Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 62 (2006) 9456–9466
Tetrahedron

Tautomeric equilibria in the reaction products of asymmetric 1,3-diamines with β-dicarbonyl compounds

Olga A. Maloshitskaya,[a,b,*] Valery V. Alekseyev,[b] Jari Sinkkonen,[a] Kirill N. Zelenin[b,✠] and Kalevi Pihlaja[a]

[a]*Department of Chemistry, Structural Chemistry Group, University of Turku, FI-20014 Turku, Finland*
[b]*Russian Military Medical Academy, 194044 St. Petersburg, Russian Federation*

Received 18 April 2006; revised 19 June 2006; accepted 6 July 2006
Available online 14 August 2006

Dedicated to the late Professor Kirill N. Zelenin

Abstract—The reaction products of 1,3-butanediamine and 2-methyl-2,4-pentanediamine with β-keto aldehydes were shown by ^{1}H and ^{13}C NMR spectroscopy to exist as tautomeric mixtures in solutions, comprising one cyclic and two open-chain forms due to the non-equivalence of the amino groups. The chain products exist as *Z*- and *E*-isomers. After equilibration, the products from 1,3-butanediamine contain relatively less of the cyclic form than those from 2-methyl-2,4-pentanediamine. The products of 2-methyl-2,4-pentanediamine with *p*-substituted aroylacetaldehydes, exhibit a linear correlation between log *K* of the ring–chain equilibria and Hammett's σ values of the aromatic ring substituents. α-Substitution of β-keto aldehydes notably increased the relative amounts of the chain *E*-isomers in their condensation products and also resulted in the formation of two diastereomers for each of the cyclic products. No ring–chain equilibria were observed in the products of 1,3-butanediamine and 2-methyl-2,4-pentanediamine with β-diketones, β-keto esters, or β-keto amides.

1. Introduction

Various ring–chain, ring–ring, and ring–chain–ring tautomeric equilibria have been discussed in recent years.[1–3] In particular, ring–chain equilibria were observed in solutions of hexahydropyrimidines, where only one open-chain tautomer (the diamine Schiff base) could be formed in each system, either because of substitution at the other amino group[4,5] or because of molecular symmetry.[6] For tetrahydroquinazolines derived from 2-aminomethylaniline and aromatic aldehydes, only one of the two possible open-chain forms was observed.[7]

We have observed for the first time chain–ring–chain tautomerism[8] in 2-aryl-4-methylhexahydropyrimidines obtained from 1,3-diaminobutane and aromatic aldehydes. However, the reaction mixtures frequently contained bis-imino products, which were inseparable from the target products of 1:1 condensation. A similar difficulty for other compounds was previously mentioned in the literature.[9]

In search for a suitable alternative to aromatic aldehydes in condensations with asymmetric 1,3-diamines, we turned to β-dicarbonyl compounds. Tautomerism in their various nitrogen derivatives is well described.[10] Moreover, their reaction products with diamines were expected to contain considerable amounts of the keto enamine tautomers, similarly to the previously observed cases of ring–chain tautomerism in their condensation products with aminoamides[11,12] and 2-aminomethylaniline.[13] In the latter case, similarly to the aromatic aldehyde derivatives,[7] only one of two possible chain (keto enamine) tautomers was observed.

In the present work, effects of the electronic factors on the tautomeric equilibria were probed by preparing derivatives of *p*-substituted benzoylacetic aldehydes. Steric effects of a bulky substituent in the β-dicarbonyl reaction component were studied using derivatives of pivaloylacetic aldehyde. Derivatives of propionylpropionaldehyde and its alicyclic analogs, 2-formylcyclopentanone and 2-formylcyclohexanone, were used to clarify the effects of α-substitution in the dicarbonyl component. Finally, derivatives of β-diketones, β-keto esters, and β-keto amides were approached, where we expected increased amounts of the imine tautomers to be observed.

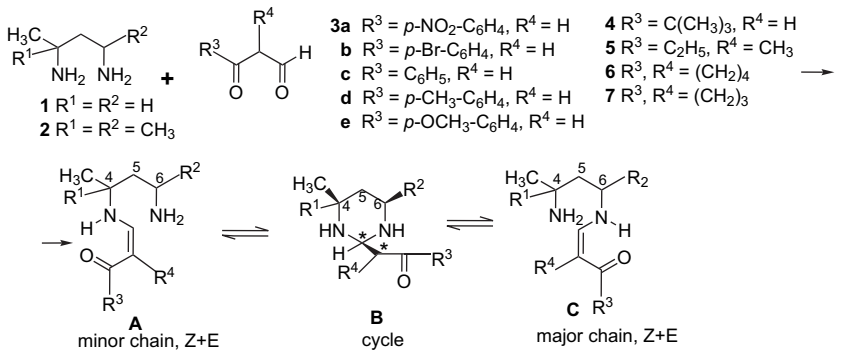
2. Results and discussion

2.1. Reactions of 1,3-butanediamine and 2-methyl-2,4-pentanediamine with β-keto aldehydes

The 1:1 condensation products existed in solutions as tautomeric mixtures of one cyclic tautomer (**B**) and two chain

Keywords: Ring–chain tautomerism; Hexahydropyrimidines; β-Dicarbonyl compounds; 1,3-Diamines.
* Corresponding author. Tel.: +358 2 3336752; fax: +358 2 3336700; e-mail: maloshitskaya@mail.ru
✠ Deceased.

0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.07.033



8 $R^1 = R^2 = R^4 = H$, $R^3 = Ph$, **9** $R^1 = R^2 = R^4 = H$, $R^3 = C(CH_3)_3$, **10** $R^1 = R^2 = H$, $R^3 = C_2H_5$, $R^4 = CH_3$.
11a-e $R^1 = R^2 = CH_3$, R^3 = *p*-substituted Ph, $R^4 = H$, **12** $R^1 = R^2 = CH_3$, $R^3 = C(CH_3)_3$, $R^4 = H$
13 $R^1 = R^2 = R^4 = CH_3$, $R^3 = C_2H_5$, **14** $R^1 = R^2 = CH_3$, $R^3, R^4 = (CH_2)_4$, **15** $R^1 = R^2 = CH_3$, $R^3, R^4 = (CH_2)_3$

Scheme 1.

ene–amines (**A** and **C**) formed due to the non-equivalent amino groups (Scheme 1). The tautomeric mixtures reached equilibria after 10–15 h standing. Their ^1H and ^{13}C NMR spectra were assigned using DEPT 135, COSY, HSQC, and HMBC.

