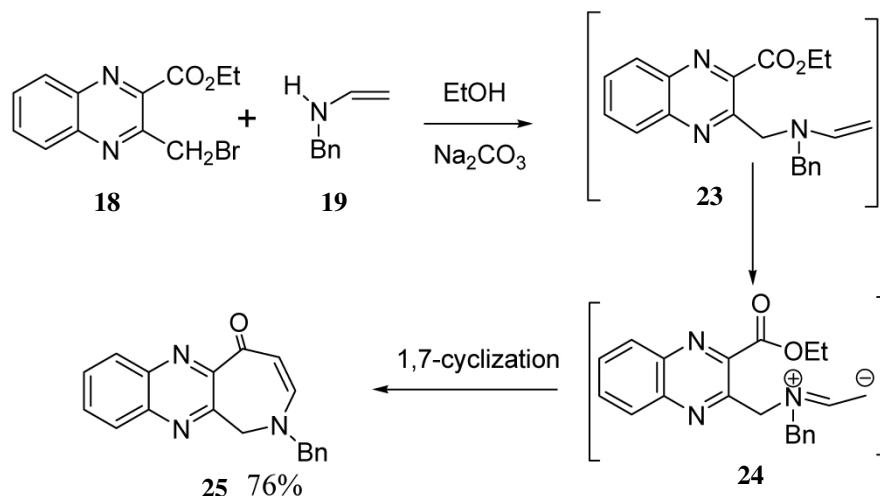
By the same mechanism, the bromo-quinoxaline derivative **18** reacted with *N*-benzyl enamine derivative **19** to

give the azepino-quinoxaline derivative **25**, via the intermediates **23** and **24** (Scheme 5). The IR spectrum of **25** indicated the presence of an α,β -unsaturated ketone at 1682 cm^{-1} and its ¹H NMR spectrum confirmed the appearance of two vinyl protons for 4-CH and 3-CH at δ 5.30 and 5.95 ppm, respectively. Also the ¹³C NMR data revealed an increase of the value of chemical shift of 3-C than 4-C atom.

This new mode of ring closure in the synthesis of the non-fused azepine ring has been further explored by the fusion of *N*-benzylaminofumarate **26**¹⁰ with ethyl 4-bromobutyrate, which afforded the azepine derivative **29**. The proposed mechanism for this cyclization includes the enamine-ester **27** (Scheme 6), as was described above. The carbanion **28** (formed from tertiary enamine species),⁵ could add to the butyrate ester in a favoured 7-exo-trig⁶ mode, forming the azepine derivative **29**. IR data for compound **29** reflect the presence of two different carbonyl absorptions for ester groups at 1721 and 1716 cm^{-1} , in addition to the α,β -unsaturated ketone at 1683 cm^{-1} . ¹H NMR spectrum for compound **29** showed the disappearance of ethyl ester protons but still contain the two



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methyl ester protons at δ 3.72 and 3.85 ppm for 3-C and 2-C ester groups.

Azepine derivative **32** has been formed by a further refluxing of ethyl acetoacetate with ethyl *N*-phenyl-4-aminobutyrate **30**^{2b} in toluene and in the presence of *p*-toluenesulfonic acid, by the same mechanism of formation as for compound **29**. The enaminoester **31** was detected by TLC test during the reaction and could cyclize to the azepine derivative **32** (Scheme 7). The IR spectrum for compound **32** showed the carbonyl absorption for ester at 1712 cm^{-1} and for α,β -unsaturated ketone at 1679 cm^{-1} . ¹H NMR spectrum for compound **32** showed the presence for one set of ethyl ester protons in addition to the upfield chemical shielding of the allylic methyl group protons to δ 2.34 ppm.

