On the reaction of fused benzodiazepines with alkynes containing electron-withdrawing groups

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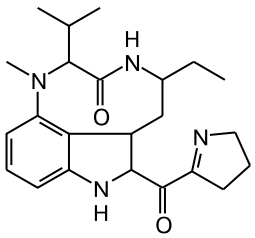
Fused benzodiazepines were found to react with activated alkynes to effect either vinylation of unsubstituted nitrogen atom or dealkylation of nitrogen and its further vinylation. For benzodiazepinones bearing lactam fragment, the reactions with alkynes proceed by several pathways: formation of vinyl-substituted benzodiazepines, the Stevens rearangement products, and expansion of the diazepine ring: benzodiazonine and diazecine.

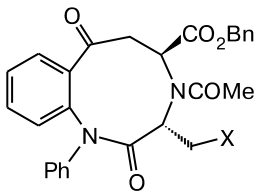
Key words: tetrahydrobenzo-1,4-diazepines, benzopyrrolo-1,4-diazonine, octahydrobenzo-1,7-diazecine, the Stevens rearangement, tandem expansion, tandem cleavage.

By the present time, four general methods for the synthesis of fused diazonines have been described: a copper-complex catalyzed closing of a nine-membered ring in the reaction of *o*-halophosphoamidates with carbamates[1], transformation of *o*-(azetidinon-1-yl)aminoethylarenes (hetarenes),[2] and a ring expansion resulting from either the oxidation[3] or the Sommlet—Hauser rearangement.[4]

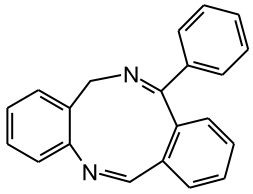
The scientific literature has only separate examples of synthesis of 1,2- and 1,5-diazonines, benzo- and dibenzodiazonines, indolodiazonines. Meanwhile, chemical compounds containing a diazonine ring in the molecule display various biological activity. Such alkaloids as teleocidin and lingbiatoxin were found in bacteria of the family *Streptomyces mediocidicus*.[5] Physiological action of these alkaloids is variable: they stimulate the nervous system, possess antifungal and antihypertensive properties. Besides alkaloids, there are synthetically prepared compounds containing a diazonine fragment, as well; they are given below.



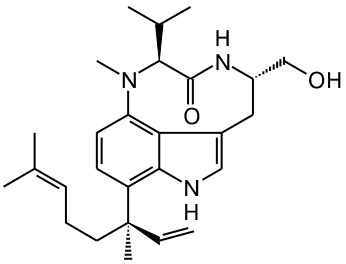
Teleocidine



2,7-Dioxo-2,3,4,5,6,7-hexahydro-1*H*-benzo[*h*]-[1,4]diazonine



5-Phenyl-7*H*-dibenzo-[b,g]-[1,5]diazonine



Lingbiatoxine

The indicated compounds exhibit various biological activity; 2,7-dioxo-2,3,4,5,6,7-hexahydro-1*H*-benzo[*h*][1,4]-diazonine is a CCK_2-receptor antagonist,[6] 5-phenyl-7*H*-dibenzo[*b*,*g*][1,5]diazonine can be used as antidepressant.[7]

Heterocyclic system having a diazonine fragment are studied poorly, and there are no literature data on fused pyrrolobenzodiazonines at all.

Recently,[8] we have described a synthesis of azoninoindoles by a tandem reaction of the azepine ring expansion in hexahydroazepinoindoles upon the action of alkynes with electron-withdrawing substituents. Azoninoindoles were obtained in 64—88% yields.

In the present work, we planned to develop an approach to the synthesis of fused diazonines based on this reaction.

We involved into the reactions with dimethyl acetylenedicarboxylate (DMAD), methyl propiolate, and acetylacetylene the following substrates: methyl 4-methyl- (**1**)

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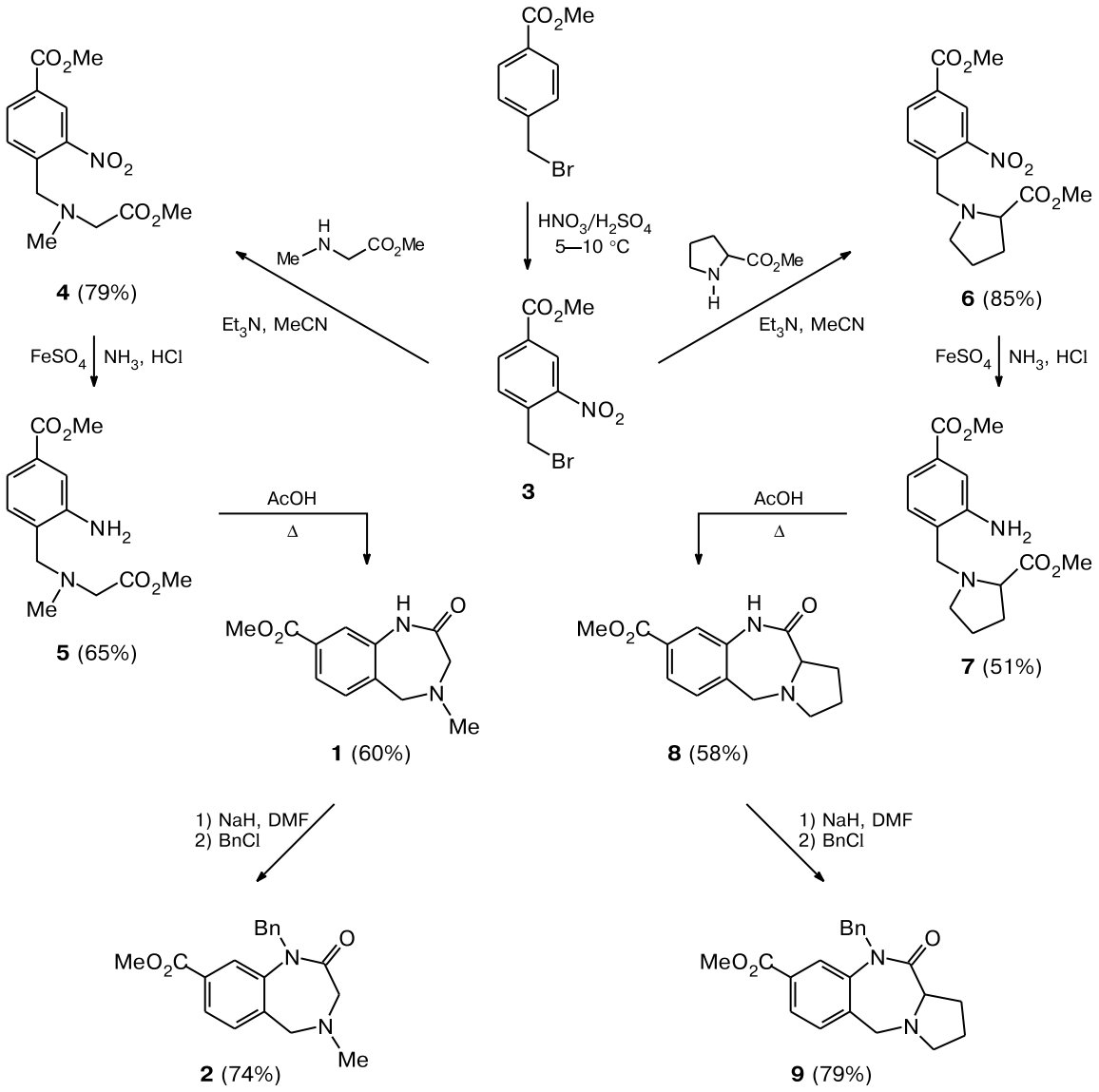
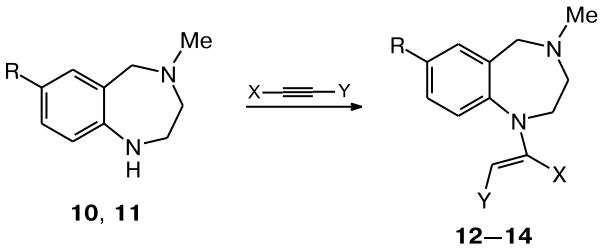
Scheme 1



and methyl 1-benzyl-4-methyl-2-oxo-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine-8-carboxylate (**2**) (Scheme 1), methyl 11-oxo- (**8**) and methyl 10-benzyl-11-oxo-2,3,5,10,11,11a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-8-carboxylate (**9**) (see Scheme 1), as well as 4-methyl- and 7-fluoro-4-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepines (**10**, **11**) (Scheme 2), 1-acetyl-4-methyl- (**15**) and 1-acetyl-7-fluoro-4-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepines (**16**) (Scheme 3).

The synthesis of the starting diazepinones **1**, **2**, **8**, and **9** is given in Scheme 1. Diazepines **10** and **11** were obtained according to the procedure described in the work.[9] Their transformations to *N*-acetyl-substituted **15** and **16** was effected by acetylation with acetic anhydride under standard conditions.