The presence of two chain tautomers was confirmed by pairwise =C*H*–NH signals at 6.5–7.0 and 7.2–7.9 ppm for the *Z*- and *E*-isomers, respectively; N*H*–CH= signals at 9.0–10.7 (*Z*-isomers, intramolecular hydrogen bonding) and 6.4–8.4 ppm (*E*-isomers); and the carbon signals at 186.5–206.2 (conjugated C=O), 139.5–154.3 (*C*H–NH), and 89.8–105.9 ppm (=*C*–C=O). These two open-chain forms were confirmed as **A** and **C** by HMBC spectra. To simplify the following discussion, the numbering of atoms in the hexahydropyrimidine ring was preserved in the open-chain forms.

For example, in the HMBC spectra of compound **8** there were observed correlations between =C*H*–NH (6.96 ppm, dd) and *C*H_2NH (C-6, 46.7 ppm) indicating the **C** tautomer, and between =C*H*–NH (7.00 ppm, dd) and *C*H–CH_3 (C-4, 52.3 ppm) indicating the **A** tautomer. Similar HMBC correlations were also observed for all the compounds **8**–**10**. Signals originating from the vicinity of the amino groups further confirmed the presence of **A** and **C** tautomers. In the NMR spectra of **8**–**10** (R^1=R^2=H), the **A** tautomer gave the signals of H-4 at 3.36–3.47 and those of C-4 at 51.6–52.6 ppm, whereas the tautomer **C** gave the respective signals at 2.81–3.02 and 44.0–44.5 ppm. For the **A** tautomers, the H-6 signals were found at 2.57–2.80 and those of C-6 at 38.3–38.7 ppm, whereas the **C** tautomer gave the respective signals at 3.24–3.36 and 45.2–46.7 ppm.

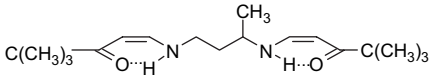
Similarly, the presence of **A** and **C** forms in the substituted diamine derivatives (**11**–**15**, R^1=R^2=CH_3) was confirmed by HMBC spectra. Thus, for compound **11c** cross-peaks indicating **C** form were observed between =C*H*–NH (7.01 ppm) and *C*H–CH_3 (C-6, 52.2 ppm), and those indicating **A** form between =C*H*–NH (7.11 ppm) and *C*$(CH_3)_2$ (C-4, 54.4 ppm). Furthermore, compounds **11**–**15** gave signals for the **A** tautomer at 3.00–3.19 (H-6) and at 43.6–44.6 ppm (C-6) as compared to those of the **C** tautomer at 3.46–3.62 (H-6) and 49.7–52.1 ppm (C-6). The signals of C-4 for the **A** and **C** tautomers were found at 53.84–54.63 and 49.2–50.0 ppm, respectively. Notably, the NH signal for **A** was a broadened doublet (J=12–14 Hz) due to a coupling to =CH, whereas that of **C** gave a broadened triplet (or rather dd, due to a coupling to both =CH and C*H*–CH_3, see Scheme 1).

Diastereomers of the cyclic structures **B** were identified from the signals at 3.6–4.2 (H-2) and at 61.8–73.4 (C-2), 198.7–220.9 (unconjugated C=O), and 43.7–51.5 ppm (*C*H–CO).

Generally, for all of compounds **8**–**15** the **A** tautomers (produced by condensation to the sterically more hindered amino group) were less abundant than the **C** tautomers. As to the cyclic tautomers, they were less abundant for the 1,3-butanediamine (**8**–**10**) than for the 2-methyl-2,4-pentanediamine derivatives **11**–**13**. A similar tendency was previously observed for the condensation products of **1** and **2** with aromatic aldehydes.[8] These observations are in line with the well-known rule for ring–chain tautomeric equilibria that highly substituted ring tautomers are relatively more stable (i.e., they predominate over the open-chain forms in equilibrated mixtures).[14] Also, the relative stability of the cyclic tautomers derived from diamines **1** and **2** conforms to the so-called *gem*-dimethyl effect:[14] the presence of geminal methyl substituents in cyclic tautomers usually increases their relative stability in ring–chain equilibria.

Compositions of the equilibrated tautomeric mixtures are listed in Table 1 (note that some of the isomers gave indistinguishably overlapping signals).

Upon storing (2–15 days, depending on the starting ketoaldehyde), the 1:1 condensation products partially disproportionated into free diamines and bis-imines. The latter were also formed as by-products of the main reaction, but was successfully removed by column chromatography. One of the bis-imino products (**16**, Fig. 1) was purposefully synthesized as a reference compound and characterized by NMR spectroscopy. In chloroform solution it existed in the



16

Figure 1.

Table 1. Compositions of equilibrium mixtures (% of the total)

Compd	DMSO-d_6					$CDCl_3$				
	E_{major}	E_{minor}	Z_{major}	Z_{minor}	Cyclic	E_{major}	E_{minor}	Z_{major}	Z_{minor}	Cyclic
8	Σ52		Σ48		—	—	—	63	33	4
9	Σ42		37	19	2	—	—	59	27	14
10	57	34	5	4	—	22	8	41	20	4+5
11c	Σ35		45	8	12	—	—	42	11	47
12	21	1	35	6	36	—	—	16	4	80
13	61	11	4	—	Σ24	26	9	23	5	22+15
14	Overlapping signals					20	7	34	8	13+18
15	65	18	7	2	4+4	38	18	20	5	9+10

Quantitative data were obtained by integration of ═C*H*–NH (linear forms) and H-2 (cyclic forms) signals.

Z-configuration ($J_{CH=CH}$=8.0) stabilized by intramolecular hydrogen bonding (IMHB).