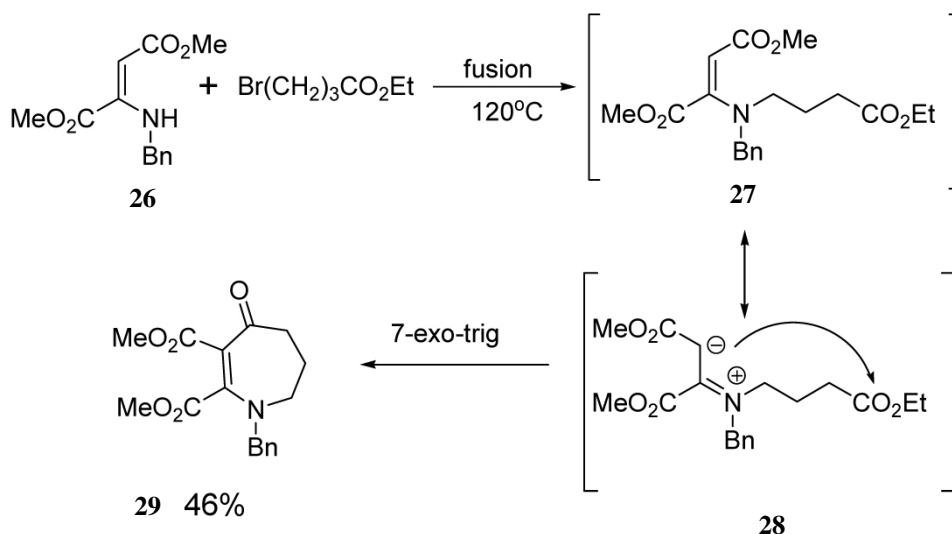
3. Conclusion

It can be concluded that tertiary enamines could exist in the quaternary resonating structure with a negative

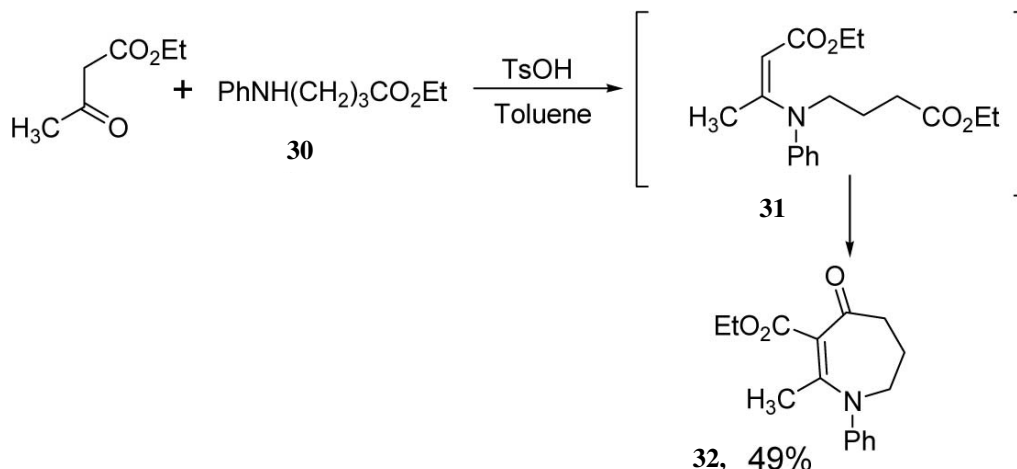
charge on their β carbon.⁵ This will lead to a great efficiency of an intramolecular attack on the esters carbonyl group, forming azepine ring. The yields in the case of the fused azepines are somewhat higher than for the non-fused azepines obtained by the described method. This new cyclization can be referred to as a carbonyl-enamine ring closure and will be further utilized in the syntheses of various ring sizes in future work.

4. Experimental

Silica gel plates (Merck F 254) and silica gel 60 (Merck, 70–230 mesh) were used for TLC and column chromatography, respectively. All melting points were determined on a Gallenkamp melting point apparatus. Microanalyses were performed with a Perkin-Elmer 260 elemental analyzer for C, H, and N, and the results were within $\pm 0.4\%$ of the theoretical values. The IR spectra were recorded with a Perkin-Elmer 1420 spectrometer in Nujol



Shema 6



Schema 6

mulls for the solids and on KBr discs in the case of liquids, peaks are expressed in cm^{-1} . The ^1H NMR spectra were recorded with Varian EM 390 instrument at 200 MHz using CDCl_3 as a solvent. ^{13}C NMR spectra were recorded at 50 MHz. The chemical shifts are reported in δ (ppm). All the exchangeable protons were confirmed by addition of D_2O .