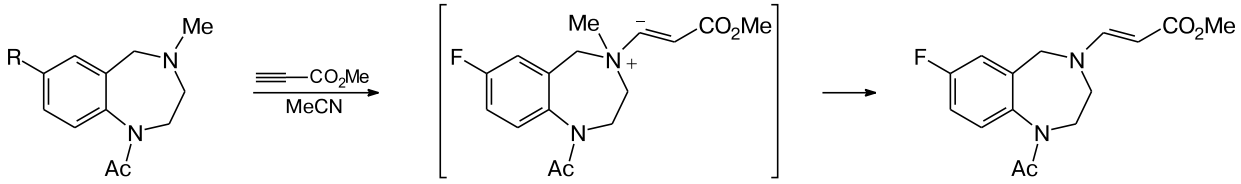
Scheme 2



R = H (**10**, **12**); F (**11**, **13**, **14**); X = H, Y = CO_2Me (**12** (88%), **13** (72%)); X = Y = CO_2Me (**14** (78%))

Methyl 4-bromo-3-nitrobenzoate (**3**) obtained by the nitration of methyl 4-bromomethylbenzoate was convert-

Scheme 3



15, **16** **A** **17** (34%)

R = H (**15**), F (**16**)

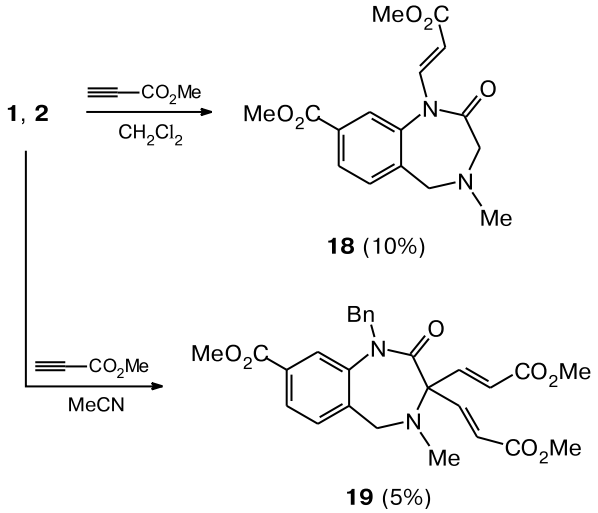
ed into compound **4** upon the action of methyl ester of sarcosine. Compound **4** was reduced with iron sulfate to the corresponding amine **5**, reflux of which in glacial acetic acid led to benzodiazepine **1**. Benzylation of the amide fragment was carried out using benzyl chloride in the presence of sodium hydride, finally obtaining benzylated benzodiazepine **2**. Benzodiazepines **8** and **9** were synthesized similarly.

When benzodiazepines **10**, **11**, and **16** were treated with alkynes in methanol and in acetonitrile, no expected products of the diazepine fragment expansion, *i.e.*, benzodiazonines and products of their cleavage, were obtained. Treatment of benzodiazonines **10** and **11** with DMAD and methyl propiolate in methanol at 20 °C leads to the exclusive vinylation of the unsubstituted nitrogen atom with the formation of 1-vinyl-substituted derivatives **12**—**14** (see Scheme 2). According to the ^{1}H NMR spectroscopic data, the vinyl fragment in diazepines **12**—**14** has *E*-configuration (J = 13.0 Hz).

N-Acetyl-substituted diazepines **15** and **16** do not react with DMAD and methyl propiolate in refluxing methanol, moreover, diazepine **15** is inreactive in acetonitrile with a large excess of alkyne, either. Diazepine **16** upon the action of excessive methyl propiolate in refluxing acetonitrile for 5 days was converted to 4-acryloyl-substituted benzodiazepine **17** in 34% yield (see Scheme 3). Apparently, the latter resulted from elimination of the methyl group from the intermediate zwitterion **A**.

Reactions of 1,4-benzodiazepine **1** with activated alkynes are complicated and proceed with the formation of multi-component mixtures. No individual compounds in the case of the reactions with methyl propiolate, acetylacetylene, and DMAD in methanol were isolated. In the reaction of 1,4-benzodiazepine **1** with methyl propiolate in CH_2Cl_2, *N*-vinylated benzodiazepine **18** was obtained (Scheme 4), which is the product of vinylation of the nitrogen atom of the lactam fragment, that was unambiguously confirmed by X-ray crystallography (Fig. 1). In acetonitrile, *N*-benzylbenzodiazepine **2** reacts with methyl propiolate to give compound **19** resulting from the twice Stevens rearangement. In methanol, *N*-benzylbenzodiazepine **2** does not react with methyl propiolate even under several-days reflux with a large excess of the reactant.

Scheme 4



R = H (**15**), F (**16**)

Benzopyrrolodiazepinone **8** was involved into the reaction with methyl propiolate and acetylacetylene in dichloromethane and methanol. The reactions proceeded

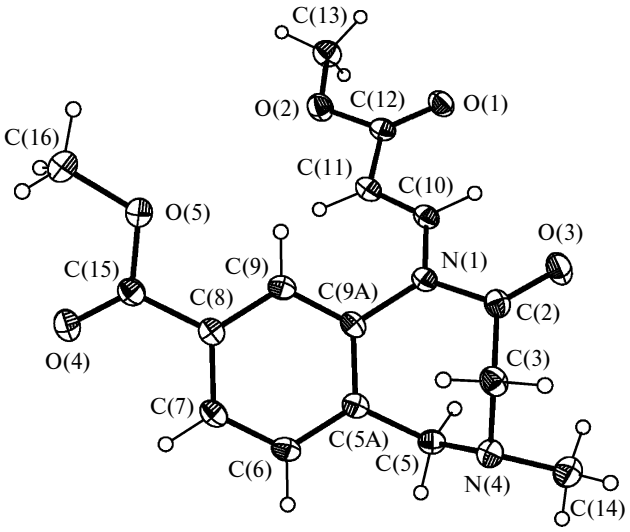
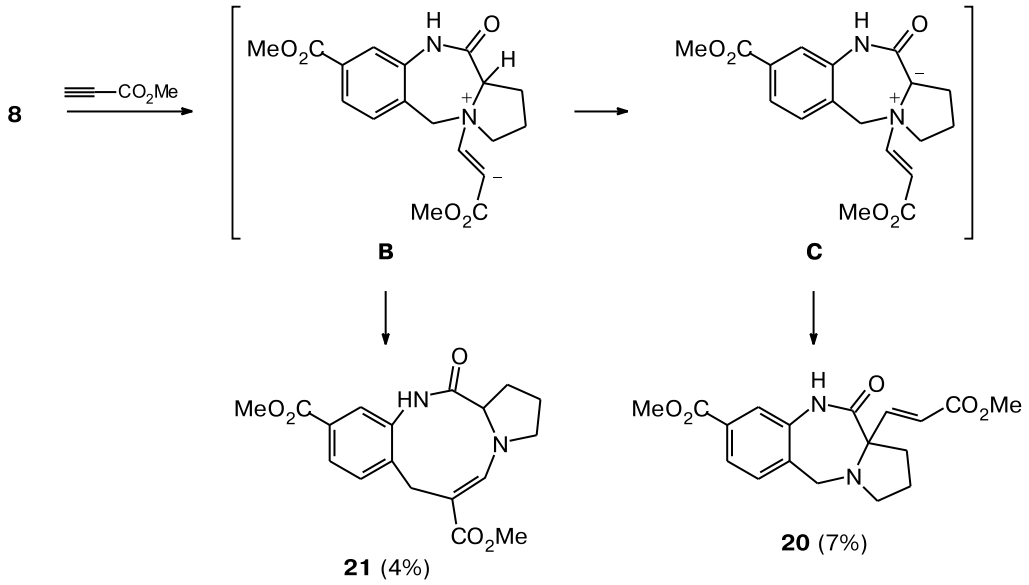


Fig. 1. Molecular structure of compound **18**.

Scheme 5



by several pathways with the formation of multi-component reaction mixtures. After chromatographic separation of the reaction mixture obtained in the reaction of benzopyrrolodiazepinone **8** with methyl propiolate in dichloromethane at 25 °C, 11a-methylacryloyl-substituted benzopyrrolodiazepine **20** (7%) and the expected product of the diazepine ring expansion, *i.e.*, dimethyl 13-oxo-2,3,7,12,13,13a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazonine-6,10-dicarboxylate **21** (4%) were isolated (Scheme 5). When the reaction was carried out in methanol, only benzopyrrolodiazepine **20** (30%) was isolated from the reaction mixture by chromatography.

The processes shown in Scheme 5, by analogy with the work,[10] proceed presumably through the ammonium zwitterion **B** formed by the Michael reaction. A nucleophilic attack by the anionic center of the intermediate **B** on the methylene group of the fragment $Ar—CH_2—N^+$ causes the ring expansion and results in the preparation of diazonine **21**. Due to the high CH-acidity of the carbon atom neighboring to the amide group, formation of ylide **C** is possible, in which migration of the acryloyl substituent by the Stevens rearrangement yields diazepine **20**.

From the products of the reaction of benzopyrrolodiazepinone **8** with acetylacetylene in dichloromethane, only the products of its *C*- and *C*,*N*-vinylation, *i.e.*, benzopyrrolodiazepines **22** (4%) and **23** (17%), were isolated in the individual states (Scheme 6). Such a course of the process is probably due to the lower nucleophilicity of the anionic center in the possible intermediate of the zwitterionic type **B**, since the excess of electrons apparently is delocalized more efficiently with participation of the carbonyl group of the ketone fragment than with participation of the ester fragment. Therefore, the probability of the diazepine ring expansion in the reaction of nucleophilic expansion essentially is decreased. It can be suggested that after the formation of the Stevens rearrangement product, *i.e.*, butenoyl-substituted diazepinone **22**, its quaternization to the zwitterion **D** takes place with further transformation to the amide anion **E**. The latter through the 1,4-sigmatropic rearrangement is converted into benzopyrrolodiazepine **23**. The structure of compound **23** was unambiguously confirmed using X-ray crystallography (Fig. 2).