2.1.1. Reactions with pivaloylacetic and *p*-substituted benzoylacetic aldehydes. The derivatives of aroylacetic aldehydes (**8**, **11a–e**) and pivaloylacetic aldehyde (**9**, **12**) in chloroform solutions exist as mixtures of two chain tautomers **A** and **C** (*Z*-isomers, $J_{CH=CH}$=7.4–8.0 stabilized by IMHB) and cyclic tautomers **B**. For the latter, only one diastereomeric form was observed, in which the substituents of the hexahydropyrimidine ring are equatorial, so there is no *syn*-axial interactions between R^3COCH_2 and R^1 (Fig. 2). For example, in the NOESY spectrum of **12** (R^1=R^2=CH_3, R^3=*t*-Bu), a correlation was observed between H-2 (4.02 ppm, dd, J_1=4.75, J_2=6.0 Hz) and H-6 (2.97 ppm, m). Similarly, only one of the two possible diastereomers was previously detected for the analogous hexahydropyrimidines derived from diamine **2**.[8] Cyclic forms of diamine **1** derivatives were observed as a mixture of both possible diastereomers, but the concentration of one of them was very low (ratio approx. 1:10).[8]

When dissolved in DMSO-d_6, which is a highly polar solvent, compounds **8**, **9**, **11**, and **12** gave a smaller amount of cyclic **B** tautomer than when dissolved in chloroform, and also *E*-forms of the chain tautomers could be observed in DMSO-d_6. Being more polar than the corresponding *Z*-isomers, the *E*-isomers are better stabilized by non-specific solvation, e.g., intermolecular hydrogen bonding between the solvent and the NH groups.[14] Formation of the *E*-isomers in DMSO-d_6 was confirmed by the proton signals of –CH═C*H*–CO (5.3–6.0 ppm, d, $J_{CH=CH}$=12.5–12.8 Hz). We noted that the *E*-isomers produced broadened signals, especially in the carbon spectra of **11** and **12**, although the corresponding C–H correlations were clearly observed in the HSQC spectra. However, the signals for *Z*-isomers were sharp. This indicates that some dynamic processes, which are slow in NMR time scale, take place in the case of *E*-isomers. The cause for the broadening is most likely hindered rotation at the N–C bond (in –HN–CH═C– moiety), which has a partial double bond character. This has been previously observed for secondary enaminones by Kozerski et al.[15] Also the observation that N*H* and C*H* protons (in the moiety above) exhibit the most broadened signals, is in harmony with the hindered rotation at N–C bond.

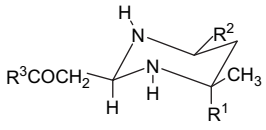


Figure 2.

As the temperature was increased from room temperature to 57 °C, the signals for *E*-isomers sharpened, but were still rather broad. The decomposition of the structure inhibited extensive measurements at higher temperatures. The lowering of temperature was unfortunately not possible because of the melting point of DMSO-d_6 (and *E*-isomers were not observed in $CDCl_3$). We also noted that the relative amounts of *E*- and *Z*-isomers changed as the temperature was changed. This further proves the existence of ring–chain tautomeric equilibrium system as presented in Scheme 1.

Upon equilibration, the relative content of the linear tautomers (sum total of [**A**]+[**C**]) is higher for the aroylacetaldehyde derivatives (i.e., [**8A+C**]>[**9A+C**], [**11A+C**]>[**12A+C**]), probably due to stabilizing effect of conjugation between the aromatic ring and C═C–C═O fragments in **8A**, **8C** and **11A**, **11C**, which cannot be achieved in the pivaloylacetaldehyde derivatives **9** and **12**.

For the series **11a–e**, in which substantial amounts of the tautomers **B** were observed, the ring–chain equilibrium constants in $CDCl_3$ correlated closely with the electronic properties of the substituents on the aromatic rings (Table 2,

Table 2. Compositions of equilibrium mixtures (% relative to the major chain tautomer) for the condensation products of 2-methyl-2,4-pentanediamine with *p*-substituted benzoylacetaldehydes in $CDCl_3$ solutions

Compd	Substituent	σ	Chain tautomer **C** (major)	Chain tautomer **A** (minor)	Cyclic tautomer **B**	*K*=[A+C]/[B]
11a	NO_2	0.78	100	25	11	0.088
11b	Br	0.23	100	24	54	0.435
11c	H	0	100	25	116	0.928
11d	CH_3	−0.17	100	22	173	1.430
11e	OCH_3	−0.27	100	24	240	1.927

Eq. 1). In DMSO-d_6, the equilibrium constants of **11a–e** could not be determined with a sufficient precision because of the interference with broadened signals of the *E*-isomers.

$$\log K_{eq}(CDCl_3) = -(0.0558 \pm 0.007) - (1.282 \pm 0.019)\sigma, \quad r = -0.999 \qquad (1)$$

Apart from this, the aromatic ring substituents were expected to affect the IMHB strength and, thereby, the chemical shifts of the NH protons. Indeed, linear correlations between their chemical shifts and the σ constants were observed (Eqs. 2 and 3). Compounds **11a–e** were dissolved in similar concentrations:

$$\delta_{NH\ major} = (0.34 \pm 0.03)\sigma + (10.43 \pm 0.01), \quad r = 0.982 \qquad (2)$$

$$\delta_{NH\ minor} = (0.38 \pm 0.03)\sigma + (10.86 \pm 0.01), \quad r = 0.987 \qquad (3)$$

The yields and properties of **11a–e** are listed in Table 3. The ^{1}H and ^{13}C NMR parameters for their major (**C**) and minor chain tautomers (**A**), and cyclic tautomers (**B**) are shown in Tables 4–9.

2.1.2. Reaction with propionylpropionaldehyde. Substitution at the α-position in the dicarbonyl component (compounds **10** and **13**, R^4=CH_3) resulted in the formation of *E*-isomers of their chain tautomers already in chloroform solutions (see Table 1). Also, *Z*-isomers and cyclic tautomers were detected, although open-chain forms of **10** and **13** in DMSO solutions exist exclusively as *E*-isomers. It has been noted previously[16] that the presence of R^4 substituent greatly affects *Z*/*E* equilibria in enaminones.