3-Bromo-1-phenylazepane-2,4-dione (5)

To a solution of 2,4-azepanedione (**4**, 4.06 g, 0.02 mol) in glacial acetic acid (15 mL) a solution of bromine (3.2 g, 0.02 mol) in glacial acetic acid (15 mL) was added with stirring during 15 min at room temperature. The reaction mixture was stirred for further 3 h and poured into water-ice mixture (100 mL). The crude product **5** was collected by filtration and recrystallized from ethyl acetate to give pure product **5** (4.2 g, 75%), mp 50–53 °C. IR (Nujol) ν 1732 (CO, ketone), 1680 (CO, amide) cm^{-1} . ^1H NMR (200 MHz, CDCl_3) δ 1.91 (t, 2H, $J = 10.1$ Hz, 5- CH_2), 2.21 (m, 2H, 6- CH_2), 2.52 (t, 2H, $J = 10.1$ Hz, 7- CH_2), 7.32 (m, 5H, Ph), 12.36 (br, 1H, exch. OH). Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{BrNO}_2$ (281.133): C, 51.09; H, 4.29; Br, 28.32; N, 4.96. Found: C, 51.32; H, 4.30; Br, 28.53; N, 4.61.

Condensation of 1,2-diamine with α -bromoketone

To a solution of the diamine (0.01 mol) in acetonitrile (20 mL) and sodium carbonate (3 gm) in dry ice bath (-78 °C) a solution of the corresponding α -bromoketone (0.01 mol) in acetonitrile (10 mL) was added dropwise during 10 min. After the addition was completed, the reaction mixture was left to reach room temperature and the room temperature was maintained for 8 h with continuous stirring. The solid material was removed by filtration and the solvent was removed *in vacuo*. The crude material was purified by the column chromatography and recrystallized from proper solvent to give the desired pure product.

1,2,3,4,6,7,8,9-Octahydro-6-phenyl-5H-pyrazino[2,3-c]azepin-5-one (7)

Compound **7** was prepared from the reaction of compound **5** with 1,2-diaminoethane following the procedure described above. The product was recrystallized from ethyl acetate to give yellow powder (1.36 g, 56%), mp 130–133 °C (ethyl acetate). IR (Nujol) ν 1660 (CO, amide) cm^{-1} . ^1H NMR (200 MHz, CDCl_3) δ 2.04 (m, 2H, 8- CH_2), 2.43 (t, 2H, $J = 10.1$ Hz, 9- CH_2), 3.05–3.34 (2m, 4H, 2- CH_2 , 3- CH_2), 3.62 (t, 2H, $J = 10.1$ Hz, 7- CH_2), 7.51 (br, 1H, exch. 1-NH), 8.26 (br, 1H, exch. 4-NH), 7.73 (m, 5H, Ph). ^{13}C NMR (50 MHz, CDCl_3) δ 171.8, 142.5, 140.2, 133.2, 128.4, 125.3, 121.5, 55.2, 54.5, 48.2, 36.2, 31.4. Anal. Calcd for $\text{C}_{14}\text{H}_{17}\text{N}_3\text{O}$ (243.304): C, 69.11; H, 7.04; N, 17.27. Found: C, 69.32; H, 7.22; N, 17.04.