The reaction of benzopyrrolodiazepinone **8** with acetylacetylene in methanol, besides butenoyl-substituted diazepinone **22** (yield 4%), led to methyl 3-methoxy-2-oxo-1,7-bis[(1*E*)-3-oxobut-1-en-1-yl]-1,2,3,4,5,6,7,8-octahydro-1,7-benzodiazecine-11-carboxylate (**24**) as a result of the bridged C—N bond cleavage (Scheme 7). Diazecine **24**

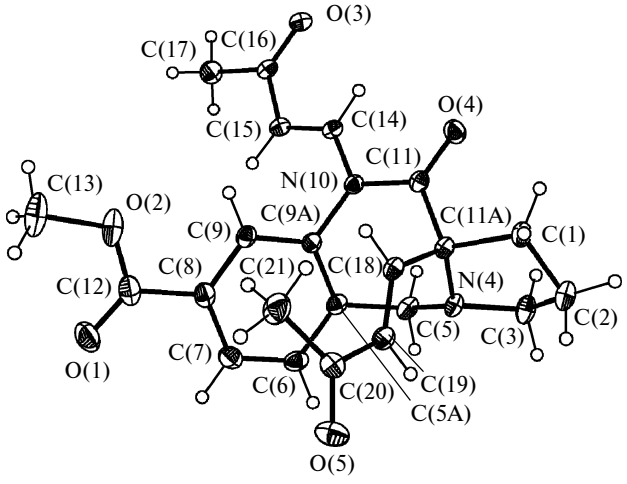
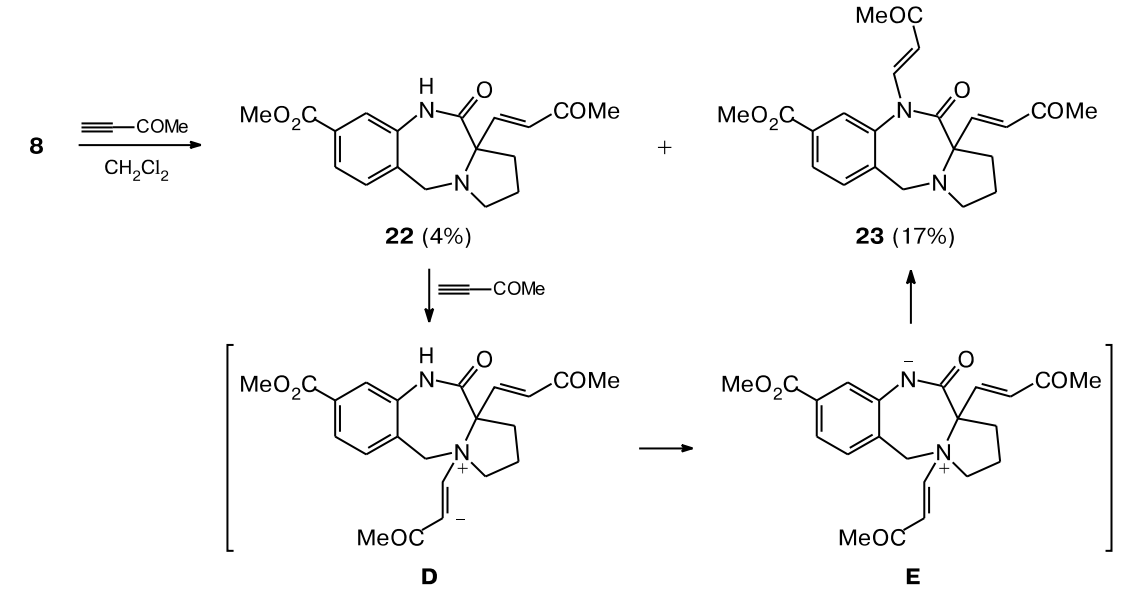
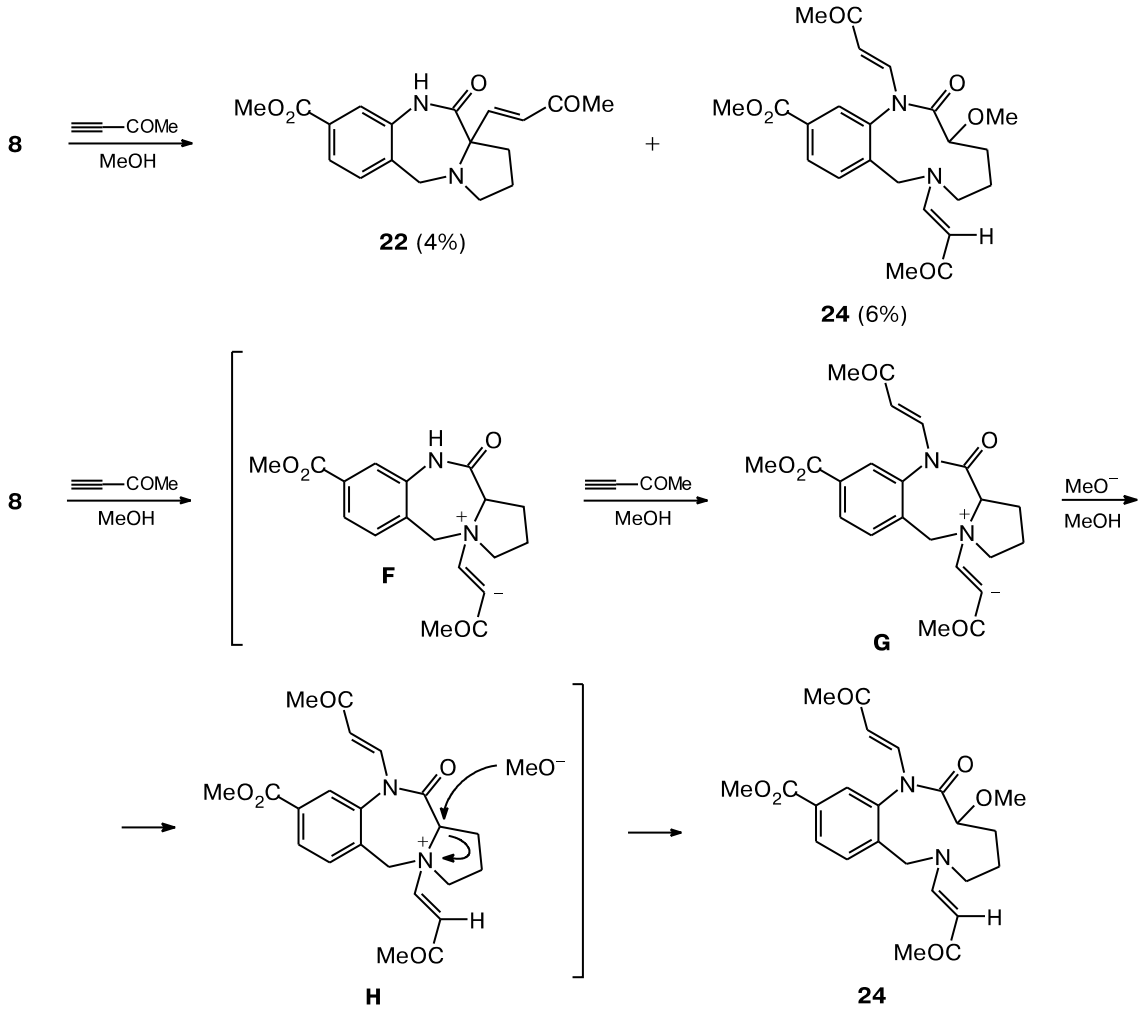


Fig. 2. Molecular structure of compound **23**.

Scheme 6



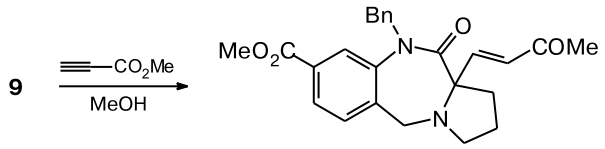
Scheme 7



apparently was formed from the intermediate **F**, the product of the *N*-vinylation of the starting molecule **8**, which after the addition of an acetylacetylene molecule to the angular N atom was protonated with methanol. The thus arising methoxide anion cleaved the C—N bridged bond, which is a fairly general approach to the preparation of medium-sized azaheterocycles from their quaternary salts.[11]

The reaction of *N*-benzyl-substituted benzopyrrolodiazepinone **9** with methyl propiolate in methanol led to the formation of the Stevens rearangement product, benzopyrrolodiazepine **25**, in 21% yield (Scheme 8).

Scheme 8



25 (21%)

The structures of compounds **12**—**14** and **17**—**25** were inferred from the spectral data, whereas the structures of compounds **18** and **23** were additionally confirmed by X-ray crystallography. The IR spectra of compounds **12**—**14** and **17**—**25** exhibit absorption bands of the stretching vibrations of the amide, ester, and keto groups in the region 1621—1727 cm^{-1}.

The mass spectra of all the compounds have peaks of molecular ions corresponding to their molecular formulas. The ^1H and ^{13}C NMR spectra exhibit signals for all the protons and carbon atoms present in their molecules, with the chemical shifts and the spin-spin coupling constants corresponding to their positions. The ^1H NMR spectra of vinyl-substituted diazepines **12**—**14**, **17**—**20**, and **22**—**25** are characterized by the presence of two doublet signals in the regions δ 4.93—6.05 and 6.62—7.70 with the spin-spin coupling constants ranging from 13.7 to 16.2 Hz, that unambiguously indicate the *E*-configuration of the vinyl fragment. The terminal proton of the *N*-vinyl group in diazepine **14** was found as a broadened singlet at δ 4.69. The ^1H NMR spectrum of diazonine **21** is characterized by the presence of a singlet at δ 7.76 due to the presence of the proton H(5) of the enamine fragment.

Compounds **18** and **23** include the fused bicyclic and tricyclic systems, respectively (see Figs 1 and 2). According to the data of X-ray crystallography, the diazepine rings of the molecules of **18** and **23** are in the *twist-boat* conformation, whereas the pyrrolidine rings are in the *envelope* conformation. The vinyl fragments on the nitrogen atoms in both compounds are involved into conjugation with both the carbonyl group of the carboxyl (in compound **18**) or the acyl (in compound **23**) substituents and the amide group, forming an extensive planar systems O=C—C=C—N—C=O. The angles between the planes of these conjugated systems and the benzene rings are equal to 51.91(5) and 57.64(4)°, respectively. Due to the presence of the conjugation described above, the nitrogen atoms N(1) in compound **18** and N(10) in compound **23** adopt a trigonal-planar configuration, while the nitrogen atoms N(4) have a trigonal-pyramidal geometry. The second vinyl fragment in compound **23** is also involved into the conjugation with the carbonyl group of the corresponding acyl substituent, resulting in the formation of the planar system O=C—C=C situating over the benzene fragment (the dihedral angle between the corresponding planes is equal to 30.68(9)°). The carbooxyl substituents in both compounds slightly deviate from the plane of the benzene rings (the corresponding dihedral angles are equal to 7.34(17) and 12.25(12)°). Compound **23** possesses an asymmetric center at the carbon atom C(11a). Crystal of compound **23** is a racemate.

