Study of alkaloids of the Siberian and Altai flora
14.* Synthesis of alkaloid-based tertiary *N*-(3-arylprop-2-ynyl)amines**

S. A. Osadchii,[a] E. E. Shults,[a] E. V. Polukhina,[a] M. M. Shakirov,[a] S. F. Vasilevskii,[b] A. A. Stepanov,[b] and G. A. Tolstikov[a]*

[a]*N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, 9 prosp. Akad. Lavrent´eva, 630090 Novosibirsk, Russian Federation. Fax: +7 (383) 330 9752. E-mail: schultz@nioch.nsc.ru*

[b]*Institute of Chemical Kinetics and Combustion, Siberian Branch of the Russian Academy of Sciences, 3 ul. Institutskaya, 630090 Novosibirsk, Russian Federation. Fax: +7 (383) 330 7350*

3-Arylprop-2-ynylamines containing the key fragment of known alkaloids of the Altai flora were synthesized by the Sonogashira and Mannich reactions.

Key words: Sonogashira reaction, Mannich reaction, alkaloids, (−)-anabasine, (−)-cytisine, (−)-ephedrine, (+)-pseudoephedrine, alkynes.

Acetylenic nitrogen-containing compounds have medically valuable biological properties. Some of these compounds serve as efficient anticancer agents,[2,3] antitumor antibiotics,[4] HIV reverse transcriptase inhibitors,[5] and important synthetic intermediates.[6—10] Among 3-arylprop-2-ynyldialkylamine derivatives of the general formula Ar—C≡C—CH_2—N(Alk)$_2$ (**1**), enzyme inhibitors, *viz.*, inhibitors of mammalian squalene epoxidase, were found.[11]

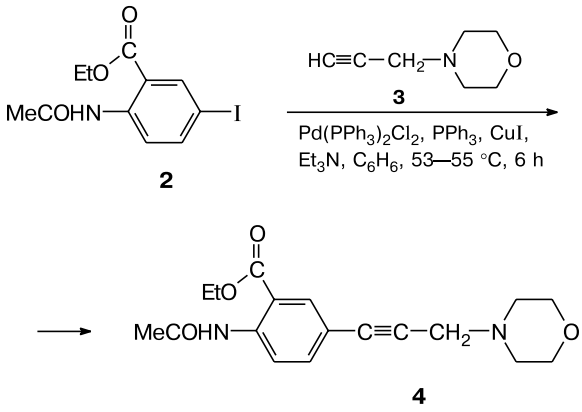
The aim of the present study was to synthesize 3-arylprop-2-ynylamines **1** starting from 2-(*N*-acetylamino)-5-iodobenzoates and secondary amines, including those based on available alkaloids of the Altai flora.

Results and Discussion

One of approaches to the synthesis of compounds **1** is based on the Sonogashira reaction,[12] *viz.*, the cross-coupling of aryl halides with alkynes (in the case under consideration, with 3-dialkylaminoprop-1-ynes) catalyzed by the palladium complex and copper(I) salts. Another approach to the synthesis of these compounds is based on the classical Mannich reaction involving the three-component reaction of terminal arylalkyne, formaldehyde (generated *in situ* from paraformaldehyde), and secondary amine.[13,14] The use of CuCl [5,9] or CuI [15] as the catalyst substantially extended the scope of the Mannich reaction, particularly, for poorly active alkynes.

Initially, we have tested the synthesis of compounds **1** using one of the known modifications of the Sonogashira cross-coupling reaction of ethyl 2-(*N*-acetylamino)-5-iodobenzoate (**2**) with 3-*N*-morpholinopropyne (**3**) as an example.[16] This reaction afforded the target ethyl 2-(*N*-acetylamino)-5-(3-morpholinoprop-1-yn-1-yl)benzoate (**4**) in 66% yield (Scheme 1).

Scheme 1



The Mannich condensation proved to be the method of choice for the synthesis of compounds **1** because the starting reagents are more readily available. We chose methyl 2-(*N*-acetylamino)-5-ethynylbenzoate (**5**) as the acetylenic component; diethylamine (**6a**), pyrrolidine (**6b**), piperidine (**6c**), morpholine (**6d**), and alkaloids, such as (−)-anabasine (**6e**), (−)-cytisine (**6f**), (−)-ephe-

* For Part 13, see Ref. 1.

** Dedicated to the memory of Academician N. N. Vorozhtsov on the 100th anniversary of his birth.

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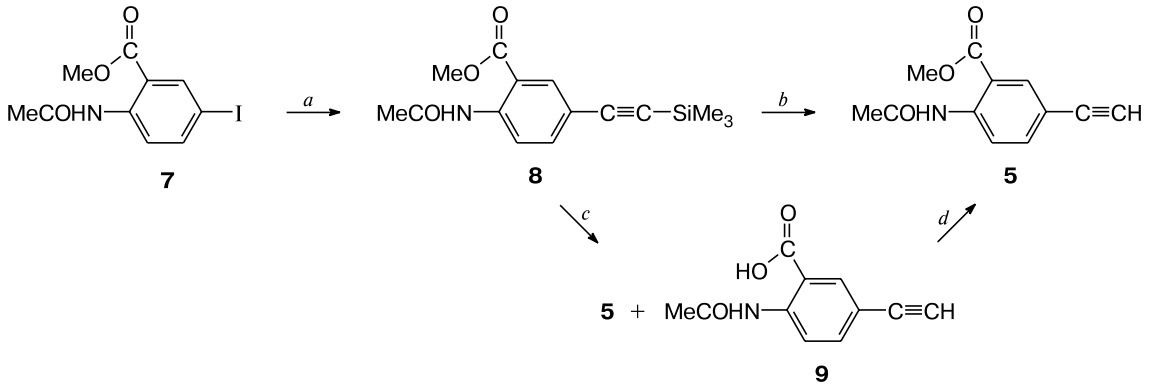
Scheme 2



Reagents and conditions: *a*. $Me_3SiC{\equiv}CH$, $Pd(PPh_3)_2Cl_2$, PPh_3, CuI, Et_3N, C_6H_6, 53—55 °C, 8 h. *b*. Bu_4NF, CH_2Cl_2. *c*. K_2CO_3, MeOH. *d*. CH_2N_2, Et_2O.

drine (**6g**), and (+)-pseudoephedrine (**6h**), were used as secondary amines.

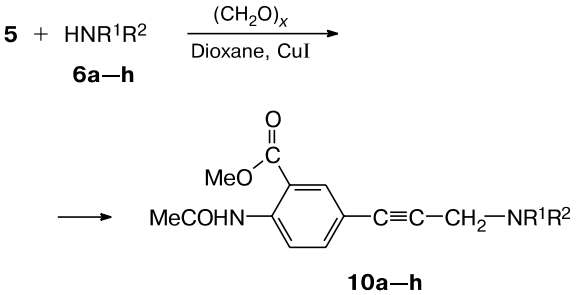
Methyl 2-(*N*-acetylamino)-5-ethynylbenzoate (**5**) necessary for the Mannich reaction was synthesized according to Scheme 2. The condensation reaction of methyl 2-(*N*-acetylamino)-5-iodobenzoate (**7**) with trimethylsilylacetylene was carried out under the conditions described in the study.[16] Desilylation of methyl 2-(*N*-acetylamino)-5-(trimethylsilylethynyl)benzoate (**8**) thus prepared (in 95% yield) with Bu_4NF in CH_2Cl_2 afforded target compound **5** in 77% yield. The use of the less expensive reagent, K_2CO_3, for the cleavage of silyl derivative **8** also gave rise to product **5** (in 76% yield), but this reaction additionally produced 2-(*N*-acetylamino)-5-ethynylbenzoic acid (**9**) in ~2% yield. The structure of the latter product was confirmed by spectroscopic data and as well as by its transformation into compound **5** by methylation with diazomethane.

