# Synthesis of 4-amino-substituted but-2-en-4-olides

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Previously unknown 4-amino derivatives of spiro-annelated $\Delta^2$-butenolide were synthesized by the addition of various amines at the activated triple bond of 4-hydroxy-2-alkynoic esters.

**Key words:** methyl 3-(1-hydroxycyclohexyl)prop-2-ynoate, amines, but-2-en-4-olides, Michael reaction, spiro compounds, 1-oxaspiro[4.5]dec-3-en-2-ones.

Certain furan-2(5*H*)-one (but-2-en-4-olide) derivatives are known to act on enzymes[1,2] and possess bactericidal, fungicidal,[3,4] or antibacterial[5,6] properties. A series of natural compounds (alkaloids, steroids, tetronic and ascorbic acids, pheromones, and fragrances)[7—13] contain $\Delta^2$-butenolide fragments. Earlier,[14] we have developed a facile procedure for the synthesis of 4-aminofuran-2(5*H*)-ones spiro-annelated at position 5, which are of interest as biologically active compounds and intermediates in the synthesis of natural compounds.[15—20] This procedure involves the reaction of esters of 4-hydroxyalk-2-ynoic acid derivatives, in particular, of compound **1**, with primary (**2**) and secondary (**3**) amines (Scheme 1). Under the reaction conditions, the initially formed linear Michael adducts **4** and **5** undergo cyclization to give the corresponding furan-2(5*H*)-one derivatives **6** and **7**.

The aim of the present study was to examine the scope of application of this one-pot procedure and to synthesize a series of amino derivatives of but-2-en-4-olides containing pharmacophoric substituents in the amine component. For this purpose, we studied the reactions of methyl (1-hydroxycyclohexyl)propiolate **1** with various amines **2a—z** and **3a—z**. The reactions were carried out in the absence of catalysts in dry diethyl ether or in a 2 : 1 diethyl ether—methanol mixture at 20—60 °C. The reactions with salts of amines were performed by refluxing in methanol in the presence of sodium acetate. In most cases, the desired amino derivatives of but-2-en-4-olides **6** and **7** were isolated in high yields. As expected, the reaction rate depends on the structure of the starting amine, the number of substituents, and their size. Benzylic amines **2a—d** and **3e,f,h** are most reactive. Thus, their reactions proceed readily in diethyl ether at room temperature, and the corresponding products **6** and **7** were obtained in 61—78% yields (Tables 1 and 2). N-Nucleophiles, which are components of heterocycles, such as piperidine (**3i—l,o**), piperazine (**3q,s,t**), and some other heterocycles (**3v,x**), react under more drastic conditions. For example, refluxing of (−)-anabasine **3o** in butanol selectively afforded (in 74% yield) $\Delta^2$-butenolide **7o** containing a chiral center in the α position with the respect to the nitrogen atom ($[\alpha_D]^{24}$ −198.70 (*c* 1.00, $CHCl_3$)). It should be noted that the analogous reaction of anabasine with nitrile of (1-hydroxycyclohexyl)propiolic acid (EtOH, 40 °C) gave only linear adduct **9** instead of iminolactone **8**.[21] Under the above-mentioned conditions, both amino groups in 1,2-diaminopropane are involved in the reaction to give bislactone **10**.

The addition of benzoylhydrazine **2x** occurs at the C≡C bond through the terminal nitrogen atom to give lactone **6x** in 77% yield. Arylhydrazines (*o*-nitro- and *o*-methoxyphenylhydrazines) were not involved in the reaction at room temperature, whereas refluxing of these compounds in methanol afforded complex mixtures of products. Apparently, high temperature promotes *Z*/*E*-isomerization of adducts **4** and **5**, which is responsible for a decrease in selectivity of the process.[22—24] The reactions of amino derivatives of imidazoles **2z** and **3y** with compound **1** gave mixtures of linear and cyclic products (**4z+6z** and **5y+7y**, respectively). Attempts to separate these mixtures into individual components by crystallization or chromatography failed. Some reactions were accompanied by partial hydrolysis of ester **1** into the corresponding acid. According to the results of IR spectroscopy (absorption bands at 2240—2260 $cm^{-1}$), products **6b,k,y** and **7m,n** contain triple bonds due, apparently, to the presence of impurities of propiolates of the corresponding amines. In the reactions of ester **1** with piperidin-4-one and dicyclohexylamine, hydrolysis of the ester giving rise to the corresponding acid becomes the main process. The structures of salts **11a,b** were established by analytical and spectroscopic methods.

To summarize, we studied the influence of the structure of the amine component on their reactions with me-

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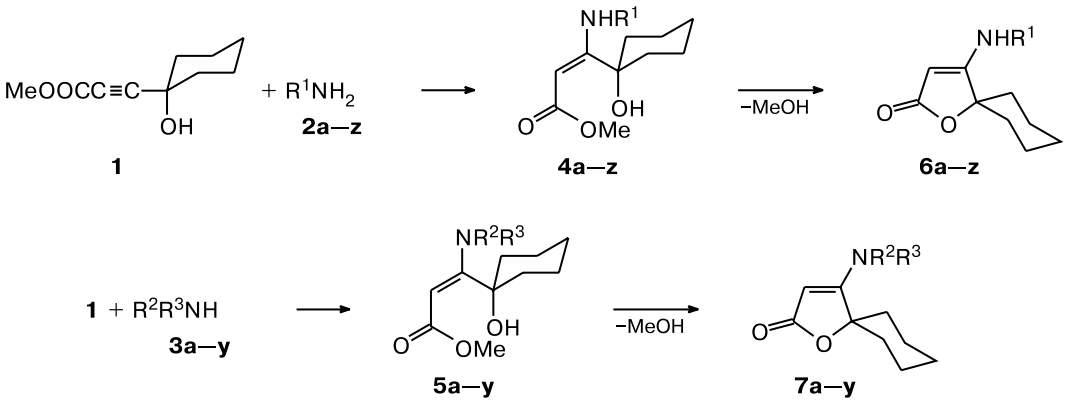
**Scheme 1**




**2**, **4**, **6:** $R^1$ = –$CH_2$–(4-pyridyl) (**a**), –$CH_2$–(2-Cl-4-Cl-phenyl) (**b**), –$CH_2$–(1-adamantyl) (**c**), (1-imidazolyl-2-$CH_2$–phenyl) (**d**), Me–CH(I)–(4-morpholinophenyl) (**e**),

Me–CH(I)–(4-morpholinophenyl) (**f**), Et–CH(I)–(1-adamantyl) (**g**), Ph–CH(I)–(1-adamantyl) (**h**), –$CHPh_2$ (**i**), –$CH_2$–$CH_2$–(4-Cl-phenyl) (**j**),

–$CH_2$–$CH_2$–(4-$SO_2NH_2$-phenyl) (**k**), –$CH_2$–$CH_2$–(3,4-dimethoxyphenyl) (**l**), –$CH_2$–$CH_2$–(3,4-diethoxyphenyl) (**m**), –$CH_2$–$CH_2$–(1,2-dimethylindol-3-yl) (**n**),

–$CH_2$–$CH_2$–(2-methyl-1-ethylindol-3-yl) (**o**), –$CH_2$–$CH_2$–O–(1-adamantyl) (**p**), –$CH_2$–$CH_2$–NH–$C_6Cl_5$ (**q**), –$CH_2$–$CH_2$–(1-imidazolyl) (**r**),

–$CH_2$–$(CH_2)_2$–NH–(2-$O_2N$-4-$CF_3$-phenyl) (**s**), –$CH_2$–$(CH_2)_2$–(morpholin-4-yl) (**t**), –$CH_2$–$(CH_2)_2$–(imidazol-1-yl) (**u**), (4-NEt-cyclohexyl) (**v**),

(1,1-dioxotetrahydrothiophen-3-yl) (**w**), –NH–C(=O)–(2-methylphenyl) (**x**), (1-adamantyl) (**y**), –$CH_2$–$(CH_2)_2$–(2-methylimidazol-1-yl) (**z**)

**3**, **5**, **7:** $R^2$–N–$R^3$ = $NBu^i_2$ (**a**), (*cyclo*-$C_5H_{11}$)$_2$N (**b**), $Pr^n$–N–$CH_2$–(cyclopropyl) (**c**), $MeN(CH_2)_2OH$ (**d**), $MeNCH_2Ph$ (**e**), $EtNCH_2Ph$ (**f**),

