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Synthesis of novel azides and triazoles on the basis of 1*H*-pyrazole-3(5)-carboxylic acids

Aleksander I. Dalinger[1], Alexey V. Medved'ko[1], Alexandra I. Balalaeva[1], Irina A. Vatsadze[2], Igor L. Dalinger[2], Sergey Z. Vatsadze[1]*

[1] *Lomonosov Moscow State University*
1, Build. 3, Leninskie Gory, Moscow 119992, Russia

[2] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,*
47 Leninsky Ave., Moscow 119991, Russia; e-mail: szv@org.chem.msu.ru

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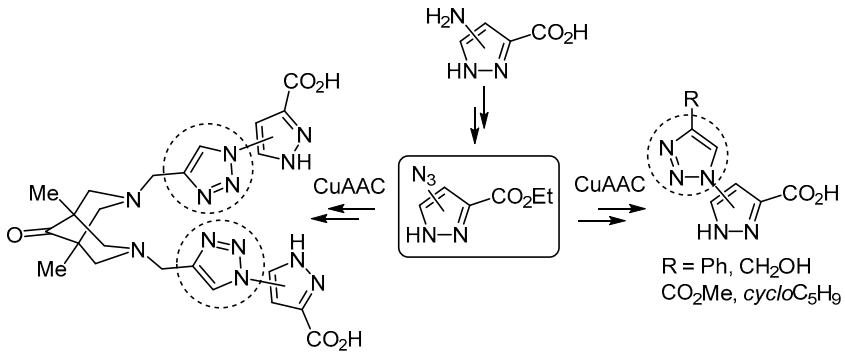


The goal of this work was to obtain novel ligands based on 1*H*-pyrazole-3(5)-carboxylic acids containing the triazole moiety at positions 3(5) or 4. Another goal was to study the possibility of joining pyrazole carboxylic acid fragments with various framework structures to create polychelated ligands that can be used in medicinal chemistry and metal complex catalysis. Methods have been developed for the synthesis of previously unknown *N*-unsubstituted 5- and 4-azido-1*H*-pyrazole-3-carboxylic acids from the corresponding available amino derivatives in high yields. For the first time, the joining of bispidines to azoles was carried out using the copper-catalyzed [3+2] cycloaddition reaction.

Keywords: azides, bispidines, pyrazole, catalysis, click chemistry, complexes, CuAAC reaction, [3+2] cycloaddition, ligands.

1*H*-Pyrazole-3(5)-carboxylic acids, in particular 5-aryl-1*H*-pyrazole-3-carboxylic acids, exhibit a wide spectrum of biological activity.[1] They are partial agonists of nicotinic acid receptors,[2] inhibitors of protein-protein interactions of replication protein A,[3] play the role of frameworks of protein tyrosine phosphatase 1B inhibitors,[4] are inhibitors of tissue-nonspecific alkaline phosphatase.[5] 5-Hetaryl-1*H*-pyrazole-3-carboxylic acids are known inhibitors of human carbonic anhydrases I, II, IX, and XII.[6]

Earlier, we demonstrated the possibility of using isomeric *N*-substituted 5(3)-aryl(hetaryl)-1*H*-pyrazole-3(5)-carboxylic acids as ligands in lanthanide luminescent complexes.[7,8] Of principal importance was not only the presence of the carboxyl group, which allows such structures to form stable chelate complexes, but also the presence in the adjacent position of a nitrogen atom of the pyridine type capable of interacting with metal ions. At the same time, such structures should be of considerable interest as ligands for use in metal complex catalysis.

As part of the project to create novel catalytic systems being developed for use in metal complex catalysis, the design of organic molecules that would combine not one but two pyrazolecarboxylates in their structure so that they could force both chelating systems for coordination to one metal moiety was carried out (Fig. 1). Such a structure may have a higher binding constant with metals, which will increase the stability of the catalyst, and additional spatial limitations will lead to an increase in selectivity.

To study the possibility of joining a conformationally rigid bicyclic core of a potential catalyst (in this case, bispidine) to the coordinating moiety (pyrazole fragments), it was decided to use the 1,2,3-triazole ring as a linker, the formation of which easily occurs as a result of the copper-catalyzed [3+2] cycloaddition reaction of azides with alkynes.

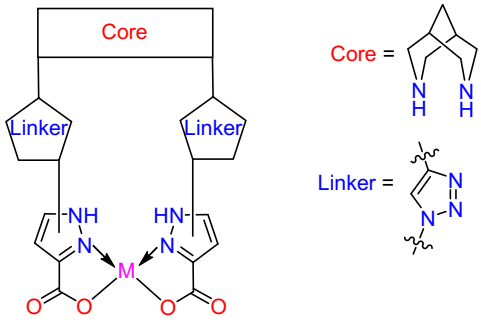


Figure 1. Design of bispyrazolecarboxylates. The core is bispidine derivatives, the linker is triazole.

A review of the literature showed that 1-(1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazoles have been little studied: there are only a few examples of the synthesis of 1-(1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazoles;[9–15] derivatives of 1-(1*H*-pyrazol-4-yl)-1*H*-1,2,3-triazoles have not been studied at all. Moreover, derivatives of 1-(1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazoles containing the $MeSO_2$ pharmacophore group have proven themselves as potential selective inhibitors of human cyclooxygenase-2 (COX-2) with excellent anti-inflammatory activity at the level of clinically used anti-inflammatory drugs.[9]

The goal of this work was to obtain novel ligands based on *N*-unsubstituted 1*H*-pyrazole-3(5)-carboxylic acids containing the triazole fragment at position 3(5) or 4, as well as to study the possibility of joining pyrazolecarboxylic acids with 3,7-diazabicyclo[3.3.1]nonane-type framework structures to create polychelating ligands. The presence of an unsubstituted nitrogen atom in the pyrazole ring of the target compounds is important because it creates additional opportunities for functionalization.[16,17]

It should be noted that 5-(1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylic acids and 4-(1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylic acids, as well as the corresponding carboxylates are not described in the literature.

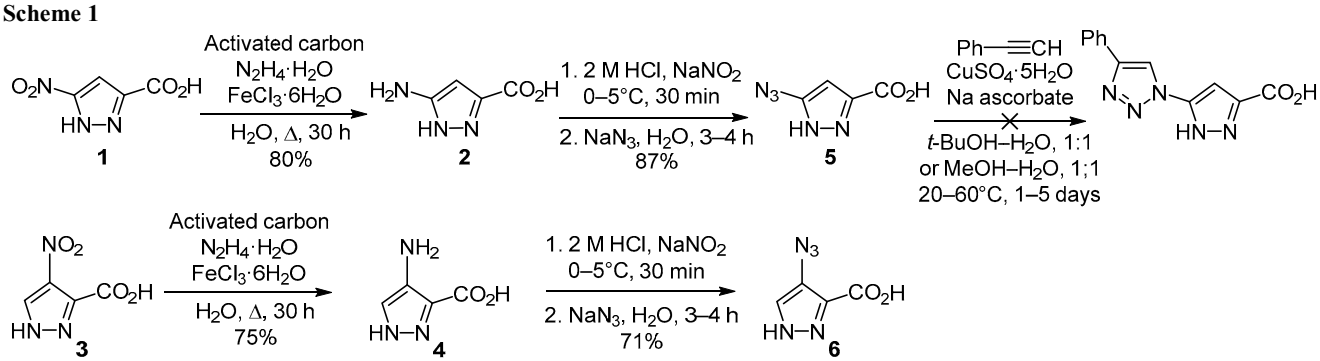
In our opinion, the optimal approach for the synthesis of triazolylpyrazoles is based on the use of the corresponding azidopyrazoles, since the introduction of a triple bond into *N*-unsubstituted pyrazolecarboxylates is synthetically more complicated than the introduction of the azido group.[18,19] Despite the fact that *N*-unsubstituted azidopyrazoles are well studied,[10,20] azidopyrazolecarboxylic acids and their derivatives are not described. Therefore, the first objective of this work was the development of methods for introducing the azido group into *N*-unsubstituted pyrazolecarboxylic acids.

In the synthesis of triazoles, 3-azido- and 4-azido-1*H*-pyrazole-5-carboxylic acids, which were obtained by us for the first time, were used as the 1,3-dipoles. Phenylacetylene, propargyl alcohol, methyl propiolate, and cyclopentylacetylene were selected as acetylene derivatives. This choice can be explained by the need to test acetylenes with different electronic and steric properties in reactions with new substrates.

For the synthesis of 5- and 4-azido-1*H*-pyrazole-3-carboxylic acids **5**, **6**, 5- and 4-amino-1*H*-pyrazole-3-carboxylic acids **2**, **4** were employed as the precursors. Amino acids **2**, **4** were obtained in 70–80% yields *via* reduction of the nitro group of the corresponding nitro acids **1**, **3** by heating under reflux with hydrazine hydrate in the presence of catalytic amounts of $FeCl_3·6H_2O$ and activated carbon in H_2O according to the literature procedure[21] (Scheme 1). The corresponding nitro acids **1**, **3** were synthesized from 3(5)-methyl-1*H*-pyrazole according to the published procedures.[22–24] 5-Azido- and 4-azido-1*H*-pyrazole-3-carboxylic acids **5**, **6** were obtained by diazotization of the corresponding amino acids **2**, **4** with $NaNO_2$ in 2 M aqueous HCl at 0–5°C. The diazonium salt formed in this case was without isolation subjected to a reaction with an aqueous solution of NaN_3. The presence of the azido group in compounds **5**, **6** was determined by the appearance of characteristic absorption bands in the IR spectrum at 2125 and 2150 cm^{-1}. An additional confirmation of the presence of the azido group in compound **6** is the signal at –138.07 ppm in the ^{14}N NMR spectrum.