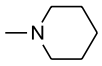
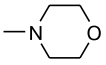
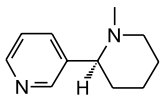
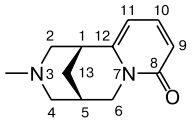
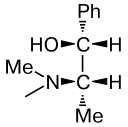
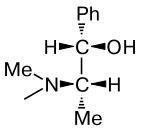
The condensation of methyl 2-(*N*-acetylamino)-5-ethynylbenzoate (**5**) with secondary amines **6a—h** and formaldehyde, which was generated *in situ* from paraformaldehyde, was carried out by the modified Mannich reaction[5] in the presence of catalytic amounts of CuI in dioxane at 85—90 °C. The yields of target compounds **10a—g** were 75—92% based on consumed arylacetylene **5** (Scheme 3); the yield of compound **10h** was somewhat lower (51%).

The reaction of (−)-ephedrine (**6g**) produced target Mannich base **10g** (in 86% yield) along with (4*S*,5*R*)-3,4-dimethyl-5-phenyloxazolidine (**11**). The reaction of (+)-pseudoephedrine (**6h**) gave not only target product **10h** (in 51% yield) but also (4*S*,5*S*)-3,4-dimethyl-5-phenyloxazolidine (**12**).

The formation of by-products **11** and **12** can be explained as follows. The hemiaminals (1*R*,2*S*)-2-(*N*-hydroxymethyl-*N*-methylamino)-1-phenylpropan-1-ol (**13**) and (1*S*,2*S*)-2-(*N*-hydroxymethyl-*N*-methyl-

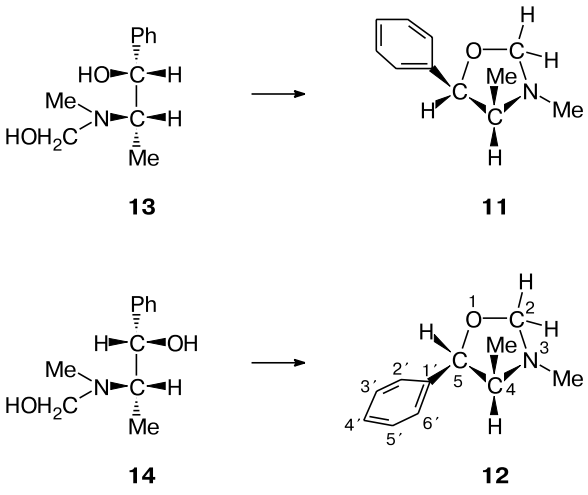
Scheme 3



6, 10	NR^1R^2	Yield of **10** (%)
a	NEt_2	90
b		92
c		87
d		75
e		77
f		92
g		86
h		51

amino)-1-phenylpropan-1-ol (**14**) are potential intermediates of the reaction of formaldehyde with (−)-ephedrine and (+)-pseudoephedrine, respectively. These compounds can undergo also intramolecular cyclization to form by-products, *viz.*, oxazolidines **11** and **12**, respectively (Scheme 4). Since oxazolidine **11** contains the phenyl and 4-methyl groups in the sterically hindered *cis* positions, the cyclization of compound **13** evidently proceeds more slowly than the cyclization of compound **14** producing oxazolidine **12** with the nonhindered *trans* arrangement of these groups. This accounts for the fact that compound **14** is more rapidly consumed in the side cyclization reaction yielding oxazolidine **12** compared to compound **13** (*cf.* Ref. 17).

Scheme 4



3-Arylprop-2-ynyldialkylamines synthesized in the present study can be of interest as pharmacologically active compounds or their precursors.

Experimental

Freshly distilled solvents were used. The reagents CuI, K_2CO_3, PPh_3, diethylamine, piperidine, and morpholine of high-purity grade (Russia) and the commercial reagents trimethylsilylacetylene and pyrrolidine were used without additional purification. Tetra-*n*-butylammonium fluoride (Sigma—Aldrich) was dried according to a known procedure.[18] Methyl 2-(*N*-acetylamino)-5-iodobenzoate (**7**),[19] ethyl 2-(*N*-acetylamino)-5-iodobenzoate (**2**),[1] and 3-*N*-morpholinopropyne (**3**)[20] were synthesized according to known procedures. The $Pd(PPh_3)_2Cl_2$ complex was synthesized in 90% yield according to a procedure published earlier[21] with the use of DMF (45 mL per gram of $PdCl_2$) instead of benzonitrile as the solvent under reflux until the starting components were dissolved. The product was identified as *trans*-dichlorobis(triphenylphosphine)palladium(II) based on the results of crystallographic analysis (Bruker P4 diffractometer).[22] The alkaloids used in the reactions were isolated from plant sources. (−)-Anabasine ((2*R*)-3-(2-piperidinyl)pyridine) (**6e**), b.p. 104—105 °C (2 Torr) (*cf.* lit. data[23]: b.p. 145—146 °C (14 Torr), n_D^{20} 1.5428; *cf.* lit. data[24]: n_D^{20} 1.5430, $[\alpha]^{23}_{578}$ −62 (*c* 5, C_6H_6), $[\alpha]_D$ −71.24 (*c* 6.9, C_6H_6)) was extracted from the aerial part of the plant Anabasis (*Anabasis aphylla L.*) according to a known procedure.[25] (−)-Cytisine ((1*R*,5*S*)-methano-8*H*-pyrido[1,2-*a*][1,5]diazocin-8-one) (**6f**), m.p. 153—154 °C (from acetone) (*cf.* lit. data[26]: m.p. 153—154 °C (from acetone), $[\alpha]^{20}_{578}$ −122 (*c* 2, H_2O); *cf.* lit. data[23]: $[\alpha]_D^{17}$ −119.6 (H_2O)) was extracted from seeds of the plant *Thermopsis lanceolata R. Br.* (lanceleaf false lupine) according to a procedure published earlier.[26] (−)-Ephedrine ((1*R*,2*S*)-2-methylamino-1-phenylpropan-1-ol) (**6g**), m.p. 38—39 °C (from hexane) (*cf.* lit. data[27]: m.p. 38—39 °C (from petroleum ether)) was prepared from hydrochloride, m.p. 216—217 °C (from EtOH), $[\alpha]^{20}_{578}$ −36 (*c* 2, H_2O) (*cf.* lit. data[27]: m.p. 216—217 °C (from EtOH), $[\alpha]_{589}$ −34.4 (*c* 1.5, H_2O)). The latter was synthesized from ephedrine, which was extracted from the softwood aerial part of *Ephedra equisetina Bunge* (Mongolian ephedra) according to a known procedure.[28] (+)-Pseudoephedrine ((1*S*,2*S*)-2-methylamino-1-phenylpropan-1-ol) (**6h**), m.p. 118—119 °C (sublimed at 100 °C (12 Torr) after crystallization from benzene), $[\alpha]^{20}_{578}$ +53 (*c* 3, EtOH) (*cf.* lit. data[27]: m.p. 118—119 °C (was purified as described above), $[\alpha]_{589}$ +55.5 (*c* 8.1, EtOH)) was isolated from ephedra through hydrochloride without prepurification. Analytical TLC of compounds **5—8** was performed on Silufol UV 254 (Kavalier, Czech Republic) or Sorbfil UV 254 (Sorbpolimer, Russia) plates using an ethyl acetate—hexane mixture (1 : 4, v/v) as the eluent. Analytical TLC of Mannich bases **10a—h** was carried out on 7.5×2.5 cm glass plates coated with a layer of the sorbent (0.04 g cm^{-2}), *viz.*, silica gel G with gypsum (10—40 μm (Sigma)) containing 1 wt.% of the luminophore K-35 (TU 6-09-458-76, Russia) and 1% Na_2CO_3, which were prepared according to a known procedure,[29] with the use of a Pr^iOH—Et_2O mixture (5 : 95, v/v) as the eluent. The components of the mixtures were visualized with UV light or iodine vapor. Iodoaromatic compounds **2** and **7** were detected by irradiation of the plates with UV light for 5 min, resulting in the appearance of brown spots. The preparative chromatography was performed on Al_2O_3 (50—150 μm, TU 6-09-3916-75, Russia, Brockmann activity II) and silica gel (35—70 μm, Acros Organics). To visually monitor the separation and elution of the compounds by the observation under UV light, the sorbents were mixed with the luminophore K-35 (1 wt.%). The melting points were determined on a Kofler apparatus. The optical rotation was measured on a Polamat A polarimeter (Carl Zeiss, λ = 578 nm). The specific rotation was expressed in (deg mL) (g dm)$^{-1}$; the concentrations of the solutions, in g (100 mL)$^{-1}$. The IR spectra were recorded on a Vector 22 spectrometer in KBr pellets or in the pure state. The UV spectra were measured on a Specord UV-Vis spectrophotometer in ethanol ($c = 10^{-4}$ mol L^{-1}). The high-resolution mass spectra were obtained on a Finnigan MAT model 8200 instrument (EI, 70 eV). The elemental analysis was carried out on a CHN-analyzer (model 1106, Carlo Erba, Italy). The NMR spectra were recorded on Bruker AV-300 (300.13 for ^1H and 75.47 MHz for ^{13}C), Bruker AM-400 (400.13 for ^1H and 100.61 MHz for ^{13}C), and Bruker DRX-500 (500.13 for ^1H and 125.76 MHz for ^{13}C) instruments for 10% solutions in $CDCl_3$ at 25 °C, unless other solvent is indicated. The chemical shifts were measured relative to the residual signals of the solvent $CHCl_3$ (δ_H 7.24 and δ_C 76.90) or DMSO (δ_H 2.50 and δ_C 39.50).

