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Mendeleev Commun., 2016, **26**, 391–394
Mendeleev Communications

Diastereoselective synthesis of 1,3-di- and 1,3,3-trisubstituted diaziridines coupled with neurotransmitter amino acids

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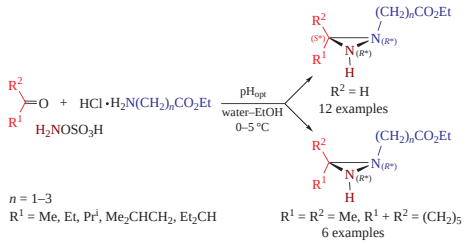
DOI: 10.1016/j.mencom.2016.09.008

The pH-controlled one-pot three-component condensation of carbonyl compounds, amino acid ethyl esters and hydroxylamine-*O*-sulfonic acid in water–ethanol mixture at 0–5 °C diastereoselectively affords conjugates of 1,3-di- or 1,3,3-trisubstituted diaziridines with neurotransmitter amino acids.

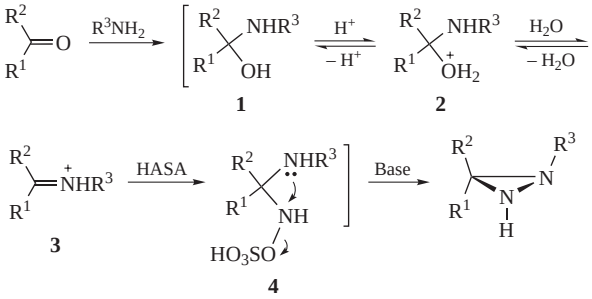


A fundamental trend in modern medicinal chemistry is development of new drugs with complex pharmacological effect possessing an alternative mechanism of action as compared with known drugs of analogous profile, having lower toxicity and lower effective dose. This goal can be achieved by combining two or more pharmacologically active moieties in one molecule.[1] Amino acids can serve as one of these moieties.[2–4] Previously it was found that diaziridine derivatives (1,2-diazacyclopropanes) have a pronounced action on the central nervous system (CNS);[5] in particular, 1-[2-(3,3-dimethyldiaziridin-1-yl)ethyl]-3,3-dimethyldiaziridine was recently shown to have a high antidepressive activity.[6] The association of diaziridine ring and neurotransmitter amino acid in one molecule could give rise to compounds with new specific action on the CNS.

We have the great experience in the chemistry of diaziridines.[7] Three key approaches are known for the construction of monocyclic diaziridines:[7(a),8] (i) three-component condensation of the carbonyl compounds, primary aliphatic amines or ammonia, and aminating reagents [hydroxylamine-*O*-sulfonic acid (HASA) or halo(alkyl)amines], (ii) reaction of the aminating reagents with the condensation products of carbonyl compounds and primary aliphatic amines, and (iii) reaction of primary aliphatic amines or ammonia with the condensation products of carbonyl compounds and aminating reagents. The first approach is the most simple and attractive one and so is widely explored.

Earlier,[7(a),9] we have found that the formation of monocyclic diaziridines upon three-component condensation of carbonyl compounds, primary aliphatic amines, and HASA in protic medium substantially depends on its pH value. To explain the influence of pH on the reaction outcome, a reaction mechanism was proposed. The first step is the reaction of the carbonyl compound with amine (or ammonia) resulting in α-amino carbinol **1**, which is protonated to give oxonium ion **2**, and its subsequent dehydration affords carbenium-iminium cation **3**. The reaction of the latter with the aminating reagent (HASA) generates aminal **4**, which would rapidly cyclize to final diaziridine **8** in the presence of base (Scheme 1).

Here we present the effective, diastereoselective, facile one-pot synthesis of earlier unknown 1,3-di- and 1,3,3-trisubstituted diaziridines coupled with neurotransmitter amino acids. The



Scheme 1

method is the extension of chemistry outlined in Scheme 1 when amino component R^3NH_2 is an ethyl ester of the proper amino acid hydrochloride, such as glycine (**5a**), β-alanine (**5b**) and γ-aminobutyric acid (GABA) (**5c**).