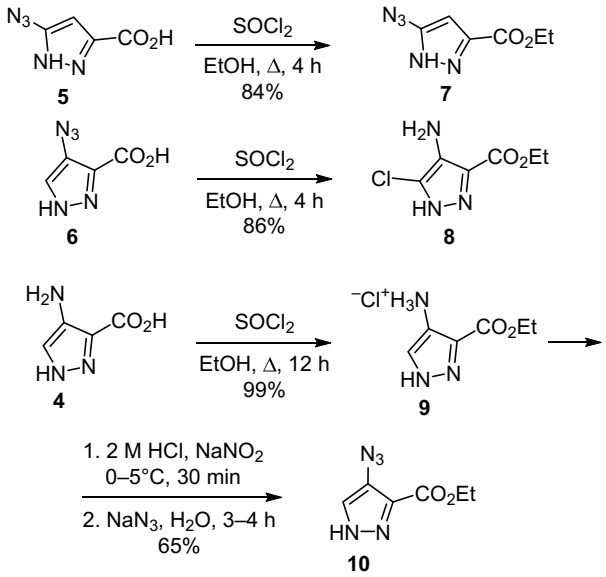
Attempts to directly access 5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylic acid by cycloaddition of phenylacetylene to azido acid **5** were unsuccessful (Scheme 1). The reactions of equimolar amounts of azide **5** and phenylacetylene were carried out in the presence of $CuSO_4·5H_2O$ (1–10 mol %) and Na ascorbate (5–30 mol %) in *t*-BuOH–H_2O, 1:1 or MeOH–H_2O, 1:1 at 20–60°C in an inert atmosphere for 1–5 days. In no case was triazole formation observed; only the starting reagents were isolated. The reason for this is probably the coordination of Cu(I) ions with azido acid **5** and their removal from the reaction. The coordination of Cu(I) ions prevents the formation of copper acetylenides, which is a prerequisite in the mechanism of copper-catalyzed azide-alkyne cycloaddition (CuAAC) (Scheme 1). Another reason for the unsuccessful reaction may be the high value of the stability constant of the pyrazolecarboxylic acid complex with the Cu(II) ion, which also removes the catalytically active

Scheme 1



metal from the reaction. To prevent coordination of Cu ions, it was decided to esterify the carboxyl group of azido acids **5**, **6**. Ethyl 5-azido-1*H*-pyrazole-3-carboxylate (**7**) was obtained in 84% yield by heating the corresponding azido acid **5** in unhydrous EtOH under reflux in the presence of 2 equiv of $SOCl_2$ for 4 h (Scheme 2). The isolated product did not require additional purification. An attempt to obtain ethyl 4-azido-1*H*-pyrazole-3-carboxylate (**10**) from the corresponding azido acid **6** by a similar method led to an unexpected result. Instead of the expected ethyl azidocarboxylate **10**, heating azido acid **6** in unhydrous EtOH in the presence of 2 equiv $SOCl_2$ afforded amino chloro derivative **8** with a yield of 86% as the sole product.

Scheme 2



The proposition of the formation of an amino chloro derivative with structure **8** was made on the basis of the obtained ^{1}H, ^{13}C NMR, IR spectroscopy, and mass spectrometry data. The ^{1}H NMR spectrum of compound **8** shows signals at 4.28 ppm (2H, q, J = 7.1 Hz) and 1.28 ppm (3H, t, J = 7.1 Hz) indicating the formation of an OCH_2CH_3 fragment, an NH_2 group signal at 4.84 ppm (2H, br. s), and a singlet at 13.19 ppm with an intensity of 1H, corresponding to the proton at the nitrogen atom of the pyrazole ring. In this case, there is no signal of a proton at the carbon atom in the pyrazole ring in the aromatic region, which indicates its possible substitution. The ^{13}C NMR spectrum shows a signal at 159.3 ppm corresponding to the carboxylate carbon atom $\underline{C}OOCH_2CH_3$, signals of three carbon atoms of the pyrazole ring at 131.9, 126.5, and 117.3 ppm, as well as signals of the CH_2CH_3 fragment at 60.2 and 14.3 ppm. The arrangement of the substituents in the ring is confirmed by comparing the obtained signals of the carbon atoms of the pyrazole ring with those described in the literature for similar amino chloro derivatives.[25–27] In the IR spectra of the starting azido acid **6** and the obtained amino chloro derivative **8**, absorption bands of the carbonyl group are observed at 1710 cm^{-1}. However, in comparison with the IR spectrum of compound **6**, the IR spectrum of compound **8** does not have an absorption band at 2160–2120 cm^{-1}, indicative of the absence of an azido group in this structure. The presence in the mass spectrum of compound **8** of $[M]^+$ signals with m/z 189 and 191 with an intensity ratio of 3:1 confirms the presence of a chlorine atom.

No examples of such transformations have been found in the literature for pyrazoles. Some studies have shown a possible mechanism for a similar acid-catalyzed conversion of aryl azides to amines.[28–30] It should be noted that this transformation is observed only during the esterification of azido acid **6** with an azido group in position **4** of the pyrazole ring and is not observed in the case of the presence of an azido group in position **5** (for azido acid **5**) A study of the limits of applicability of the new reaction to other pyrazole systems will be the subject of a separate publication.

In order to avoid such reactions, the synthesis strategy of ethyl azidocarboxylate **10** was changed. It was decided first to esterify the corresponding amino acid **4** with the formation of ethyl 4-amino-1*H*-pyrazole-3-carboxylate (**9**) and its subsequent conversion to azidocarboxylate **10** (Scheme 2). Ethyl 4-amino-1*H*-pyrazole-3-carboxylate (**9**) was obtained in the form of hydrochloride with a quantitative yield by heating amino acid **4** in the presence of an equivalent amount of $SOCl_2$ in absolute EtOH for 12 h. The structure of the product was confirmed by ^{1}H and ^{13}C NMR spectroscopy. Ethyl 4-azido-1*H*-pyrazole-3-carboxylate (**10**) was obtained by diazotization of the corresponding aminocarboxylate **9** with $NaNO_2$ in 2 M aqueous HCl at 0–5°C. The diazonium salt formed in this case, without isolation, was subjected to a reaction with NaN_3 in the form of an aqueous solution. The product was isolated in 65% yield and did not require further purification. The substance was fully characterized using ^{1}H, ^{13}C NMR, IR spectroscopy, high-resolution mass spectrometry, and elemental analysis. The formation of the azido group was determined by the appearance of the absorption band in the IR spectrum (2101 cm^{-1}) corresponding to the azido group.

In the ^{1}H and ^{13}C NMR spectra of 4-azido-substituted pyrazolecarboxylic acids and their esters, strongly broadened signals were observed due to slow (in the NMR time scale) dynamic processes, which did not allow reliable determination of the structure of these compounds. To establish the reason for the existence of the dynamic phenomena in the NMR spectra, as well as an unambiguous correlation between the signals of protons and carbon atoms in the ^{1}H and ^{13}C NMR spectra of compounds **6**, **7**, and **10**, ^{1}H–^{13}C HSQC, ^{1}H–^{13}C HMBC, ^{1}H–^{15}N HMBC experiments were performed, which completely confirmed the structure of the obtained compounds.

Our approach to use esters of the azido acids, not acids themselves in the cycloaddition reactions turned out to be successful.

The addition of phenylacetylene to ethyl azidocarboxylate **7** in the presence of $CuSO_4 \cdot 5H_2O$ (5 mol %) and Na ascorbate (10 mol %) was carried out in *t*-BuOH–H_2O, 1:1 system under an inert atmosphere. At room temperature, the addition proceeds very slowly, so it was decided to increase the temperature of the reaction mixture

(60°C). Under such conditions, the reaction was complete in 10–12 h. Triazole **11a** was isolated in 57% yield. Triazoles **11b**–**c** were obtained similarly (Scheme 3). The addition of ethyl azidocarboxylate **7** to an equimolar amount of propargyl alcohol both at room temperature and at 60°C resulted in an incomplete conversion of azide **7**. Therefore, we took a fourfold excess of propargyl alcohol; in this case, the reaction took place at 60°C in 10–12 h with a complete conversion of azide and with an 86% yield of triazole **11b**. Triazole **11c** was obtained by addition of an equimolar amount of methyl propiolate to azide **7**. The reaction readily proceeds with complete conversion at 25°C in 12 h. The yield of the corresponding triazole **11c** was also 86%. The addition of cyclopentylacetylene to azide **7** at room temperature is slow. Even after a week, complete conversion of the azide was not observed. It was decided to carry out the reaction by heating. Indeed, when heated to 60°C, the reaction proceeds completely in 10–12 h. The corresponding triazole **11d** was isolated in 91% yield. In all cases, compounds **11a**–**d** formed as the only products and did not require additional purification.

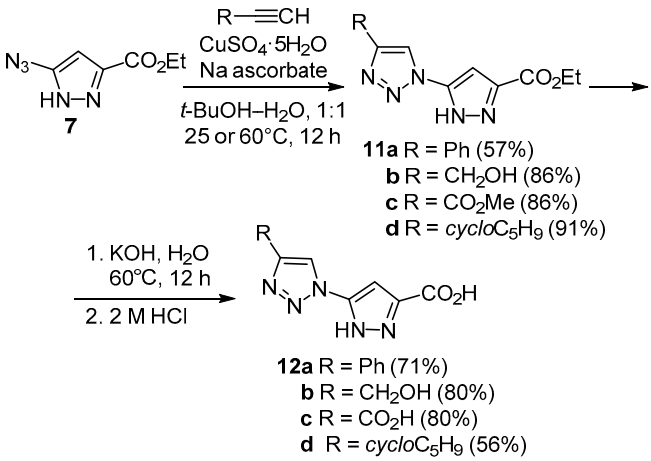
The products were identified by the appearance of triazole proton signals in the 9.28–8.40 ppm range and signals of the R substituents of the triazole fragment in the ^{1}H NMR spectrum, as well as the disappearance of the absorption band of the azido group in the IR spectrum at 2160–2120 cm^{-1}. In the ^{13}C NMR spectrum, the signals of the carbon atoms of the pyrazole and triazole rings are observed in the 152.0–99.4 ppm range. In addition, the structure of the obtained compounds was confirmed by high-resolution mass spectrometry and elemental analysis.