In conclusion, we for the first time studied transformation of benzo-1,4-diazepines, benzo-1,4-diazepinones, as well as benzopyrrolo-1,4-diazepinones upon the action of activated alkynes. Benzo-1,4-diazepines were found to be relatively inert with respect to the to activated alkynes. The presence in the diazepine ring of an amide group activates its in the reactions with alkynes. Alkynes predominantly react with the nitrogen atom of the amide group and the neighboring CH-acidic center, resulting in the formation of the Stevens rearangement products and vinylation of the amide nitrogen atom. Methyl 11-oxo-2,3,5,10,11,11a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]-benzodiazepine-8-carboxylate **8** upon the action of methyl propiolate in dichloromethane gives the expected ring expansion product, dimethyl 13-oxo-2,3,7,12,13,13a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazonine-6,10-dicarboxylate **21**, whereas its treatment with acetylacetylene in methanol gives methyl 3-methoxy-2-oxo-1,7-bis[(1*E*)-3-oxobut-1-en-1-yl]-1,2,3,4,5,6,7,8-octahydro-1,7-benzodiazecine-11-carboxylate **24** as a result of the bridged C—N bond cleavage. *N*-Benzyl-substituted benzopyrrolodiazepinone **9** reacts with methyl propiolate in methanol to give the Stevens rearangement product, *i.e.*, methyl 10-benzyl-11-oxo-11a-[(1*E*)-3-oxobut-1-en-1-yl]-2,3,5,10,11,11a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]-benzodiazepine-8-carboxylate **25**. The low yields of the products of benzodiazepine transformations are attributed to the fact that the reactions proceed at several reaction centers and lead to the formation of multi-component mixtures.

Experimental

IR the spectra were recorded on an Infralyum FT-801 Fourier-transform spectrometer in KBr pellets (for crystalline compounds) or in neat films (for oils). Mass spectra were recorded on a Thermo Scientific MAT 95XL chromato-mass spectrome-

ter (70 eV). The spectra of liquid chromato-mass spectrometry (GLC-MS) were recorded using a system including an Agilent 1100 liquid chromatograph and Agilent Technologies LC/MSD VL, ELSD Sedex 75 mass spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker-100, Bruker-400 and JEOL JNM-ECA600 spectrometers in DMSO-d_6 and $CDCl_3$, using Me_4Si as an internal standard. X-ray crystallographic data were obtained on a Bruker SMART APEX2 CCD automatic circle diffractometer.

Thin-layer chromatography was performed on plates precoated with Sorbfil silica gel (visualization in the iodine vapors). Neutral alumina (Fluka-507C, 0.05—0.15-mm grains) and silica gel (Merk, 230—400 mesh) were used for chromatographic separation.

Methyl *N*-[4-(methoxycarbonyl)-2-nitrobenzyl]-*N*-methylaminoacetate (4) and methyl 1-[4-(methoxycarbonyl)-2-nitrobenzyl]pyrrolidine-2-carboxylate (6). A solution of methyl 4-bromomethyl-3-nitrobenzoate **4** (1.50 g, 1.8 mmol) in acetonitrile (7 mL) was added to a solution of methyl ester of L-proline (0.23 g, 1.8 mmol) or methyl ester of sarcosine (0.19 g, 1.8 mmol) and triethylamine (0.28 g, 2.7 mmol) in anhydrous acetonitrile (10 mL) at 20 °C with vigorous stirring. After 2 h (the reaction progress was monitored by TLC), acetonitrile was evaporated *in vacuo*. The residue was diluted with water (10 mL) and extracted with diethyl ether (3×15 mL). The extract was dried with magnesium sulfate. The solvent was evaporated to obtain compounds **4** and **6** as orange oils.

Compound **4**. The yield was 79%, R_f 0.75 (sorbfil, ethyl acetate—hexane (1 : 1)). Found (%): C, 52.81; H, 5.53; N, 9.55. $C_{13}H_{16}N_2O_6$. Calculated (%): C, 52.70; H, 5.44; N, 9.46. IR, ν/cm^{-1}: 1740, 1657 (CO), 1532, 1362 (NO_2). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.37 (s, 3 H, NMe); 3.84 (s, 2 H, C$\underline{H}_2$CO$_2$Me); 3.71 (s, 3 H, CO_2Me); 3.95 (s, 3 H, CO_2Me); 4.09 (s, 2 H, C$\underline{H}_2$Ar); 7.81 (d, 1 H, C(6)H, J = 7.6 Hz); 8.21 (d, 1 H, C(5)H, J = 7.6 Hz); 8.49 (s, 1 H, C(3)H). MS (ESI+), m/z: 297 $[M + H]^+$.

Compound **6**. The yield was 85%, R_f 0.71 (sorbfil, ethyl acetate—hexane (1 : 1)). Found (%): C, 55.99; H, 5.73; N, 8.80. $C_{15}H_{18}N_2O_6$. Calculated (%): C, 55.90; H, 5.63; N, 8.69. IR, ν/cm^{-1}: 1727 (CO); 1535, 1355 (NO_2). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.85—2.01 (m, 2 H, CH_2); 2.09—2.21 (m, 2 H, CH_2); 2.98 (m, 1 H, CH_2); 3.41 (m, 1 H, CH_2); 3.48—3.52 (m, 1 H, C$\underline{H}$CO$_2$Me); 3.63 (s, 3 H, CO_2Me); 3.95 (s, 3 H, CO_2Me); 4.03 (d, 1 H, C$\underline{H}_2$Ar, J = 15.8 Hz); 4.13 (d, 1 H, C$\underline{H}_2$Ar, J = 15.8 Hz); 7.87 (td, 1 H, C(6)H, J = 1.4 Hz, J = 8.3 Hz); 8.18 (dd, 1 H, C(5)H, J = 1.4 Hz, J = 8.3 Hz); 8.48 (d, 1 H, C(3)H, J = 1.4 Hz). MS (ESI+), m/z: 323 $[M + H]^+$.

Methyl *N*-[2-amino-4-(methoxycarbonyl)benzyl]-*N*-methylaminoacetate (5) and methyl 1-[2-amino-4-(methoxycarbonyl)benzyl]pyrrolidine-2-carboxylate (7). A solution of nitro-substituted compound **4** (0.27 g, 0.9 mmol) or compound **6** (0.29 g, 0.9 mmol), $FeSO_4 \cdot 7H_2O$ (1.5 g, 5.5 mmol), concentrated HCl (0.07 mL) in aqueous methanol (1 : 1, 5 mL) was heated to 90 °C, followed by addition of concentrated aq. NH_4OH (1.25 mL). Then, another 6 portions of conc. NH_4OH (0.25 mL each) were added every 2 min, the mixture was kept at 65 °C for 25 min (TLC monitoring, sorbfil, ethyl acetate—hexane (2 : 3)), cooled to 0 °C, and basified with K_2CO_3 to pH 8—9. Then, the mixture was extracted with diethyl ether (3×35 mL), dried with magnesium sulfate. Diethyl ether was evaporated *in vacuo* to obtain compounds **5** and **7** as brown oils.

Compound **5**. The yield was 65%, R_f 0.34 (sorbfil, ethyl acetate—hexane (2 : 3)). Found (%): C, 58.72; H, 6.90; N, 10.61. $C_{13}H_{18}N_2O_4$. Calculated (%): C, 58.63; H, 6.81; N, 10.52. IR, ν/cm^{-1}: 1720, 1623 (CO). ^{1}H NMR (600 MHz, $CDCl_3$), δ: 2.29 (s, 3 H, NMe); 3.23 (s, 2 H, C$\underline{H}_2$CO$_2$Me); 3.62 (s, 2 H, CH_2Ar); 3.71 (s, 3 H, CO_2Me); 3.87 (s, 3 H, CO_2Me); 4.95 (br.s, 2 H, NH_2); 7.01—7.04 (m, 1 H, C(5)H); 7.29—7.32 (m, 2 H, C(3)H, C(6)H)GLC-MS with detector (evaporating detector of light scattering), m/z: 267 $[M + H]^+$.

Compound **7**. The yield was 51%, R_f 0.45 (sorbfil, ethyl acetate—hexane (2 : 3)). Found (%): C, 61.69; H, 6.97; N, 9.66. $C_{15}H_{20}N_2O_4$. Calculated (%): C, 61.63; H, 6.90; N, 9.58. IR, ν/cm^{-1}: 1727, 1628 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.74—1.84 (m, 2 H, CH_2); 1.88—1.96 (m, 1 H, CH_2); 2.14—2.30 (m, 2 H, CH_2); 2.85—2.92 (m, 1 H, CH_2); 3.18 (t, 1 H, C$\underline{H}$CO$_2$Me, J = 6.9 Hz); 3.32 (d, 1 H, CH_2Ar, J = 12.4 Hz); 3.98 (d, 1 H, C$\underline{H}_2$Ar, J = 12.4 Hz); 3.69 (s, 3 H, CO_2Me); 3.87 (s, 3 H, CO_2Me); 5.01 (br.s, 2 H, NH_2); 7.03 (d, 1 H, C(5)H, J = 7.8 Hz); 7.26—7.30 (m, 2 H, C(3)H, C(6)H). LC/MSD, ELSD (EIC), m/z: 293 $[M + H]^+$.

Methyl 4-methyl-2-oxo-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine-8-carboxylate (1) and methyl 11-oxo-2,3,5,10,11,11a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]-benzodiazepine-8-carboxylate (8). A solution of compound **5** (2.66 g, 0.01 mmol) or compound **7** (2.92 g, 0.01 mmol) in glacial acetic acid (50 mL) was refluxed for 13 h (the reaction progress was monitored by TLC, sorbfil, ethyl acetate). The solvent was evaporated *in vacuo*, aq. Na_2CO_3 (10%, 20 mL) was added to the residue to pH 10 and the mixture was extracted with ethyl acetate, the extract was dried with magnesium sulfate. Recrystallization from a mixture of ethyl acetate—hexane yielded diazepines **1** and **8**.