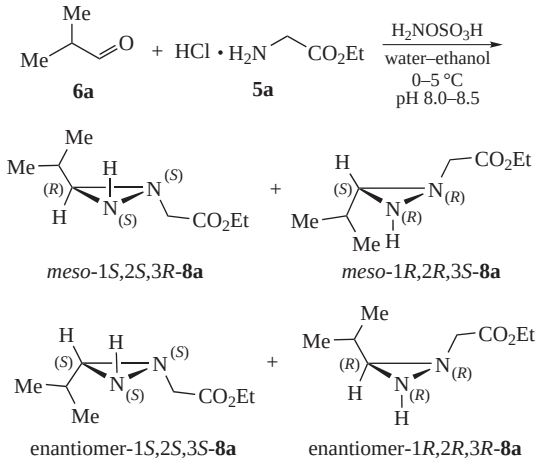
Various aldehydes **6** (isobutyraldehyde **6a**, acetaldehyde **6b**, propionaldehyde **6c**, isovaleraldehyde **6d**, and 2-ethylbutyraldehyde **6e**) and ketones **7** (acetone **7a** and cyclohexanone **7b**) were taken as the starting carbonyl compounds. Since HASA and compounds **5a–c** are water-soluble, while some carbonyl compounds are soluble in organic solvents, a water–ethanol mixture was selected as the reaction medium.

As it was earlier established,[7(a),9] the highest yield of diaziridines in aqueous medium for any amine/carbonyl compound pair was achieved at an optimal pH value (pH_{opt}) that was shifted to less alkaline region when electron-withdrawing substituents were present in the amine or carbonyl compound molecule. In addition, the pH_{opt} for diaziridine synthesis from aliphatic aldehydes was found to differ from the pH_{opt} for diaziridine synthesis from aliphatic ketones. Therefore, the pH_{opt} for the synthesis of target diaziridines coupled with neurotransmitter amino acids was determined separately for aldehydes and ketones.

Isobutyraldehyde **6a** and glycine ethyl ester hydrochloride **5a** were selected as model compounds. Compounds **5a**, **6a**, in equimolar ratio, and HASA (1.05 equiv.) were reacted in a water–ethanol mixture (1:1 v/v) at 0–5 °C. To perform the first step (formation of amino carbinol), free glycine ethyl ester was prepared *in situ* from the hydrochloride by adding 30% aqueous

NaOH to the mixture of reactants **5a** and **6a** up to pH 9.0. To optimize the reaction conditions, various pH ranges (7.5–8.0, 8.0–8.5, 8.5–9.0, and 9.0–9.5) were examined with simultaneous addition of HASA (1 equiv.) and 30% aqueous NaOH to neutralize H_2SO_4 that formed. The desired 1-(ethoxycarbonylmethyl)-3-isopropyldiaziridine **8a** was formed in all cases, however, the maximum (65%) yield was achieved at pH 8.0–8.5 (for pH ranges of 7.5–8.0, 8.5–9.0, and 9.0–9.5 the yields of **8a** were 30, 40, and 25%, respectively). Such a low pH_{opt} value is attributable to the reduced basicity of starting ester glycine as compared to aliphatic amines owing to the presence of electron-withdrawing CO_2Et group. About 1 h was needed to complete the addition of HASA and the reaction was completed within 3 h when pH stabilized. The resulting diaziridine **8a** was extracted with $CHCl_3$ and the yield of the crude product was estimated by iodometric titration.