2,3,4,5-Tetrahydro-2-phenyl-1H-azepino[3,4-b]quinoxalin-1-one (9)

Compound **9** was prepared from the reaction of compound **5** with *o*-phenylenediamine following the procedure described above. The product was recrystallized from ethyl acetate to give brownish powder (1.95 g, 68%), mp 195–197 °C (ethyl acetate-methanol). IR (Nujol) ν 1680 (CO, amide) cm^{-1} . ^1H NMR (200 MHz, CDCl_3) δ 1.94 (m, 2H, 4- CH_2), 2.46 (t, 2H, $J = 10.1$ Hz, 5- CH_2), 3.52 (t, 2H, $J = 10.1$ Hz, 3- CH_2), 6.84–7.06 (m, 4H, Ar), 7.21 (m, 5H, Ph). ^{13}C NMR (50 MHz, CDCl_3) δ 175.4, 155.8, 148.3, 146.1, 142.5, 140.1, 138.2, 136.6, 133.5, 131.2, 128.4, 125.5, 125.5, 48.2, 44.4, 30.2. MS (m/z) 290 (100%, M^+). Anal. Calcd for $\text{C}_{18}\text{H}_{15}\text{N}_3\text{O}$ (289.33): C, 74.72; H, 5.23; N, 14.52. Found: C, 74.80; H, 5.42; N, 14.35.

Ethyl 3-methylquinoxaline-2-carboxylate (17)

Compound **17** was prepared from the reaction of ethyl bromoacetoacetate (**15**)⁶ with *o*-phenylenediamine following the procedure described above. The product was recrystallized from ethanol (95%) to give brownish

powder (1.55 g, 72%), mp 220–222 °C. IR (Nujol) ν 1694 (CO, aromatic ester) cm^{-1} . ^1H NMR (200 MHz, CDCl_3) δ 1.13 (t, 3H, $J = 7.1$ Hz, OCH_2CH_3), 1.75 (s, 3H, 3- CH_3), 4.23 (m, 2H, OCH_2CH_3), 6.72–6.91 (m, 4H, Ar). ^{13}C NMR (50 MHz, CDCl_3) δ 173.3, 160.3, 152.3, 150.2, 144.3, 135.2, 133.4, 131.1, 130.1, 64.2, 22.4, 18.2. Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_2$ (216.236): C, 66.65; H, 5.59; N, 12.96. Found: C, 66.43; H, 5.76; N, 12.88.

Ethyl 3-(bromomethyl)quinoxaline-2-carboxylate (18)

A mixture of compound **17** (2.16 g, 0.01 mol), *N*-bromosuccinimide (2.1 g, 0.012 mol) and dibenzoyl peroxide as catalyst (0.01 g) in methyl formate (20 mL) was irradiated with lamp (60 W) for 2 h. Cold water (50 mL) and chloroform (50 mL) were added and the organic layer was separated, washed with cold water (20×3 mL), dried over anhydrous Na_2SO_4 and evaporated *in vacuo*. The pure product **18** was obtained by recrystallization from ethyl acetate (2.5 g, 85%), mp 102–105 °C. IR (Nujol) ν 1700 (CO, ester) cm^{-1} . ^1H NMR (200 MHz, CDCl_3) δ 1.24 (t, 3H, $J = 7.1$ Hz, OCH_2CH_3), 4.21 (q, 2H, $J = 7.1$ Hz, OCH_2CH_3), 4.43 (s, 2H, CH_2Br), 6.72–6.91 (m, 4H, Ar). Anal. Calcd for $\text{C}_{12}\text{H}_{11}\text{BrN}_2\text{O}_2$ (295.132): C, 48.84; H, 3.76; Br, 27.07; N, 9.49. Found: C, 49.11; H, 3.60; Br, 27.23; N, 9.40.

N-Benzylethenamine (19)

Benzylamine (10 g, 0.1 mol), vinyl acetate (8.6 g, 0.1 mol) and sodium carbonate (15 g) in absolute ethanol (30 mL) were refluxed for 1 h and stirred for further 8 h at room temperature. The reaction mixture was poured into water (100 mL), extracted with chloroform, dried over anhydrous Na_2SO_4 and evaporated *in vacuo* to give pure yellow oil (R_f 0.35, dichloromethane : ethanol : ammonia = 300 : 8 : 1) (10 g, 75%). IR (neat) ν 3321 (br, NH), 1610 (C=C) cm^{-1} . ^1H NMR (200 MHz, CDCl_3) δ 4.02 (s, 2H, CH_2Ph), 5.21–5.48 (dd, 2H, $J_1 = 6.4$ Hz, $J_2 = 9.7$ Hz, N- $\text{CH}=\text{CH}_2$), 5.76 (br, 1H, exch. NH), 6.39 (d, 1H, $J = 6.4$ Hz, N- $\text{CH}=\text{CH}_2$), 7.29 (m, 5H, Ph). Anal. Calcd for $\text{C}_9\text{H}_{11}\text{N}$ (133.19): C, 81.16; H, 8.32; N, 10.52. Found: C, 81.32; H, 8.43; N, 10.45.