Diazepine **1**. The yield was 60%, light brown crystals, m.p. 129—131 °C, R_f 0.26 (sorbfil, ethyl acetate). Found (%): C, 61.61; H, 6.09; N, 12.01. $C_{12}H_{14}N_2O_3$. Calculated (%): C, 61.53; H, 6.02; N, 11.96. IR, ν/cm^{-1}: 1717, 1651 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.55 (s, 3 H, NMe); 3.45 (s, 2 H, C(5)H_2); 3.84 (s, 2 H, C(3)H_2); 3.95 (s, 3 H, CO_2Me); 7.33 (d, 1 H, C(6)H, J = 7.8 Hz); 7.60 (d, 1 H, C(9)H, J = 1.6 Hz); 7.65 (br.s, 1 H, NH); 7.80 (dd, 1 H, C(7)H, J = 1.6 Hz, J = 7.8 Hz). MS (ESI+), m/z: 235 $[M + H]^+$.

Diazepine **8**. The yield was 58%, beige crystals, m.p. 132—134 °C. Found (%): C, 64.70; H, 6.27; N, 10.67. $C_{14}H_{16}N_2O_3$. Calculated (%): C, 64.60; H, 6.20; N, 10.76. IR, ν/cm^{-1}: 1726, 1665 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.82—1.92 (m, 2 H, C(2)H_2); 1.98—2.04 (m, 1 H, C(1)H_2); 2.48 (ddd, 1 H, C(1)H_2, J = 2.8 Hz, J = 7.5 Hz, J = 9.7 Hz); 2.66 (dd, 1 H, C(3)H_2, J = 3.8 Hz, J = 16.5 Hz); 3.04—3.08 (m, 1 H, C(3)H_2); 3.64 (dd, 1 H, C(11a)H, J = 2.8 Hz, J = 7.5 Hz); 3.69 (d, 1 H, C(5)H_2, J = 12.0 Hz); 3.93 (s, 3 H, CO_2Me); 4.00 (d, 1 H, C(5)H_2, J = 12.0 Hz); 7.41 (d, 1 H, C(6)H, J = 7.8 Hz); 7.50 (br.s, 1 H, NH); 7.65 (d, 1 H, C(9)H, J = 1.6 Hz); 7.83 (dd, 1 H, C(7)H, J = 7.8 Hz, J = 1.6 Hz). MS (ESI+), m/z: 261 $[M + H]^+$.

Methyl 1-benzyl-4-methyl-2-oxo-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine-8-carboxylate (2) and methyl 10-benzyl-11-oxo-2,3,5,10,11,11a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-8-carboxylate (9). Sodium hydride (0.14 g, 5.8 mmol) was added in portions to a solution of benzodiazepine **1** (1.23 g, 5.3 mmol) or benzodiazepine **8** (1.33 g, 5.1 mmol) in anhydrous DMF (30 mL) at 25 °C under argon. The reaction mixture was cooled in an ice-salt bath, followed by a dropwise addition of a solution of benzyl chloride (0.58 g, 4.6 mmol) in anhydrous DMF (25 mL). The mixture was allowed to stand at 25 °C for 1 h (the reaction progress was monitored by TLC, sorbfil, ethyl acetate),

diluted with water (60 mL), and extracted with diethyl ether (3×40 mL). The extract was dried with magnesium sulfate. The solvent was evaporated *in vacuo* to obtain benzyl-substituted diazepines **2** and **9**, a yellow oil solidifying on standing.

Diazepine **2**. The yield was 74%, R_f 0.42 (sorbfil, ethyl acetate). Found (%): C, 70.28; H, 6.11; N, 8.55. $C_{19}H_{20}N_2O_3$. Calculated (%): C, 70.35; H, 6.21; N, 8.64. IR, ν/cm^{-1}: 1721, 1674 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.50 (s, 3 H, NMe); 3.17 (s, 2 H, C(5)H_2); 3.42 (s, 2 H, C(3)H_2); 3.91 (s, 3 H, CO_2Me); 5.12 (s, 2 H, CH_2Ph); 7.20—7.24 (m, 5 H, Ph); 7.31 (d, 1 H, C(6)H, J = 7.8 Hz); 7.84 (dd, 1 H, C(7)H, J = 1.5 Hz, J = 7.8 Hz); 7.95 (d, 1 H, C(9)H, J = 1.5 Hz). MS (ESI+), m/z: 325 $[M + H]^+$.

Diazepine **9**. The yield was 79%, R_f 0.52 (sorbfil, ethyl acetate). Found (%): C, 72.06; H, 6.39; N, 8,05. $C_{21}H_{22}N_2O_3$. Calculated (%): C, 71.98; H, 6.33; N, 7.99. IR, ν/cm^{-1}: 1724, 1663 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.84—1.92 (m, 1 H, C(1)H_2); 2.05—2.14 (m, 1 H, C(1)H_2); 2.44—2.56 (m, 2 H, C(2)H_2); 3.06—3.11 (m, 1 H, C(3)H_2); 3.19 (d, 1 H, C(5)H_2, J = 10.9 Hz); 3.61 (dd, 1 H, C(3)H_2, J = 2.1 Hz, J = 7.7 Hz); 3.74 (d, 1 H, C(5)H_2, J = 10.9 Hz); 3.91—3.92 (s, 1 H, C(11a)H); 3.93 (s, 3 H, CO_2Me); 4.81 (d, 1 H, CH_2Ph, J = 14.7 Hz); 5.42 (d, 1 H, CH_2Ph, J = 14.7 Hz); 7.21—7.25 (m, 5 H, Ph); 7.36 (d, 1 H, C(6)H, J = 7.8 Hz); 7.84 (dd, 1 H, C(7)H, J = 1.6 Hz, J = 7.8 Hz); 7.96 (d, 1 H, C(9)H, J = 1.6 Hz). MS (ESI+), m/z: 351 $[M + H]^+$.

4-Methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (10) and 7-fluoro-4-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (11). A mixture of 2*H*-3,1-benzoxazine-2,4(1*H*)-dione (11.66 g, 61.30 mmol) or 6-fluoro-2*H*-3,1-benzoxazine-2,4(1*H*)-dione (12.76 g, 61.30 mmol) with sarcosine (5.46 g, 61.30 mmol) in pyridine (22 mL) was refluxed for 7 h, cooled to 5 °C. Precipitates of benzodiazepinediones were filtered off and recrystallized from ethanol to obtain 4-methyl-3,4-dihydro-1*H*-1,4-dibenzodiazepine-2,5-dione. The yield was 70%, m.p. 246—247 °C. Found (%): C, 63.18; H, 5.32; N, 14.82. $C_{10}H_{10}N_2O_2$. Calculated (%): C, 63.15; H, 5.30; N, 14.73. IR, ν/cm^{-1}: 1632 (CO); 1698 (CO); 3212 (NH). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 3.12 (s, 3 H, NMe); 3.84 (s, 2 H, CH_2); 7.10 (d, 1 H, Ar, J = 8.0 Hz); 7.21—7.24 (m, 1 H, Ar); 7.14 (d, 1 H, Ar, J = 8.0 Hz); 7.50 (m, 1 H, Ar); 10.46 (s, 1 H, NH). MS, m/z (I_{rel} (%)): 190 $[M]^+$ (100), 161 (69), 146 (13), 119 (69), 92 (50), 64 (13), 44 (46). In addition, 7-fluoro-4-methyl-3,4-dihydro-1*H*-1,4-dibenzodiazepine-2,5-dione was isolated. The yield was 76%, m.p. 213—215 °C. Found (%): C, 57.78; H, 4.21; N, 13.52. $C_{10}H_9FN_2O_2$. Calculated (%): C, 57.69; H, 4.36; N, 13.46. IR, ν/cm^{-1}: 1636 (CO); 1703 (CO); 3248 (NH). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 3.11 (s, 3 H, NMe); 3.86 (s, 2 H, CH_2); 7.13 (m, 1 H, Ar); 7.45 (m, 2 H, Ar); 10.49 (s, 1 H, NH). MS, m/z (I_{rel} (%)): 208 $[M]^+$ (4), 179 (13), 137 (24), 109 (25), 82 (31), 42 (100).

The thus obtained benzodiazepinediones (54.76 mmol) were added in portions to a suspension of lithium aluminum hydride (10.3 g, 0.27 mmol) in anhydrous dioxane (200 mL) at 0—5 °C under argon. The reaction mixture was refluxed for 4 h cooled to ~20 °C, quenched with aq. dioxane and 15% aq. NaOH. The organic layer was decanted. The solvent was evaporated *in vacuo*. The residue was subjected to chromatography on silica gel, using chloroform as an eluent. Benzodiazepines **10** or **11** were obtained as colorless crystals.

Benzodiazepine **10**. The yield was 64%, m.p. 42—44 °C (from a mixture of hexane—ethyl acetate). Found (%): C, 73.92; H, 8.80; N, 17.30. $C_{10}H_{14}N_2$. Calculated (%): C, 74.03; H, 8.70; N, 17.27. IR, ν/cm^{-1}: 3303 (NH). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 2.41 (s, 3 H, Me); 2.88 (m, 2 H, CH_2); 3.15 (m, 2 H, CH_2); 3.72 (s, 2 H, CH_2); 3.88 (br.s, 1 H, NH); 6.74 (m, 1 H, Ar); 6.85 (m, 1 H, Ar); 7.11 (m, 2 H, Ar). MS, m/z (I_{rel} (%)): 162 $[M]^+$ (61), 147 (36), 130 (32), 118 (100), 91 (97), 77 (34), 65 (51), 44 (44).