The multiplicities of the signals in the ^{13}C NMR spectra were determined using *J*-modulated (JMOD) experiments and proton off-resonance techniques. The assignment of the signals for the carbon atoms in compound **5** was made by determining the multiplicities of the signals based on the results of $^{13}C—^{1}H$ decoupling experiments (monoresonance mode). The assignment of the signals for the carbon atoms in the anabasine and cytisine fragments in the ^{13}C NMR spectra of compounds **10e,f** was made taking into account the chemical shifts of the corresponding carbon atoms for (–)-anabasine[30] and (–)-cytisine.[31] The assignment of the signals for the carbon atoms of the aromatic rings in the ^{13}C NMR spectra of acetylenic compounds **4**, **5**, **8**, **9**, and **10a—h** was performed taking into account the chemical shifts of the corresponding carbon atoms in methyl 2-(*N*-acetylamino)-5-(3-hydroxyprop-1-ynyl)benzoate.[1]

Ethyl 2-(*N*-acetylamino)-5-(3-morpholinoprop-1-yn-1-yl)benzoate (4). Ethyl 2-(*N*-acetylamino)-5-iodobenzoate (**2**) (1.00 g, 3 mmol), CuI (7 mg, 0.04 mmol, 1.3 mol.%), $Pd(PPh_3)_2Cl_2$ (15 mg, 0.02 mmol, 0.7 mol.%), 3-*N*-morpholinopropyne (**3**) (0.50 g, 4 mmol), and triethylamine (2 mL) were successively added with stirring to benzene (20 mL) under argon flow. The reaction mixture was heated at 53—55 °C for 6 h and then cooled to 25 °C. Then $Et_3N \cdot HI$ was filtered off, and the precipitate was washed on a filter with benzene (3×5 mL). The filtrate was concentrated *in vacuo* to ~3 mL, the residue was chromatographed on a short column packed with Al_2O_3 (2×1 cm layer of the sorbent), and the products were eluted with ethyl acetate (30 mL). The eluate was concentrated *in vacuo*, and the residue was crystallized from benzene. Compound **4** was obtained in a yield of 0.65 g (66%), m.p. 113—115 °C. High-resolution mass spectrum, found: *m/z* 330.1539 $[M]^+$. $C_{18}H_{22}N_2O_4$. Calculated: M = 330.1579. ^1H NMR (300.13 MHz), δ: 1.44 (t, 3 H, $C\underline{H}_3CH_2$, *J* = 7 Hz); 2.25 (s, 3 H, MeCO); 2.66 (t, 4 H, $C(3)H_2$, $C(5)H_2$, *J* = 6 Hz); 3.52 (s, 2 H, $C(1')H_2$); 3.80 (t, 4 H, $C(2)H_2$, $C(6)H_2$, *J* = 6 Hz); 4.40 (q, 2 H, $CH_3C\underline{H}_2$, *J* = 7 Hz); 7.58 (dd, 1 H, H(6″), *J* = 9 Hz, *J* = 2 Hz); 8.13 (d, 1 H, H(2″), *J* = 2 Hz); 8.68 (d, 1 H, H(5″), *J* = 9 Hz); 11.15 (br.s, 1 H, NH). ^{13}C NMR (75.47 MHz), δ: 14.3 ($CH_2\underline{C}H_3$); 25.5 ($\underline{C}H_3CO$); 48.1 (C(1′)); 52.5 ($C(3)H_2$, $C(5)H_2$); 61.7 ($\underline{C}H_2CH_3$); 66.9 ($C(2)H_2$, $C(6)H_2$); 84.1, 84.3 (C(2′), C(3′)); 114.9 (C(3″)); 117.0 (C(1″)); 120.2 (C(5″)); 134.2 (C(2″)); 137.3 (C(6″)); 141.3 (C(4″)); 167.7 (COO); 169.0 ($CH_3\underline{C}O$). IR (KBr), ν/cm^{-1}: 749, 791, 858, 908, 1026, 1092, 1118, 1222, 1262, 1313, 1450, 1472, 1524, 1592; 1682, 1702 (C=O); 2206 (C≡C); 2811, 2931; 3264, 3301, 3410 (NH). UV (EtOH), λ_{max}/nm (logε): 235 (4.21), 273 (4.11), 281 (4.12), 325 (3.46).