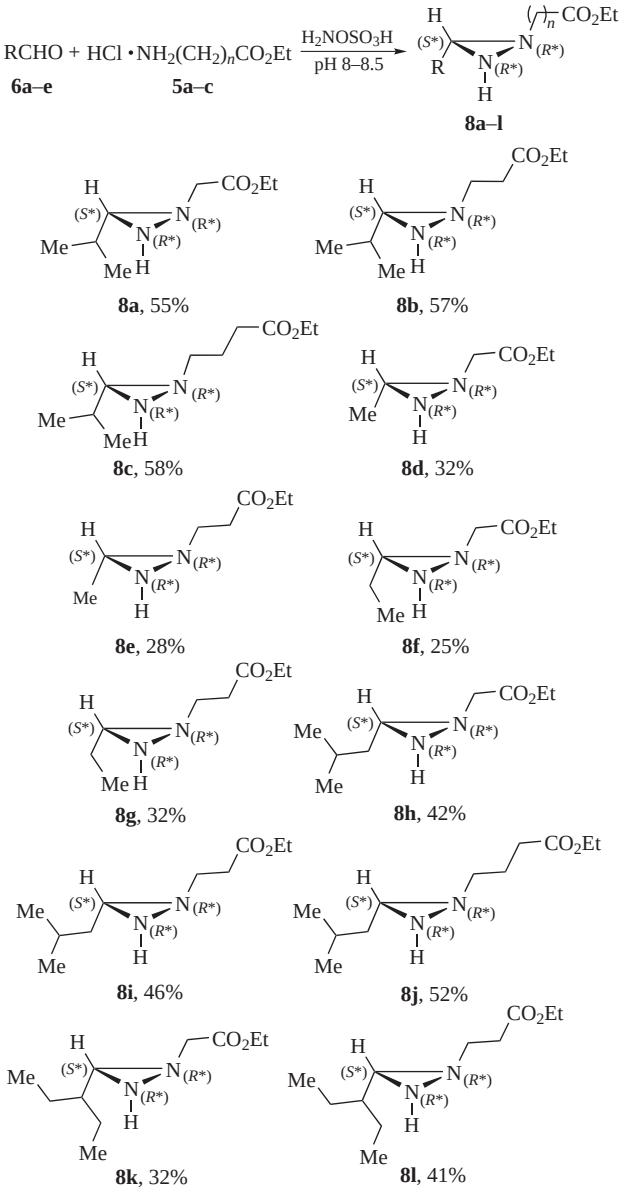
1-(Ethoxycarbonyl)-3-isopropyldiaziridine **8a** was formed as a mixture of two diastereomers in ~10:1 ratio (TLC and ^{1}H NMR data). It is known that the diaziridine ring has two stereogenic nitrogen centers, which are stereolabile and, therefore, prone to interconversion with rather high barriers (18–24 kcal mol^{-1}). The adjacent substituents at the nitrogen atoms of the diaziridine ring occur only in the antiperiplanar conformation, which results in coupled interconversion and, hence, both nitrogen atoms in each diaziridine ring have the same absolute configuration.[10] The diaziridine ring in the molecule of **8a** contains a chiral carbon atom along with chiral nitrogen atoms. Therefore, this molecule exists as a mixture of four stereoisomers (two *meso* forms, 1*S*,2*S*,3*R* and 1*R*,2*R*,3*S*, and two enantiomeric forms, 1*S*,2*S*,3*S* and 1*R*,2*R*,3*R*). Thus, the two diastereomers of **8a** observed in TLC and ^{1}H NMR spectra correspond, evidently, to two racemic mixtures of 1*S*,2*S*,3*S* + 1*R*,2*R*,3*R* and 1*R*,2*R*,3*S* + 1*S*,2*S*,3*R*, in which one of the racemates significantly predominates (Scheme 2).