Benzodiazepine **11**. The yield was 62%, m.p. 48—50 °C (from a mixture of hexane—ethyl acetate). Found (%): C, 66.91; H, 7.14; N, 15.25. $C_{10}H_{13}FN_2$. Calculated (%): C, 66.64; H, 7.27; N, 15.54. IR, ν/cm^{-1}: 3263 (NH). ^{1}H NMR (400 MHz, DMSO-d_6), δ: 2.39 (s, 3 H, Me); 2.86 (m, 2 H, C(2)H_2); 3.09 (m, 2 H, C(3)H_2); 3.67 (s, 2 H, C(5)H_2); 3.80 (br.s, 1 H, NH); 6.68 (dd, 1 H, C(9)H, J = 4.9 Hz, J = 8.6 Hz); 6.78 (ddd, 1 H, C(8)H, J = 2.9 Hz, J = 8.6 Hz, J = 9.3 Hz); 6.85 (dd, 1 H, C(6)H, J = 2.9 Hz, J = 9.1 Hz). MS, m/z (I_{rel} (%)): 180 $[M]^+$ (81), 165 (24), 148 (16), 138 (77), 109 (95), 83 (51), 44 (100).

Reaction of benzodiazepines 10 and 11 with alkynes (general procedure). Methyl propiolate or methyl acetylenedicarboxilate (2.78 mmol) was added to a solution of benzodiazepine **10** or **11** (1.85 mmol) in methanol (15 mL) at 20 °C. After 1 h (TLC monitoring), the solvent was evaporated *in vacuo*, the residue was subjected to chromatography on silica gel, using chloroform—methanol (20 : 1) as an eluent to obtain 5-methyl-1-vinylbenzodiazepines **12**—**14**.

Methyl (2*E*)-3-(4-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepin-1-yl)acrylate (12). The yield was 88%, yellow oil. Found (%): C, 68.35; H, 7.21; N, 11.30. $C_{14}H_{18}N_2O_2$. Calculated (%): C, 68.27; H, 7.37; N, 11.37. IR, ν/cm^{-1}: 1687 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.38 (s, 3 H, NMe); 2.89 (m, 2 H, C(2)H_2); 3.56 (m, 2 H, C(3)H_2); 3.69 (s, 3 H, CO_2Me); 3.71 (s, 2 H, C(5)H_2); 4.84 (br.s, 1 H, =CH); 7.20 (m, 3 H, Ar); 7.21 (m, 1 H, Ar); 7.72 (d, 1 H, =CH, J = 13.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 43.4 (Me); 49.2 (CH_2); 50.5 (Me); 55.8 (CH_2); 59.8 (CH_2); 88.2 (CH=); 124.8 (CH); 126.6 (CH); 128.8 (CH); 130.7 (C); 133.4 (C); 145.1 (C); 149.9 (=CH); 169.9 (CO). MS, m/z (I_{rel} (%)): 246 $[M]^+$ (57), 231 (67), 215 (38), 203 (85), 188 (22), 170 (44), 144 (88), 130 (100), 117 (51), 91 (62), 77 (42), 65 (31).

Methyl (2*E*)-3-(7-fluoro-4-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepin-1-yl)acrylate (13). The yield was 72%, yellow oil. Found (%): C, 63.58; H, 6.55; N, 10.62. $C_{14}H_{17}FN_2O_2$. Calculated (%): C, 63.62; H, 6.50; N, 10.58. IR, ν/cm^{-1}: 1616 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.38 (s, 3 H, NMe); 2.91 (m, 2 H, C(2)H_2); 3.55 (m, 2 H, C(3)H_2); 3.68 (br.s, 5 H, CO_2Me, C(5)H_2); 4.79 (br.s, 1 H, =CH); 6.97 (m, 2 H, Ar); 7.16 (m, 1 H, Ar); 7.64 (d, 1 H, =CH, J = 13.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 43.2 (Me); 48.2 (CH_2); 50.7 (Me); 55.4 (CH_2); 59.4 (CH_2); 88.0 (=CH); 115.2 (d, CH, J = 22 Hz); 117.4 (d, CH, J = 22 Hz); 126.6 (C); 136.4 (C); 140.9 (C); 149.9 (=CH); 160.6 (d, C—F, J = 248 Hz); 169.6 (CO). MS, m/z (I_{rel} (%)): 264 $[M]^+$ (49); 249 (29), 233 (19), 221 (100), 206 (19), 188 (20), 162 (92), 148 (85), 135 (38), 109 (19), 83 (14), 42 (18).

Dimethyl 2-(7-fluoro-4-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepin-1-yl)but-2-enedioate (14). The yield was 78%, colorless crystals, m.p. 106—107 °C (from a mixture of ethyl acetate—hexane). Found (%): C, 59.78; H, 6.10; N, 8.51. $C_{16}H_{19}FN_2O_4$. Calculated (%): C, 59.62; H, 5.94; N, 8.69. IR, ν/cm^{-1}: 1693, 1737 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.34 (s, 3 H, NMe); 2.80—3.90 (m, 12 H, C(2)H_2, C(3)H_2, C(5)H_2, 2 CO_2Me); 4.69 (br.s, 1 H, =CH); 6.98 (m, 2 H, Ar); 7.19 (m, 1 H, Ar). MS, m/z (I_{rel} (%)): 322 $[M]^+$ (48); 307 (38), 290 (28), 263

(22), 219 (100), 203 (61), 160 (29), 136 (30), 109 (18), 83 (16), 59 (16), 42 (15).

1-Acetyl-4-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (15) and 1-acetyl-7-fluoro-4-methyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (16). Acetic anhydride (0.75 g, 7.39 mmol) was added dropwise to a solution of benzodiazepine **10** (1.26 g, 7.8 mmol) or benzodiazepine **11** (1.37 g, 7.6 mmol) in acetonitrile (40 mL) at 20 °C. The mixture was refluxed for 1 h, acetonitrile was evaporated *in vacuo*. The residue was diluted with water (50 mL), basified with soda to pH 9, and extracted with chloroform (5×50 mL). The extract was dried with sodium sulfate. The residue after evaporation of chloroform was recrystallized from hexane to obtain *N*-acetyl-substituted **15** and **16** as colorless crystals.

Diazepine **15**. The yield was 86%, m.p. 67—69 °C. Found (%): C, 70.43; H, 8.10; N, 13.53. $C_{12}H_{16}N_2O$. Calculated (%): C, 70.56; H, 7.90; N, 13.71. IR, ν/cm^{-1}: 1645 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.92 (s, 3 H, COMe); 2.32 (s, 3 H, NMe); 2.95 (m, 3 H, $C(2)H_2$, $C(3)H_2$); 3.56 (d, 1 H, $C(5)H_2$, J = 13.9 Hz); 3.81 (d, 1 H, $C(5)H_2$, J = 13.9 Hz); 4.60 (m, 1 H, $C(2)H_2$); 7.15 (m, 1 H, Ar); 7.26 (m, 3 H, Ar). MS, m/z (I_{rel} (%)): 204 [M]$^+$ (52), 189 (25), 161 (100), 146 (49), 130 (63), 118 (87), 91 (95).

Diazepine **16**. The yield was 84%, m.p. 101—103 °C. Found (%): C, 64.38; H, 6.82; N, 12.70. $C_{12}H_{15}FN_2O$. Calculated (%): C, 64.85; H, 6.80; N, 12.60. IR, ν/cm^{-1}: 1664 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.92 (s, 3 H, COMe); 2.34 (s, 3 H, NMe); 2.95 (m, 3 H, $C(2)H_2$, $C(3)H_2$); 3.53 (d, 1 H, $C(5)H_2$, J = 14.0 Hz); 3.82 (d, 1 H, $C(5)H_2$, J = 14.0 Hz); 4.57 (m, 1 H, $C(2)H_2$); 7.00—7.04 (m, 2 H, Ar); 7.16 (dd, 1 H, Ar, J = 5.1 Hz, J = 8.4 Hz). MS, m/z (I_{rel} (%)): 222 [M]$^+$ (57), 189 (25), 207 (32), 179 (80), 163 (35), 148 (72), 136 (100), 109 (92), 83 (78), 43 (65).

Methyl (2*E*)-3-(1-acetyl-7-fluoro-1,2,3,5-tetrahydro-4*H*-1,4-benzodiazepin-4-yl)acrylate (17). A solution of benzodiazepine **16** (0.1 g, 0.45 mmol) and methyl propiolate (0.076 g, 0.90 mmol) in acetonitrile (5 mL) was refluxed for 5 days with addition of methyl propiolate (0.076 g, 0.9 mmol) every day. The solvent was evaporated *in vacuo*. The residue was subjected to chromatography on silica gel, using hexane—ethyl acetate (from 7 : 3 to 0 : 1 (v/v)) as an eluent to obtain compound **17** (0.045 g, 34%), colorless oil crystallizing on standing, m.p. 110—112 °C (from ethyl acetate). Found (%): C, 61.76; H, 5.93; N, 9.56. $C_{15}H_{17}FN_2O_3$. Calculated (%): C, 61.63; H, 5.86; N, 9.58. IR, ν/cm^{-1}: 1601, 1641 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.92 (s, 3 H, COMe); 2.79 (m, 1 H, $C(2)H_2$); 3.56 (m, 2 H, $C(3)H_2$); 3.65 (s, 3 H, CO_2Me); 4.23 (m, 2 H, $C(5)H_2$); 4.72 (d, 1 H, =CH, J = 13.3 Hz); 4.78 (m, 1 H, $C(2)H_2$); 7.05 (ddd, 1 H, C(8)H, J = 2.9 Hz, J = 8.6 Hz, J = 9.3 Hz); 7.12 (dd, 1 H, C(6)H, J = 2.9 Hz, J = 8.2 Hz), 7.22 (dd, 1 H, C(9)H, J = 5.1 Hz, J = 8.6 Hz); 7.33 (d, 1 H, =CH, J = 13.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 22.4 (Me); 46.6 (CH_2); 50.6 (Me); 52.6 (CH_2); 54.6 (CH_2); 87.1 (=CH_2); 115.8 (d, CH, J = 22 Hz); 117.1 (d, CH, J = 22 Hz); 129.9 (d, CH, J = 9 Hz); 137.0 (C); 138.7 (C); 150.4 (=CH); 161.5 (d, C—F, J = 250 Hz); 162.3 (C); 169.7 (C). MS, m/z (I_{rel} (%)): 292 [M]$^+$ (19); 260 (25), 218 (22), 164 (14), 148 (51), 136 (63), 109 (59), 83 (30), 43 (100).