$HO(CH_2)_2NCH_2Ph$ (**g**), $N(CH_2Ph)_2$ (**h**), (2-Me-piperidin-1-yl) (**i**), (2-Et-piperidin-1-yl) (**j**), (4-Me-piperidin-1-yl) (**k**), (4-COOEt-piperidin-1-yl) (**l**), (4-$CONH_2$-piperidin-1-yl) (**m**),

(4-CON-piperidin-1-yl) (**n**), *S*-(–)-Anabasine (**o**), (4-(2-HO-ethyl)-piperazin-1-yl) (**p**), (4-(2-NC-ethyl)-piperazin-1-yl) (**q**), (4-Ph-piperazin-1-yl) (**r**), (4-(4-$NO_2$-phenyl)-piperazin-1-yl) (**s**),

(4-(4-F-phenyl)-piperazin-1-yl) (**t**), (4-(1-adamantyl)-piperazin-1-yl) (**u**), (2,6-dimethylmorpholin-4-yl) (**v**), (**w**), (1,3,3-trimethyl-6-azabicyclo[3.2.1]octan-6-yl) (**x**), (imidazol-1-yl) (**y**)

thyl (1-hydroxycyclohexyl)propiolate **1**. The structural features responsible for selectivity of the reaction and its pathway were revealed. A representative series (a library) of amino derivatives of but-2-en-4-olides **6**, **7**, and **10** containing pharmacophoric substituents at the nitrogen atom of the amino group were synthesized.

**Table 1.** Physicochemical characteristics of compounds **6a—z** and **10**

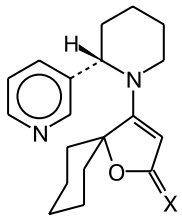
| Compound | Method of synthesis and isolation | Yield (%) | M.p./°C | Found / Calculated (%) | | | Molecular formula | MS, *m/z* (*I* (%)) |
|---|---|---|---|---|---|---|---|---|
| | | | | C | H | N | | |
| **6a** | *A*, *a* | 61* | 198—199 | 69.55<br>69.74 | 7.12<br>7.02 | 10.86<br>10.85 | $C_{15}H_{18}N_2O_2$ | 258 (5.2) |
| **6b** | *A*, *a* | 65 | 186—187 | 59.00<br>58.91 | 5.19<br>5.25 | 4.31<br>4.29 | $C_{16}H_{17}C1_2NO_2$ | 326 (2.1) |
| **6c** | *B*, *a* | 67 | 262—263 | 76.21<br>76.15 | 9.16<br>9.27 | 4.53<br>4.44 | $C_{20}H_{29}NO_2$ | 315 (13.4) |
| **6d** | *C*, *b* | 61 | 247—248 | 74.71<br>74.51 | 6.72<br>6.88 | 8.53<br>8.69 | $C_{20}H_{22}N_2O_2$ | 322 (6.7) |
| **6e** | *B*, *b* | 49 | 217—218 | 74.48<br>74.54 | 8.59<br>8.53 | 7.81<br>7.90 | $C_{22}H_{30}N_2O_2$ | 354 (5.4) |
| **6f** | *B*, *a* | 67 | 210—211 | 70.47<br>70.76 | 7.96<br>7.92 | 7.91<br>7.86 | $C_{21}H_{28}N_2O_3$ | 356 (4.3) |
| **6g** | *B*, *a* | 68 | 305—306 | 77.01<br>76.92 | 9.85<br>9.68 | 4.01<br>4.08 | $C_{22}H_{33}NO_2$ | 343 (7.4) |
| **6h** | *B*, *a* | 62 | 305—306 | 79.68<br>79.75 | 8.63<br>8.50 | 3.45<br>3.58 | $C_{26}H_{33}NO_2$ | 391 (18.5) |
| **6i** | *B*, *a* | 80 | 264—265 | 79.38<br>79.25 | 7.05<br>6.95 | 4.12<br>4.20 | $C_{22}H_{23}NO_2$ | 333 (8.4) |
| **6j** | *B*, *b* | 58 | 185—186 | 66.85<br>66.77 | 6.42<br>6.59 | 4.63<br>4.58 | $C_{17}H_{20}C1NO_2$ | 305 (9.2) |
| **6k** | *B*, *a* | 62 | 115—116 | 57.96<br>58.26 | 6.89<br>6.33 | 7.44<br>7.99 | $C_{17}H_{22}N_2O_4S$ | 350 (6.0) |
| **6l** | *A*, *a* | 74* | 162—163 | 69.01<br>68.86 | 7.43<br>7.60 | 4.38<br>4.23 | $C_{19}H_{25}NO_4$ | 331 (11.8) |
| **6m** | *A*, *a* | 69* | 150—151 | 70.23<br>70.17 | 8.08<br>8.13 | 3.98<br>3.90 | $C_{21}H_{29}NO_4$ | 359 (17.9) |
| **6n** | *D*, *b* | 43 | 222—223 | 74.61<br>74.52 | 7.65<br>7.74 | 8.39<br>8.28 | $C_{21}H_{26}N_2O_2$ | 338 (12.3) |
| **6o**** | *D*, *b* | 27 | 89—90*** | — | — | — | $C_{22}H_{28}N_2O_2$ | 352 (9.4) |
| **6p** | *A*, *a* | 70 | 221—222 | 72.62<br>73.00 | 9.26<br>9.05 | 4.24<br>4.05 | $C_{21}H_{31}NO_3$ | 345 (2.1) |
| **6q** | *B*, *a* | 58 | 206—207 | 44.80<br>44.48 | 3.37<br>3.74 | 6.28<br>6.11 | $C_{17}H_{17}C1_5N_2O_2$ | 458 (19.6) |
| **6r** | *B*, *a* | 52 | 175—175.5 | 64.41<br>64.34 | 7.47<br>7.33 | 15.93<br>16.08 | $C_{14}H_{19}N_3O_2$ | 261 (—) |
| **6s** | *B*, *a* | 64 | 174—175 | 55.18<br>55.15 | 5.29<br>5.37 | 10.14<br>10.16 | $C_{19}H_{22}F_3N_3O_4$ | 413 (—) |
| **6t** | *A*, *a* | 63 | 143—144 | 65.34<br>65.28 | 8.98<br>8.90 | 9.41<br>9.52 | $C_{16}H_{26}N_2O_3$ | 294 (4.4) |
| **6u** | *B*, *b* | 41 | 175—176 | 65.68<br>65.43 | 7.51<br>7.69 | 15.54<br>15.26 | $C_{15}H_{21}N_3O_2$ | 275 (4.9) |
| **6v** | *B*, *b* | 61 | 171—172 | 68.91<br>69.03 | 9.39<br>9.41 | 10.15<br>10.06 | $C_{16}H_{26}N_2O_2$ | 278 (4.2) |
| **6w** | *C*, *b* | 51 | 308—309 | 54.63<br>54.66 | 6.76<br>6.72 | 4.93<br>4.90 | $C_{13}H_{19}NO_4S$ | 285 (14.3) |
| **6x** | *C*, *b* | 77 | 294—295 | 67.23<br>67.11 | 6.41<br>6.34 | 9.79<br>9.78 | $C_{16}H_{18}N_2O_3$ | 286 (18.7) |
| **6y**** | *D*, *b* | 23 | >355 | — | — | — | $C_{19}H_{27}NO_2$ | 301 (21.3) |
| **4z+6z** | *D*, *b* | 22 | 99—101 | — | — | — | — | — |
| **10** | *B*, *b* | 58 | >365 | 68.19<br>68.08 | 8.11<br>8.16 | 15.04<br>15.12 | $C_{21}H_{30}N_2O_4$ | 374 (2.2) |

* Upon storage of the reaction mixture at room temperature for 1.5—3 months, the yields were increased by 7—12%.
** Compounds **6o** and **6y** contained an impurity (3—5%) of the corresponding salt **11** ($\nu_{C\equiv C}$ ~2240 $cm^{-1}$).
*** An amorphous compound, the purity was ~93%.