Methyl 2-(*N*-acetylamino)-5-(trimethylsilylethynyl)benzoate (8). Methyl 2-(acetylamino)-5-iodobenzoate (**7**) (12.8 g, 40.1 mmol), CuI (160 mg, 0.84 mmol, 2.1 mol.%), $Pd(PPh_3)_2Cl_2$ (167 mg, 0.24 mmol, 0.6 mol.%), PPh_3 (165 mg, 0.63 mmol, 1.6 mol.%), triethylamine (16.0 mL, 11.6 g, 115 mmol), and trimethylsilylacetylene (5.00 g, 7.2 mL, 50.9 mmol) were successively added with stirring to benzene (160 mL) under argon flow. The reaction mixture was heated at 53—55 °C for 8 h under argon flow, cooled to 25 °C (TLC monitoring), and kept without stirring for 16 h. The precipitate of $Et_3N \cdot HI$ was filtered off and washed on a filter with benzene (3×5 mL). The combined filtrates were concentrated *in vacuo*, and the resinous residue was kept at 60 °C (3 Torr) and extracted with diethyl ether (4×15 mL). The extract was concentrated, and the residue was crystallized from methanol. Compound **8** was obtained in the crystalline state in a yield of 11.0 g (95%), m.p. 120—121 °C. High-resolution mass spectrum, found: *m/z* 289.1140 $[M]^+$. $C_{15}H_{19}NO_3Si$. Calculated: M = 289.1134. ^1H NMR (400.13 MHz), δ: 0.21 (s, 9 H, $SiMe_3$); 2.18 (s, 3 H, MeCO); 3.88 (s, 3 H, OMe); 7.55 (dd, 1 H, H(4), *J* = 9 Hz, *J* = 2 Hz); 8.08 (d, 1 H, H(6), *J* = 2 Hz); 8.62 (d, 1 H, H(3), *J* = 9 Hz); 11.02 (br.s, 1 H, NH). ^{13}C NMR (75.47 MHz), δ: –0.2 ($SiMe_3$); 25.3 ($\underline{C}H_3CO$); 52.3 (OCH_3); 94.1 (C(2′)); 103.6 (C(1′)); 114.4 (C(1)); 117.1 (C(5)); 119.9 (C(3)); 134.4 (C(6)); 137.6 (C(4)); 141.3 (C(2)); 168.0 (COO); 168.9 ($CH_3\underline{C}O$). IR (CCl_4, *c* = 2%, *d* = 0.1 mm), ν/cm^{-1}: 847, 858, 916, 985, 1088, 1218, 1236, 1250, 1268, 1293, 1316, 1367, 1399, 1438, 1511, 1586; 1694, 1710 (C=O); 2159 (C≡C); 2956; 3281, 3319 (NH). UV (EtOH), λ_{max}/nm (logε): 237 (4.09), 277 (4.04), 285 (4.06), 325 (3.39).

Methyl 2-(*N*-acetylamino)-5-ethynylbenzoate (5) (*cf.* lit. data[5,32]). ***A.*** A solution of Bu_4NF (2.65 g, 10.1 mmol) in CH_2Cl_2 (15 mL) was added dropwise with stirring to a solution of compound **8** (2.17 g, 7.51 mmol) in CH_2Cl_2 (15 mL), the temperature being maintained at 20—25 °C using external cooling. The reaction mixture was kept at 25 °C for 5 min and then extracted with water (3×7.5 mL). The organic layer was washed and then dried with $MgSO_4$. The solvent was removed, and the crystalline precipitate was kept at 40 °C (3 Torr) and dissolved in ethyl acetate (30 mL). The resulting solution was chromatographed on a quartz column packed with silica gel (35—70 μm, Acros-Organics, 15×2.5 cm layer of the sorbent) containing 1 wt.% of the luminophore K-35 (the column was filled by suspending the sorbent in hexane). Upon the elution with ethyl acetate, an UV-absorbing fraction was collected and concentrated to dryness. The residue was suspended in hexane. The precipitate was filtered off, washed with hexane, and dried. Crystals of compound **5** were obtained in a yield of 1.26 g (77%), m.p. 147—148 °C (from AcOEt). High-resolution mass spectrum, found: *m/z* 217.0736 $[M]^+$. $C_{12}H_{11}NO_3$. Calculated: M = 217.0739. ^1H NMR (500.13 MHz), δ: 2.18 (s, 3 H, MeCO); 3.02 (s, 1 H, ≡CH); 3.87 (s, 3 H, OMe); 7.55 (dd, 1 H, H(4), *J* = 9 Hz, *J* = 2 Hz); 8.08 (d, 1 H, H(6), *J* = 2 Hz); 8.62 (d, 1 H, H(3), *J* = 9 Hz); 11.05 (br.s, 1 H, NH). ^{13}C NMR (125.77 MHz, monoresonance), δ: 25.3 (q, $\underline{C}H_3CO$, *J* = 129 Hz); 52.3 (q, OMe, *J* = 148 Hz); 77.0 (d, C(2′), *J* = 252 Hz); 82.2 (dt, C(1′), *J* = 50 Hz, *J* = 5 Hz); 114.4 (dd, C(1), *J* = 7 Hz, *J* = 2 Hz); 115.8 (dd, C(5), *J* = 9 Hz, *J* = 4 Hz); 119.9 (ddd, C(3), *J* = 169 Hz, *J* = 5 Hz, *J* = 1.5 Hz); 134.4 (dd, C(6), *J* = 166 Hz, *J* = 7 Hz); 137.6 (dd, C(4), *J* = 164 Hz, *J* = 7 Hz); 141.5 (td, C(2), *J* = 9 Hz, *J* = 1.5 Hz); 167.8 (m, COO, $\Delta\nu_{1/2}$ = 12 Hz); 168.9 (qd, $CH_3\underline{C}O$, *J* = 6 Hz, *J* = 3 Hz). IR (KBr), ν/cm^{-1}: 795, 848, 1087, 1201, 1235, 1267, 1294, 1322, 1436, 1516, 1595; 1680, 1699 (C=O); 2848, 2956, 3025. IR (CCl_4, *c* = 2%, *d* = 0.1 mm), ν/cm^{-1}: 2119 (C≡C), 3311 (NH, ≡CH). UV (EtOH), λ_{max}/nm (logε): 234 (4.08), 270 (3.93), 278 (3.04), 323 (3.34).

B. Finely dispersed anhydrous K_2CO_3 (0.60 g, 4.35 mmol) was added in one portion to a mixture of compound **8** (9.13 g, 31.6 mmol) and anhydrous MeOH (77 mL) with stirring at 50 °C under argon flow. Then the reaction mixture was stirred without heating for 3 h. The precipitate was filtered off, dried, and extracted with ethyl acetate (30 mL) under reflux. Compound **5** was isolated from the concentrated extract upon cooling in a yield of 5.21 g (76%), m.p. 147—148 °C, and identified based on the IR spectrum. The solvent was removed from the methanolic filtrate at 60 °C (30 Torr). Ethyl acetate (10 mL)

was added to the residue, and the mixture was heated to boiling and cooled. The precipitate was filtered off, dried, treated with AcOH (2 mL), filtered off, washed with water, again dried, and recrystallized from MeOH. **2-(*N*-Acetylamino)-5-ethynylbenzoic acid (9)** was obtained in a yield of 0.15 g (2%), m.p. 245—247 °C (with decomp.). High-resolution mass spectrum, found: *m/z* 203.0580 $[M]^+$. $C_{11}H_9NO_3$. Calculated: M = 203.0582. ^{1}H NMR (DMSO-d_6, 300.13 MHz), δ: 2.13 (s, 4 H, COMe, CO_2H); 4.12 (s, 1 H, ≡CH); 7.60 (dd, 1 H, H(4), J = 9 Hz, J = 2 Hz); 7.97 (d, 1 H, H(6), J = 2 Hz); 8.46 (d, 1 H, H(3), J = 9 Hz); 11.11 (br.s, 1 H, NH). ^{13}C NMR (100.63 MHz), δ: 25.0 ($\underline{C}H_3CO$); 82.4 (C(1′)); 80.3 (C(2′)); 115.5 (C(1)); 116.5 (C(5)); 120.0 (C(3)); 134.3 (C(6)); 136.8 (C(4)); 141.1 (C(2)); 168.6 (COO, $CH_3\underline{C}O$). IR (KBr), ν/cm^{-1}: 791, 847, 1086, 1148, 1202, 1235, 1265, 1294, 1318, 1366, 1400, 1435, 1512, 1590; 1688, 1703 (C=O); 2151 (C≡C); 2957; 3266, 3317 (NH). UV (EtOH), λ_{max}/nm (logε): 227 (4.48), 232 (4.47), 270 (4.38), 278 (4.38), 317 (3.69).