Methyl 1-[(1*E*)-3-methoxy-3-oxoprop-1-en-1-yl]-4-methyl-2-oxo-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine-8-carboxylate (18). A solution of benzodiazepine **1** (0.40 g, 1.7 mmol) and methyl propiolate ((0.29 g, 3.4 mmol) in dichloromethane (15 mL) was kept at 30 °C for 90 h (TLC monitoring, sorbfil, ethyl acetate—heptane (1 : 1)). The solvent was evaporated, the residue was purified using column chromatography on silica gel and ethyl acetate—hexane (1 : 1) as an eluent. Compound **18** (0.05 g, 10%) was collected as white crystals, m.p. 141—142 °C (from a mixture of ethyl acetate—hexane), R_f 0.24 (sorbfil, ethyl acetate—hexane (1 : 1)). Found (%): C, 60.46; H, 5.83; N, 8.69. $C_{16}H_{18}N_2O_5$. Calculated (%): C, 60.37; H, 5.70; N, 8.80. IR, ν/cm^{-1}: 1632, 1694, 1723 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.16 (s, 2 H, $C(3)H_2$); 2.51 (s, 3 H, NMe); 3.15 (br.s, 2 H, $C(5)H_2$); 3.73 (s, 3 H, CO_2Me); 3.94 (s, 3 H, $ArCO_2\underline{Me}$); 5.39 (d, 1 H, CH=$\underline{CH}CO_2Me$, J = 14.4 Hz); 7.49 (d, 1 H, C(6)H, J = 8.3 Hz); 7.98 (d, 1 H, C(9)H, J = 2.0 Hz); 8.04 (dd, 1 H, C(7)H, J = 2.0 Hz, J = 8.3 Hz); 8.54 (d, 1 H, $\underline{CH}$=$CHCO_2Me$, J = 14.4 Hz). MS (ESI+), m/z: 319 [M + H]$^+$.

Methyl 1-benzyl-3,3-bis[(1*E*)-3-methoxy-3-oxoprop-1-en-1-yl]-4-methyl-2-oxo-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine-8-carboxylate (19). A solution of benzodiazepine **2** (0.40 g, 1.2 mmol) and methyl propiolate (0.21 g, 2.5 mmol) in acetonitrile (15 mL) was kept at 30 °C for 120 h (TLC monitoring, sorbfil, ethyl acetate—heptane (1 : 1)). The solvent was evaporated, the residue was purified using column chromatography on silica gel and ethyl acetate—hexane (1 : 3) as an eluent. Compound **19** (0.03 g, 5%) was collected as white crystals, m.p. 145—146 °C (from a mixture of ethyl acetate—hexane), R_f 0.40 (sorbfil, ethyl acetate—hexane (1 : 1)). Found (%): C, 65.70; H, 5.84; N, 5.59. $C_{27}H_{28}N_2O_7$. Calculated (%): C, 65.84; H, 5.73; N, 5.69. IR, ν/cm^{-1}: 1719, 1687, 1677 (CO), 1623, 1586 (C=C). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.40 (s, 3 H, NMe); 3.49 (s, 2 H, $C(5)H_2$); 3.63 (s, 6 H, 2 CO_2Me); 3.91 (s, 3 H, $ArCO_2Me$); 5.10 (s, 2 H, $C\underline{H}_2Ph$); 5.74 (d, 2 H, 2 CH=C$\underline{H}CO_2Me$, J = 15.9 Hz); 6.80 (d, 2 H, 2 $C\underline{H}$=$CHCO_2Me$, J = 15.9 Hz); 7.22 (d, 1 H, C(6)H, J = 7.8 Hz); 7.24 (m, 5 H, Ph); 7.81 (dd, 1 H, C(7)H, J = 1.6 Hz, J = 7.8 Hz); 7.89 (d, 1 H, C(9)H, J = 1.6 Hz). MS (ESI+), m/z: 493 [M + H]$^+$.

Methyl 11a-[(1*E*)-3-methoxy-3-oxoprop-1-en-1-yl]-11-oxo-2,3,5,10,11,11a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-8-carboxylate (20) and dimethyl 13-oxo-2,3,7,12,13,13a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazonine-6,10-dicarboxylate (21). A solution of benzodiazepine **8** (0.4 g, 1.5 mmol) and methyl propiolate (0.26 g, 3.0 mmol) in dichloromethane (20 mL) was kept at 25 °C for 94 h (TLC monitoring, sorbfil, ethyl acetate—heptane (1 : 1)). The solvent was evaporated *in vacuo*. The residue was subjected to chromatography on silica gel to sequentially isolate compounds **20** and **21**.

Diazepine **20**. The yield was 7%, ethyl acetate—hexane (1 : 2) was an eluent, white crystals, m.p. 152—154 °C (from a mixture of ethyl acetate—hexane), R_f 0.32 (sorbfil, ethyl acetate—hexane (1 : 1)). Found (%): C, 62.69; H, 5.92; N, 8.23. $C_{18}H_{20}N_2O_5$. Calculated (%): C, 62.78; H, 5.85; N, 8.13. IR, ν/cm^{-1}: 1633, 1657, 1720 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.72—1.88 (m, 2 H, $C(2)H_2$); 2.68—2.79 (m, 2 H, $C(1)H_2$); 3.11—3.17 (m, 2 H, $C(3)H_2$); 3.62 (s, 3 H, CO_2Me); 3.79 (d, 1 H, $C(5)H_2$, J = 13.2 Hz); 3.91 (s, 3 H, CO_2Me); 4.04 (d, 1 H, $C(5)H_2$, J = 13.2 Hz); 5.86 (d, 1 H, C$\underline{H}$=CH, J = 15.6 Hz); 6.9 (d, 1 H, CH=C$\underline{H}CO_2Me$, J = 15.6 Hz); 7.31 (d, 1 H, C(6)H, J = 7.8 Hz); 7.52 (d, 1 H, C(9)H, J = 1.5 Hz); 7.59 (br.s, 1 H, NH); 7.75 (dd, 1 H, C(7)H, J = 1.5 Hz, J = 7.8 Hz). MS (ESI+), m/z: 345 [M + H]$^+$.

Diazonine **21**. The yield was 4%, ethyl acetate—hexane (1 : 1) was an eluent, white crystals, m.p. 225—227 °C (from a mixture of ethyl acetate—hexane), R_f 0.20 (sorbfil, ethyl acetate—hexane (1 : 1)). Found (%): C, 62.69; H, 5.92; N, 8.23.

$C_{18}H_{20}N_2O_5$. Calculated (%): C, 62.78; H, 5.85; N, 8.13. IR, ν/cm^{-1}: 1620, 1678, 1714 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.76—1.88 (m, 2 H, C(1)H_2); 2.06—2.15 (m, 1 H, C(2)H_2); 2.28—2.36 (m, 1 H, C(2)H_2); 3.29—3.35 (m, 1 H, C(3)H_2); 3.44 (d, 1 H, C(7)H_2, *J* = 14.7 Hz); 3.67—3.72 (m, 1 H, C(3)H_2); 3.78 (s, 3 H, CO_2Me); 3.92 (s, 3 H, ArCO_2Me); 3.95 (dd, 1 H, C(13a)H, *J* = 3.3 Hz, *J* = 7.8 Hz), 3.99 (d, 1 H, C(7)H_2, *J* = 14.7 Hz); 7.10 (br.s, 1 H, NH); 7.61 (d, 1 H, C(8)H, *J* = 8.0 Hz); 7.76 (s, 1 H, C(5)H); 7.78 (d, 1 H, C(11)H, *J* = 1.8 Hz); 7.88 (dd, 1 H, C(9)H, *J* = 1.8 Hz, *J* = 8.0 Hz). MS (ESI+), *m*/*z*: 345 [M + H]$^+$.

Methyl 11-oxo-11a-[(1*E*)-3-oxobut-1-en-1-yl]-2,3,5,10,11,11a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]benzodiazepine-8-carboxylate (22) and methyl 11-oxo-10,11a-bis[(1*E*)-3-oxobut-1-en-1-yl]-2,3,5,10,11,11a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]-benzodiazepine-8-carboxylate (23). A solution of benzodiazepine **8** (0.40 g, 1.5 mmol) and acetylacetylene ((0.31 g, 4.6 mmol) in dichloromethane (20 mL) was kept at 30 °C for 30 h (the reaction progress was monitored by TLC, sorbfil, ethyl acetate). The solvent was evaporated, the residue was subjected to chromatography on silica gel to sequentially elute compounds **22** and **23**.

Diazepine **22**. The yield was 4%, ethyl acetate—hexane (1 : 2) was an eluent, yellow oil, R_f 0.28 (sorbfil, ethyl acetate—hexane (1 : 2)). Found (%): C, 65.70; H, 6.00; N, 8.45. $C_{18}H_{20}N_2O_4$. Calculated (%): C, 65.84; H, 6.14; N, 8.53. IR, ν/cm^{-1}: 1633, 1667, 1678, 1722 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.73—1.85 (m, 2 H, C(2)H_2); 2.00 (s, 3 H, COMe); 2.70—2.84 (m, 2 H, C(1)H_2); 3.14—3.18 (m, 2 H, C(3)H_2); 3.79 (d, 1 H, C(5)H_2, *J* = 13.0 Hz); 3.90 (s, 3 H, ArCO_2Me); 4.03 (d, 1 H, C(5)H_2, *J* = 13.0 Hz); 6.05 (d, 1 H, CH=CHCOMe, *J* = 16.0 Hz); 6.62 (d, 1 H, CH=CHCOMe, *J* = 16.0 Hz); 7.33 (d, 1 H, C(6)H, *J* = 7.8 Hz); 7.50 (d, 1 H, C(9)H, *J* = 1.6 Hz); 7.69 (dd, 1 H, C(7)H, *J* = 1.6 Hz, *J* = 7.8 Hz); 8.08 (br.s, 1 H, NH). MS (ESI+), *m*/*z*: 329 [M + H]$^+$.