Compounds **12a**–**d** were obtained by alkaline hydrolysis of the corresponding triazolylcarboxylates **11a**–**d** by treatment with aqueous KOH (3 equiv) at 60°C for 12 h, followed by acidification with 2 M aqueous HCl to pH 1. The formed precipitate was filtered off. The corresponding 5-(1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylic acids **12a**–**d** were isolated in 56–80% yields (Scheme 3). The structure of compounds **12a**–**d** was determined by ^{1}H, ^{13}C NMR, IR spectroscopy and confirmed by high-resolution mass spectrometry, and, for compounds **12a**,**c**, also by elemental analysis.

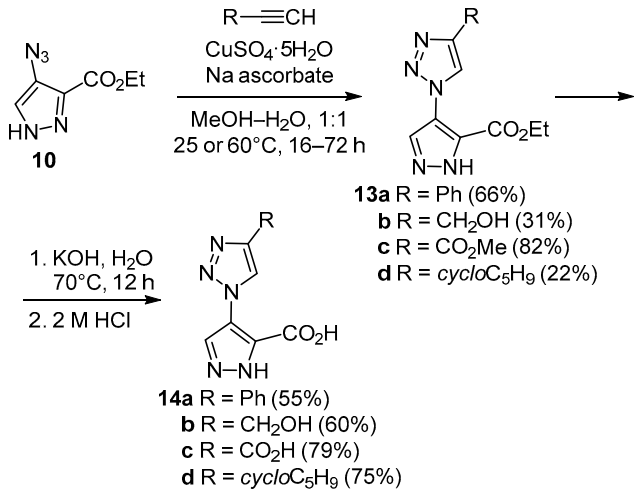
4-(1*H*-1,2,3-Triazol-1-yl)-1*H*-pyrazole-3-carboxylates **13a**–**d** were obtained analogously to the preparation of the isomeric triazolylcarboxylates **11a**–**d**. Due to poor solubility of ethyl azidocarboxylate **10** in *t*-BuOH, all acetylene addition reactions were carried out in MeOH–H_2O, 1:1 system under an inert atmosphere (Scheme 4).

The addition of phenylacetylene to azidocarboxylate **10** in the presence of $CuSO_4 \cdot 5H_2O$ (5 mol %) and Na ascorbate (10 mol %) requires more drastic conditions than in the case of azidocarboxylate **7**. The reaction proceeds with complete conversion of azide **10** at 60°C in 48 h. Product **13a** was isolated in 66% yield. The addition of ethyl azidocarboxylate **10** to an equimolar amount of propargyl alcohol both at room temperature and when heated to 60°C occurred with incomplete conversion of azide **10**, as in the case of azide **7**. Therefore, a fourfold excess of propargyl alcohol was employed, in which case the reaction took place at 60°C in 16–17 h with complete conversion of the azide producing triazole **13b** in 31% yield. The low yield of the product is probably due to its good solubility in H_2O, which makes it difficult to isolate. In the ^{1}H NMR spectrum, individual broadened signals are observed in the region of NH protons and pyrazole protons with the ratio of intensities of 0.2 to 0.8 with the total intensity of one proton each. The explanation for this observation may be the presence of two NH tautomers. The remaining signals of both tautomers coincide. Triazole **13c** was obtained by addition of an equimolar amount of methyl propiolate to azide **10**. The reaction readily proceeds at 25°C with complete conversion in 16 h. The yield of the corresponding triazole **13c** was 82%. The addition of cyclopentylacetylene to azide **7** was only possible upon heating. The reaction proceeds completely in 72 h at 60°C. The corresponding triazole **13d** was isolated in 22% yield.

Scheme 3



Scheme 4



The products were identified by the appearance of triazole proton signals in the ^{1}H NMR spectrum in the 9.15–8.18 ppm range and signals of the R substituents of the triazole fragment, as well as the disappearance of the absorption band of the azide group in the IR spectrum at 2160–2120 cm^{-1}. It should be noted that, in contrast to the ^{1}H and ^{13}C NMR spectra of the isomeric triazolylcarboxylates **11a**–**d**, the ^{1}H NMR spectra of compounds **13a**–**d** show a strongly broadened signal of the pyrazole proton in the range of 8.55–8.28 ppm, while the ^{13}C NMR

spectra exhibit strongly broadened signals of carbon atoms of the triazole and pyrazole rings in the 150.8–120.3 ppm range. The signal broadening is probably related either to the existence of products in two tautomeric forms, which correlates with ^{1}H and ^{13}C NMR spectra of the corresponding azidocarboxylates **6** and **10** or to intramolecular dynamic processes due to steric constraints.

Compounds **14a**–**d** were obtained *via* alkaline hydrolysis of the corresponding triazolylcarboxylates **13a**–**d** by treatment with an aqueous KOH solution (3 equiv) at 70°C for 12 h, followed by acidification with 2 M aqueous HCl solution to pH 1. The formed precipitate was filtered off. The corresponding 4-(1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylic acids **14a**–**d** were isolated in 55–79% yields. The structure of compounds **14a**–**d** was determined by ^{1}H, ^{13}C NMR, IR spectroscopy and confirmed by high-resolution mass spectrometry.

To synthesize bispyrazolecarboxylic acids **18** and **20** based on 3,7-diazabicyclo[3.3.1]nonanes, we used the method that we developed earlier by introducing azidopyrazolecarboxylates into the [3+2] cycloaddition reaction, namely, joining of the bispidine framework with pyrazole moieties *via* triazole linkers. In order to achieve this, a method was developed for introducing acetylene fragments into bispidine by bis-*N*-alkylation with propargyl bromide. 1,5-Dimethylbispidin-9-one (**15**) was taken as the starting framework (Scheme 4), which we already obtained previously according to a published procedure.[31] Bispropargylation of bispidine **15** was carried out by heating in MeCN under reflux in the presence of 2 equiv of propargyl bromide and 2 equiv DIPEA for 10 h. Purification of the isolated bispropargylbispidine **16** was carried out using column chromatography. The yield of pure product was 73% (Scheme 5). Bistriazolylpyrazole carboxylate **17** was obtained by addition of 2 equiv of azidopyrazole carboxylate **7** to bispropargylbispidine in an inert atmosphere in the *t*-BuOH–H_2O, 1:1 system in the presence of $CuSO_4 \cdot 5H_2O$ (5 mol %) and Na ascorbate (10 mol %). The reaction proceeds at room temperature for 48 h with a good yield (88%). Compound **17** is formed as the only product. Bistriazolylpyrazolecarboxylate **19** was obtained by addition of 2 equiv of azidopyrazolecarboxylate **10** to bispropargylbispidine **16** in an inert atmosphere in the MeOH–H_2O, 1:1 system in the presence of $CuSO_4 \cdot 5H_2O$ (5 mol %) and Na ascorbate (10 mol %). The reaction proceeds at room temperature for 12 h also with a good yield (78%). Compound **19** formed as the only product.

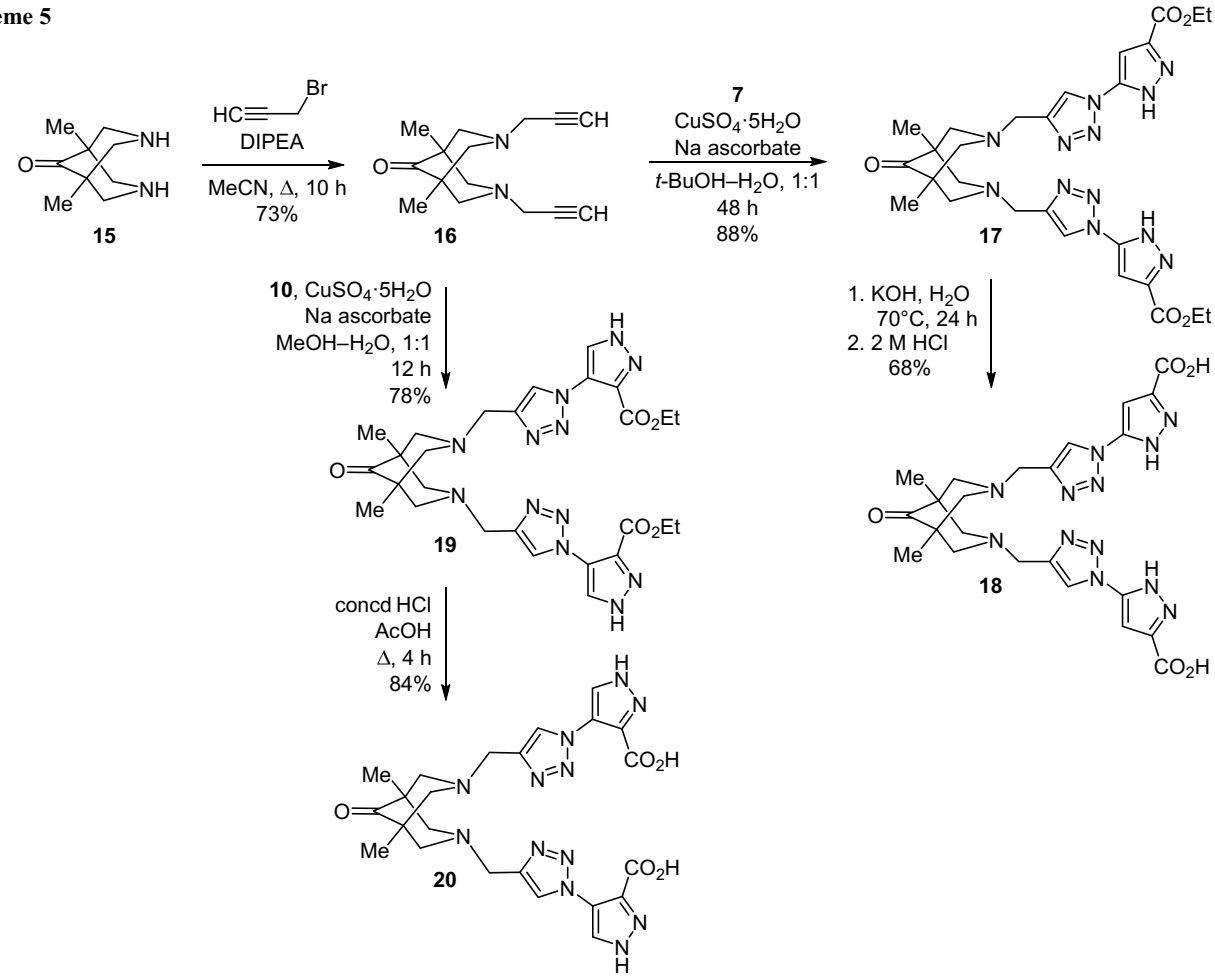
The products were identified by the appearance of triazole proton signals in the ^{1}H NMR spectrum at 8.51 ppm for compound **17** and at 8.32 ppm for compound **19**, the appearance of signals of pyrazole fragments and the disappearance of the signal of acetylene protons, as well as the disappearance of the absorption band of the azide group in the IR spectrum at 2160–2120 cm^{-1}. In the ^{1}H NMR spectrum of compound **19**, a strongly broadened signal of the pyrazole proton is observed at 8.36 ppm, which is superimposed on the signal of the triazole proton at 8.32 ppm. The structure of the obtained compounds was also established using ^{13}C NMR spectroscopy and confirmed by high-resolution mass spectrometry, and for compound **17**, by elemental analysis. It is worth noting that before introduction into the subsequent hydrolysis reaction, bistriazolylpyrazolecarboxylates **17** and **19** must be thoroughly purified of traces of Cu(II) either by washing with a large amount of H_2O or by passing through a short column with silica gel using $CHCl_3$–MeOH, 1:5 as an eluent.