Acid **9** (29 mg) was treated with a 0.7 *N* ethereal solution of CH_2N_2 (3 mL). After removal of excess CH_2N_2 and the solvent, compound **5** was obtained in a yield of 28 mg, m.p. 147—148 °C. Compound **5** was identified based on the ^{1}H NMR spectrum.

Synthesis of Mannich bases 10a—h (general procedure). Paraformaldehyde (67 mg, 2.2 mmol), the corresponding secondary amine **6** (2.0 mmol), CuI (8 mg, 0.02 mmol), and methyl 2-(acetylamino)-5-ethynylbenzoate (**5**) (439 mg, 2.0 mmol) were successively added with stirring to dioxane (3.8 mL) under argon flow. The reaction mixture was heated at 85—90 °C for 3 h and cooled to 25 °C. The solvent was removed *in vacuo* (the bath temperature was 80 °C). The residue was dried at 80 °C (3 Torr) and extracted with diethyl ether (4×5 mL). The extract was concentrated to 3 mL, and then the solvent was allowed to spontaneously evaporate. The residue was triturated with hexane (3 mL), and the crystalline Mannich bases were filtered off.

Mannich base **10c** was purified by preparative TLC on an unfixed layer of Al_2O_3 (1 wt.% of the luminophore K-35, the sorbent layer thickness was 2 mm, the length of the starting band was 60 cm, Et_2O as the eluent). The broadest UV-absorbing band was collected. The product was eluted from the sorbent with chloroform.

Compounds **10e,f** were isolated by filtration of the reaction mixture from traces of impurities followed by the removal of the solvent at 80 °C (30 Torr). The residues were dried at 80 °C (3 Torr).

To isolate compound **10g**, the solvent was removed from the reaction mixture at 80 °C (3 Torr). According to the ^{1}H NMR spectroscopic data, the residue contained the following three compounds: starting arylacetylene **5**, compound **10g**, and (4*S*,5*R*)-3,4-dimethyl-5-phenyloxazolidine (**11**). After preparative TLC under the conditions described above for compound **10c** ($CHCl_3$ as the eluent), two UV-absorbing bands of the sorbent were collected. The products were eluted from the sorbent with a MeOH—$CHCl_3$ mixture (1 : 10, v/v). Starting arylacetylene **5** (12%) was isolated from the upper band. After the elution with the same mixture and removal of the solvents from the eluate at 80 °C (3 Torr), the sorbent from the lower band gave an amorphous residue containing a mixture of compounds **10g** and **11** (^{1}H NMR spectroscopic data). The latter compound was removed from this mixture by evacuation at 100 °C (3 Torr) for 1 h.

To isolate compound **10h**, the solvent was removed from the reaction mixture at 80 °C (3 Torr). The residue contained (^{1}H NMR spectroscopic data) the following three compounds: starting arylacetylene **5**, compound **10h**, and (4*S*,5*S*)-3,4-dimethyl-5-phenyloxazolidine (**12**). After preparative TLC under the conditions described above for compound **10g**, starting arylacetylene **5** was isolated from the upper band of the sorbent in 48% yield. After the elution with the same mixture and removal of the solvents from the eluate at 80 °C (3 Torr), the sorbent from the lower band gave an amorphous residue containing a mixture of compounds **10h** and **12** (^{1}H NMR spectroscopic data). The latter compound was removed from this mixture by evacuation at 100 °C for 1 h (3 Torr).

Authentic samples of oxazolidines **11** ($[\alpha]^{20}_{578}$ +5.9 (*c* 4, C_6H_6)) (*cf.* lit. data[33]: $[\alpha]^{21}_{589}$ +5.6 (*c* 0.36, C_6H_6)) and **12** ($[\alpha]^{20}_{578}$ +49.5 (*c* 2, C_6H_6)) (*cf.* lit. data[33]: $[\alpha]^{21}_{589}$ +50.8 (*c* 0.56, C_6H_6)) were synthesized from (−)-ephedrine (**6g**) and (+)-pseudoephedrine (**6h**), respectively, under the conditions of the Mannich reaction in the absence of arylacetylene **5** and CuI. The yield of the products was 90—92%. The ^{1}H and ^{13}C NMR spectroscopic data were consistent with the published data.[34]

Methyl 2-(*N*-acetylamino)-5-(3-diethylaminoprop-1-yn-1-yl)benzoate (10a). The yield was 90%, crystals, m.p. 65—66 °C. High-resolution mass spectrum, found: *m/z* 302.1623 $[M]^+$. $C_{17}H_{22}N_2O_3$. Calculated: M = 302.1630. ^{1}H NMR (300.13 MHz), δ: 1.03 (t, 6 H, $(C\underline{H}_3CH_2)_2$, J = 7 Hz); 2.14 (s, 3 H, MeCO); 2.53 (q, 4 H, $(CH_3C\underline{H}_2)_2$, J = 7 Hz); 3.54 (s, 2 H, $C(3)H_2$); 3.83 (s, 3 H, OMe); 7.46 (dd, 1 H, H(6′), J = 9 Hz, J = 2 Hz); 7.98 (d, 1 H, H(2′), J = 2 Hz); 8.57 (d, 1 H, H(5′), J = 9 Hz); 10.96 (br.s, 1 H, NH). ^{13}C NMR (75.48 MHz), δ: 12.4 ($(\underline{C}H_3CH_2)_2$); 25.2 ($\underline{C}H_3CO$); 41.2 (C(3)); 47.1 ($(CH_3\underline{C}H_2)_2$); 52.2 (OMe); 83.4, 84.2 (C(1), C(2)); 114.3 (C(3′)); 117.2 (C(1′)); 119.8 (C(5′)); 133.8 (C(2′)); 137.3 (C(6′)); 140.7 (C(4′)); 167.8 (COO); 168.6 ($CH_3\underline{C}O$). IR (KBr), ν/cm^{-1}: 792, 846, 999, 1092, 1237, 1298, 1323, 1363, 1431, 1525, 1599; 1684, 1703 (C=O); 2815, 2969; 3268, 3317 (NH). UV (EtOH), λ_{max}/nm (logε): 235 (4.49), 273 (4.39), 281 (4.40), 326 (3.73).