The cyclic tautomers **B** can in principle exist in four diastereomeric forms of which only two were actually detected in ca. 1:1 ratio. The same ratio of diastereomers was observed for the cyclic reaction product of propionylpropionaldehyde with 2-aminobenzenesulfonamide,[12] which had only two chiral centers, the C-2 of the ring and C-1′ of the side chain. So it can be concluded that the two diastereomers of **10B** and **13B** are due to the chiral center at C-1′ since only one diastereomer was detected when R^4=H (compare **8** and **9** with **11** and **12**, respectively). The cyclic forms are relatively less stable in **10** (derived from the less substituted diamine **1**) than in **13** (derived from **2**), similarly to the derivatives of **1** and **2** with other aldehydes (see Table 1). Also, cyclic tautomers are generally less stable in DMSO than in $CDCl_3$.

The presence of both *Z*- and *E*-isomers of **10** and **13** was confirmed by the NOE spectra. Thus, the spectrum of **13** in $CDCl_3$ showed correlations between the C*H*═ (6.72 and 6.61 ppm) and ═C–CH_3 (1.81 and 1.83 ppm) of the *Z*-isomers and the absence of such correlation for the corresponding signals of the *E*-isomers. Moreover, the presence of the *E*,*E*′-conformation (Fig. 3) of the latter was proved by NOE correlations observed between the C*H*═ signals and CH_2–CH_3 (2.40–2.50 ppm, m). It is known from the literature on the geometrical isomerism of enaminones[16] that NH signals of their *Z*-forms are shifted downfield from the corresponding *E*-form signals due to IMHB. Indeed, we observed the NH signals of the *Z*- and *E*-isomers at 9.07–10.86 and 6.48–8.48 ppm, respectively. Moreover,

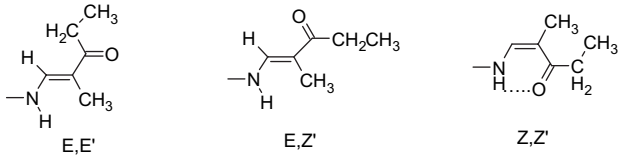


Figure 3.

the carbon signals of ═C*H*–NH (*E*-) and ═*C*–C═O (*E*-) were shifted by 2–3 ppm to higher field than the corresponding *Z*-form signals.

The *Z*-isomers are destabilized by steric interactions involving the methyl substituent, which are minimized in the *E*,*E*′-conformation (Fig. 3). In DMSO-d_6 solutions, the chain tautomers of **10** and **13** predominantly existed in the *E*,*E*′-conformation, similarly to the analogous derivatives of 2-aminobenzenesulfonamide.[12]

2.1.3. Reactions with 2-formylcyclohexanone and 2-formylcyclopentanone. In these compounds, an additional structural constraint is introduced apart from the α-substitution, which could be expected to affect the tautomeric equilibria. Unfortunately, the condensation products of **1** with the title ketoaldehydes were unstable, and rapidly decomposed.

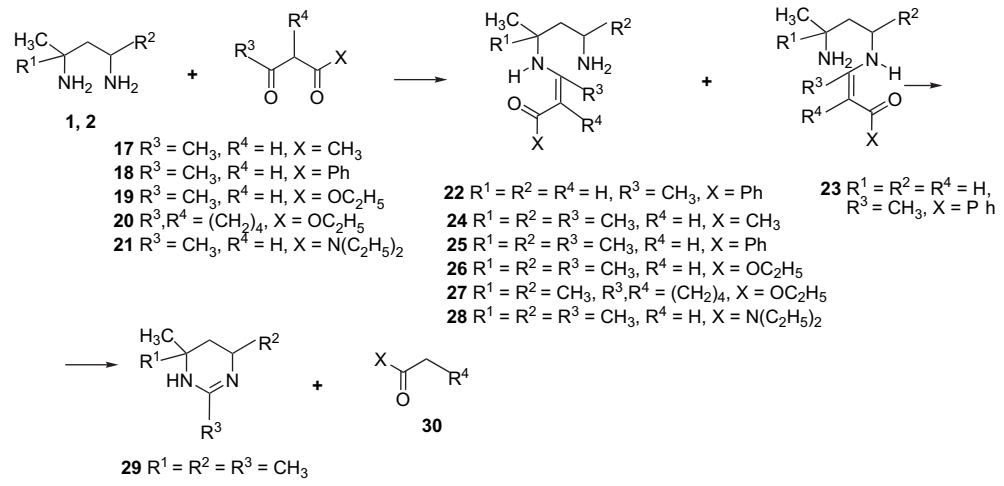
Derivatives of the substituted diamine **2** (**14** and **15**) were more stable, and their behavior resembled that of **13**. The *E*-isomers of the chain forms were observed even in chloroform solutions, and two diastereomers of each cyclic tautomer were detected (Table 1). In principle, the compositions of equilibrium mixtures should not differ much for the structurally very similar compounds **13** (R^3=Et, R^4=Me) and **14** [R^3R^4=–$(CH_2)_4$–]. The slightly decreased stability of **14B** relative to **13B** may be explained by the presence of alicyclic substructure, as noted in the literature.[14] The presence of a cyclic moiety usually decreases the fraction of a ring tautomer.[14]

For the 2-formylcyclopentanone derivative **15** in $CDCl_3$, the total content of the *E*-isomers (38%+18%) is higher than for the 2-formylcyclohexanone derivative **14** (20%+7%). Moreover, the size of the aliphatic carbocycle seems to affect the total content of the heterocyclic tautomers (19% for **15** vs 31% for **14**), a trend also observed in the previous study.[12]

2.2. Reactions of 1,3-butanediamine and 2-methyl-2,4-pentanediamine with β-diketones, β-keto esters, and β-keto amides

As shown in Scheme 2, the reactions always occurred at the more reactive acetylic carbonyl (as in **18**) or, in general, at the keto group of keto esters and keto amides **19–21**.