Scheme 2

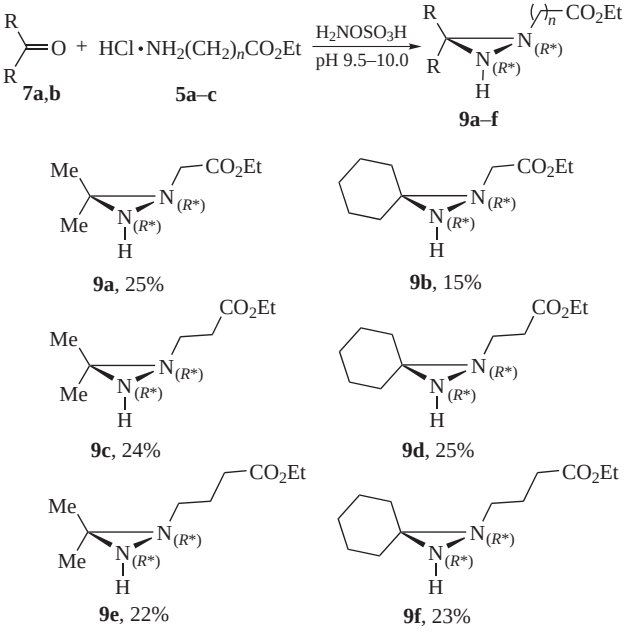
The attempted chromatographic resolution of the diastereomers on SiO_2 failed; however, the major diastereomer was isolated. A little amount of the minor diastereomer was detected in the NMR spectrum after the first distillation, while only the predominant diastereomer was isolated after the second distillation. Apparently, epimerization of the minor diastereomer to the major one *via* the coupled interconversion takes place under these conditions. The structure of the major diastereomer was determined by elemental analysis and spectral methods (^{1}H and ^{13}C NMR, IR spectroscopy and mass spectrometry), including the {^{1}H-^{1}H}g NOESY 2D spectrum for **8a** (see Online Supplementary Materials). Considering the coupling of the N–CH_2 and CH_{ring} protons observed in the NOESY 2D spectrum, it is evident that the isopropyl and ethoxycarbonylmethyl substituents occupy *trans*-positions in the diaziridine ring and, hence, the major diastereomer represents the racemic mixture of two *meso*-forms, 1*R**,2*R**,3*S**. The minor diastereomer is evidently the racemic mixture of two enantiomers 1*S**,2*S**,3*S**. It was characterized only by the ^{1}H and ^{13}C NMR spectra of the diastereomer mixture.

With the optimized conditions in hand, we performed the three-component condensation with aldehydes **6a–d**, amino acid ethyl ester hydrochlorides **5a–c**, and HASA, and the results are summarized in Scheme 3. The desired diaziridines **8b–l** coupled with neurotransmitter amino acids were obtained in moderate to good yields as individual diastereomers (Scheme 3). Minor amounts of the second diasteremers were detected in the ^{1}H NMR spectra of crude **8d–g** synthesized from acetaldehyde and propionaldehyde; however, the minor diastereomers were epimerized after two distillations, resulting in individual diastereomers in all cases. Evidently, the final compound **8** represented the racemic mixture of two *meso* forms in which bulky substituents occupied *trans*-positions. All compounds were characterized by ^{1}H, ^{13}C NMR and MS spectral data.† (1*R**,2*R**,3*S**)-**8a** has also been transformed to phenylcarbamoyl derivative **8a′** (see Online Supplementary Materials).



Scheme 3 *Reagents and conditions*: 1 equiv. of **5**, **6** and 1.05 equiv. of HASA, water–ethanol (1:1 v/v), 0–5 °C. Isolated yields after two distillations are given.

To introduce ketones **7a**,**b** into the similar process, the search of pH_{opt} was also needed. Acetone **7a** and hydrochloride of ester **5a** were selected as model compounds. The search for pH_{opt} was carried out in more alkaline regions (9.0–9.5, 9.5–10.0, and 10.0–10.5) than those for the synthesis of diaziridine **8a**. It was found that the pH_{opt} was 9.5–10 for the synthesis of diaziridine **9a**; however, the product formed contained a considerable amount of impurity (^{1}H NMR data) that failed to be isolated pure by column chromatography or by repeated distillation. The final product contained about 5% impurity and, hence, it was characterized only by the ^{1}H and ^{13}C NMR spectra. The same picture was observed in the reaction of ketone **7b** with ester **5a** under analogous conditions, diaziridine **9b** being characterized by the ^{1}H NMR spectrum. Evidently, the pH requirement for ketones **7a**,**b** (more alkaline region) and ester **5a** (less alkaline region) were at variance with each other. To our delight, the reactions of both ketones **7a**,**b** with compounds **5b**,**c**, in which the electron-withdrawing CO_2Et group is spaced apart from the NH_2 group, and with HASA at pH 9.5–10 was more successful and the desired diaziridines **9c**–**f** were isolated as individual compounds and characterized by elemental analysis and spectral data (Scheme 4).† However, the yields of diaziridines **9** were rather low in all cases. Presumably, an alternative pathway of the reaction with ketones **7** is formation of their condensation products with amino acid esters **5** without participation of HASA. Since the synthesized 1,3,3-trisubstituted diaziridines **9** contain only two chiral nitrogen atoms in the molecule, they are racemic 1*R**,2*R**-**9**.