Bistriazolylpyrazolecarboxylic acid **18** was obtained by alkaline hydrolysis of carboxylate **17** at 70°C for 1 day, followed by acidification with 2 M aqueous HCl. It turned out that in order to achieve a good result, it is very important to carefully acidify to at least pH 3–4, since it is in this case that a precipitate forms, which is then filtered. In a more acidic environment, the product turns into a water-soluble protonated form, which greatly complicates the isolation of the product which is free of inorganic salts. Target compound **18** was isolated in 68% yield. The structure of the product was established by IR, ^{1}H, ^{13}C NMR spectroscopy and confirmed by high-resolution mass spectrometry. The results of elemental analysis suggest that the compound crystallizes in the form of hydrate **18**·$4H_2O$.

During the synthesis of bistriazolylpyrazolecarboxylic acid **20** by alkaline hydrolysis of the corresponding carboxylate **19** by a similar method, great difficulties arose at the product isolation step. When acidified with 2 M aqueous HCl, it was not possible to select a suitable pH value of the medium at which an unprotonated form exists. At pH 5–6, a precipitate formed, which contained a partially protonated form of the product. At lower pH values, the product was completely converted to a protonated water-soluble form. In order to exclude the formation of inorganic salts and facilitate the isolation of the product, it was decided to obtain the target bistriazolylpyrazolecarboxylic acid **20** by hydrolysis of carboxylate **19** in an acidic medium. Compound **20** was obtained by heating carboxylate **19** under reflux for 4 h in concentrated HCl with addition of glacial AcOH (1:1) to ensure good solubility (Scheme 5). The structure of the product was established by IR, ^{1}H, ^{13}C NMR spectroscopy, and confirmed by high-resolution mass spectrometry. In the ^{1}H NMR spectrum, there is a signal of the methyl group of AcOH at 1.90 ppm in a 1:1 ratio in respect to the signals of compound **20**, which does not change even after prolonged drying of the product under reduced pressure at 80°C. The results of elemental analysis allow us to propose the following composition of the product: **20**·3HCl·AcOH. Probably, three HCl molecules protonate the three main centers of the molecule, and AcOH is located in the cavity of the molecule, which thus acts as a receptor.

An unexpected additional confirmation of certain receptor properties of compounds **18** and **20** was found when studying their solubility in DMF, which was carried out in order to obtain single crystals suitable for X-ray structural analysis. Upon evaporation of the solution of acid **18** and subsequent drying under reduced pressure of the obtained solid sample it was found (by NMR spectroscopy) that the resulting dry product contained a complex of composition **18**·DFM. If similar manipulations are carried out with a product of the composition **20**·3HCl·AcOH, then the replacement of the AcOH molecule with the DMF molecule is clearly seen from the NMR spectrum.

Scheme 5



To conclude, we have developed methods for the synthesis of previously unknown *N*-unsubstituted 5- and 4-azido-1*H*-pyrazole-3-carboxylic acids from the corresponding available amino derivatives. The possibility of catalytic cycloaddition of alkynes with substituents of various nature with the formation of the corresponding triazoles was studied. For the first time, joining of bispidines with azoles was carried out using the copper-catalyzed [3+2] cycloaddition reaction. Along with the successful synthesis of the target compounds, we established fundamental spectral differences as well as differences in the reactivity of 5- and 4-azido-1*H*-pyrazole-3-carboxylates. For the first time, additional two-dimensional NMR experiments were carried out for these compounds, which made it possible to unequivocally establish their structures.

Experimental

IR spectra were registered on a Thermo Scientific Nicolet iS5 FTIR spectrometer with iD1 Transmission and iD7 ATR (diamond) accessories. ^{1}H and ^{13}C NMR spectra were acquired on Bruker Avance 400 (400 and 101 MHz, respectively), Bruker DRX-500 (500 and 126 MHz, respectively), Bruker AM-300 (300 and 75 MHz, respectively), and Bruker Avance IIIHD 500 (500 and 126 MHz, respectively) spectrometers at 298 K (unless other temperature is indicated). ^{14}N NMR spectrum of compound **6** was registered on a Bruker DRX-500 (36 MHz) spectrometer in DMSO-d_6. For ^{1}H and ^{13}C nuclei, TMS was used as internal standard, for ^{14}N nuclei, nitromethane was used. Mass spectra were recorded on a Finnigan MAT INCOS-50 (direct injection, EI ionization, 70 eV) mass spectrometer. High-resolution mass spectra were recorded on a Bruker MicroOTOFII mass spectrometer with electrospray ionization. Elemental analysis was performed on a PerkinElmer Series II 2400 CHNS/O analyzer. Melting points were determined by the capillary method on Stuart SMP20 and Electrothermal IA9000 apparatuses. Monitoring of the reaction progress and assessment of the purity of synthesized compounds were done by TLC on Merck TLC Silica gel 60G F254 plates. Carl Roth Silica gel 60, 0.04–0.063 mm was used for column chromatography.

All reagents and solvents used in the work (purity 90.0–99.9+ %) were supplied by commercial sources (Sigma-Aldrich, abcr, IREA 2000), and, if necessary, subjected to further purification by standard routines immediately before use to achieve analytical purity.

5-Nitro-1*H*-pyrazole-3-carboxylic acid (1) was obtained from 3(5)-methyl-1*H*-pyrazole (41 g) according to published methods.[22,23] Yield of the oxidation step 33 g (85%), mp 175–176°C (mp 174–175°C[23]). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 15.02 (2H, br. s, NH, COOH); 7.41 (1H, s, H-4 pyrazole).

4-Nitro-1*H*-pyrazole-3-carboxylic acid (3) was obtained from 3(5)-methyl-1*H*-pyrazole (30 g) according to

a published method.[24] Combined yield over nitration and oxidation steps 34 g (59%), colorless solid, mp 208–209°C (mp 206–208°C[24]).

Synthesis of 5- and 4-amino-1*H*-pyrazole-3-carboxylic acids 2, 4 (General method). Reduction of the nitro group was carried out according to a published method.[21] The corresponding nitro acid **1**, **3** (0.032 mol) was suspended in H_2O (30 ml). Activated carbon (0.8 g), $N_2H_4 \cdot H_2O$ (95%, ρ 1.023 g/cm^3) (6.55 ml, 6.71 g, 0.134 mol), and $FeCl_3 \cdot 6H_2O$ (64 mg) were added to the suspension with stirring. The reaction mixture was heated under reflux for 30 h. The hot solution was filtered, the filtrate was evaporated to dryness under reduced pressure. The resulting dry residue was dissolved in H_2O (20 ml) and carefully acidified with 2 M aqueous HCl to pH 4–5. The formed precipitate was filtered off and washed with a small amount of H_2O. The product was dried in a vacuum desiccator over P_2O_5 to constant weight.

5-Amino-1*H*-pyrazole-3-carboxylic acid (2). Yield 3.25 g (80%), colorless solid, mp 245–246°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 5.77 (1H, s, H-4 pyrazole). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 162.2; 152.8; 138.3; 92.3. ^{1}H NMR spectrum and mp of the obtained compound correspond to the published data.[23]

4-Amino-1*H*-pyrazole-3-carboxylic acid (4). Yield 3.05 g (75%), purple solid, mp 212–213°C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 7.05 (1H, s, H-5 pyrazole); 5.23 (2H, br. s, NH_2). ^{13}C NMR spectrum (75 MHz, DMSO-d_6), δ, ppm: 162.4; 136.2; 125.5; 119.5.

Synthesis of 5- and 4-azido-1*H*-pyrazole-3-carboxylic acids 5, 6 (General method). The corresponding amino acid **2**, **4** (0.0173 mol) was dissolved in 2 M aqueous HCl (50 ml), and the formed solution was cooled to 0°C in an ice bath. Aqueous $NaNO_2$ (0.019 mol) was dropwise added to the reaction mixture. The mixture was stirred for 30 min, then aqueous NaN_3 (0.026 mol) was carefully added. The reaction mixture was stirred for 3–4 h. The formed precipitate was filtered off on a fritted glass filter and washed with a small amount of H_2O, then dried in a vacuum desiccator over P_2O_5 to constant weight. The filtrate was extracted with EtOAc, the organic phase was separated and dried over anhydrous Na_2SO_4. The dried organic phase was evaporated under reduced pressure on the rotary evaporator to afford a solid. Both solids were combined.