**Table 2.** Physicochemical characteristics of compounds **7a—y**

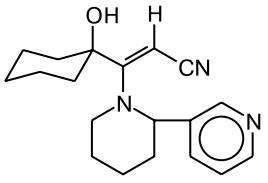
| Compound | Method of synthesis and isolation | Yield (%) | M.p./°C | Found / Calculated (%) | | | Molecular formula | MS, *m/z* (*I* (%)) |
|---|---|---|---|---|---|---|---|---|
| | | | | C | H | N | | |
| **7a** | *B*, *b* | 56 | 128—129 | 72.88<br>73.07 | 10.63<br>10.46 | 5.01<br>5.01 | $C_{17}H_{29}NO_2$ | 279 (17.0) |
| **7b** | *B*, *b* | 43 | 91—92 | 74.12<br>74.22 | 10.93<br>10.81 | 4.51<br>4.56 | $C_{19}H_{33}NO_2$ | 307 (22.0) |
| **7c** | *A*, *b* | 76 | 86—87 | 71.38<br>71.67 | 10.21<br>10.03 | 5.53<br>5.57 | $C_{16}H_{25}NO_2$ | 263 (29.4) |
| **7d** | *B*, *b* | 46 | 99—100 | 64.01<br>63.97 | 8.47<br>8.50 | 6.29<br>6.22 | $C_{12}H_{19}NO_3$ | 225 (25.1) |
| **7e** | *A*, *a* | 78 | 118—119 | 75.17<br>75.24 | 7.99<br>7.80 | 5.19<br>5.16 | $C_{17}H_{21}NO_2$ | 271 (11.7) |
| **7f** | *A*, *b* | 79 | 82—83 | 75.63<br>75.75 | 8.15<br>8.12 | 4.97<br>4.91 | $C_{18}H_{23}NO_2$ | 285 (39.0) |
| **7g** | *B*, *b* | 67 | 128—129 | 71.79<br>71.73 | 7.57<br>7.69 | 4.81<br>4.65 | $C_{18}H_{23}NO_3$ | 287 (—) |
| **7h** | *A*, *a* | 78 | 161—162 | 79.52<br>79.50 | 7.35<br>7.25 | 4.06<br>4.03 | $C_{23}H_{25}NO_2$ | 347 (29.6) |
| **7i** | *A*, *b* | 82 | 134—135 | 72.39<br>72.25 | 9.31<br>9.30 | 5.57<br>5.62 | $C_{15}H_{23}NO_2$ | 249 (31.3) |
| **7j** | *B*, *b* | 69 | 112—113 | 72.81<br>72.96 | 9.64<br>9.57 | 5.43<br>5.32 | $C_{16}H_{25}NO_2$ | 263 (10.6) |
| **7k** | *A*, *a* | 74 | 136—137 | 72.38<br>72.25 | 9.24<br>9.30 | 5.63<br>5.62 | $C_{15}H_{23}NO_2$ | 249(47.2) |
| **7l** | *B*, *b* | 67* | 150—151 | 66.45<br>66.42 | 8.36<br>8.20 | 4.41<br>4.56 | $C_{17}H_{25}NO_4$ | 307 (100) |
| **7m** | *B*, *a* | 55* | 236—237 | 64.81<br>64.72 | 8.01<br>7.97 | 10.01<br>10.07 | $C_{15}H_{22}N_2O_3$ | 278 (56.2) |
| **7n** | *B*, *b* | 57 | 184—185 | 69.01<br>69.33 | 8.73<br>8.73 | 8.04<br>8.09 | $C_{20}H_{30}N_2O_3$ | 346 (36.4) |
| **7o** | *D*, *b*<br>*C*, *b* | 74<br>62 | 221—222 | 72.84<br>73.04 | 7.79<br>7.74 | 8.69<br>8.97 | $C_{19}H_{24}N_2O_2$ | 312 (62.3) |
| **7p** | *B*, *b* | 63 | 156—158 (decomp.) | 64.51<br>64.26 | 8.67<br>8.63 | 10.08<br>9.99 | $C_{15}H_{24}N_2O_3$ | 280 (11.4) |
| **7q** | *B*, *b* | 69 | 151—152 | 66.22<br>66.41 | 8.12<br>8.01 | 14.19<br>14.52 | $C_{16}H_{23}N_3O_2$ | 289 (53.6) |
| **7r** | *B*, *b* | 47 | 206—207 | 72.91<br>73.04 | 7.85<br>7.74 | 9.08<br>8.97 | $C_{19}H_{24}N_2O_2$ | 312 (65.4) |
| **7s** | *B*, *b* | 72 | 268—269 | 63.91<br>63.85 | 6.53<br>6.48 | 11.57<br>11.76 | $C_{19}H_{23}N_3O_4$ | 357 (100) |
| **7t** | *A*, *a* | 70* | 191—192 | 69.15<br>69.07 | 7.13<br>7.02 | 8.33<br>8.48 | $C_{19}H_{23}FN_2O_2$ | 330 (38.3) |
| **7u** | *B*, *b* | 69 | 242—243 | 74.59<br>74.55 | 9.34<br>9.25 | 7.43<br>7.56 | $C_{23}H_{34}N_2O_2$ | 370 (43.4) |
| **7v** | *C*, *b* | 49 | 187.5—189 | 67.81<br>67.89 | 8.85<br>8.74 | 5.41<br>5.28 | $C_{15}H_{23}NO_3$ | 265 (100) |
| **7w** | *D*, *b* | 36 | 264—265 | 73.21<br>73.28 | 5.83<br>5.92 | 6.51<br>6.33 | $C_{27}H_{26}N_2O_4$ | 442 (1.0) |
| **7x** | *B*, *b* | 49* | 144—145 | 75.15<br>75.20 | 9.85<br>9.63 | 4.51<br>4.62 | $C_{19}H_{29}NO_2$ | 303 (37.8) |
| **5y+7y** | *B*, *b* | 43* | 125—135 | — | — | — | — | — |

* Upon storage of the reaction mixture at room temperature for 1.5—3 months, the yields were increased by 7—12%.

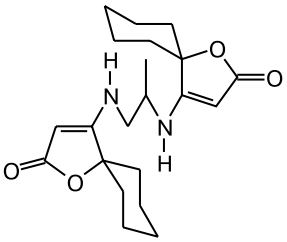


**7o**, **8**

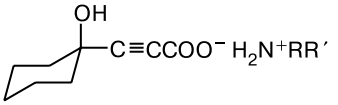
X = O (**7o**), NH (**8**)



**9**



**10**



**11a,b**

RR′N =  (**a**),

(*cyclo*-$C_6H_{11})_2N$ (**b**)

The resulting but-2-en-4-olides will be tested for antitumor activity at the M. M. Shemyakin and Yu. A. Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences. The database of their physicochemical and spectroscopic properties (Tables 1—5) can be used for identification of biologically active compounds belonging to furan derivatives.

## Experimental

The $^1$H NMR spectra were recorded on a Bruker DRX-500 instrument (500.13 MHz) in DMSO-$d_6$ with $Me_4Si$ as the internal standard. The UV spectra were measured on a Specord M-40 spectrometer in ethanol. The IR spectra were recorded on a Specord M-80 instrument in KBr pellets. The mass spectra were obtained on a Finnigan MAT.INCOS 50 instrument (EI, 70 eV) using a direct inlet system.

The melting points were measured on a Boetius hot-stage apparatus and are uncorrected.

The reagents were purchased from Acros Organics and Chemical Blocks. The specific rotation was measured on a PU-7 polarimeter. The specific rotation is given in deg mL $g^{-1}$ $dm^{-1}$, and the concentrations of solutions in chloroform are given in g $(100\ mL)^{-1}$.

Elemental analysis was carried out on a Perkin—Elmer 2400 C,H,N analyzer.

The course of the reactions was monitored by TLC on Silufol (UV-254) in a 9 : 1 : 1 chloroform—methanol—ethyl acetate mixture; spots were visualized with iodine vapor.

**Addition of amines 2a—z and 3a—y to methyl 3-(1-hydroxycyclohexyl)propiolate (1) (general procedure).** Method *A*. A solution of propiolate **1** (1.18 g, 7 mmol) and the corresponding amine (9—10 mmol) in dry diethyl ether (20 mL) was kept at room temperature for 10—12 days.