Unlike the ketoaldehyde derivatives (where R^3=H), reaction products **22–28** do not form cyclic tautomers at all. Inspection of the conformations of the possible cyclic isomers shows that the destabilizing interactions of CH_3 and $XCOCH_2$ groups with *syn*-axial H or CH_3 cannot be avoided in any of the conformers as shown in Figure 4.



Scheme 2.

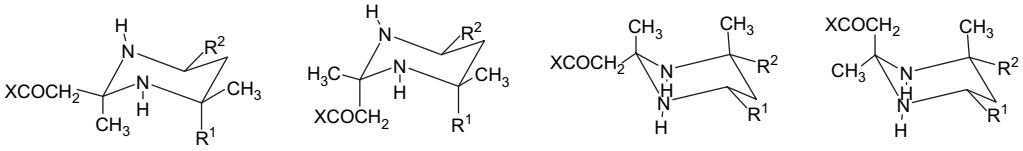


Figure 4.

The derivatives of diamine **1** invariably contained considerable amounts of the bis-condensation products, which could not be removed by column chromatography except the benzoylacetone derivative, which was obtained as a 4:1 mixture of regioisomers **22** and **23**. Their ratio remained constant in different solvents, indicating the absence of chain–chain tautomerism.

Condensations with the substituted diamine **2** occurring to the less hindered amino group produced a single regioisomer in each case (**24**–**28**), all of which were pure *Z*-isomers except the acetoacetic ester derivative **26** (*Z*/*E*=100:16). Possible effects of α-substitution (R^4=CH_3) in the dicarbonyl component on the *Z*/*E* isomerism could not be studied because the condensation products of α-substituted acetylacetone and acetoacetic ester (R^3=R^4=X=CH_3 and R^3=R^4=CH_3, X=OC_2H_5) were unstable.

Upon prolonged storage in solutions, compounds **24**–**28** decomposed to form **29** (Scheme 2) which, according to the ^{13}C NMR spectra, does not contain a carbonyl group. The double bond position in **29** was determined by comparing the chemical shifts of C-4 (49.3 ppm) and C-6 (43.4 ppm) with the corresponding signals for **12B** (C-4, 49.2 and C-6, 46.5 ppm) and with the previously reported[8] spectrum of 4,4,6-trimethyl-2-phenylhexahydropyrimidine (C-4, 49.5 and C-6, 46.9 ppm). The high-field shift of C-6 signal in **29** indicates a double bond between N-1 and C-2.

3. Conclusion

Ring–chain tautomerism involving two open-chain regioisomers is for the first time reported for the 1:1 condensation products of β-keto aldehydes with substituted aliphatic 1,3-diamines possessing non-equivalent amino groups. The equilibrium mixtures contained relatively higher amounts of the cyclic tautomers in the case of the more substituted diamine **2**.

For a series of condensations products of diamine **2** with *para*-substituted benzoylacetic aldehydes, the ring–chain equilibrium constants correlated closely with the Hammett σ constants for the aromatic substituents.

Increasing the solvent polarity (i.e., $CDCl_3$ vs DMSO-d_6) decreased the equilibrium content of the cyclic tautomers.

In addition to the ring–chain tautomerism, *Z*- and *E*-forms of the chain tautomers were also observed. In $CDCl_3$, *Z*-isomers prevail, whereas in DMSO-d_6 the amounts of *E*-isomers become much higher. Substitution at the α-position of the starting ketoaldehyde increased the amounts of the *E*-forms in the equilibria and resulted in the formation of diastereomeric mixtures of the cyclic tautomers.

The condensation products of **1** and **2** with β-diketones, β-keto esters, and β-keto amides did not exhibit any ring–chain tautomerism. No imine structures could be observed for any of the reaction products.

4. Experimental

4.1. General

In general, the ring–chain equilibria were reached in NMR tubes at 10–15 h after dissolving the compound. The equilibria were considered to be settled when two consecutive measurements at 2 h intervals indicated no change in the ratio of the chain and cyclic forms.

4.2. Spectrometry

NMR spectra were acquired using Bruker Avance 500 and 600 spectrometers (equipped with BBI-5mm-Zgrad-ATM and BBO-5mm-Zgrad probes) operating at 500.13 and 600.13 MHz for ^{1}H and 125.77 and 150.90 MHz for ^{13}C, respectively. Spectra were recorded at 25 °C using DMSO-d_6 and $CDCl_3$ as a solvent with a non-spinning sample in 5 mm NMR tubes. Spectra were processed by a PC with Windows XP operating system and XWin-NMR software. Proton and carbon spectra were referenced internally to TMS signal using value 0.00 ppm. ^{1}H NMR spectra and ^{13}C NMR proton-decoupled spectra were acquired with single-pulse excitation and 30° flip angle. Exponential weighting (1 Hz) was applied prior to Fourier transformation (in carbon spectra). Gradient selected DQF-COSY spectra were acquired with cosygpmfqf pulse program (pulse programs refer to original ones installed by Bruker). Gradient selected NOESY spectra were acquired with noesygpph pulse program. Gradient selected ^{1}H–^{13}C HSQC spectra were acquired with hsqcetgpsisp.2 pulse program (using shaped pulses). Gradient selected ^{1}H–^{13}C HMBC spectra were acquired with hmbcgplpndqf pulse program.

Mass-spectral measurements of the $M^{+\bullet}$ compositions were obtained in the EI ionization mode, direct insertion probe, on a VG ZABSpec instrument at a resolving power of 7000–8000 (10% valley definition).

4.3. General synthetic procedures

The starting keto aldehydes were prepared according to the standard methods[17] and used immediately for condensations with the diamines.

4.3.1. Reaction of 1,3-diamines with β-keto aldehydes (procedure A, substances 8–15, 22, 23, 25). To a solution of diamine (2–3 mmol) in 10 mL of dry ether stirred and cooled on an ice bath, a solution of equimolar amount of β-keto aldehyde (2–3 mmol) in 10 mL of dry ether was slowly added. In the course of addition, ammonium salt of the keto aldehyde precipitated. The reaction mixture was stirred at a room temperature overnight, concentrated in vacuo, and chromatographed on silica gel (100–250 mesh, elution with ether/methanol 2:1).