Methyl 2-(*N*-acetylamino)-5-(3-pyrrolidinoprop-1-yn-1-yl)benzoate (10b). The yield was 92%, crystals, m.p. 80—81 °C. High-resolution mass spectrum, found: *m/z* 300.1477 $[M]^+$. $C_{17}H_{20}N_2O_3$. Calculated: M = 300.1474. ^{1}H NMR (300.13 MHz), δ: 1.73 (br.s, 4 H, $C(3)H_2$, $C(4)H_2$); 2.12 (s, 3 H, MeCO); 2.57 (br.s, 4 H, $C(2)H_2$, $C(5)H_2$); 3.50 (br.s, 2 H, $C(1')H_2$); 3.81 (s, 3 H, OMe); 7.45 (dd, 1 H, H(6″), J = 9 Hz, J = 2 Hz); 7.97 (d, 1 H, H(2″), J = 2 Hz); 8.54 (d, 1 H, H(5″), J = 9 Hz); 10.95 (br.s, 1 H, NH). ^{13}C NMR (75.48 MHz), δ: 23.5 (C(3)); 25.1 ($\underline{C}H_3CO$, C(4)); 43.5 (C(1′)); 52.1 (CH_3O); 52.5 (C(2), C(5)); 82.7, 85.2 (C(2′), C(3′)); 114.2 (C(3″)); 117.1 (C(1″)); 119.7 (C(5″)); 133.8 (C(2″)); 137.2 (C(6″)); 140.7 (C(4″)); 167.8 (COO); 168.6 ($CH_3\underline{C}O$). IR (KBr), ν/cm^{-1}: 791, 857, 1088, 1236, 1275, 1295, 1321, 1372, 1438, 1510, 1588; 1687, 1704 (C=O); 2731, 2791, 2874, 2955; 3268 (NH). UV (EtOH), λ_{max}/nm (logε): 235 (4.50), 273 (4.39), 280 (4.40), 325 (3.74).

Methyl 2-(*N*-acetylamino)-5-(3-piperidinoprop-1-yn-1-yl)benzoate (10c). The yield was 87%, crystals, m.p. 76—77 °C. High-resolution mass spectrum, found: *m/z* 314.1625 $[M]^+$. $C_{18}H_{22}N_2O_3$. Calculated: M = 314.1630. ^{1}H NMR (300.13 MHz), δ: 1.42 and 1.53 (both m, 2 H and 4 H, respectively, $C(3)H_2$—$C(5)H_2$); 2.11 (s, 3 H, CH_3CO); 2.43 (m, 4 H, $C(2)H_2$, $C(6)H_2$); 3.34 (br.s, 2 H, $C(1')H_2$); 3.80 (s, 3 H, MeO); 7.45 (dd, 1 H, H(6″), J = 9 Hz, J = 2 Hz); 7.97 (d, 1 H, H(2″),

J = 2 Hz); 8.54 (d, 1 H, H(5″), *J* = 9 Hz); 10.94 (br.s, 1 H, NH). ^{13}C NMR (75.48 MHz), δ: 52.2 (C(2), C(6)); 25.6 (C(3), C(5)); 23.6 (C(4)); 48.1 (C(1′)); 83.4, 84.8 (C(2′), C(3′)); 117.1 (C(1″)); 133.8 (C(2″)); 114.2 (C(3″)); 140.7 (C(4″)); 119.7 (C(5″)); 137.2 (C(6″)); 25.6 ($\underline{C}H_3CO$); 52.1 (CH_3O); 167.8 (COO); 168.6 ($CH_3\underline{C}O$). IR (KBr), ν/cm^{-1}: 791, 844, 1235, 1272, 1294, 1321, 1442, 1517, 1592; 1683, 1699 (C=O); 2770, 2814, 2851, 2937; 3267, 3317 (NH). UV (EtOH), λ_{max}/nm (logε): 232 (4.45), 272 (4.37), 325 (3.75).

Methyl 2-(*N*-acetylamino)-5-(3-morpholinoprop-1-yn-1-yl)benzoate (10d). The yield was 75%, crystals, m.p. 118—119 °C. High-resolution mass spectrum, found: *m/z* 316.1421 $[M]^+$. $C_{17}H_{20}N_2O_4$. Calculated: M = 316.1423. ^{1}H NMR (300.13 MHz), δ: 2.17 (s, 3 H, COMe); 2.57 (t, 4 H, C(3)H$_2$, C(5)H$_2$, *J* = 4.5 Hz); 3.43 (s, 2 H, C(1′)H$_2$); 3.71 (t, 4 H, C(2)H$_2$, C(6)H$_2$, *J* = 4.5 Hz); 3.86 (s, 3 H, OMe); 7.50 (dd, 1 H, H(6″), *J* = 9 Hz, *J* = 2 Hz); 8.03 (d, 1 H, H(2″), *J* = 2 Hz); 8.60 (d, 1 H, H(5″), *J* = 9 Hz); 11.01 (br.s, 1 H, NH). ^{13}C NMR (100.63 MHz), δ: 25.3 ($\underline{C}H_3CO$); 47.8 (C(1′)); 52.2 (C(3)H$_2$, C(5)H$_2$); 52.3 (OMe); 66.6 (C(2)H$_2$, C(6)H$_2$); 83.9, 84.1 (C(2′), C(3′)); 114.4 (C(3″)); 116.8 (C(1″)); 119.9 (C(5″)); 134.0 (C(2″)); 137.3 (C(6″)); 141.0 (C(4″)); 167.9 (COO); 168.8 ($CH_3\underline{C}O$). IR (KBr), ν/cm^{-1}: 842, 863, 888, 915, 1005, 1069, 1091, 1117, 1133, 1201, 1235, 1278, 1295, 1316, 1338, 1362, 1437, 1516, 1594; 1695 (C=O); 2815, 2855, 2926, 2960; 3311 (NH). UV (EtOH), λ_{max}/nm (logε): 235 (4.45), 273 (4.35), 280 (4.36), 326 (3.73).

(2*S*)-1-{3-[4-(*N*-Acetylamino)-3-(methoxycarbonyl)phenyl]prop-2-ynyl}-2-(3-pyridyl)piperidine (10e). The yield was 77%, viscous oil, $[\alpha]^{20}_{578}$ −72.5 (*c* 7.7, $CHCl_3$). High-resolution mass spectrum, found: *m/z* 391.1891 $[M]^+$. $C_{23}H_{25}N_3O_3$. Calculated: M = 391.1896. ^{1}H NMR (400.14 MHz), δ: 1.31 (qt, 1 H, *J* = 12 Hz, *J* = 4 Hz), 1.52 (qd, 1 H, *J* = 12 Hz, *J* = 3 Hz), 1.62—1.75 (m, 4 H) (H(3a), H(3b), H(4a), H(4b), H(5a), H(5b)); 2.14 (s, 3 H, MeCO); 2.54 (td, 1 H, *J* = 12 Hz, *J* = 3 Hz), 2.96 (br.d, 1 H, *J* = 12 Hz), 3.28 (dd, 1 H, *J* = 11 Hz, *J* = 3 Hz) (H(2), H(6a), H(6b)); 3.14 and 3.27 (both d, 1 H each, AB system, C(1′)H$_2$, *J* = 17 Hz); 3.84 (s, 3 H, OMe); 7.18 (dd, 1 H, H(5‴), *J* = 8 Hz, *J* = 5 Hz); 7.48 (dd, 1 H, H(6″), *J* = 9 Hz, *J* = 2 Hz); 7.64 (br.d, 1 H, H(4‴), *J* = 8 Hz); 7.98 (d, 1 H, H(2″), *J* = 2 Hz); 8.43 (dd, 1 H, H(6‴), *J* = 5 Hz, *J* = 1.5 Hz); 8.53 (d, 1 H, H(2‴), *J* = 1.5 Hz); 8.59 (d, 1 H, H(5″), *J* = 9 Hz); 10.94 (br.s, 1 H, NH). ^{13}C NMR (100.63 MHz), δ: 24.4 (C(4)); 25.2 ($\underline{C}H_3CO$); 25.7 (C(5)); 35.4 (C(3)); 44.7 (C(1′)); 52.2 (CH_3O); 53.0 (C(6)); 63.1 (C(2)); 83.8, 84.4 (C(2′), C(3′)); 114.4 (C(3″)); 117.0 (C(1″)); 119.9 (C(5″)); 123.3 (C(5‴)); 133.8 (C(2″)); 134.7 (C(4‴)); 137.3 (C(6″)); 138.9 (C(3‴)); 140.8 (C(4″)); 148.6 (C(6‴)); 149.3 (C(2‴)); 167.8 (COO); 168.7 ($CH_3\underline{C}O$). IR (film), ν/cm^{-1}: 565, 664, 686, 717, 754, 793, 843, 984, 1002, 1026, 1088, 1113, 1236, 1294, 1320, 1367, 1400, 1438, 1513, 1589; 1691, 1700 (C=O); 2801, 2855, 2936; 3273, 3314 (NH). UV (EtOH), λ_{max}/nm (logε): 235 (4.40), 272 (4.32), 281 (4.31), 325 (3.62).