Method *B*. A solution of propiolate **1** (7 mmol) and the corresponding amine (9—10 mmol) in a ~2 : 1 diethyl ether—methanol mixture (20 mL) was kept at room temperature for 2 days and then heated at 55—60 °C for 10—12 h.

Method *C*. A solution of a mixture of compound **1** (7 mmol), the corresponding amine hydrochloride (5 mmol), and sodium acetate (10 mmol) in methanol (20 mL) was refluxed for 15—20 h.

Method *D*. The mixture was refluxed in butanol (20 mL) for 12—15 h analogously to the method *B*.

All expected compounds were isolated and purified according to one of procedures described below.

(*a*) The solid product that precipitated was filtered off, thoroughly washed on a filter with a saturated sodium bicarbonate solution, water, and petroleum ether with small additives (2—5%) of ethyl acetate and methanol, dried in air, and recrystallized from a petroleum ether—ethyl acetate mixture.

(*b*) The hot reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The residue (solid and oily) was refluxed in petroleum ether (10—15 mL) for 7—10 min, and the unconsumed starting compounds were removed by decantation. The solid residue was filtered off and worked up analogously to the procedure *a*. In the case of oily products (**6l,o**), the residues were subjected to silica gel flash chromatography using a solution of methanol in ethyl acetate (5—12%) as the eluent.

The following compounds were synthesized according to the procedure *A*, *a*: 4-(3-pyridyl)methylamino- (**6a**), 4-(3,4-dichlorobenzylamino)- (**6b**), 4-[2-(3,4-dimethoxyphenyl)ethylamino]- (**6l**), 4-[2-(3,4-diethoxyphenyl)ethylamino]- (**6m**), 4-[2-(adamantan-1-yloxy)ethylamino]- (**6p**), 4-(3-morpholinopropylamino)- (**6t**), 4-(*N*-benzyl-*N*-methylamino)- (**7e**), 4-dibenzylamino- (**7h**), 4-(4-methylpiperidin-1-yl)- (**7k**), and 4-[4-(4-fluorophenyl)piperazin-1-yl]-1-oxaspiro[4.5]dec-3-en-2-one (**7t**).

The procedure *A*, *b* was used to synthesize 4-(*N*-cyclopropylmethyl-*N*-propylamino)- (**7c**), 4-(*N*-benzyl-*N*-ethylamino)- (**7f**), and 4-(2-methylpiperidin-1-yl)-1-oxaspiro[4.5]dec-3-en-2-one (**7i**).

The following compounds were synthesized according to the procedure *B*, *a*: 4-(adamantan-1-yl)methylamino- (**6c**), 4-[1-(4-morpholinophenyl)ethylamino]- (**6f**), 4-[1-(adamantan-1-yl)propylamino]- (**6g**), 4-[α-(adamantan-1-yl)benzylamino]- (**6h**), 4-benzhydrylamino- (**6i**), 4-[2-(4-aminosulfonylphenyl)ethylamino]- (**6k**), 4-[2-(pentachlorophenylamino)ethylamino]- (**6q**), 4-[2-(pyrazol-1-yl)ethylamino]- (**6r**), 4-[3-(2-nitro-4-trifluoromethylanilino)propyl]- (**6s**), and 4-[4-aminocarbonylpiperidin-1-yl)-1-oxaspiro[4.5]dec-3-en-2-one (**7m**).

The following compounds were synthesized according to the procedure *B*, *b*: 4-[1-(4-piperidinophenyl)ethylamino]- (**6e**), 4-[2-(4-chlorophenyl)ethylamino]- (**6j**), 4-[3-(imidazol-1-yl)propylamino]- (**6u**), 4-(1-ethylpiperidin-3-yl)amino- (**6v**), 4-diisobutylamino- (**7a**), 4-dipentylamino- (**7b**), 4-[*N*-(2-hydroxyethyl)-*N*-methylamino]- (**7d**), 4-[*N*-benzyl-*N*-(2-hydroxyethyl)amino]- (**7g**), 4-(2-ethylpiperidin-1-yl)- (**7j**), 4-[(4-ethoxycarbonyl)piperidin-1-yl]- (**7l**), 4-[4-(piperidinocarbonyl)piperidin-1-yl]- (**7n**), 4-[4-(2-hydroxyethyl)piperazin-1-yl]- (**7p**), 4-[4-(2-cyanoethyl)piperazin-1-yl]- (**7q**),