1,4-Diacetyl-6-benzyl-1,2,3,4,5,6-hexahydro-9H-pyrazino[2,3-*c*]azepin-9-one (22)

A solution of the bromopiperazine derivative **13** (3.47 g, 0.01 mol), *N*-benzyl enamine **19** (1.33 g, 0.01 mol) in absolute ethanol (50 mL) and sodium carbonate (3 g) was refluxed for 6 h. After cooling, the reaction mixture was poured into cold water (100 mL) and the precipitate was filtered off. The pure product **22** was obtained by crystallization from ethanol (95%) (2 g, 57%), mp 240–242 °C. IR (Nujol) ν 1660 (CO, 4- NCOCH_3), 1665 (CO, 1- NCOCH_3), 1689 (CO, 9-C) cm^{-1} . ^1H NMR (200 MHz, CDCl_3) δ 2.25–2.27 (2s, 6H, 4- NCOCH_3 , 1- NCOCH_3), 3.03–3.32 (m, 4H, 2- CH_2 , 3- CH_2), 3.69 (s, 2H, 5- CH_2), 4.22 (s, 2H, CH_2Ph), 5.20 (d, 1H, $J = 8.6$ Hz, 8-

CH), 5.90 (d, 1H, $J = 8.6$ Hz, 7-CH), 7.55 (m, 5H, Ar). ^{13}C NMR (50 MHz, CDCl_3) δ 180.2, 177.4, 172.4, 171.3, 144.5, 140.6, 138.1, 136.2, 133.4, 130.8, 120.9, 118.7, 50.2, 48.8, 47.3, 28.4, 23.3. Anal. Calcd for $\text{C}_{19}\text{H}_{21}\text{N}_3\text{O}_3$ (339.388): C, 67.24; H, 6.24; N, 12.38. Found: C, 67.30; H, 6.11; N, 12.42.

2-Benzyl-1,2-dihydro-5H-azepino[3,4-*b*]quinoxalin-5-one (25)

A solution of the bromoquinoxaline derivative **18** (2.95 g, 0.01 mol), *N*-benzyl enamine **19** (1.33 g, 0.01 mol) and sodium carbonate (3 g) in absolute ethanol (50 mL) was refluxed for 9 h. After cooling, the reaction mixture was poured into cold water (100 mL) and the precipitate was filtered off. The pure product **25** was obtained by crystallization from absolute ethanol (2.3 g, 76%), mp 193–200 °C. IR (Nujol) ν 1682 (CO, 6-C) cm^{-1} . ^1H NMR (200 MHz, CDCl_3) δ 3.03 (s, 2H, 1- CH_2), 4.22 (s, 2H, CH_2Ph), 5.30 (d, 1H, $J = 8.6$ Hz, 4-CH), 5.95 (d, 1H, $J = 8.6$ Hz, 3-CH), 6.72–7.76 (m, 9H, Ar). ^{13}C NMR (50 MHz, CDCl_3) δ 193.2, 172.2, 160.6, 158.2, 144.1, 141.3, 136.4, 134.8, 133.7, 132.8, 132.6, 130.1, 129.5, 129.3, 129.1, 110.6, 50.3. Anal. Calcd for $\text{C}_{19}\text{H}_{15}\text{N}_3\text{O}$ (301.342): C, 75.73; H, 5.02; N, 13.94. Found: C, 75.54; H, 5.20; N, 14.10.