(1*R*,5*S*)-3-{3-[4-(*N*-Acetylamino)-3-(methoxycarbonyl)phenyl]prop-2-ynyl}-1,2,3,4,5,6-hexahydro-8*H*-1,5-methanopyrido[1,2-*a*][1,5]diazocin-8-one (10f). The yield was 92%, amorphous powder, $[\alpha]^{20}_{578}$ −102.9 (*c* 4.0, $CHCl_3$). High-resolution mass spectrum, found: *m/z* 419.1847 $[M]^+$. $C_{24}H_{25}N_3O_4$. Calculated: M = 419.1845. ^{1}H NMR (300.13 MHz) δ: 1.65—1.79 (m, 2 H, C(13)H$_2$); 2.12 (s, 3 H, MeCO); 2.38 and 2.89 (both br.s, 1 H each, H(1), H(5)); 2.54—2.60 and 2.71—2.82 (both m, 2 H each, C(2)H$_2$, C(4)H$_2$); 3.34 and 3.26 (both d, 1 H each, AB system, C(1′)H$_2$, *J* = 17 Hz); 3.79 (dd, 1 H, H(6b), *J* = 15.5 Hz, *J* = 6.5 Hz); 3.82 (s, 3 H, OMe); 3.94 (d, 1 H, H(6a), *J* = 15.5 Hz); 5.87 (d, 1 H, H(9), *J* = 7 Hz); 6.30 (d, 1 H, H(11), *J* = 9 Hz); 7.15 (dd, 1 H, H(10), *J* = 9 Hz, *J* = 7 Hz); 7.42 (dd, 1 H, H(6″), *J* = 9 Hz, *J* = 2 Hz); 7.94 (d, 1 H, H(2″), *J* = 2 Hz); 8.54 (d, 1 H, H(5″), *J* = 9 Hz); 10.93 (br.s, 1 H, NH). ^{13}C NMR (75.48 MHz), δ: 25.0 (C(13)); 25.1 ($\underline{C}H_3CO$); 27.5 (C(5)); 35.0 (C(1)); 47.2 (C(1′)); 49.6 (C(2)); 52.1 (OMe); 58.2 (C(4)); 58.8 (C(6)); 83.5, 84.2 (C(2′), C(3′)); 104.3 (C(11)); 114.3 (C(3″)); 116.3 (C(9)); 116.8 (C(1″)); 119.8 (C(5″)); 133.7 (C(2″)); 137.1 (C(6″)); 138.3 (C(10)); 140.8 (C(4″)); 151.0 (C(12)); 163.3 (C(8)); 167.7 (COO), 168.6 ($CH_3\underline{C}O$). IR (KBr), ν/cm^{-1}: 749, 793, 844, 1001, 1058, 1087, 1135, 1159, 1235, 1293, 1319, 1366, 1399, 1437, 1510, 1547, 1585; 1653, 1692 (C=O); 2801, 2938; 3312, 3393 (NH). UV (EtOH), λ_{max}/nm (logε): 234 (4.51), 281 (4.37), 312 (4.05).

(1*R*,2*S*)-2-{*N*-[3-(4-Acetylamino-3-methoxycarbonylphenyl)prop-2-ynyl]-*N*-methylamino}-1-phenylpropan-1-ol (10g). The yield was 86%, viscous oil, $[\alpha]^{20}_{578}$ +52.8 (*c* 10, $CHCl_3$). High-resolution mass spectrum, found: *m/z* 394.1896 $[M]^+$. $C_{23}H_{26}N_2O_4$. Calculated: M = 394.1892. ^{1}H NMR (300.13 MHz), δ: 0.87 (d, 3 H, C(2)H$_3$, *J* = 6.7 Hz); 2.18 (s, 3 H, MeCO); 2.48 (s, 3 H, H(1), MeN); 2.85 (dq, 1 H, H(2), *J* = 3.2 Hz, *J* = 6.7 Hz); 3.38 (br.s, 1 H, OH); 3.64 and 3.70 (both d, 1 H each, AB system, C(1′)H$_2$, *J* = 17.6 Hz); 3.88 (s, 3 H, OMe); 4.97 (d, 1 H, H(1), *J* = 3.2 Hz); 7.16—7.31 (m, 5 H, Ph); 7.52 (dd, 1 H, H(6″), *J* = 9 Hz, *J* = 2 Hz); 8.04 (d, 1 H, H(2″), *J* = 2 Hz); 8.63 (d, 1 H, H(5″), *J* = 9 Hz); 11.02 (br.s, 1 H, NH). ^{13}C NMR (75.48 MHz), δ: 10.13 (C(2)H$_3$); 25.2 ($\underline{C}H_3CO$); 39.5 (MeN); 44.2 (C(1′)); 52.2 (OMe); 62.3 (C(2)); 71.8 (C(1)); 83.9, 84.5 (C(2′), C(3′)); 114.4 (C(3″)); 117.0 (C(1″)); 119.9 (C(5″)); 125.6 (C(2‴), C(6‴)); 126.6 (C(4‴)); 127.8 (C(3‴), C(5‴)); 133.8 (C(2″)); 137.3 (C(6″)); 140.9 (C(1‴)); 141.9 (C(4″)); 167.8 (COO); 168.7 ($CH_3\underline{C}O$). IR (film), ν/cm^{-1}: 685, 703, 754, 793, 844, 1001, 1088, 1151, 1236, 1294, 1320, 1368, 1399, 1438, 1517, 1589; 1696 (C=O); 2797, 2891, 2953, 2986; 3272, 3314, 3421 (NH, OH). UV (EtOH), λ_{max}/nm (logε): 231 (4.40), 273 (4.31), 281 (4.30), 326 (3.66).