**Table 3.** Main spectroscopic characteristics of compounds **6a—y** and **10**

| Compound | IR, ν/cm$^{-1}$ | | UV, $\lambda_{max}$/nm ($\varepsilon \cdot 10^{-3}$) | $^1$H NMR, δ (*J*/Hz) | |
|---|---|---|---|---|---|
| | C=C [C=O] | NH | | HC= (s) | Signals of other protons |
| **6a** | 1608 [1704] | 3308 | 255 (25.2) | 4.52 | 1.24, 1.47—1.55, 1.71, 1.86 (all m, 1 H, 4 H, 3 H, 2 H, $CH_2$ of cyclohexane); 4.33 (d, 2 H, $NCH_2$, *J* = 5.6); 7.39 (dd, 1 H, H of pyridine, *J* = 6.0, *J* = 4.0); 7.69 (d, 1 H, H of pyridine, *J* = 6.0); 7.83 (t, 1 H, NH, *J* = 5.6); 8.49 (d, 1 H, H of pyridine, *J* = 4.0); 8.54 (s, 1 H, H of pyridine) |
| **6b** | 1608 [1700] | 3080, 3260, 3276 | 255 (27.3) | 4.49 | 1.24, 1.47—1.56, 1.69, 1.85 (all m, 1 H, 4 H, 3 H, 2 H, $CH_2$ of cyclohexane); 4.28 (d, 2 H, $NCH_2$, *J* = 6.0); 7.38 (dd, 1 H, H arom., *J* = 8.0, *J* = 0.4); 7.59 (d, 1 H, H arom., *J* = 0.4); 7.64 (d, 1 H, H arom., *J* = 8.0); 7.86 (t, 1 H, NH, *J* = 6.0) |
| **6c** | 1608 [1700] | 3084, 3248 | 258 (19.6) | 4.46 | 1.26, 1.33—1.72, 1.49, 1.94 (two m, s, m, 1 H, 13 H, 6 H, 2 H, $CH_2$ of cyclohexane, $CH_2$, Ad); 1.94 (s, 3 H, CH, Ad); 2.73 (d, 2 H, $NCH_2$, *J* = 5.4); 7.06 (t, 2 H, NH, *J* = 5.4) |
| **6d** | 1604 sh, 1616 [1692] | 3064, 3224 | 255 (24.2) | 4.21 | 1.22, 1.42—1.60, 1.66, 1.84 (all m, 1 H, 4 H, 3 H, 2 H, $CH_2$ of cyclohexane); 4.09 (d, 2 H, $NCH_2$, *J* = 6.0); 6.26, 7.01 (both s, 2 H each, H of pyrrole); 7.34 (m, 1 H, H arom.); 7.43 (m, 3 H, H arom.); 7.35 (t, 1 H, NH, *J* = 6.0) |
| **6e** | 1604 [1696] | 3060, 3268 | 258 (29.0) | 4.21 | 1.17—1.74, 1.93 (both m, 14 H, 2 H, $CH_2$ of cyclohexane, $CH_2$ of piperidine); 1.40 (d, 3 H, Me, *J* = 7.0); 3.09 (t, 4 H, $NCH_2$, *J* = 7.0); 4.26 (quint, 1 H, NCH, *J* = 7.0); 6.89, 7.12 (both d, 2 H each, H arom., *J* = 8.0); 7.53 (d, 1 H, NH, *J* = 7.0) |
| **6f** | 1604 [1700] | 3056, 3268 | 258 (37.8) | 4.21 | 1.27, 1.51, 1.67, 1.83 (all m, 2 H, 3 H, 3 H, 2 H, $CH_2$ of cyclohexane); 1.40 (d, 3 H, Me, *J* = 7.0); 3.07 (t, 4 H, $NCH_2$, *J* = 5.5); 3.72 (t, 4 H, $OCH_2$, *J* = 5.5); 4.28 (quint, 1 H, NCH, *J* = 7.0); 6.90, 7.16 (both d, 2 H each, H arom., *J* = 8.0); 7.55 (d, 1 H, NH, *J* = 7.0) |
| **6g** | 1603 [1696] | 3088, 3253 | 258 (27.2) | 4.43 | 0.81 (t, 3 H, Me, *J* = 7.0); 1.30, 1.36—1.72 (both m, 20 H, $CH_2$ of cyclohexane, $CH_2$, Ad); 1.93 (s, 3 H, CH, Ad); 1.91, 2.05 (both t, 2 H, $C\underline{H}_2CH_3$, *J* = 7.0); 6.62 (d, 1 H, NH, *J* = 7.0) |
| **6h** | 1600 [1700] | 3060, 3292 | 257 (23.9) | 4.37 | 1.17, 1.36, 1.40—1.75, 1.53, 2.07 (three m, s, m, 1 H, 1 H, 12 H, 6 H, 2 H, $CH_2$ of cyclohexane, $CH_2$, Ad); 1.92 (s, 3 H, CH, Ad); 3.91 (d, 2 H, NCH, *J* = 8.0); 7.06 (d, 1 H, NH, *J* = 8.0); 7.22—7.33 (m, 5 H, H arom.) |
| **6i** | 1600 [1700] | 3244 | 257 (29.5) | 4.41 | 1.25, 1.43, 1.53, 1.68, 2.06 (all m, 1 H, 2 H, 2 H, 3 H, 2 H, $CH_2$ of cyclohexane); 5.62 (d, 1 H, NH, *J* = 7.0); 7.28—7.32 (m, 6 H, H arom.); 7.36—7.39 (m, 4 H, H arom.); 7.98 (d, 1 H, NH, *J* = 7.0) |
| **6j** | 1604 [1704] | 3068, 3228 | 220 (12.5), 257 (29.7) | 4.40 | 1.24, 1.38, 1.52—1.81 (all m, 1 H, 2 H, 7 H, $CH_2$ of cyclohexane); 2.81 (t, 2 H, *J* = 7.0); 3.27 (q, 2 H, $NCH_2$, *J* = 7.0); 7.12 (br.s, 1 H, NH); 7.23 (d, 2 H, H arom., *J* = 8.0); 7.29 (d, 2 H, H arom., *J* = 7.0) |
| **6k** | 1616 [1700] | 3064, 3320, 3572 | 256 (26.1) | 4.53 | 1.19, 1.43, 1.54, 1.60—1.81 (all m, 1 H, 2 H, 2 H, 5 H, $CH_2$ of cyclohexane); 2.87 (t, 2 H, $CH_2Ar$, *J* = 6.8); 3.30 (q, 2 H, $NCH_2$, *J* = 6.8); 7.32 (br.s, 3 H, $NH_2$, NH); 7.44, 7.75 (both d, 2 H each, H arom., *J* = 7.0) |
| **6l** | 1608 [1700] | 3080, 3276 | 257 (26.5) | 4.42 | 1.22, 1.43, 1.52—1.75, 1.79 (all m, 1 H, 2 H, 5 H, 2 H, $CH_2$ of cyclohexane); 2.74 (t, 2 H, $CH_2Ar$, *J* = 6.8); 3.24 (q, 2 H, $NCH_2$, *J* = 6.8); 3.73, 3.77 (both s, 6 H, OMe); 6.72 (d, 1 H, H arom., *J* = 8.0); 6.83 (s, 1 H, H arom.); 6.86 (d, 1 H, H arom., *J* = 8.0); 7.12 (br.s, 1 H, NH) |
| **6m** | 1604 [1700] | 3064, 3232 | 256 (28.0) | 4.48 | 1.20, 1.40, 1.33, 1.67, 1.78 (all m, 1 H, 2 H, 2 H, 3 H, 2 H, $CH_2$ of cyclohexane); 1.31 (t, 6 H, Me, *J* = 6.4); 2.72 (t, 2 H, $CH_2Ar$, *J* = 6.8); 3.22 (q, 2 H, $NCH_2$, *J* = 6.8); 3.90—4.10 (both t, 4 H, $OCH_2$, 2 *J* = 6.4); 6.71 (dd, 1 H, H arom., *J* = 8.0, *J* = 2.0); 6.83 (t*, H arom.); 6.86 (br.s, 1 H, H arom.); 7.27 (t, 1 H, NH, *J* = 6.8) |
| **6n** | 1604 [1700] | 3076, 3272 | 229 (36.9), 258 (25.7) | 4.43 | 1.21, 1.43, 1.55, 1.67, 1.76 (all m, 1 H, 2 H, 2 H, 3 H, 2 H, $CH_2$ of cyclohexane); 2.33 (s, 3 H, MeC=); 2.86 (t, 2 H, $C\underline{H}_2C=$, *J* = 7.0); 3.21 (q, 2 H, $NCH_2$, *J* = 7.0); 3.64 (s, 3 H, NMe); 6.99, 7.07 (both t, 1 H each, H arom., *J* = 6.0); 7.35 (d, 1 H, H arom., *J* = 6.0); 7.36 (br.s, 1 H, NH); 7.44 (d, 1 H, H arom., *J* = 6.0) |

(*to be continued*)