4.3.1.1. 1-(3-Phenyl-3-oxoprop-1-enylamino)-3-aminobutane (8). Yield 37% (220 mg), yellowish oil. HRMS: $C_{13}H_{18}N_2O$ $M^{+\bullet}$ calcd 218.1419; obsd 218.1411. Compound *Z*-**8C** (major chain): δ_H ($CDCl_3$): 1.11 (3H, d, J_{CH_3CH}=6.4, CH_3), 1.57 (1H, m, H-a from CH_2–CH), 1.67 (1H, m, H-b from CH_2–CH), 3.02 (1H, m, CHCH$_3$), 3.36 (2H, m, CH_2NH), 5.69 (1H, d, $J_{CH=CH}$=7.6, =CH–CO), 6.96 (1H, dd, $J_{CH=CH}$=7.6, J_{CH-NH}=12.8, =CH–NH), 7.41 (3H, m, H-3′, H-4′, H-5′), 7.87 (2H, d, J=7.8, H-2′, H-6′), 10.38 (1H, br s, NH). δ_C ($CDCl_3$): 24.8 (CH_3), 40.6 (CH_2CH), 44.5 (CH–CH_3), 46.7 (CH_2–NH), 90.1 (CH–CO), 127.0 (C-2′, C-6′), 128.2 (C-3′, C-5′), 130.8 or 130.9 (C-4′), 139.8 (C-1′), 154.3 (CHNH), 189.8 (CO). Compound *Z*-**8A** (minor chain): δ_H ($CDCl_3$): 1.29 (3H, d, J_{CH-CH_3}=6.8, CH_3), 1.67 (2H, m, CH_2CH), 2.79 (2H, m, CH_2NH$_2$), 3.46 (1H, m, CHCH$_3$), 5.69 (1H, d, $J_{CH=CH}$=7.6, =CH–CO), 7.00 (1H, dd, $J_{CH=CH}$=7.2, J_{CH-NH}=12.8, =CH–NH), 7.41 (3H, m, H-3′, H-4′, H-5′), 7.86 (2H, d, J=7.8, H-2′, H-6′), 10.38 (1H, br s, NH). δ_C ($CDCl_3$): 22.3 (CH_3), 38.7 (CH_2NH_2), 41.3 (CH_2CH), 52.3 (CH_3CH), 89.8 (CHCO), 127.0 (C-2′, C-6′), 128.2 (C-3′, C-5′), 130.8 or 130.9 (C-4′), 139.8 (C-1′), 154.2 (CHNH), 189.7 (CO). Compound **8B** (cyclic), observed signals: δ_H ($CDCl_3$): 4.04 (1H, t, J_{CH-CH_2}=5.6, H-2). δ_C ($CDCl_3$): 23.0 (CH_3), 35.0 (C-5), 45.7 (C-6), 51.3 (C-4), 68.3 (C-2), 133.4 (C-4′), 136.8 (C-1′), 198.8 (CO).

4.3.1.2. 1-(4.4-Dimethyl-3-oxopent-1-enyl)amino-3-aminobutane (9). Yield 46% (210 mg), yellowish oil. HRMS: $C_{11}H_{22}N_2O$ $M^{+\bullet}$ calcd 198.1732; obsd 198.1739. Compound *Z*-**9C** (major chain): δ_H ($CDCl_3$): 1.10 (3H, d, J_{CH_3CH}=6.5, CH_3), 1.14 (9H, s, (CH_3)$_3$C), 1.53 (1H, m, H-a from CH_2–CH), 1.63 (1H, m, H-b from CH_2–CH), 3.00 (1H, m, CHCH$_3$), 3.28 (2H, m, CH_2NH), 5.15 (1H, d, $J_{CH=CH}$=8.0, =CH–CO), 6.76 (1H, dd, $J_{CH=CH}$=7.5, J_{CH-NH}=12.5, =CH–NH), 9.90 (1H, br s, NH). δ_C ($CDCl_3$): 24.7 (CH_3), 27.7 ((CH_3)$_3$C), 40.6 (CH_2CH), 41.5 (C(CH$_3$)$_3$), 44.4 (CH–CH_3), 46.4 (CH_2–NH), 88.9 (CH–CO), 153.3 (=CHNH), 206.1 (CO). Compound *Z*-**9A** (minor chain): δ_H ($CDCl_3$): 1.14 (9H, s, (CH_3)$_3$C), 1.24 (3H, d, J_{CH-CH_3}=6.5, CH_3), 1.62 (2H, m, CH_2CH), 2.70–2.80 (2H, m, CH_2NH$_2$), 3.36 (1H, m, CHCH$_3$), 5.14 (1H, d, $J_{CH=CH}$=7.5, =CH–CO), 6.80 (1H, dd, $J_{CH=CH}$=7.5, J_{CH-NH}=13.0, =CH–NH), 9.84 (1H, br s, NH). δ_C ($CDCl_3$): 22.3 (CH_3), 27.7 ((CH_3)$_3$C), 38.7 (CH_2NH_2), 41.4 (CH_2CH), 41.5 (C(CH$_3$)$_3$), 52.6 (CH_3CH), 88.6 (=CHCO), 151.9 (=CHNH), 206.1 (CO). Compound **9B** (cyclic): δ_H ($CDCl_3$): 1.08 (3H, d, J_{CH_3CH}=6.5, CH_3), 1.14 (9H, s, (CH_3)$_3$C), 1.25 (1H, m, H-5ax), 1.60 (1H, m, H-5eq), 2.70–2.85 (3H, m, CH_2CO, CH–CH_3), 3.00 (2H, m, H-4ax, H-6ax), 3.13 (1H, ddd, J_{6eq6ax}=13.0, J_{6eq5ax}=4.4, J_{6eq5eq}=1.9, H-6eq), 3.81 (1H, t, J_{CH-CH_2}=5.7, H-2). δ_C ($CDCl_3$): 23.0 (CH_3), 26.7 ((CH_3)$_3$C), 35.0 (C-5), 41.6 (C(CH$_3$)$_3$), 43.6 (CH_2CO), 45.7 (C-6), 51.3 (C-4), 68.1 (C-2), 215.4 (CO).