Scheme 4 *Reagents and conditions*: 1 equiv. of **5**, **7** and HASA (1.05 equiv.), water–ethanol (1:1, v/v), 0–5 °C. Isolated yields after two distillations are given.

In summary, a general, facile, diastereoselective method for the preparation of new hybrid structures, previously unknown 1,3-di- and 1,3,3-trisubstituted diaziridines coupled with neurotransmitter amino acids, was developed. This method is based on one-pot three-component condensation of carbonyl compounds, amino acid ethyl ester taken as hydrochlorides, and hydroxylamine-*O*-sulfonic acid under very mild conditions (aqueous ethanol, 0–5 °C) at controlled pH (pH_{opt}). Diaziridines obtained from aldehydes were shown to form as mixtures of two diastereomers, the predominant diastereomers being racemic mixtures of two *meso* forms. The minor diasetromers (racemic mixture of two enantiomers) epimerize to the major ones in the course of distillation, resulting in only one diastereomer. The advantages of the method are operational simplicity, step economy, and the use of simple and accessible initial compounds. In the whole, the developed method provides a powerful tool for the synthesis of the extensive series of new kind of structures containing two neurotropic active fragments in one molecule – a neurotransmitter amino acid and diaziridine ring.

This work was supported by the Russian Foundation for Basic Research (grant no. 13-03-00153).

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2016.09.008.

References

1 (*a*) V. P. Ananikov, E. A. Khokhlova, M. P. Egorov, A. M. Sakharov, S. G. Zlotin, A. V. Kucherov, L. M. Kustov, M. L. Gening and N. E. Nifantiev, *Mendeleev Commun.*, 2015, **25**, 75; (*b*) L. L. Fershtat, M. A. Epishina,

† *General procedure for the synthesis of diaziridines* **8a**–**l** *and* **9a**–**f**. Freshly distilled carbonyl compound (**6a**–**e** or **7a**,**b**, 30 mmol) was added to 30 mmol of amino acid ethyl ester hydrochloride (**5a**–**c**) in the mixture of 30 ml of water and 30 ml of ethanol at 0 °C and pH 9.0 was achieved by addition of 30% aqueous NaOH. Then hydroxylamine-*O*-sulfonic acid (35 mmol, 90%) was poured in small portions for 1 h at 0–5 °C and pH 8.0–8.5 (for aldehydes) or 9.5–10.0 (for ketones) achieved by simultaneous addition of 30% aqueous NaOH. The reaction mixture was stirred at 0–5 °C for additional 3 h at corresponding pH value, then warmed to room temperature, saturated with NaCl and extracted with $CHCl_3$. Organic phase was dried with K_2CO_3 for 30 min, solvent was removed on a rotatory evaporator and the residue was twice distilled *in vacuo*.