**Table 3** (*continued*)

| Compound | IR, ν/cm$^{-1}$ | | UV, $\lambda_{max}$/nm ($\varepsilon \cdot 10^{-3}$) | $^1$H NMR, δ (*J*/Hz) | |
|---|---|---|---|---|---|
| | C=C [C=O] | NH | | HC= (s) | Signals of other protons |
| **6o** | 1608 [1712] | 3064, 3284 | 226 (38.4), 258 (25.5) | 4.42 | 1.22 (t, 3 H, $CH_2C\underline{H}_3$, *J* = 8.0); 1.40—1.82 (m, 10 H, $CH_2$ of cyclohexane); 2.32 (s, 3 H, MeC=); 2.80 (m, 4 H, $NC\underline{H}_2C\underline{H}_2C$=); 3.21 (q, 2 H, $CH_2$, Ar, *J* = 8.0); 6.82 (d, 1 H, H arom., *J* = 8.0); 6.88 (t, 1 H, H arom., *J* = 8.0); 7.22 (d, 1 H, H arom., *J* = 8.0); 7.37 (t, 1 H, NH, *J* = 6.0); 10.60 (s, 1 H, NH of pyrrole) |
| **6p** | 1604, 1616 sh [1700] | 3084, 3256 | 255 (28.0) | 4.46 | 1.22, 1.43, 1.56—1.73, 1.61, 1.82 (three m, s, m, 1 H, 2 H, 11 H, 6 H, 2 H, $CH_2$ of cyclohexane, $CH_2$, Ad); 2.08 (s, 3 H, CH, Ad); 3.13 (q, 2 H, $NCH_2$, *J* = 6.0); 3.45 (t, 2 H, $OCH_2$, *J* = 6.0); 7.31 (t, 1 H, NH, *J* = 6.0) |
| **6q** | 1608 [1700] | 3072, 3240, 3276, 3340 | 227 (32.1), 255 (28.8) | 4.47 | 1.18, 1.37, 1.51, 1.65 (all m, 1 H, 2 H, 2 H, 5 H, $CH_2$ of cyclohexane); 3.20, 3.53 (both q, 2 H each, $NCH_2$, *J* = 6.7); 5.47, 7.18 (both t, 1 H each, NH, *J* = 6.7) |
| **6r** | 1614 [1718] | 3026, 3121, 3145, 3214 | 254 (25.3) | 4.46 | 1.25, 1.40—1.74, 1.81 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 2.96 (q, 2 H, $HNC\underline{H}_2$, *J* = 6.8); 4.02 (t, 2 H, $C\underline{H}_2$N of pyrazole, *J* = 6.8); 6.86, 7.21, 7.59 (all s, 1 H, 1 H, 1 H, H of pyrazole); 7.31 (t, 1 H, NH, *J* = 6.8) |
| **6s** | 1604, 1640 sh [1696] | 3088, 3288, 3384 | 351 (38.9) | 4.42 | 1.25, 1.47, 1.52—1.83, 1.91 (all m, 1 H, 2 H, 7 H, 2 H, $CH_2$ of cyclohexane, $NCH_2C\underline{H}_2CH_2N$); 3.26 (d, 2 H, $NCH_2$, *J* = 7.0); 3.49 (q, 2 H, $NCH_2$, *J* = 7.0); 7.12 (br.s, 1 H, NH); 7.26, 7.74 (d, 1 H, H arom., *J* = 8.0); 8.32 (s, 1 H, H arom.); 8.43 (br.s, 1 H, NH) |
| **6t** | 1608 [1700] | 3060, 3232 | 256 (23.2) | 4.42 | 1.23, 1.44, 1.46—1.74, 1.78 (all m, 1 H, 2 H, 7 H, 2 H, $CH_2$ of cyclohexane, $NCH_2C\underline{H}_2CH_2N$); 2.25—2.38 (m, 6 H, $NCH_2$); 3.08 (q, 2 H, $NCH_2$, *J* = 6.8); 3.55 (t, 4 H, $OCH_2$, *J* = 7.0); 7.22 (t, 1 H, NH, *J* = 6.8) |
| **6u** | 1612 [1720] | 3212 | 255 (21.1) | 4.41 | 1.22, 1.42, 1.56, 1.68, 1.82 (all m, 1 H, 2 H, 2 H, 3 H, 2 H, $CH_2$ of cyclohexane); 1.92 (quint, 2 H, $CH_2$, *J* = 7.0); 2.94 (q, 2 H, $NCH_2$, *J* = 6.8); 3.98 (t, 2 H, $NCH_2$, *J* = 6.8); 6.89, 7.18, 7.61 (all s, 1 H each, H of imidazole); 7.25 (t, 1 H, NH, *J* = 6.8) |
| **6v** | 1604 [1700] | 3080, 3248 | 255 (23.7) | 4.38 | 1.02 (t, 3 H, Me, *J* = 7.0); 1.26, 1.38—1.98 (both m, 2 H, 14 H, $CH_2$ of cyclohexane, $CH_2$ of piperidine); 2.38 (q, 2 H, $NCH_2$); 2.71, 2.86 (both d, 2 H, $NCH_2$); 3.16 (br.s, 3 H, NCH, $NCH_2$); 6.79 (br.s, 1 H, NH) |
| **6w** | 1604 [1696] | 3272 | 253 (7.8) | 4.63 | 1.22, 1.39—1.58, 1.68, 1.80 (all m, 1 H, 4 H, 3 H, 2 H, $CH_2$ of cyclohexane); 2.11 (sextet, 1 H, β′-$CH_2$ of sulfolane, *J* = 7.5); 2.47 (q, 1 H, β′-$CH_2$ of sulfolane, *J* = 6.6); 2.93 (dd, 1 H, α-$CH_2$S, *J* = 13.7, *J* = 6.2); 3.14 (dt, 1 H, α′-$CH_2$S, *J* = 8.5, *J* = 7.8); 3.32 (q, 1 H, α-$CH_2$S, *J* = 8.1); 3.57 (dd, 1 H, α-$CH_2$S, *J* = 13.7, *J* = 8.1); 7.44 (d, 1 H, NH, *J* = 6.6) |
| **6x** | 1608 [1700] | 3008, 3244 | 248 (14.7) | 4.51 | 1.12, 1.27, 1.32, 1.92 (all m, 1 H, 4 H, 3 H, 2 H, $CH_2$ of cyclohexane); 7.54 (t, 2 H, H arom., *J* = 8.0); 7.61 (t, 1 H, H arom., *J* = 8.0); 7.81 (d, 2 H, H arom., *J* = 8.0); 9.38, 9.74 (both s, 1 H each, NH) |
| **6y** | 1600 [1700] | 3068, 3300 | 258 (27.6) | 4.62 | 1.18, 1.42—1.72, 1.85, 1.92 (two m, s, m, 2 H, 12 H, 6 H, 2 H, $CH_2$ of cyclohexane, $CH_2$, Ad); 2.06 (s, 3 H, CH, Ad); 6.54 (s, 1 H, NH) |
| **10** | 1608 [1700] | 3080, 3272 | 260 (35.1) | 4.42, 4.51 | 1.14 (d, 3 H, Me, *J* = 7.6); 1.19, 1.37, 1.51, 1.56—1.76 (all m, 2 H, 4 H, 4 H, 10 H, $CH_2$ of cyclohexane); 3.00—3.16 (m, 2 H, $NCH_2$); 3.44 (septet, 1 H, NCH, *J* = 7.6); 6.97 (d, 1 H, NH, *J* = 7.6); 7.24 (t, 1 H, NH, *J* = 6.8) |

* The degenerate triplet.

4-(4-phenylpiperazin-1-yl)- (**7r**), 4-[4-(4-nitrophenyl)piperazin-1-yl]- (**7s**), 4-[4-(adamantan-1-yl)piperazin-1-yl]- (**7u**), 4-(1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl)-1-oxaspiro[4.5]dec-3-en-2-one (**7x**), and *N*,*N*-bis(2-oxo-1-oxaspiro[4.5]dec-3-en-4-yl)-1,2-diaminopropane (**10**).

The *C*, *b* was used to synthesize 4-[2-(pyrrol-1-yl)benzylamino]- (**6d**), 4-(1,1-dioxotetrahydrothiophen-3-yl)amino- (**6w**), 4-*N*′-benzoylhydrazino- (**6x**), 4-[(*S*)-2-(3-pyridyl)piperidin-1-yl]- (**7o**), and 4-(2,6-dimethylmorpholin-4-yl)-1-oxaspiro[4.5]dec-3-en-2-one (**7v**).

The following compounds were synthesized according to the procedure *D*, *b*: 4-[2-(1,2-dimethylindol-3-yl)ethylamino]- (**6n**), 4-[2-(8-ethyl-2-methylindol-3-yl)ethylamino]- (**6o**), 4-(adamantan-1-yl)amino- (**6y**), and 4-[(1-phthalimidomethyl)-