5-Azido-1*H*-pyrazole-3-carboxylic acid (5). Yield 2.32 g (87%), yellow solid, mp 164–165°C. IR spectrum, ν, cm^{-1}: 3309 (NH), 3101 (OH), 2125 (N_3), 1675 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 13.76 (2H, br. s, NH, COOH); 6.48 (1H, s, H-4 pyrazole). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 160.3; 147.6; 136.9; 98.9. Found, *m*/*z*: 154.0363 $[M+H]^+$. $C_4H_4N_5O_2$. Calculated, *m*/*z*: 154.0360. Found, %: C 31.51; H 1.82; N 45.37. $C_4H_3N_5O_2$. Calculated, %: C 31.38; H 1.98; N 45.74.

4-Azido-1*H*-pyrazole-3-carboxylic acid (6). Yield 1.88 g (71%), brown solid, mp 139–140°C. IR spectrum, ν, cm^{-1}: 3249 (NH), 3145 (CO<u>OH</u>), 2150 (N_3), 1710 (C=O). ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 13.46 (2H, br. s, NH, COOH); 7.75 (1H, s, H-5 pyrazole). ^{1}H NMR spectrum (500 MHz, DMSO-d_6, 343 K), δ, ppm: 13.14 (2H, br. s, NH, COOH); 7.69 (1H, s, H-5 pyrazole). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 161.5; 129.6 (br. s); 124.2. ^{13}C NMR spectrum (126 MHz, DMSO-d_6, 343 K), δ, ppm: 161.4; 130.5; 128.7; 124.2. ^{14}N NMR spectrum, δ, ppm: –138.07 (N_3). Found, *m*/*z*: 154.0354 $[M+H]^+$. $C_4H_4N_5O_2$. Calculated, *m*/*z*: 154.0360. Found, %: C 31.43; H 1.83; N 45.74. $C_4H_3N_5O_2$. Calculated, %: C 31.38; H 1.98; N 45.74.

Ethyl 5-azido-1*H*-pyrazole-3-carboxylate (7). 3-Azido-1*H*-pyrazole-5-carboxylic acid (**5**) (1.5 g, 0.0098 mol) was dissolved in absolute EtOH (20 ml). $SOCl_2$ (1.45 ml, 2.38 g, 0.020 mol) was added dropwise to the solution, and the mixture was heated under reflux for 4 h. The solvent was evaporated under reduced pressure on the rotary evaporator. H_2O was added to the solid residue, and the mixture was extracted with EtOAc. The organic phase was separated and dried over anhydrous Na_2SO_4, then evaporated under reduced pressure. Yield 1.51 g (84%), yellow solid, mp 92–93°C. IR spectrum, ν, cm^{-1}: 3261 (NH), 2125 (N_3), 1701 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 13.92 (1H, s, NH); 6.55 (1H, s, H-4 pyrazole); 4.30 (2H, q, *J* = 7.1, OC<u>H</u>$_2$CH$_3$); 1.28 (3H, t, *J* = 7.2, OCH$_2$C<u>H</u>$_3$). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 158.4; 147.5; 135.1; 98.7; 61.2; 14.1. Found, *m*/*z*: 182.0671 $[M+H]^+$. $C_6H_8N_5O_2$. Calculated, *m*/*z*: 182.0673. Found, %: C 39.84; H 3.80; N 38.22. $C_6H_7N_5O_2$. Calculated, %: C 39.78; H 3.90; N 38.66.

Ethyl 4-amino-5-chloro-1*H*-pyrazole-3-carboxylate (8). 4-Azido-1*H*-pyrazole-3-carboxylic acid (**6**) (1.19 g, 0.0078 mol) was dissolved in absolute EtOH (25 ml). $SOCl_2$ (1.3 ml, 2.14 g, 0.0179 mol) was added dropwise to the solution, and the mixture was heated under reflux for 4 h. The reaction mixture was evaporated to dryness on the rotary evaporator under reduced pressure, washed with a small amount of H_2O, and extracted with EtOAc. The organic phase was separated and dried over anhydrous Na_2SO_4. The dried extract was evaporated to dryness under reduced pressure. The resulting brown oil was dried to constant weight in a vacuum desiccator over P_2O_5. The product gradually crystallizes upon standing. Yield 1.27 g (86%), yellow solid, mp 101–102°C. IR spectrum, ν, cm^{-1}: 3407 (NH_2), 1710 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 13.19 (1H, br. s, NH); 4.84 (2H, br. s, NH_2); 4.28 (2H, q, *J* = 7.1, OC<u>H</u>$_2$CH$_3$); 1.28 (3H, t, *J* = 7.1, OCH$_2$C<u>H</u>$_3$). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 159.3; 131.9; 126.5; 117.3; 60.2; 14.3. Mass spectrum, *m*/*z* (I_{rel}, %): 189 $[M]^+$ (64), 191 $[M]^+$ (21), 161 $[M–C_2H_4]^+$ (35), 143 $[M–EtOH]^+$ (100). Found, *m*/*z*: 212.01967 $[M+Na]^+$. $C_6H_8ClN_3NaO_2$. Calculated, *m*/*z*: 212.01972.

Ethyl 4-amino-1*H*-pyrazole-3-carboxylate hydrochloride (9). Amino acid **4** (2 g, 0.0157 mol) was suspended in absolute EtOH (20 ml). $SOCl_2$ (1.17 ml, 1.92 g, 0.0161 mol) was added dropwise to the suspension. The mixture was heated under reflux for 12 h until homogenization. A cherry-colored solution formed. The solvent was evaporated to dryness under reduced pressure on the rotary evaporator. The solid residue was dried in a vacuum desiccator to constant weight. Yield 3.0 g (99%), pink solid, mp 114–115°C. ^{1}H NMR spectrum (400 MHz,

DMSO-d_6), δ, ppm (*J*, Hz): 10.22 (4H, br. s, NH, $^+NH_3$); 8.03 (1H, s, H-3 pyrazole); 4.28 (2H, q, *J* = 7.0, OC$\underline{H}_2$CH$_3$); 1.30 (3H, t, *J* = 7.1, OCH$_2$C$\underline{H}_3$). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 160.5; 133.7; 127.3; 116.6; 60.8; 14.1. Found, *m*/*z*: 178.05868 $[M+Na]^+$. $C_6H_9N_3NaO_2$. Calculated, *m*/*z*: 178.05870.

Ethyl 4-azido-1*H*-pyrazole-3-carboxylate (10). Hydrochloride **9** (3 g, 0.0157 mol) was dissolved in 2 M aqueous HCl (80 ml), and the solution was cooled to 0°C in the ice bath. Aqueous $NaNO_2$ (1.38 g, 0.02 mol) was added dropwise to the solution. The mixture was stirred for 30 min, then aqueous NaN_3 (0.025 mol) was carefully added. The reaction mixture was stirred for 3–4 h. The formed precipitate was filtered off and washed with a small amount of H_2O, then dried in a vacuum desiccator over P_2O_5 to constant weight. The filtrate was extracted with EtOAc, the organic phase was separated and dried over anhydrous Na_2SO_4. The dried organic phase was evaporated under reduced pressure on the rotary evaporator to afford a solid. Both solids were combined. Yield 1.86 g (65%), light-pink solid, mp 122–123°C. IR spectrum, ν, cm^{-1}: 3210 (NH), 2101 (N_3), 1678 (C=O). ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 13.97 (0.4H, br. s, NH); 13.64 (0.6H, br. s, NH); 7.92 (0.7H, br. s, H-5 pyrazole); 7.68 (0.3H, br. s, H-5 pyrazole); 4.29 (2H, q, *J* = 7.1, OC$\underline{H}_2$CH$_3$); 1.29 (3H, t, *J* = 7.0, OCH$_2$C$\underline{H}_3$). ^{1}H NMR spectrum (500 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 12.20 (1H, br. s, NH); 7.70 (1H, s, H-5 pyrazole); 4.50 (2H, q, *J* = 7.1, OC$\underline{H}_2$CH$_3$); 1.46 (3H, t, *J* = 7.0, OCH$_2$C$\underline{H}_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 161.5; 158.5; 134.6; 133.8; 123.7; 60.9; 14.6. ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 160.8; 131.8; 126.6; 124.4; 61.6; 14.4. Found, *m*/*z*: 204.0496 $[M+Na]^+$. $C_6H_7N_5NaO_2$. Calculated, *m*/*z*: 204.0492.

Synthesis of 5-(1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylates 11a–c (General method). Ethyl 5-azido-1*H*-pyrazole-3-carboxylate **7** (1.7 mmol) and the corresponding acetylene (phenylacetylene, propargyl alcohol, methyl propiolate, and cyclopentylacetylene; in the case of compound **11b**, a 4-fold excess of propargyl alcohol was used) (1.7 mmol) were dissolved in *t*-BuOH (4 ml). A solution of Na ascorbate (34 mg, 0.17 mmol, 10 mol %) in H_2O (2 ml) was added with vigorous stirring to the reagent solution. The flask was evacuated and filled with argon. A solution of $CuSO_4 \cdot 5H_2O$ (21 mg, 0.085 mmol, 5 mol %) in H_2O (2 ml) was then added to the reaction mixture. The reaction mixture was stirred at 60°C (for compounds **11a**,**b**,**d**) and at 25°C (for compound **11c**) for 12 h, and the mixture was poured into ice water. The formed precipitate was filtered off and washed with a small amount of H_2O, then dried in a vacuum desiccator over P_2O_5. The filtrate was extracted with EtOAc, the organic phase was separated and dried over anhydrous Na_2SO_4. The dried organic phase was evaporated under reduced pressure on the rotary evaporator to afford a solid. Both solids were combined.