Dimethyl 1-benzyl-4,5,6,7-tetrahydro-4-oxo-1H-azepine-2,3-dicarboxylate (29)

A mixture of compound **26** (2.49 g, 0.01 mol) and ethyl 4-bromobutyrate (1.95 g, 0.01 mol) was heated at 120 °C for 6 h. After cooling, the reaction mixture was purified by column chromatography using mixture of dichloromethane, ethanol and ammonia (300 : 8 : 1) to give pure yellow oil ($R_f = 0.2$) (1.45 g, 46%). IR (neat) ν 1721 (CO, 2-C-ester), 1716 (CO, 3-C-ester), 1683 (CO, 4-C-ketone) cm^{-1} . ^1H NMR (200 MHz, CDCl_3) δ 1.92 (m, 2H, 6- CH_2), 2.63 (t, 2H, $J = 9.6$ Hz, 5- CH_2), 3.11 (t, 2H, $J = 9.6$ Hz, 7- CH_2), 3.72 (s, 3H, 3- CO_2CH_3), 3.85 (s, 3H, 2- CO_2CH_3), 4.23 (s, 2H, N- CH_2Ph), 7.33–7.53 (m, 5H, Ar). ^{13}C NMR (50 MHz, CDCl_3) δ 211.3, 178.2, 173.3, 170.3, 140.6, 133.2, 130.5, 125.2, 110.1, 58.9, 55.3, 54.2, 53.3, 45.4, 28.3. Anal. Calcd for $\text{C}_{17}\text{H}_{19}\text{NO}_5$ (317.34): C, 64.34; H, 6.03; N, 4.41. Found: C, 64.25; H, 6.42; N, 4.65.

Ethyl 4,5,6,7-tetrahydro-2-methyl-4-oxo-1-phenyl-1H-azepine-3-carboxylate (32)

A solution of ethyl acetoacetate (1.13 g, 0.01 mol) and ethyl 4-(*N*-phenylamino)butyrate (2.07 g, 0.01 mol) in dry toluene (20 mL) in the presence of *p*-toluenesulfonylchloride (0.05 g, catalyst) was refluxed for 12 h. After cooling, the reaction mixture was washed with water (3×10 mL), dried over anhydrous Na_2SO_4 and evaporated *in vacuo*. The residue was purified by column chromatography using mixture of dichloromethane, ethanol and ammonia (300 : 8 : 1) to produce pure product **32** ($R_f = 0.3$) (1.33 g, 49%). IR (neat) ν 1712 (CO, ester), 1679

(CO, ketone) cm^{-1} . ^1H NMR (200 MHz, CDCl_3) δ 1.33 (t, 3H, $J = 7.1$ Hz, OCH_2CH_3), 1.76 (m, 2H, 6- CH_2), 2.34 (s, 3H, 2- CH_3), 2.78 (t, 2H, $J = 9.6$ Hz, 5- CH_2), 3.37 (t, 2H, $J = 9.6$ Hz, 7- CH_2), 4.21 (q, 2H, $J = 7.1$ Hz, OCH_2CH_3), 7.67–7.83 (m, 5H, Ar). ^{13}C NMR (50 MHz, CDCl_3) δ 210.3, 175.5, 168.3, 150.4, 133.6, 120.5, 120.2, 108.8, 63.2, 50.6, 44.3, 28.3, 27.4, 17.2. Anal. Calcd. for $\text{C}_{16}\text{H}_{19}\text{NO}_3$ (273.33) C, 70.31; H, 7.01; N, 5.12. Found: C, 70.43; H, 7.26; N, 5.37.

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Povzetek

Pirazino[2,3-*c*]azepin in azepino[3,4-*b*]kinoksalin predstavljata nova obročna sistema, ki sta bila pripravljena s pomočjo spajanja pirazinskega obroča z azepinskim derivatom ali pa obratno. Kot nov način za pripravo azepinskih ciklov je bila proučevana intramolekularna 1,7-karbonil-enaminska ciklizacija. Raziskani so bili različni primeri in različni reakcijski pogoji za to ciklizacijo.