*Ethyl (1*R**,2*R**,3*S**)-2-(3-isopropyldiaziridin-1-yl)acetate* **8a**. Colorless liquid, yield 55%, bp 73–75 °C (1 Torr). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.00, 1.12 (both d, 6 H, 2 Me, *J* 6.0 Hz), 1.25 (t, 3 H, CH_2*Me*, *J* 6.0 Hz), 1.40 (m, 1H, CH), 1.90 (d, 1H, NH, *J* 6.6 Hz), 2.35 (t, 1H, CH_{ring}, *J* 6.6 Hz), 3.15 (d, 1H, N-CH_A, ^2J 15.0 Hz), 3.22 (d, 1H, N-CH_B, ^2J 15.0 Hz), 4.20 (q, 2 H, OCH_2, *J* 6.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.21 (Me), 16.15 (Me), 16.85 (Me), 33.15 (CH), 60.85 (CH_{ring}), 61.97 (NCH_2), 66.01 (OCH_2), 169.50 (C=O). IR (ν/cm^{-1}): 3436, 3379, 3249, 2963, 2876, 1745, 1469, 1372, 1275, 1196, 1169, 1089, 1038, 940, 927, 841. MS (EI, 70 eV), *m*/*z* (%): 172 (M^+, 9), 171 ($[M-H]^+$, 47), 99 (100), 84 ($[Me_2CH–CHN_2]^+$, 12), 70 ($[Me_2CH–CHN]^+$, 22), 55 ($[Me_2CH–C]^+$, 21), 43 (Pr^i, 58). HRMS (ESI), *m*/*z*: 173.1286 $[M+H]^+$ (calc. for $C_8H_{16}N_2O_2$, *m*/*z*: 173.1285). Found (%): C, 55.85; H, 9.31; N, 16.19. Calc. for $C_8H_{16}N_2O_2$ (%): C, 55.79; H, 9.36; N, 16.27.

*Ethyl (1*R**,2*R**,3*S**)-2-(3-isobutyldiaziridin-1-yl)acetate* **8h**. Colorless liquid, yield 42%, bp 92–94 °C (1 Torr). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.00 (d, 6 H, Me_2CH, *J* 6.0 Hz), 1.31 (t, 3 H, *Me*CH_2O, *J* 7.4 Hz), 1.43 (m, 1H, Me_2C*H*), 1.57 (m, 1H, CH_AC_{ring}), 1.85 (m, 2 H, CH_BC_{ring}, NH), 2.60 (m, 1H, HC_{ring}), 3.12, 3.32 (both d, 2 H, NCH_2, ^2J 16.4 Hz), 4.20 (q, 2 H, OCH_2, *J* 7.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.2 (*Me*CH_2O), 22.6 (*Me*CH), 22.8 (*Me*CH), 26.2 (*C*HMe_2), 43.4 (CH_2C_{ring}), 59.1 (C_{ring}), 60.9 (NCH_2), 61.7 (CH_2O), 169.7 (C=O). IR (ν/cm^{-1}): 3468, 3247, 2959, 3211, 2935, 2907, 2873, 1747, 1468, 1371, 1348, 1248, 1192, 1098, 1032, 975, 900, 846, 811. MS (EI, 70 eV), *m*/*z*: 186 $[M]^+$, 185 $[M-H]^+$, 171 $[M-Me]^+$, 156 [M – H, Et]$^+$, 113 [M – C(O)OEt]$^+$, 98 $[Me_2CH_2CHN_2]^+$, 97 $[Me_2CH_2CHN_2-H]^+$, 84 $[Me_2CH_2CHN-H]^+$, 71 $[Me_2CH_2CH-H]^+$, 43 $[Me_2CH_2CH-H, Me]^+$. HRMS (ESI), *m*/*z*: 187.1445 $[M+H]^+$ (calc. for $C_9H_{18}N_2O_2$, *m*/*z*: 187.1442). Found (%): C, 58.10; H, 9.67; N, 14.99. Calc. for $C_9H_{18}N_2O_2$ (%): C, 58.04; H, 9.74; N, 15.04.

*Ethyl (1*R**,2*R**)-4-(1,2-diazaspiro[2.5]octan-1-yl)butanoate* **9f**. Colorless liquid, yield 24%, bp 115 °C (1 Torr). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.21 (t, 3 H, *Me*CH_2, *J* 7.1 Hz), 1.56 [m, 10 H, $(CH_2)_5$], 1.88 (m, 3 H, NCH_2CH_2, NH), 2.38 (m, 3 H, CH_2C=O, NCH_B), 2.70 (dt, 1H, NCH_A, *J* 12.4 and 7.1 Hz), 4.08 (q, 2 H, OCH_2, *J* 7.1 Hz). HRMS (ESI), *m*/*z*: 227.1751 $[M+H]^+$ (calc. for $C_{12}H_{22}N_2O_2$, *m*/*z*: 227.1755). Found (%): C, 63.65; H, 9.83; N, 12.30. Calc. for $C_{12}H_{22}N_2O_2$ (%): C, 63.68; H, 9.80; N, 12.38.