4.3.1.3. 1-(2-Methyl-3-oxopent-1-enyl)amino-3-aminobutane (10). Yield 42% (150 mg), yellowish oil. HRMS: $C_{10}H_{20}N_2O$ $M^{+\bullet}$ calcd 184.1576; obsd 184.1574. Compound *E*-**10C** (trans-major chain): δ_H (DMSO-d_6): 0.95 (3H, t,

Table 3. *p*-Substituted 4-(3-aryl-3-oxoprop-1-enyl)amino-2-amino-2-methylpentanes **11a–e**

Compd	Yield, %	Yield, mg	Appearance	$M^{+\bullet}$	HRMS	
					Calculated	Observed
11a	27	80	Yellow oil	$C_{15}H_{21}N_3O_3$	291.1583	291.1582
11b	50	330	Yellow oil	$C_{15}H_{21}BrN_2O$	324.0837 (^{79}Br)	324.0820 (^{79}Br)
11c	35	230	Yellowish oil	$C_{15}H_{22}N_2O$	246.1732	246.1729
11d	30	70	Yellowish oil	$C_{16}H_{24}N_2O$	260.1889	260.1878
11e	50	280	Yellowish oil	$C_{16}H_{24}N_2O_2$	276.1838	276.1840

Table 4. The ^{1}H NMR data ($CDCl_3$, chemical shifts in ppm and coupling constants in Hz) of the major chain tautomers **C** of *p*-substituted 4-(3-aryl-3-oxoprop-1-enyl)amino-2-amino-2-methylpentanes **11a–e**

R	CH_3, s	CH_3, s	CH_3–CH, d	J_{CH-CH_3}	H-a, dd (CH_2)	J_{gem}	J_{CH-CH_a}	H-b, dd (CH_2)	J_{CH-CH_b}	CH–CH_3, m
NO_2	1.17	1.19	1.34	6.6	1.61	14.4	3.3	1.72	9.0	3.66
Br	1.14	1.15	1.29	7.0	1.58	14.8	3.2	1.69	8.8	3.57
H	1.15	1.16	1.31	6.4	1.58	14.5	3.4	1.70	8.8	3.57
CH_3	1.15	1.16	1.30	6.6	1.57	14.4	3.0	1.70	8.7	3.55
OCH_3	1.14	1.15	1.30	6.6	1.57	14.4	3.0	1.69	8.7	3.55

R	=CH–CO, d	J_{CHCH}	=CHNH, dd	J_{CHNH}	H-2′, H-6′, d	H-3′, H-5′, d	J_{arom}	NH, br t	H_R
NO_2	5.69	7.2	7.13	13.2	7.99	8.24	9.0	10.72	—
Br	5.63	7.5	7.03	13.0	7.73	7.52	8.5	10.47	—
H	5.70	7.4	7.01	12.9	7.87	7.40	n.d.	10.45	7.44
CH_3	5.68	7.2	6.99	12.9	7.77	7.20	7.8	10.40	2.38
OCH_3	5.66	7.2	6.97	13.4	7.85	6.90	9.0	10.34	3.83

$J_{CH_3-CH_2}$=7.5, CH_3CH_2), 1.00 (3H, d, J_{CH_3-CH}=6.5, CH_3–CH), 1.41 (1H, m, H-a from CH_2–CH), 1.50 (1H, m, H-b from CH_2–CH), 1.53 (3H, s, CH_3–C=), 2.41 (2H, q, $J_{CH_3-CH_2}$=7.5, CH_2CH_3), 2.81 (1H, m, CH–CH_3), 3.24 (2H, m, CH_2NH), 6.55 (1H, m, NH), 7.42 (1H, d, J_{CH-NH}=13.5, =CH). δ_C (DMSO-d_6): 8.9 (CH_3C=), 10.4 (CH_3CH_2), 24.3 (CH_3CH), 28.2 (CH_2CH_3), 40.7 (CH_2–CH), 44.0 (CH–CH_3), 45.2 (CH_2NH), 103.4 (=$C(CH_3)$–CO), 149.6 (=CH–NH), 195.4 (CO). Compound *E*-**10A** (trans-minor chain): δ_H (DMSO-d_6): 0.95 (3H, t, $J_{CH_3-CH_2}$=7.5, CH_3CH_2), 1.15 (CH_3–CH), 1.41 (1H, m, H-a from CH_2–CH), 1.50 (1H, m, H-b from CH_2–CH), 1.54 (3H, s, CH_3–C=), 2.41 (2H, q, $J_{CH_3-CH_2}$=7.5, CH_2CH_3), 2.57 (2H, m, CH_2–NH_2), 3.47 (1H, m, CH–CH_3), 6.42 (1H, m, NH), 7.44 (1H, d, J_{CH-NH}=13.5, =CH). δ_C (DMSO-d_6): 9.1 (CH_3C=), 10.3 (CH_3CH_2), 22.0 (CH_3CH), 28.2 (CH_2CH_3), 38.3 (CH_2NH_2), 40.0 (CH_2–CH), 51.6 (CH–CH_3), 103.2 (=C–CH_3), 148.3 (=CH), 195.5 (CO).