Ethyl 5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylate (11a). Yield 275 mg (57%), beige solid, mp 210–211°C. IR spectrum, ν, cm^{-1}: 3203 (NH), 1710 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.53 (1H, s, NH); 9.19 (1H, s, H-5 triazole); 7.97 (2H, d, *J* = 7.5, H Ph); 7.48 (2H, t, *J* = 7.6, H Ph); 7.37 (1H, t, *J* = 7.3, H Ph); 7.23 (1H, s, H-4 pyrazole); 4.37 (2H, q, *J* = 7.0, OC$\underline{H}_2$CH$_3$); 1.34 (3H, t, *J* = 7.07, OCH$_2$C$\underline{H}_3$). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 158.3; 146.9; 146.3; 135.4; 130.0; 129.0; 128.4; 125.5; 119.5; 99.7; 61.5; 14.1. Found, *m*/*z*: 284.1140 $[M+H]^+$. $C_{14}H_{14}N_5O_2$. Calculated, *m*/*z*: 284.1142. Found, %: C 58.86; H 4.55; N 24.97. $C_{14}H_{13}N_5O_2$. Calculated, %: C 59.36; H 4.63; N 24.72.

Ethyl 5-[4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl]-1*H*-pyrazole-3-carboxylate (11b). Yield 347 mg (86%), yellow solid, mp 223–224°C. IR spectrum, ν, cm^{-1}: 3384 (OH), 3218 (NH), 1701 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.45 (1H, s, NH); 8.48 (1H, s, H-5 triazole); 7.19 (1H, s, H-4 pyrazole); 5.31 (1H, t, *J* = 5.6, CH$_2$O$\underline{H}$); 4.60 (2H, d, *J* = 4.2, C$\underline{H}_2$OH); 4.36 (2H, q, *J* = 6.8, OC$\underline{H}_2$CH$_3$); 1.33 (3H, t, *J* = 6.7, OCH$_2$C$\underline{H}_3$). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 158.3; 148.7; 146.4; 135.3; 121.0; 99.6; 61.4; 54.8; 14.1. Found, *m*/*z*: 238.0937 $[M+H]^+$. $C_9H_{12}N_5O_3$. Calculated, *m*/*z*: 238.0935.

Methyl 1-[3-(ethoxycarbonyl)-1*H*-pyrazol-5-yl]-1*H*-1,2,3-triazole-4-carboxylate (11c). Yield 390 mg (86%), beige solid, mp 190–191°C. IR spectrum, ν, cm^{-1}: 3196 (NH), 1719 (C=O), 1684 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.59 (1H, s, NH); 9.28 (1H, s, H-5 triazole); 7.29 (1H, s, H-4 pyrazole); 4.35 (2H, q, *J* = 6.9, OC$\underline{H}_2$CH$_3$); 3.86 (3H, s, OCH$_3$); 1.33 (3H, t, *J* = 6.9, OCH$_2$C$\underline{H}_3$). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 160.4; 158.2; 145.4; 139.2; 135.4; 127.4; 100.6; 61.5; 52.1; 14.1. Found, *m*/*z*: 266.0886 $[M+H]^+$. $C_{10}H_{12}N_5O_4$. Calculated, *m*/*z*: 266.0884. Found, %: C 45.31; H 4.08; N 26.43. $C_{10}H_{11}N_5O_4$. Calculated, %: C 45.29; H 4.18; N 26.41.

Ethyl 5-(4-cyclopentyl-1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylate (11d). Yield 425 mg (91%), beige solid, mp 179–180°C. IR spectrum, ν, cm^{-1}: 3246 (NH), 2955 (CH), 1711 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.40 (1H, s, NH); 8.40 (1H, s, H-5 triazole); 7.14 (1H, s, H-4 pyrazole); 4.34 (2H, q, *J* = 7.1, OC$\underline{H}_2$CH$_3$); 3.16 (1H, q, *J* = 7.4, CH cyclopentane); 2.06–1.96 (2H, m, CH$_2$ cyclopentane); 1.74–1.60 (6H, m, CH$_2$ cyclopentane); 1.32 (3H, t, *J* = 7.1, OCH$_2$C$\underline{H}_3$). ^{13}C NMR spectrum (75 MHz, DMSO-d_6), δ, ppm: 158.4; 152.0; 146.8; 135.2; 119.2; 99.4; 61.4; 36.1; 32.7; 24.7; 14.1. Found, *m*/*z*: 276.1451 $[M+H]^+$. $C_{13}H_{18}N_5O_2$. Calculated, *m*/*z*: 276.1455.

Synthesis of 5-(1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylic acids 12a–d (General method). The corresponding carboxylate **11a**–**d** (0.0019 mol) was dissolved in aqueous KOH (330 mg, 0.0059 mol; 25 ml of solution). The formed solution was stirred at 60°C for 12 h. Then, the solution was passed through a thin layer of silica gel and acidified by 2 M aqueous HCl to pH 1. The formed precipitate was filtered off and dried in a vacuum desiccator over P_2O_5. The filtrate was extracted with EtOAc, the organic phase was separated and dried over anhydrous Na_2SO_4. The dried organic phase was evaporated under reduced pressure on the rotary evaporator to afford a solid. Both solids were combined.

5-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylic acid (12a). Yield 344 mg (71%), colorless solid,

mp 269–270°C. IR spectrum, ν, cm^{-1}: 3141 (NH), 2985 (OH), 1689 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.38 (1H, s, NH); 13.88 (1H, br. s, COOH); 9.18 (1H, s, H-5 triazole); 7.98 (2H, d, *J* = 7.3, H Ph); 7.48 (2H, t, *J* = 7.5, H Ph); 7.37 (1H, t, *J* = 7.3, H Ph); 7.19 (1H, s, H-4 pyrazole). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 159.8; 146.9; 146.2; 136.5; 130.0; 129.0; 128.4; 125.5; 119.5; 99.6. Found, *m*/*z*: 256.0834 $[M+H]^+$. $C_{12}H_{10}N_5O_2$. Calculated, *m*/*z*: 256.0829.

5-[4-(Hydroxymethyl)-1*H*-1,2,3-triazol-1-yl]-1*H*-pyrazole-3-carboxylic acid (12b). Yield 318 mg (80%), orange solid, mp 264–265°C. IR spectrum, ν, cm^{-1}: 3213 (OH), 2971–2350 (CO<u>OH</u>), 1699 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 14.27 (1H, s, NH); 13.81 (1H, br. s, COOH); 8.45 (1H, s, H-5 triazole); 7.11 (1H, s, H-4 pyrazole); 5.29 (1H, br. s, CH_2O<u>H</u>); 4.58 (2H, s, C<u>H</u>$_2$OH). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 160.0; 148.7; 146.2; 136.6; 120.9; 99.4; 54.8. Found, *m*/*z*: 210.0614 $[M+H]^+$. $C_7H_8N_5O_3$. Calculated, *m*/*z*: 210.0622.

1-(3-Carboxy-1*H*-pyrazol-5-yl)-1*H*-1,2,3-triazole-4-carboxylic acid (12c). Yield 340 mg (80%), colorless solid, mp 190–191°C. IR spectrum, ν, cm^{-1}: 3142 (NH), 3088–2526 (CO<u>OH</u>), 1694 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 14.38 (1H, s, NH); 13.59 (2H, br. s, COOH); 9.13 (1H, s, H-5 triazole); 7.20 (1H, s, H-4 pyrazole). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 161.4; 159.7; 145.5; 140.3; 136.6; 127.1; 100.4. Found, *m*/*z*: 224.0414 $[M+H]^+$. $C_7H_6N_5O_4$. Calculated, *m*/*z*: 224.0414.

5-(4-Cyclopentyl-1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylic acid (12d). Yield 263 mg (56%), colorless solid, mp 244–245°C. IR spectrum, ν, cm^{-1}: 3300 (NH), 3200–2574 (CO<u>OH</u>), 2957 (cyclopentyl), 1664 (C=O). ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.22 (1H, s, NH); 13.75 (1H, br. s, COOH); 8.38 (1H, s, H-5 triazole); 7.08 (1H, s, H-4 pyrazole); 3.18 (1H, q, *J* = 7.9, CH cyclopentane); 2.06–1.97 (2H, m, CH_2 cyclopentane); 1.83–1.55 (6H, m, CH_2 cyclopentane). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 159.8; 152.0; 146.4; 136.5; 119.2; 99.3; 36.1; 32.8; 24.7. Found, *m*/*z*: 248.1144 $[M+H]^+$. $C_{11}H_{14}N_5O_2$. Calculated, *m*/*z*: 248.1142.

Synthesis of 4-(1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylate 13a–d (General method). Ethyl 4-azido-1*H*-pyrazole-3-carboxylate (**10**) (3.3 mmol) and the corresponding acetylene (phenylacetylene, propargyl alcohol, methyl propiolate, and cyclopentylacetylene; in the case of compound **13b**, a 4-fold excess of propargyl alcohol was used) (3.3 mmol) were dissolved in MeOH (15 ml). A solution of Na ascorbate (67 mg, 0.33 mmol, 10 mol %) in H_2O (7.5 ml) was added with vigorous stirring to the reagent solution. The flask was evacuated and filled with argon. A solution of $CuSO_4 \cdot 5H_2O$ (43 mg, 0.17 mmol, 5 mol %) in H_2O (7.5 ml) was then added to the reaction mixture. The reaction mixture was stirred at 25°C for 48 h (for compound **13a**), 16 h (for compounds **13b**,**c**), or at 60°C for 72 h (for compound **13d**). The solvent was removed from the reaction mixture under reduced pressure on the rotary evaporator. The dry residue was extracted with EtOAc, the organic layer was washed with H_2O and separated, and then dried over anhydrous Na_2SO_4 and evaporated under reduced pressure on the rotary evaporator to obtain a solid residue.

Ethyl 4-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-5-carboxylate (13a). Yield 617 mg (66%), beige solid, mp 220–221°C. IR spectrum, ν, cm^{-1}: 3240 (NH), 1703 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.15 (1H, br. s, NH); 8.93 (1H, s, H-5 triazole); 8.54 (1H, br. s, H-3 pyrazole); 7.91 (2H, d, *J* = 7.6, H Ph); 7.48 (2H, t, *J* = 7.6, H Ph); 7.36 (1H, t, *J* = 7.4, H Ph); 4.20 (2H, q, *J* = 7.2, OC<u>H</u>$_2$CH$_3$); 1.12 (3H, t, *J* = 7.1, OCH$_2$C<u>H</u>$_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 160.5; 146.0; 136.0; 130.4; 129.0; 128.1; 125.2; 124.4; 121.1; 60.6; 13.7. Found, *m*/*z*: 284.1144 $[M+H]^+$. $C_{14}H_{14}N_5O_2$. Calculated, *m*/*z*: 284.1142.