For more data, see Online Supplementary Materials.

A. S. Kulikov, M. I. Struchkova and N. N. Makhova, *Chem. Heterocycl. Compd*., 2015, **51**, 176 (*Khim. Geterotsikl. Soedin*., 2015, **51**, 176); (*c*) S. G. Zlotin, A. M. Churakov, O. A. Luk'yanov, N. N. Makhova, A. Yu. Sukhorukov and V. A. Tartakovsky, *Mendeleev Commun*., 2015, **25**, 399; (*d*) S. Guglielmo, D. Cortese, F. Vottero, B. Rolando, V. P. Kommer, D. L. Williams, R. Fruttero and A. Gasco, *Eur. J. Med. Chem*., 2014, **84**, 135; (*e*) E. Borretto, L. Lazzarato, F. Spallotta, C. Cencioni, Yu. D'Alessandra, C. Gaetano, R. Fruttero and A. Gasco, *ACS Med. Chem. Lett*., 2013, **4**, 994.

2 (*a*) A. Nortcliffe, N. B. Botting and D. O'Hagan, *Org. Biomol. Chem*., 2013, **11**, 4657; (*b*) C. J. Moody and R. A. Hughes, *Angew. Chem. Int. Ed*., 2007, **46**, 7930; (*c*) A. Dondoni and A. Massi, *Acc. Chem. Res.*, 2006, **39**, 451; (*d*) T. K. Chakraborty, S. Ghosh and S. Jayaprakash, *Curr. Med. Chem*., 2002, **9**, 421; (*e*) D. L. Steer, R. A. Lew, P. Perlmutter, A. I. Smith and M. I. Aguilar, *Curr. Med. Chem*., 2002, **9**, 811.

3 M. D. Mashkovskii, *Lekarstvennye sredstva (Drugs)*, Novaya Volna, Moscow, 2000, vol. 1, p. 124 (in Russian).

4 M. D. Mashkovskii, *Lekarstvennye sredstva (Drugs)*, Novaya Volna, Moscow, 2000, vol. 1, p. 113 (in Russian).

5 (*a*) A. Z. Baichurina, I. I. Semina and R. S. Garaev, *Bull. Exp. Biol. Med*., 1996, **121**, 584; (*b*) R. G. Kostyanovsky, G. V. Shustov, O. G. Nabiev, S. N. Denisenko, S. A. Sukhanova and E. F. Lavretskaya, *Pharm. Chem. J*., 1986, **20**, 385 [*Khim.-Farm. Zh*., 1986, **20** (6), 671]; (*c*) C. J. Paget and C. S. Davis, *J. Med. Chem*., 1964, **7**, 626.

6 (*a*) M. Kamuf and O. Trapp, *Chirality*, 2011, **23**, 113; (*b*) A. A. Prokopov, L. I. Kotlova and A. S. Berlyand, *Pharm. Chem. J*., 2007, **41**, 7 [*Khim.-Farm. Zh*., 2007, **41** (1), 8]; (*c*) V. Yu. Petukhova, Yu. A. Strelenko, K. A. Lyssenko and N. N. Makhova, *Russ. Chem. Bull., Int. Ed*., 2007, **56**, 1550 (*Izv. Akad. Nauk, Ser. Khim.*, 2007, 1491); (*d*) A. A. Prokopov, L. I. Kotlova and A. S. Berlyand, *Pharm. Chem. J*., 2006, **40**, 463 [*Khim.-Farm. Zh*., 2006, **40** (9), 3]; (*e*) A. A. Prokopov, L. I. Kotlova and A. S. Berlyand, *Pharm. Chem. J*., 2005, **39**, 345 [*Khim.-Pharm. Zh*., 2005, **39** (7), 8].