**Table 4.** Main spectroscopic characteristics of compounds **7a—x**

| Compound | IR, ν/cm$^{-1}$ | | UV, $\lambda_{max}$/nm ($\varepsilon \cdot 10^{-3}$) | $^1$H NMR, δ (*J*/Hz) | |
|---|---|---|---|---|---|
| | C=C [C=O] | Other groups | | HC= (s) | Signals of other protons |
| **7a** | 1584 [1720] | | 271 (29.7) | 4.53 | 0.87 (d, 12 H, $CH(C\underline{H}_3)_2$, *J* = 7.6); 1.31, 1.57—1.74, 1.93 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 2.04 (septet, 2 H, $C\underline{H}Me_2$, *J* = 7.6); 3.11 (d, 4 H, $NCH_2$, *J* = 7.6) |
| **7b** | 1576 [1716] | — | 270 (28.2) | 4.43, 4.52 (1 H) | 0.82—1.03, 1.16, 1.38—1.92, 2.06 (all m, 12 H, 1 H, 14 H, 1 H, $CH_2$ of cyclohexane, $C\underline{H}_2C\underline{H}_2C\underline{H}_2C\underline{H}_3$); 3.09—3.29 (m, 4 H, $NCH_2$) |
| **7c** | 1588 [1724] | — | 269 (24.9) | 4.53 | 0.30, 0.54 (both q, 2 H, 2 H, $CH_2$ of cyclopropane, *J* = 4.4); 0.86 (t, 3 H, Me, *J* = 7.4); 0.92 (t, 1 H, CH of cyclopropane, *J* = 7.2); 1.33, 1.54—1.72, 1.93 (all m, 1 H, 9 H, 2 H, $CH_2$ of cyclohexane, $NCH_2C\underline{H}_2CH_3$); 3.18 (d, 2 H, $NC\underline{H}_2CH$, *J* = 7.0); 3.26 (t, 2 H, $NC\underline{H}_2CH_2$, *J* = 7.0) |
| **7d** | 1592 [1696] | 3368 (OH) | 267 (20.8) | 4.42 | 1.32, 1.53—1.75, 2.02 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 2.96 (s, 3 H, Me); 3.35 (t, 2 H, $NCH_2$, *J* = 7.2); 3.62 (q, 2 H, $OCH_2$, *J* = 7.2); 4.68 (t, 1 H, OH, *J* = 7.2) |
| **7e** | 1588 [1716] | — | 266 (33.5) | 4.59 | 1.33, 1.52—1.71, 2.04 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 2.94 (s, 9 H, NMe); 4.59 (s, 2 H, $NCH_2$); 7.19 (d, 2 H, H arom., *J* = 8.0); 7.31 (t, 1 H, H arom., *J* = 8.0); 7.39 (t, 2 H, H arom., *J* = 8.0) |
| **7f** | 1584 [1720] | — | 266 (30.2) | 4.50 | 1.28, 1.63, 2.01 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 1.09 (t, 3 H, Me, *J* = 8.0); 3.32 (br.s, 2 H, $NCH_2$); 4.55 (s, 2 H, $NC\underline{H}_2Ar$); 7.22 (d, 2 H, H arom., *J* = 8.0); 7.29 (t, 1 H, H arom., *J* = 8.0); 7.38 (t, 2 H, H arom., *J* = 8.0) |
| **7g** | 1580 [1692] | 3388 (OH) | 267 (29.9) | 4.52 | 1.30, 1.61, 2.03 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 3.35 (br.s, 2 H, $NCH_2$); 3.55 (q, 2 H, $OCH_2$, *J* = 5.4); 4.64 (br.s, 2 H, $NC\underline{H}_2Ar$); 4.87 (br.s, 1 H, OH); 7.19 (d, 2 H, H arom., *J* = 8.0); 7.30 (t, 1 H, H arom., *J* = 8.0); 7.39 (t, 2 H, H arom., *J* = 8.0) |
| **7h** | 1596 [1724] | 1572 (Ar) | 267 (25.3) | 4.72 | 1.31, 1.60, 2.00 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 4.55 (br.s, 4 H, $NC\underline{H}_2Ar$); 7.20 (d, 4 H, H arom., *J* = 8.0); 7.28 (t, 2 H, H arom., *J* = 8.0); 7.38 (t, 4 H, H arom., *J* = 8.0) |
| **7i** | 1584, 1708 | — | 270 (27.6) | 4.59 | 1.16 (d, 3 H, Me, *J* = 7.6); 1.36, 1.49—1.71, 1.95 (all m, 2 H, 12 H, 2 H, $CH_2$ of cyclohexane, $CH_2$ of piperidine); 3.11 (td, 1 H, $NCH_2$, *J* = 7.0, *J* = 1.9); 3.54 (d, 1 H, $NCH_2$, *J* = 7.0); 3.91 (br.s, 1 H, NCH) |
| **7j** | 1572 [1720] | — | 270 (30.3) | 4.62 | 0.84 (t, 3 H, Me, *J* = 7.2); 1.35, 1.50—1.75, 1.95 (all m, 2 H, 14 H, 2 H, $CH_2$ of cyclohexane, $CH_2$ of piperidine, $C\underline{H}_2CH_3$); 3.08 (t, 1 H, $NCH_2$, *J* = 7.6); 3.63 (m, 2 H, NCH, $NCH_2$) |
| **7k** | 1584 [1717] | — | 270 (29.1) | 4.64 | 0.89 (d, 3 H, Me, *J* = 7.2); 1.09, 1.37, 1.50—1.72, 1.96 (all m, 2 H, 1 H, 10 H, 2 H, $CH_2$ of cyclohexane, $CH_2$, CH of piperidine) |
| **7l** | 1580 [1720] | 1736 (COOEt) | 268 (27.7) | 4.74 | 1.19 (t, 3 H, Me, *J* = 7.6); 1.36, 1.47—1.71, 1.85—2.02 (all m, 1 H, 9 H, 4 H, $CH_2$ of cyclohexane, $CH_2$ of piperidine); 2.67 (m, 1 H, CH of piperidine); 3.12 (td, 2 H, $NCH_2$, *J* = 12.0, *J* = 2.0); 3.69, 3.73 (both t, 2 H, $NCH_2$, *J* = 2.0); 4.08 (q, 2 H, $OCH_2$, *J* = 7.6) |
| **7m** | 1576, 1684, [1696 sh] | 3180, 3376 ($NH_2$) | 268 (26.6) | 4.69 | 1.35, 1.45—1.82, 1.96 (all m, 1 H, 11 H, 2 H, $CH_2$ of cyclohexane, $CH_2$ of piperidine); 2.42 (m, 1 H, CH of piperidine); 3.04 (t, 2 H, $NCH_2$, *J* = 12.0); 3.76 (d, 2 H, $NCH_2$, *J* = 12.0); 6.85, 7.32 (both c, 2 H, $NH_2$) |
| **7n** | 1580 [1624] | 1724, 1424, 1204 (amide) | 268 (30.4) | 4.66 | 1.27—1.72, 1.91 (both m, 18 H, 2 H, $CH_2$ of cyclohexane, $CH_2$ of piperidine); 2.92 (br.t, 1 H, CH of piperidine, *J* = 13.0); 3.11 (br.t, 2 H, $NCH_2$, *J* = 13.0); 3.42, 3.49 (both t, 4 H, $NCH_2$, *J* = 6.0); 3.78 (br.d, 2 H, $NCH_2$, *J* = 13.0) |
| **7o** | 1580 [1712] | — | 268 (25.7) | 4.70 | 1.38, 1.49—1.75, 1.82—2.02, 2.12, 2.36 (all m, 2 H, 10 H, 2 H, 1 H, 1 H, $CH_2$ of cyclohexane, $CH_2$ of piperidine); 3.08 (t, 1 H, $NCH_2$, *J* = 13.0); 3.76 (d*, 1 H, $NCH_2$); 5.18 (br.s, 1 H, NCH); 7.43 (dd, 1 H, H of pyridine, *J* = 8.0, *J* = 4.0); 7.63 (d, 1 H, H of pyridine, *J* = 8.0); 8.46 (s, 1 H, H of pyridine); 8.51 (d, 1 H, H of pyridine, *J* = 4.0) |

(*to be continued*)

**Table 4** (*continued*)

| Compound | IR, ν/cm$^{-1}$ | | UV, $\lambda_{max}$/nm ($\varepsilon \cdot 10^{-3}$) | $^1$H NMR, δ (*J*/Hz) | |
|---|---|---|---|---|---|
| | C=C [C=O] | Other groups | | HC= (s) | Signals of other protons |
| **7p** | 1584 [1728] | 3190 (OH) | 266 (13.0) | 4.67 | 1.32, 1.50—1.73, 1.91 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 2.40—2.70 (br.s, 6 H, $NCH_2$); 3.35 (br.s, 4 H, $NCH_2$); 3.54 (q, 2 H, $OCH_2$, *J* = 5.4); 4.42 (br.s, 1 H, NH) |
| **7q** | 1592 [1720] | 2248 (C≡N) | 267 (30.8) | 4.70 | 1.32, 1.53—1.72, 1.90 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 2.47 (t, 4 H, $CH_2CN$, $NCH_2$, *J* = 4.6); 2.62, 2.69 (both t, 2 H each, $NCH_2$, *J* = 4.6); 3.38 (t, 4 H, $NCH_2$, *J* = 4.6) |
| **7r** | 1592 [1720] | — | 267 (37.9) | 4.76 | 1.35, 1.54—1.74, 2.01 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 3.39, 3.53 (both t, 4 H each, $NCH_2$, *J* = 4.6); 6.83 (t, 1 H, H arom., *J* = 8.0); 6.97 (d, 2 H, H arom., *J* = 8.0); 7.50 (t, 2 H, H arom., *J* = 8.0) |
| **7s** | 1596, 1604 [1712] | — | 266 (26.5), 376 (18.8) | 4.73 | 1.34, 1.54—1.75, 2.01 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 3.21 (s, 2 H, $NCH_2$); 3.60 (s, 6 H, $NCH_2$); 7.01, 8.09 (both d, 2 H each, H arom., 2 *J* = 8.0) |
| **7t** | 1588 [1716] | — | 268 (30.2) | 4.78 | 1.35, 1.60, 1.67, 2.01 (all m, 1 H, 4 H, 3 H, 2 H, $CH_2$ of cyclohexane); 3.11, 3.53 (both t, 4 H each, $NCH_2$, 2 *J* = 4.6); 6.80, 6.98 (both d, 2 H each, H arom., 2 *J* = 6.0); 7.09 (t, 2 H, H arom., *J* = 9.0) |
| **7u** | 1584 [1728] | — | 268 (29.7) | 4.51 | 1.28, 1.56—1.79, 1.93 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 1.69 (s, 12 H, $CH_2$, Ad); 2.11 (s, 3 H, CH, Ad); 2.64, 3.32 (both br.s, 4 H each, $NCH_2$) |
| **7v** | 1580 [1716] | — | 268 (26.2) | 4.64, 4.70** | **A**: 1.22 (d, 6 H, Me, *J* = 7.2); 1.36, 1.55—1.72, 1.95 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 3.12 (dd, 2 H, $NCH_2$, *J* = 12.0, *J* = 4.0); 3.43 (d, 2 H, $NCH_2$, *J* = 12.0); 3.96 (t, 2 H, OCH, *J* = 4.0) **B**: 1.20 (d, 6 H, Me, *J* = 7.2); 1.36, 1.55—1.72, 1.95 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 2.68 (t, 2 H, $NCH_2$, *J* = 12.0); 3.55 (m, 2 H, OCH); 3.61 (d, 2 H, $NCH_2$, *J* = 12.0) |
| **7w** | 1568 [1712] | 1724 (amide) | 220 (33.5), 267 (11.8) | 4.52 | 1.08, 1.32—1.70, 1.96 (all m, 1 H, 7 H, 2 H, $CH_2$ of cyclohexane); 2.82 (m, 2 H, $C\underline{H}_2Ar$); 3.78 (m, 1 H, $NCH_2$); 3.96 (m, 2 H, $NCH_2$); 4.13 (br.t, 1 H, $NCH_2$, *J* = 12.0); 5.01 (br.s, 1 H, NCH of piperidine); 7.26 (br.s, 4 H, H arom.); 7.88 (m, 4 H, H arom.) |
| **7x** | 1584 [1720] | — | 270 (28.1) | — | 0.89, 0.94, 1.09 (all c, 3 H each, Me); 1.18—2.20 (m, 16 H, $CH_2$ of cyclohexane, $CH_2$ of bicyclic fragment); 3.55—3.95 (both m, 2 H, $NCH_2$); 4.25—4.55 (m, 2 H, CH=, NCH) |