Ethyl 4-[4-(hydroxymethyl)-1*H*-1,2,3-triazol-1-yl]-1*H*-pyrazole-5-carboxylate (13b). Yield 241 mg (31%), pale-yellow solid, mp 164–165°C. IR spectrum, ν, cm^{-1}: 3371 (OH), 3247 (NH), 1705 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.49 (0.2H, br. s, NH); 14.04 (0.8H, br. s, NH); 8.45 (0.8H, br. s, H-3 pyrazole); 8.12 (0.2H, br. s, H-3 pyrazole); 8.31 (1H, s, H-5 triazole); 5.28 (1H, s, CH$_2$O<u>H</u>); 4.60 (2H, s, C<u>H</u>$_2$OH); 4.21 (2H, q, *J* = 7.1, OC<u>H</u>$_2$CH$_3$); 1.18 (3H, t, *J* = 7.1, OCH$_2$C<u>H</u>$_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 160.6; 147.7; 135.7; 127.9; 125.5; 121.4; 60.6; 54.9; 13.8. Found, *m*/*z*: 238.0936 $[M+H]^+$. $C_9H_{12}N_5O_3$. Calculated, *m*/*z*: 238.0935.

Methyl 1-[5-(ethoxycarbonyl)-1*H*-pyrazol-4-yl]-1*H*-1,2,3-triazole-4-carboxylate (13c). Yield 718 mg (82%), colorless solid, mp 195–196°C. IR spectrum, ν, cm^{-1}: 3150 (NH), 1740 (C=O), 1703 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.14 (1H, br. s, NH); 9.15 (1H, s, H-5 triazole); 8.55 (1H, s, H-3 pyrazole); 4.16 (2H, q, *J* = 7.1, OC<u>H</u>$_2$CH$_3$); 3.86 (3H, s, OCH$_3$); 1.12 (3H, t, *J* = 7.0, OCH$_2$C<u>H</u>$_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 160.6; 160.4; 138.3; 136.0; 132.0; 128.4; 120.3; 60.7; 52.0; 13.8. Found, *m*/*z*: 266.0890 $[M+H]^+$. $C_{10}H_{12}N_5O_4$. Calculated, *m*/*z*: 266.0884.

Ethyl 4-(4-cyclopentyl-1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-5-carboxylate (13d). Yield 200 mg (22%), brown solid, mp 149–150°C. IR spectrum, ν, cm^{-1}: 3230 (NH), 2957 (cyclopentyl), 1700 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.12 (1H, br. s, NH); 8.34 (1H, s, H-5 triazole); 8.18 (1H, s, H-3 pyrazole); 4.17 (2H, q, *J* = 7.1, OC<u>H</u>$_2$CH$_3$); 3.15 (1H, t, *J* = 7.5, CH cyclopentane); 2.02 (2H, d, *J* = 9.1, CH_2 cyclopentane); 1.73–1.60 (6H, m, CH_2 cyclopentane); 1.13 (3H, t, *J* = 7.1, OCH$_2$C<u>H</u>$_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 160.1; 150.8; 135.0; 129.4; 123.8; 121.6; 60.7; 36.1; 32.9; 24.7; 13.8. Found, *m*/*z*: 276.1449 $[M+H]^+$. $C_{13}H_{18}N_5O_2$. Calculated, *m*/*z*: 276.1455.

Synthesis of (1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-3-carboxylic acids 14a–d (General method). The corresponding carboxylate **13a**–**d** (0.0015 mol) was dissolved in aqueous KOH (295 mg, 0.0053 mol; 30 ml of solution). The formed solution was stirred at 70°C for 12 h. Then, the solution was passed through a thin layer of silica gel and acidified by 2 M aqueous HCl to pH 1. The formed precipitate was filtered off and dried in a vacuum desiccator over P_2O_5. The filtrate was extracted with

EtOAc, the organic phase was separated and dried over anhydrous Na_2SO_4. The dried organic phase was evaporated under reduced pressure on the rotary evaporator to afford a solid. Both solids were combined.

4-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-5-carboxylic acid (14a). Yield 211 mg (55%), colorless solid, mp 262–263°C. IR spectrum, ν, cm^{-1}: 3176 (NH), 3095 (OH), 1687 (C=O). ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 13.88 (2H, br. s, NH, COOH); 8.94 (1H, s, H-5 triazole); 8.36 (1H, br. s, H-3 pyrazole); 7.91 (2H, d, *J* = 7.7, H Ph); 7.48 (2H, t, *J* = 7.6, H Ph); 7.37 (1H, t, *J* = 7.4, H Ph). 13C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 161.3; 146.0; 136.3; 130.5; 129.0; 128.1; 125.3; 124.3; 121.3. Found, *m*/*z*: 256.0828 $[M+H]^+$. $C_{12}H_{10}N_5O_2$. Calculated, *m*/*z*: 256.0829.

4-[4-(Hydroxymethyl)-1*H*-1,2,3-triazol-1-yl]-1*H*-pyrazole-5-carboxylic acid (14b). Yield 188 mg (60%), light-orange solid, mp 212–213°C. IR spectrum, ν, cm^{-1}: 3154 ($CH_2\underline{O}H$), 2925 ($CO\underline{O}H$), 1716 (C=O). ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm: 8.33 (1H, s, H-5 triazole); 8.26 (1H, s, H-3 pyrazole); 4.59 (2H, s, $C\underline{H}_2OH$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 161.0; 147.6; 130.9; 130.5 (br. s); 125.3; 121.6; 54.9. Found, *m*/*z*: 210.0627 $[M+H]^+$. $C_7H_8N_5O_3$. Calculated, *m*/*z*: 210.0622.

1-(5-Carboxy-1*H*-pyrazol-4-yl)-1*H*-1,2,3-triazole-4-carboxylic acid (14c). Yield 264 mg (79%), colorless solid, mp 268–269°C. IR spectrum, ν, cm^{-1}: 3379 (NH), 3344 ($CO\underline{O}H$), 3304 ($CO\underline{O}H$), 1715 (C=O). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm: 13.98 (1H, br. s, NH); 13.26 (2H, br. s, COOH); 9.02 (1H, s, H-5 triazole); 8.41 (1H, br. s, H-3 pyrazole). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 161.6; 161.0; 139.4; 136.3; 131.6; 128.3; 120.7. Found, *m*/*z*: 224.0423 $[M+H]^+$. $C_7H_6N_5O_4$. Calculated, *m*/*z*: 224.0414.

4-(4-Cyclopentyl-1*H*-1,2,3-triazol-1-yl)-1*H*-pyrazole-5-carboxylic acid (14d). Yield 278 mg (75%), brown solid, mp 239–240°C. IR spectrum, ν, cm^{-1}: 3147 (NH), 2957 (cyclopentane), 2454 ($CO\underline{O}H$), 1681 (C=O). ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 13.69 (2H, br. s, NH, COOH); 8.25 (1H, br. s, H-3 pyrazole); 8.21 (1H, s, H-5 triazole); 3.17 (1H, q, *J* = 7.6, CH cyclopentane); 2.02 (2H, d, *J* = 8.2, CH_2 cyclopentane); 1.78–1.57 (6H, m, CH_2 cyclopentane). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 160.9; 150.8; 135.6; 127.8; 123.6; 121.8; 36.1; 32.8; 24.7. Found, *m*/*z*: 248.1152 $[M+H]^+$. $C_{11}H_{14}N_5O_2$. Calculated, *m*/*z*: 248.1142.

1,5-Dimethyl-3,7-di(prop-2-yn-1-yl)-3,7-diazabicyclo-[3.3.1]nonan-9-one (16). 1,5-Dimethyl-3,7-diazabicyclo-[3.3.1]nonan-9-one (**15**) (3.00 g, 0.018 mol) was dissolved in MeCN (50 ml). Propargyl bromide (2.71 ml, 4.25 g, 0.036 mol) and DIPA (6.3 ml, 4.65 g, 0.036 mol) were added to the solution. The reaction mixture was heated under reflux with stirring for 10 h. The progress of the reaction was monitored by TLC (visualization in iodine chamber). The solvent was evaporated to dryness under reduced pressure on the rotary evaporator. The residue was dissolved in CH_2Cl_2 (75 ml) and washed with H_2O (2×45 ml). The organic layer was separated and dried over anhydrous Na_2SO_4. The solvent was evaporated to dryness under reduced pressure on the rotary evaporator. A brown oil formed, which crystallized upon standing. The brown oil was purified by flash column chromatography on silica gel, eluent petroleum ether – EtOAc, 1:1. After purification, a colorless oil formed, which crystallized into colorless solid. Yield 3.2 g (73%), colorless solid, mp 69–70°C. IR spectrum, ν, cm^{-1}: 3299 (CH alkyne), 3268 (CH alkyne), 1729 (C=O). ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 3.39 (4H, d, *J* = 2.5, $2CH_2$); 3.09 (4H, d, *J* = 11.1, $2CH_2$); 2.60 (4H, d, *J* = 10.8, $2CH_2$); 2.24 (2H, t, *J* = 2.4, 2CH); 1.03 (6H, s, $2CH_3$). ^{13}C NMR spectrum (126 MHz, $CDCl_3$), δ, ppm: 214.6; 78.2; 73.6; 64.3; 46.3; 45.7; 19.9. Found, *m*/*z*: 245.16478 $[M+H]^+$. $C_{15}H_{21}N_2O$. Calculated, *m*/*z*: 245.16484. Found, %: C 73.63; H 8.30; N 11.38. $C_{15}H_{20}N_2O$. Calculated, %: C 73.74; H 8.25; N 11.47.