7 (*a*) N. N. Makhova, V. Yu. Petukhova and V. V. Kuznetsov, *ARKIVOC*, 2008, **i**, 128; (*b*) V. V. Kuznetsov, Yu. S. Syroeshkina, D. I. Moskvin, M. I. Struchkova, N. N. Makhova and A. A. Zharov, *J. Heterocycl. Chem.*, 2008, **45**, 497; (*c*) Yu. S. Syroeshkina, V. V. Kuznetsov, V. V. Kachala and N. N. Makhova, *J. Heterocycl. Chem*., 2009, **46**, 1195; (*d*) S. G. Zlotin and N. N. Makhova, *Russ. Chem. Rev.*, 2010, **79**, 543 (*Usp. Khim.*, 2010, **79**, 603); (*e*) N. N. Makhova, A. V. Shevtsov and V. Yu. Petukhova, *Russ. Chem. Rev*., 2011, **80**, 1035 (*Usp. Khim.*, 2011, **80**, 1087); (*f*) V. Yu. Petukhova, L. L. Fershtat, V. V. Kachala, V. V. Kuznetsov, D. V. Khakimov, T. S. Pivina and N. N. Makhova, *J. Heterocycl. Chem.*, 2013, **50**, 326; (*g*) Y. V. Vishnevskiy, J. Schwabedissen, A. N. Rykov, V. V. Kuznetsov and N. N. Makhova, *J. Phys. Chem. A*, 2015, **119**, 10871; (*h*) M. I. Pleshchev, N. V. Das Gupta, V. V. Kuznetsov, I. V. Fedyanin, V. V. Kachala and N. N. Makhova, *Tetrahedron*, 2015, **71**, 9012.

8 (*a*) E. Schmitz, *Dreiringe mit zwei Heteroatomen: Oxaziridine, Diaziridine, cyclische Diazoverbindungen*, Springer, Berlin, 1967; (*b*) H. W. Heine, in *The Chemistry of Heterocyclic Compounds*, ed. A. Hassner, Wiley-Interscience, New York, 1983, vol. 42, part 2, pp. 547–629; (*c*) E. Schmitz, in *Comprehensive Heterocyclic Chemistry*, 1st edn., ed. W. Lwowski, Pergamon Press, Oxford, 1984, vol. 7, part 5.08, pp. 195–236; (*d*) R. G. Kostyanovsky, R. Murugan and M. Sutharchanadevi, in *Comprehensive Heterocyclic Chemistry II*, eds. A. R Katritzky, C. W. Rees and E. F. V. Scriven, Pergamon Press, Oxford, 1996, vol. 1A, part 1.11, pp. 347–364; (*e*) G. D. McAllister, A. Perry and R. J. K. Taylor, in *Comprehensive Heterocyclic Chemistry III*, eds. A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor, Elsevier, Oxford, 2008, vol. 1, part 1.11, pp. 539–557.

9 (*a*) V. V. Kuznetsov, N. N. Makhova, Yu. A. Strelenko and L. I. Khmel'nitskii, *Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1991, **40**, 2496 (*Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 2861); (*b*) V. V. Kuznetsov, N. N. Makhova and L. I. Khmel'nitskii, *Russ. Chem. Bull.*, 1997, **46**, 1354 (*Izv. Akad. Nauk, Ser. Khim.*, 1997, 1410).

10 (*a*) O. Trapp, V. Schurig and R. G. Kostyanovsky, *Chem. Eur. J.*, 2004, **10**, 951; (*b*) M. Jung and V. Schurig, *J. Am. Chem. Soc*., 1992, **114**, 529; (*c*) J.-M. Lehn, *Top. Curr. Chem*., 1970, **15**, 311; (*d*) A. Mannschreck, R. Radeglia, E. Gründemann and R. Ohme, *Chem. Ber.*, 1967, **100**, 1778.

Received: 9th March 2016; Com. 16/4866