(1*S*,2*S*)-2-{*N*-[3-(4-Acetylamino-3-methoxycarbonylphenyl)prop-2-ynyl]-*N*-methylamino}-1-phenylpropan-1-ol (10h). The yield was 51%, m.p. 123—124 °C (from $CHCl_3$), $[\alpha]^{20}_{578}$ +54.8 (*c* 9.3, $CHCl_3$). High-resolution mass spectrum, found: *m/z* 394.1884 $[M]^+$. $C_{23}H_{26}N_2O_4$. Calculated: M = 394.1892. ^{1}H NMR (300.13 MHz), δ: 0.86 (d, 3 H, C(2)H$_3$, *J* = 6.7 Hz); 2.23 (s, 3 H, MeCO); 2.44 (s, 3 H, H(1), MeN); 2.89 (dq, 1 H, H(2), *J* = 9.5 Hz, *J* = 6.7 Hz); 3.57 and 3.65 (both d, 1 H each, AB system, C(1′)H$_2$, *J* = 16.7 Hz); 3.92 (s, 3 H, OMe); 4.26 (d, 1 H, H(1), *J* = 9.5 Hz); 7.28—7.39 (m, 5 H, Ph); 7.57 (dd, 1 H, H(6″), *J* = 9 Hz, *J* = 2 Hz); 8.10 (d, 1 H, H(2″), *J* = 2 Hz); 8.69 (d, 1 H, H(5″), *J* = 9 Hz); 11.08 (br.s, 1 H, NH). ^{13}C NMR (75.48 MHz), δ: 8.07 (C(2)H$_3$); 25.0 ($\underline{C}H_3CO$); 35.2 (MeN); 44.5 (C(1′)); 52.2 (OMe); 64.6 (C(2)); 74.7 (C(1)); 83.3, 85.8 (C(2′), C(3′)); 114.5 (C(3″)); 116.9 (C(1″)); 120.0 (C(5″)); 127.2 (C(2‴), C(6‴)); 127.5 (C(4‴)); 128.0 (C(3‴), C(5‴)); 133.8 (C(2″)); 137.1 (C(6″)); 141.0 (C(1‴)); 141.6 (C(4″)); 167.9 (COO), 168.7 ($CH_3\underline{C}O$). IR (KBr), ν/cm^{-1}: 685, 707, 767, 792, 849, 1040, 1087, 1234, 1296, 1316, 1372, 1399, 1433, 1455, 1519, 1596; 1689, 1708 (C=O); 2797, 2857, 2927, 2953, 2958; 3255, 3320, 3416

(NH, OH). UV (EtOH), λ_{max}/nm (logε): 232 (4.45), 273 (4.36), 326 (3.72).

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References

1. S. A. Osadchii, E. E. Shults, S. F. Vasilevskii, E. V. Polukhina, A. A. Stepanov, and G. A. Tolstikov, *Izv. Akad. Nauk, Ser. Khim.*, 2007, 344 [*Russ. Chem. Bull., Int. Ed.*, 2007, **56**, 356].
2. V. M. Dembitsky and D. O. Levitsky, *Nat. Prod. Commun.*, 2006, **1**, 405.
3. V. M. Dembitskii, G. A. Tolstikov, and A. G. Tolstikov, *Khim. Interes. Ustoichivogo Razvitiya*, 2003, **11**, 341 [*Chem. Sustainable Development*, 2003, **11** (Engl. Transl.)].
4. M. Konishi, H. Ohkuma, T. Tsuno, T. Oki, G. D. VanDuyne, and J. Clardy, *J. Am. Chem. Soc.*, 1990, **112**, 3715.
5. M. A. Huffman, N. Yasuda, A. E. DeCamp, and E. J. J. Grabowski, *J. Org. Chem.*, 1995, **60**, 1590.
6. M. Tramontini, *Synthesis*, 1973, 703.
7. M. Tramontini and L. Anglioni, *Tetrahedron*, 1990, **46**, 1791.
8. S. V. Klyatskaya, E. V. Tret´yakov, and S. F. Vasilevskii, *Izv. Akad. Nauk, Ser. Khim.*, 2002, 122 [*Russ. Chem. Bull., Int. Ed.*, 2002, **51**, 128].
9. K. Hattori, M. Miyata, and H. Yamamoto, *J. Am. Chem. Soc.*, 1993, **115**, 1151.
10. M. Miura, M. Enna, K. Okuro, and M. Nomura, *J. Org. Chem.*, 1995, **60**, 4999.
11. D. L. Musso, M. J. Clarke, J. L. Kelley, G. E. Boswell, and G. Chen, *Org. Biomol. Chem.*, 2003, **1**, 498.
12. K. Sonogashira, Y. Tohda, and N. Hagihara, *Tetrahedron Lett.*, 1975, **50**, 4467.
13. C. Mannich and F. T. Chang, *Ber. Deutsch. Chem. Ges.*, 1933, **66**, 418.
14. J. J. Li, *Name Reactions*, Springer-Verlag, Berlin—Heidelberg, 2003.
15. L. W. Bieber and M. F. da Silva, *Tetrahedron Lett.*, 2004, **45**, 8281.
16. K. Edo, T. Sakamoto, and H. Yamanaka, *Chem. Pharm. Bull.*, 1978, **26**, 3843.
17. H. Pfanz and G. Kirchner, *Justus Liebigs Ann. Chem.*, 1958, **614**, 149.
18. E. J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, 1972, **94**, 6190.
19. C. A. Osadchii, E. E. Shults, E. V. Polukhina, M. M. Shakirov, and G. A. Tolstikov, *Izv. Akad. Nauk, Ser. Khim.*, 2006, 1038 [*Russ. Chem. Bull., Int. Ed.*, 2006, **55**, 1077].
20. V. B. Mochalin and T. S. Minervina, *Zh. Org. Khim.*, 1965, **1**, 1726 [*J. Org. Chem. USSR*, 1965, **1** (Engl. Transl.)].
21. N. Miyaura and A. Suzuki, in *Organic Syntheses*, 1993, Coll. Vol. **8**, 532; 1990, Coll. Vol. **68**, 130.
22. G. Ferguson, R. McCrindle, A. J. McAlees, and M. Parvez, *Acta Crystallogr., Sect. B*, 1982, **38**, 2679.
23. T. A. Henry, *The Plant Alkaloids*, 4th ed., London, 1949.
24. A. Orechov and G. Menschikoff, *Ber. Deutsch. Chem. Ges.*, 1931, **64**, 266.
25. A. S. Sadykov, *Khimiya alkaloidov Anabasis aphylla* [*Chemistry of Alkaloids from Anabasis aphylla*], Izd-vo AN Uzb. SSR, Tashkent, 1956, 222 pp. (in Russian).
26. M. V. Tsarev, *Dokl. Akad. Nauk SSSR*, 1944, **42**, 127 [*Dokl. Chem.*, 1944 (Engl. Transl.)].
27. R. A. Konovalova, S. Yunusov, and A. P. Orekhov, *Zh. Obshch. Khim.*, 1939, **9**, 1356 [*J. Gen. Chem. USSR*, 1939, **9** (Engl. Transl.)].
28. V. G. Zakharov, N. I. Libizov, and Kh. A. Aslanov, *Lekarstvennye veshchestva iz rastenii i sposoby ikh proizvodstva* [*Drugs from Plants and Methods of Their Production*], Izd-vo FAN, Tashkent, 1980, 232 pp. (in Russian).
29. S. A. Osadchii, N. A. Pankrushina, M. M. Shakirov, E. E. Shults, and G. A. Tolstikov, *Izv. Akad. Nauk, Ser. Khim.*, 2000, 552 [*Russ. Chem. Bull., Int. Ed.*, 2000, **49**, 557].
30. M. Shamma and D. M. Hindenlang, *Carbon-13 NMR Shift Assignments of Amines and Alkaloids*, Plenum Press, New York—London, 1979, No. 24.
31. S. Takamatsu, K. Saito, S. Ohmiya, N. Ruangrundi, and J. Murakoshi, *Phytochemistry*, 1991, **30**, 3793.
32. T. Eckert and J. Ipaktschi, *Monatsh. Chem.*, 1998, **129**, 1035.
33. N. S. Khruscheva, N. M. Loim, V. I. Sokolov, and V. D. Makhaev, *J. Chem. Soc., Perkin Trans. 1*, 1997, **16**, 2425.
34. R. Contreras, F. Santiesteban, M. A. Paz-Sandoval, and B. Wrackmeyer, *Tetrahedron*, 1984, **40**, 3829.

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