Diethyl 5,5'-{4,4'-[(1,5-dimethyl-9-oxo-3,7-diazabicyclo-[3.3.1]nonane-3,7-diyl)bis(methylene)]bis(1*H*-1,2,3-triazole-4,1-diyl)}bis(1*H*-pyrazole-3-carboxylate) (17). Ethyl 5-azido-1*H*-pyrazole-3-carboxylate **7** (593 mg, 3.27 mmol) and bispropargyl **16** (400 mg, 1.64 mmol) were dissolved in *t*-BuOH (10 ml). A solution of Na ascorbate (33 mg, 0.164 mmol, 10 mol %) in H_2O (5 ml) was added to the reagent solution. The flask was evacuated and filled with argon. A solution of $CuSO_4·5H_2O$ (20 mg, 0.08 mmol, 5 mol %) in H_2O (5 ml) was then added to the reaction mixture. The reaction mixture was stirred at room temperature for 2 days. A beige precipitate formed. The progress of the reaction was monitored by TLC (eluent petroleum ether – EtOAc, 1:1) by the disappearance of spots of the reagents (visualization in the iodine chamber). The formed precipitate was filtered off, washed with H_2O, and dried in a vacuum desiccator over P_2O_5 to constant weight. The filtrate was extracted with EtOAc, washed with H_2O, the organic phase was separated and dried over anhydrous Na_2SO_4. The dried organic phase was evaporated under reduced pressure on the rotary evaporator to afford a solid. The extracted product was purified by flash chromatography on silica gel, eluent $CHCl_3$–MeOH, 5:1. Both solids were combined. Yield 878 mg (88%), beige solid, mp 202–203°C. IR spectrum, ν, cm^{-1}: 1730 (C=O), 1722 (EtO–$\underline{C=O}$). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.44 (2H, br. s, NH); 8.51 (2H, s, H-5 triazole); 7.20 (2H, s, H-4 pyrazole); 4.36 (4H, q, *J* = 7.1, $2OC\underline{H}_2CH_3$); 3.74 (4H, s, $2CH_2$); 3.08 (4H, d, *J* = 10.7, $2CH_2$); 2.40 (4H, d, *J* = 10.7, $2CH_2$); 1.33 (6H, t, *J* = 7.1, $2CH_2C\underline{H}_3$); 0.86 (6H, s, $2CH_3$). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 214.3; 158.4; 146.1; 143.8; 135.5; 121.9; 99.5; 64.4; 61.4; 50.8; 46.0; 20.0; 14.1. Found, *m*/*z*: 607.2866 $[M+H]^+$. $C_{27}H_{35}N_{12}O_5$. Calculated, *m*/*z*: 607.2848. Found, %: C 52.83; H 5.44; N 27.75. $C_{27}H_{34}N_{12}O_5$. Calculated, %: C 53.46; H 5.65; N 27.71.

5,5'-{4,4'-[(1,5-Dimethyl-9-oxo-3,7-diazabicyclo[3.3.1]-nonane-3,7-diyl)bis(methylene)]bis(1*H*-1,2,3-triazole-4,1-diyl)}bis(1*H*-pyrazole-3-carboxylic acid) hydrochloride dihydrate (18·HCl·2H$_2$O). Biscarboxylate **17** (1.543 g, 0.0025 mol) was dissolved in aqueous KOH (0.56 g, 0.01 mol; 25 ml of solution). The formed solution was stirred at 70°C for 24 h. Then, the solution was passed through a thin layer of silica gel and acidified by 2 M aqueous HCl to pH 2–3. The formed beige precipitate was filtered off, washed with a small amount of cold H_2O, and dried in a vacuum desiccator over P_2O_5 to constant weight.

Yield 933 mg (68%), light-gray solid, mp 267–268°C. IR spectrum, ν, cm^{-1}: 3111 (OH), 1713 (C=O). ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.28 (2H, s, NH); 11.52 (2H, br. s, COOH); 8.80 (2H, s, H-5 triazole); 7.11 (2H, s, H-4 pyrazole); 4.24 (4H, s, $2NCH_2$); 3.62 (4H, d, *J* = 10.6, $2CH_2$ bispidine); 2.96 (4H, d, *J* = 10.6, $2CH_2$ bispidine); 0.87 (6H, s, $2CH_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 208.7; 159.8; 146.0; 139.4; 137.1; 123.7; 99.2; 62.2; 49.6; 45.6; 16.0. Found, *m*/*z*: 551.2213 $[M+H]^+$. $C_{23}H_{27}N_{12}O_5$. Calculated, *m*/*z*: 551.2222. Found, %: C 44.40; H 5.50; N 26.90. $C_{23}H_{31}ClN_{12}O_7$. Calculated, %: C 44.34; H 5.02; N 26.98.

Diethyl 4,4'-{[(1,5-dimethyl-9-oxo-3,7-diazabicyclo-[3.3.1]nonane-3,7-diyl)bis(methylene)]bis(1*H*-1,2,3-triazole-4,1-diyl)}bis(1*H*-pyrazole-3-carboxylate) (19). Ethyl 4-azido-1*H*-pyrazole-3-carboxylate (**10**) (2.32 g, 12.8 mmol) and bispropargyl **16** (1.55 g, 6.4 mmol) were dissolved in MeOH (70 ml). A solution of Na ascorbate (127 mg, 0.64 mmol, 10 mol %) in H_2O (35 ml) was added to the reagent solution. The flask was evacuated and filled with argon. A solution of $CuSO_4 \cdot 5H_2O$ (80 mg, 0.32 mmol, 5 mol %) in H_2O (35 ml) was then added to the reaction mixture. The reaction mixture was stirred at room temperature for 12 h. A beige precipitate started to form immediately. The progress of the reaction was monitored by TLC (eluent petroleum ether – EtOAc, 1:1) by the disappearance of spots of the reagents (visualization in the iodine chamber). The formed precipitate was filtered off and washed with H_2O, and dried in a vacuum desiccator over P_2O_5 to constant weight. The filtrate was extracted with CH_2Cl_2, washed with H_2O, the organic phase was separated and dried over anhydrous Na_2SO_4. The dried organic phase was evaporated under reduced pressure on the rotary evaporator to afford a solid. The extracted and filtered products were purified by flash chromatography on silica gel, eluent $CHCl_3$–MeOH, 5:1. Both solids were then combined. Yield 3.03 g (78%), beige solid, mp 211–212°C. IR spectrum, ν, cm^{-1}: 3235 (NH), 2928 (CH_2), 1710 (C=O ester), 1682 (C=O ketone). ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 14.12 (2H, br. s, 2NH); 8.36 (2H, br. s, H-5 pyrazole); 8.32 (2H, s, H-5 triazole); 4.17 (4H, q, *J* = 7.1, $2OC\underline{H}_2CH_3$); 3.72 (4H, s, $2NCH_2$); 3.09 (4H, d, *J* = 10.6, $2CH_2$ bispidine); 2.41 (4H, d, *J* = 10.6, $2CH_2$ bispidine); 1.14 (6H, t, *J* = 7.1, $2OCH_2C\underline{H}_3$); 0.87 (6H, s, $2CH_3$). ^{13}C NMR spectrum (126 MHz, DMSO-d_6), δ, ppm: 214.4; 160.1; 142.9; 133.4; 129.0; 126.5; 121.5; 64.5; 60.7; 51.0; 46.0; 20.0; 14.0. Found, *m*/*z*: 607.2844 $[M+H]^+$. $C_{27}H_{35}N_{12}O_5$. Calculated, *m*/*z*: 607.2848.

4,4'-{[(1,5-Dimethyl-9-oxo-3,7-diazabicyclo[3.3.1]-nonane-3,7-diyl)bis(methylene)]bis(1*H*-1,2,3-triazole-4,1-diyl)}bis(1*H*-pyrazole-3-carboxylic acid) trihydrochloride monoacetate (20·3HCl·AcOH). Biscarboxylate **19** (600 mg, 0.99 mmol) was dissolved in glacial AcOH (20 ml), and aqueous HCl (6.69 M, 22%, ρ 1.108 g/cm^3, 25 ml) was added. A dark-emerald solution was formed, the color of which, when heated under reflux, gradually turned into yellow. The reaction mixture was heated under reflux for 4 h and then left overnight at room temperature. The reaction mixture was evaporated to dryness on the rotary evaporator under reduced pressure and dried in a vacuum desiccator successively over P_2O_5 and KOH for 2 days. The product was isolated as monoacetate trihydrochloride. Yield 595 mg (84%), yellow solid, mp 244–245°C. IR spectrum, ν, cm^{-1}: 2922 (OH), 1728 (C=O). ^1H NMR spectrum (400 MHz, DMSO-d_6), δ, ppm (*J*, Hz): 11.44 (2H, br. s, NH); 10.29 (2H, br. s, 2COOH); 8.69 (2H, s, H-5 triazole); 8.24 (2H, s, H-5 pyrazole); 4.25 (4H, s, $2NCH_2$); 3.60 (4H, d, *J* = 11.3, $2CH_2$ bispidine); 2.97 (4H, d, *J* = 11.2, $2CH_2$ bispidine); 1.90 (3H, s, CH_3COOH); 0.89 (6H, s, $2CH_3$). ^{13}C NMR spectrum (101 MHz, DMSO-d_6), δ, ppm: 208.6; 172.1 ($CH_3\underline{C}OOH$); 161.0; 138.6; 132.81; 130.45; 128.4; 121.3; 62.3; 49.9; 45.6; 21.2 ($\underline{C}H_3COOH$); 16.0. Found, *m*/*z*: 551.2231 $[M+H]^+$. $C_{23}H_{27}N_{12}O_5$. Calculated, *m*/*z*: 551.2222. Found, %: C 42.07; H 4.89; N 23.37. $C_{25}H_{33}Cl_3N_{12}O_7$. Calculated, %: C 41.71; H 4.62; N 23.35.

Supplementary information file, containing ^1H and ^{13}C NMR, as well as ^1H–^{13}C HSQC, ^1H–^{13}C HMBC, ^1H–^{15}N HMBC 2D NMR spectra for compounds **6**, **7**, **10**, is available at the journal website at http://link.springer.com/journal/10593.

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