Diazepine **23**. The yield was 17%, ethyl acetate—hexane (1 : 2) was an eluent, white crystals, m.p. 164—166 °C (from a mixture of ethyl acetate—hexane), R_f 0.25 (sorbfil, ethyl acetate—hexane (1 : 2)). Found (%): C, 66.73; H, 5.92; N, 7,12. $C_{22}H_{24}N_2O_5$. Calculated (%): C, 66.67; H, 6.06; N, 7.07. IR, ν/cm^{-1}: 1727, 1696, 1670, 1633 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.56—1.62 (m, 2 H, C(1)H_2); 1.74 (s, 3 H, COMe); 2.27 (s, 3 H, COMe); 1.75—1.82 (m, 1 H, C(2)H_2); 2.64—2.72 (m, 1 H, C(2)H_2); 2.92—3.02 (m, 1 H, C(3)H_2); 3.21—3.27 (m, 1 H, C(3)H_2); 3.48 (d, 1 H, C(5)H_2, *J* = 11.3 Hz); 3.86 (s, 3 H, CO_2Me); 3.90 (d, 1 H, C(5)H_2, *J* = 11.3 Hz); 5.62 (d, 1 H, CH=CHCOCH$_3$, *J* = 14.8 Hz); 5.63 (d, 1 H, CH=CHCOCH$_3$, *J* = 16.2 Hz); 6.10 (d, 1 H, CH=CHCOCH$_3$, *J* = 16.2 Hz); 7.47 (d, 1 H, C(6)H, *J* = 7.9 Hz); 7.60 (d, 1 H, C(9)H, *J* = 1.7 Hz); 7.90 (dd, 1 H, C(7)H, *J* = 1.7 Hz, *J* = 7.9 Hz); 8.47 (d, 1 H, CH=CHCOCH$_3$, *J* = 14.8 Hz). MS (ESI+), *m*/*z*: 397 [M + H]$^+$.

Methyl 3-methoxy-2-oxo-1,7-bis[(1*E*)-3-oxobut-1-en-1-yl]-1,2,3,4,5,6,7,8-octahydro-1,7-benzodiazecine-11-carboxylate (24). A solution of benzodiazepine **8** ((0.40 g, 1.5 mmol) and acetylacetylene (0.31 g, 4.6 mmol) in methanol (15 mL) was kept at 30 °C for 30 h (the reaction progress was monitored by TLC, sorbfil, ethyl acetate). The solvent was evaporated *in vacuo*, the residue was subjected to chromatography on silica gel to sequentially elute compounds **22** and **24**.

Benzodiazepine **22**. The yield was 20 mg (4%), ethyl acetate—hexane (2 : 1) was an eluent, yellow oil, R_f 0.28 (sorbfil, ethyl acetate—hexane (1 : 2)). Spectral characteristics of this compound are identical to those of the compound described above.

Benzodiazecine **24**. The yield was 41 mg (6%), ethyl acetate—hexane (1 : 1) was an eluent, colorless oil, R_f 0.61 (sorbfil, ethyl acetate). Found (%): C, 64.38; H, 6.62; N, 6.43. $C_{23}H_{28}N_2O_6$. Calculated (%): C, 64.47; H, 6.59; N, 6.54. IR, ν/cm^{-1}: 1678, 1633, 1726 (CO). ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.74—1.82 (m, 2 H, C(4)H_2); 1.86—1.94 (m, 2 H, C(5)H_2); 2.10 (s, 6 H, 2 COMe); 2.19—2.25 (m, 1 H, C(6)H_2); 2.84—2.88 (m, 1 H, C(6)H_2); 3.21 (dd, 1 H, C(3)H, *J* = 5.9 Hz, *J* = 8.9 Hz); 3.31 (d, 1 H, C(8)H_2, *J* = 14.5 Hz); 3.62 (s, 3 H, OMe); 3.74 (d, 1 H, C(8)H_2, *J* = 14.5 Hz); 3.90 (s, 3 H, CO_2Me); 4.93 (d, 1 H, CH=CHCOCH$_3$, *J* = 13.6 Hz); 4.97 (d, 1 H, CH=CHCOCH$_3$, *J* = 14.7 Hz); 7.67 (d, 1 H, C(12)H, *J* = 1.7 Hz); 7.69 (d, 1 H, CH=CHCOCH$_3$, *J* = 13.6 Hz); 7.70 (d, 1 H, CH=CHCOCH$_3$, *J* = 14.7 Hz); 7.84 (d, 1 H, C(9)H, *J* = 8.1 Hz); 8.60 (dd, 1 H, C(10)H, *J* = 1.7 Hz, *J* = 8.1 Hz). MS, *m*/*z* (I_{rel} (%)): 428 [M]$^+$ (19), 385 (34), 370 (16), 269 (59), 311 (43), 258 (100), 256 (18), 244 (46), 243 (19), 242 (22), 240 (17), 232 (30), 231 (29), 226 (79), 216 (18), 214 (20), 202 (31), 198 (20), 196 (25), 188 (51), 184 (24), 183 (17), 182 (29), 156 (37), 155 (24), 154 (44), 129 (19), 128 (33).

Methyl 10-benzyl-11-oxo-11a-[(1*E*)-3-methoxy-3-oxoprop-1-en-1-yl]-2,3,5,10,11,11a-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4]-benzodiazepine-8-carboxylate (25). A solution of benzodiazepine **9**

Table 1. The principal crystallographic data and parameters of refinement for compounds **18** and **23**

Parameter	**18**	**23**
Molecular formula	$C_{16}H_{18}N_2O_5$	$C_{22}H_{24}N_2O_5$
Molecular weight	318.32	396.43
T/K	120	100
Crystal system	Triclinic	Monoclinic
Space group	*P*-1	$P2_1/c$
a/Å	8.0457(12)	9.1135(4)
b/Å	9.9012(15)	14.0104(6)
c/Å	10.1814(15)	15.6584(6)
α/deg	96.064(3)	90
β/deg	109.828(3)	98.070(1)
γ/deg	90.660(3)	90
V/Å^3	757.7(2)	1979.53(14)
Z	2	4
d_{calc}/g cm^{-3}	1.395	1.330
F(000)	336	840
μ/mm^{-1}	0.105	0.095
$2\theta_{max}$/deg	56	61
Number of measured reflections	7836	25845
Number of independent reflections	3631	6044
Number of reflections with $I > 2\sigma(I)$	2483	4727
Number of refinement parameters	211	265
R_1 ($I > 2\sigma(I)$)	0.061	0.063
wR_2 (all the data)	0.152	0.133
GOOF	1.004	1.002

(0.50 g, 1.4 mmol) and methyl propiolate (0.24 g, 2.9 mmol) in methanol (15 mL) was kept at 30 °C for 95 h (the reaction progress was monitored by TLC, sorbfil, ethyl acetate—hexane (1 : 1)). Methanol was evaporated *in vacuo*. The residue was recrystallized. The yield was 0.14 g (21%), yellow crystals, m.p. 101—103 °C (from a mixture of hexane—ethyl acetate), R_f 0.45 (sorbfil, ethyl acetate—hexane (1 : 1)). Found (%): C, 69.17; H, 6.17; N, 6.32. $C_{25}H_{26}N_2O_5$. Calculated (%): C, 69.11; H, 6.03; N, 6.45. IR, ν/cm^{-1}: 1641, 1659, 1723 (CO). ^{1}H (400 MHz, $CDCl_3$), δ: 1.52—1.62 (m, 1 H, CH_2); 1.64—1.78 (m, 1 H, CH_2); 1.82—1.91 (m, 1 H, CH_2); 2.64—2.74 (m, 1 H, CH_2); 3.05—3.19 (m, 2 H, CH_2); 3.28 (d, 1 H, C(5)H_2, J = 11.0 Hz); 3.50 (s, 3 H, CO_2CH_3); 3.69 (d, 1 H, C(5)H_2, J = 11.0 Hz); 3.88 (s, 3 H, $ArCO_2C\underline{H}_3$); 4.81 (d, 1 H, C$\underline{H}_2$Ph, J = 14.7 Hz); 5.41 (d, 1 H, C$\underline{H}_2$Ph, J = 14.7 Hz); 5.50 (d, 1 H, C$\underline{H}$=CHCO$_2$Me, J = 15.6 Hz); 6.51 (d, 1 H, CH=C$\underline{H}$CO$_2$Me, J = 15.6 Hz); 7.22 (d, 1 H, C(6)H, J = 7.8 Hz); 7.77 (dd, 1 H, C(7)H, J = 1.4 Hz, J = 7.8 Hz); 7.52 (s, 1 H, C(9)H). MS (ESI+), m/z: 435 $[M + H]^+$.

X-ray diffraction studies. Parameters of unit cells and intensities of reflections for compounds **18** and **23** were measured on Bruker SMART 1K CCD (λ(Mo-Kα) irradiation, graphite monochromator, φ- and ω-scan techniques) and Bruker SMART APEX-II CCD (λ(Mo-Kα)-irradiation, graphite monochromator, φ- and ω-scan techniques) automatic diffractometers, respectively. The principal crystallographic data are given in Table 1. The structures were solved by direct method and refined by the full-matrix least squares method on F^2 in anisotropic approximation for nonhydrogen atoms. The hydrogen atoms, whose positions were calculated geometrically, were included into the refinement in isotropic approximation with the fixed positional (the riding model) and thermal (U_{iso}(H) = 1.5U_{eq}(C) for Me groups and U_{iso}(H) = 1.2U_{eq}(C) for all other groups) parameters. All the calculations were performed using the SHELXTL program package.[12] Tables of the atomic coordinates, bond distances, bond angles, and anisotropic temperature parameters for compounds **18** and **23** were deposited with the Cambridge Structural Database.

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