* The unresolved doublet.

** Diastereomers **A** and **B** in a ratio of ~1 : 5.

1,2,3,4-tetrahydroisoquinolin-2-yl]-1-oxaspiro[4.5]dec-3-en-2-one (**7w**).

The yields, elemental analysis data, and the melting points for compounds **6a—z** and **10** are given in Table 1; for compounds **7a—y**, in Table 2. The IR, UV, and $^1$H NMR spectroscopic data are presented, respectively, in Tables 3 and 4. The mass-spectrometric data are listed in Tables 1, 2, and 5.

**Methyl 3-(1-hydroxycyclohexyl)-3-(imidazol-1-yl)prop-2-enoate (5y) and 4-(imidazol-1-yl)-1-oxaspiro[4.5]dec-3-en-2-one (7y) (see Table 2).** A mixture of compounds **5y+7y** was obtained in a ratio of 14 : 3. Recrystallization of this mixture ($^1$H NMR data) led to enrichment with γ-lactone **7y** to form a mixture of **5y+7y** in a ratio of 12 : 5, m.p. 125—132 °C (petroleum ether—diethyl ether, 2 : 1). IR, ν/cm$^{-1}$: 1632, 1660, 1732, 1748, 3112, 3152. Compound **5y**. $^1$H NMR, δ: 3.52 (s, 3 H, OMe); 5.27 (s, 1 H, OH); 6.39 (s, 1 H, CH=); 6.95, 7.19, and 7.47 (all s, 3 H, H of imidazole). In addition, the spectrum showed signals characteristic of compound **7y** (δ): 6.54 (s, 1 H, CH=); 7.21, 7.89, and 8.49 (all s, 3 H, H of imidazole).

**Methyl 3-(1-hydroxycyclohexyl)-3-[3-(2-methylimidazol-1-yl)propylamino]prop-2-enoate (4z) and 4-[3-(2-methylimidazol-1-yl)propylamino]-1-oxaspiro[4.5]dec-3-en-2-one (6z) (see Table 1).** A mixture of compounds **4z+6z** was obtained in a ratio of 1 : 5, m.p. 99—102 °C. IR, ν/cm$^{-1}$: 1612, 1656, 1728, 3048, 3210. Compound **4z**. $^1$H NMR, δ: 1.89 (s, 3 H, MeC=); 3.07 (q, 2 H, NC(1)$H_2$, *J* = 6.7 Hz); 3.22 (s, 3 H, OMe); 3.86 (br.t, 2 H, NC(3)$H_2$, *J* = 6.2 Hz); 5.05 (br.s, 1 H, OH); 6.71 and 7.91 (both s, 2 H, H of imidazole); 6.72 (t, 1 H, NH, *J* = 6.7 Hz). In addition, the spectrum showed characteristic signals of compound **6z** (δ, *J*/Hz): 2.52 (s, 3 H, MeC=); 3.00 (q, 2 H, NC(1)$H_2$, *J* = 6.7 Hz); 3.91 (t, 2 H, NC(1)$H_2$, *J* = 6.4 Hz); 6.74 and 7.05 (both s, 2 H, H of imidazole), 7.37 (t, 1 H, NH, *J* = 6.7 Hz).

**4-Oxopiperidinium (1-hydroxycyclohexyl)ethynylcarboxylate (11a).** The yield was 47%, m.p. 253—254 °C. Found (%): N, 5.31.

**Table 5.** Mass spectra of compounds **6a,c,g,m,u,w**, **7n,o,t**, and **10**

| Compound | *m/z* (*I* (%))* |
|---|---|
| **6a** | 215 (27.7), 202 (41.0), 132 (45.1), 93 (33.4), 92 (100), 68 (38.1) |
| **6c** | 189 (24.1), 135 (100), 107 (26.8), 93 (49.3), 79 (62.2), 68 (40.0) |
| **6g** | 208 (46.6), 207 (21.1), 135 (100), 93 (40.2), 79 (62.2), 68 (35.1) |
| **6m** | 192 (88.0), 180 (31.9), 179 (100), 151 (50.2), 123 (65.4) |
| **6u** | 149 (77.3), 109 (39.8), 95 (74), 82 (100), 68 (31.5) |
| **6w** | 229 (22.9), 137 (23.6), 68 (34.7), 55 (100), 41 (84.0) |
| **7n** | 234 (90.3), 190 (100), 140 (85.3), 84 (44.1), 69 (43.0) |
| **7o** | 268 (50.2), 213 (30.9), 185 (39.3), 176 (56.3), 132 (45.3), 106 (44), 68 (30.0), 41 (100) |
| **7t** | 150 (100), 137 (22.8), 123 (67.9), 122 (58.2) |
| **10** | 194 (35.9), 181 (39.6), 91 (35.2), 55 (43.5), 44 (100) |

* The signals with intensities of no lower than 20% are given.

$C_{14}H_{21}NO_4$. Calculated (%): N, 5.24. IR, ν/cm$^{-1}$: 1560, 1640, 1660, 2208 (C≡C); 3420. $^1$H NMR, δ: 1.08—1.24 and 1.38—1.83 (both m, 3 H, 7 H, $CH_2$ of cyclohexane); 2.52 and 2.74 (both m, 2 H each, $CH_2C$=O); 3.09 (t, 2 H, $NCH_2$, $J$ = 7.2 Hz); 3.52 (br.s, 2 H, $NCH_2$); 6.23 (s, 1 H, OH); 8.52 (br.s, 2 H, NH, COOH).

**Dicyclohexylammonium (1-hydroxycyclohexyl)ethynylcarboxylate (11b).** The yield was 39%, m.p. 206—207 °C. Found (%): N, 4.01. $C_{21}H_{35}NO_3$. Calculated (%): N, 4.01. IR, ν/cm$^{-1}$: 1548, 1632, 2224 (C≡C); 3280. $^1$H NMR, δ: 1.02—2.05 (m, 30 H, $CH_2$ of cyclohexane); 2.98 (br.t, 2 H, NCH); 4.90—5.30 (br.s, 2 H, OH, NH); 8.50—10.60 (br.s, 1 H, COOH).

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