4.3.1.4. 4-(4,4-Dimethyl-3-oxopent-1-enyl)amino-2-amino-2-methylpentane (12). Yield 58% (260 mg), colorless oil. HRMS: $C_{13}H_{26}N_2O$ $M^{+\bullet}$ calcd 226.2045; obsd 226.2038. Compound *Z*-**12C** (major chain): δ_H ($CDCl_3$): 1.12 (3H, s, CH_3 from $C(CH_3)_2$), 1.13 (3H, s, CH_3 from $C(CH_3)_2$), 1.14 (9H, s, $C(CH_3)_3$), 1.25 (3H, d, J_{CH_3CH}=6.5, CH_3–CH), 1.53 (1H, dd, J_{CH_a-CH}=4.0, J_{gem}=14.5, H-a from CH_2), 1.63 (1H, dd, J_{CH_b-CH}=8.3, J_{gem}=14.7, H-b

Table 5. The ^{13}C NMR chemical shifts (in ppm, $CDCl_3$) of the major chain tautomers **C** of *p*-substituted 4-(3-aryl-3-oxoprop-1-enyl)amino-2-amino-2-methylpentanes **11a–e**

R	CH_3CH	CH_3	CH_3	Cq	CH_2	CH–CH_3	=CH–CO
NO_2	24.4	31.3	31.8	49.5	51.2	52.3	90.2
Br	24.6	31.2	31.3	49.4	51.2	52.1	89.7
H	24.7	31.4	31.5	49.4	51.4	52.1	90.0
CH_3	24.7	31.4	31.5	49.4	51.5	52.1	89.9
OMe	24.8	31.4	31.4	49.4	51.5	52.0	89.6

R	C-2′,6′	C-3′,5′	C-4′	C-1′	=CH–NH	CO	C_R
NO_2	127.9	123.5	145.3	149.0	153.5	186.5	—
Br	128.6	131.3	125.3	138.6	152.8	188.0	—
H	127.0	128.2	130.8	139.8	152.4	189.6	—
CH_3	127.1	128.9	137.1	141.1	152.1	189.5	21.5
OMe	130.3	113.8	163.7	132.5	151.9	188.8	55.3

Table 7. The ^{13}C NMR chemical shifts (in ppm, $CDCl_3$) of the minor chain tautomers **A** of *p*-substituted 2-(3-aryl-3-oxoprop-1-enyl)amino-4-amino-2-methylpentanes **11a–e**

R	CH_3–CH	CH_3	CH_3	CH–CH_3	CH_2	$(CH_3)_2C$	=CH–CO
NO_2	27.0	28.2	28.9	43.9	51.8	55.0	90.3
Br	26.5	28.1	28.8	43.7	51.9	54.5	89.8
H	26.6	28.2	28.9	43.8	52.2	54.4	90.2
CH_3	26.6	28.3	29.0	43.7	52.2	54.3	90.0
OCH_3	26.6	28.3	29.0	43.7	52.2	54.3	89.7

R	C-2′,6′	C-3′,5′	C-4′	C-1′	=CH–NH	CO	C_R
NO_2	129.3	123.5	145.5	148.8	150.9	186.3	—
Br	129.5	131.8	125.3	138.7	150.2	187.8	—
H	127.0	128.3	130.7	n.d.	149.8	189.5	—
CH_3	128.4	129.2	134.7	143.9	149.6	189.4	21.6
OMe	130.9	113.7	163.5	132.6	149.3	188.6	55.2

Table 6. The ^{1}H NMR data ($CDCl_3$, chemical shifts in ppm and coupling constants in Hz) of the minor chain tautomers **A** of *p*-substituted 2-(3-aryl-3-oxoprop-1-enyl)amino-4-amino-2-methylpentanes **11a–e**

R	CH_3CH, d	J_{CH_3-CH}	$(CH_3)_2C$, s	CH_2, m	CH–CH_3, m	=CH–CO, d	$J_{CH=CH}$
NO_2	1.14	6.6	1.40	1.64	3.17	5.71	7.2
Br	1.11	6.0	1.35	1.61	3.13	5.65	7.5
H	1.11	6.4	1.37	1.62	3.15	5.73	7.6
CH_3	1.11	6.0	1.36	1.62	3.15	5.72	7.2
OCH_3	1.11	6.0	1.36	1.60	3.15	5.69	7.8

R	=CH–NH, dd	J_{CH-NH}	H-3′,5′	H-2′,6′	J_{arom}	NH, d	H_R
NO_2	7.21	13.8	8.12	8.32	9.0	11.17	—
Br	7.12	13.5	7.59	7.80	8.5	10.90	—
H	7.11	12.8	7.45	7.94	n.d.	10.86	7.46
CH_3	7.09	13.2	7.26	7.86	7.8	10.81	2.41
OCH_3	7.07	13.2	Overlap.	7.94	n.d.	10.75	3.86

Table 8. The ^{1}H NMR data ($CDCl_3$, chemical shifts in ppm and coupling constants in Hz) of the cyclic tautomer **B** of 4,4,6-trimethyl-2-(2-aryl-2-oxoethyl)-hexahydropyrimidines **11a–e**

R	H-5ax, dd	$J_{gem}=J_{5ax6ax}$	CH_3CH, d	J_{CH_3-CH}	CH_3-eq, s	CH_3-ax, s	H-5eq, dd	J_{5eq6ax}	CHCH_3, m
NO_2	0.94	12.3	1.07	6.0	1.13	1.21	1.54	2.7	3.03
Br	0.95	12.2	1.06	6.0	1.12	1.18	1.51	3.0	3.01
H	0.96	12.4	1.07	6.4	1.13	1.19	1.52	2.8	3.03
CH_3	0.95	12.0	1.07	6.0	1.12	1.19	1.51	2.4	3.03
OCH_3	0.95	12.3	1.06	6.0	1.12	1.19	1.51	2.4	3.02

R	H_a, dd, CH_2CO	J_{CH-H_a}	H_b, dd, CH_2CO	J_{gem}	J_{CH-H_b}	H-2, dd	H-3′,5′	H-2′,6′	J_{arom}	H_R
NO_2	3.20	6.0	3.27	18.0	4.8	4.26	8.09	8.31	8.4	—
Br	3.13	6.5	3.21	17.5	4.8	4.22	7.59	7.80	8.5	—
H	3.17	6.4	3.26	17.6	4.8	4.24	7.93	7.4–7.5	7.6	7.56
CH_3	3.16	6.6	3.23	17.4	4.2	4.23	7.25	7.83	7.8	2.40
OCH_3	3.12	6.3	3.21	17.7	4.5	4.22	6.92	7.91	9.0	3.86

Table 9. The ^{13}C NMR chemical shifts (in ppm, $CDCl_3$) of cyclic tautomer **B** of 4,4,6-trimethyl-2-(2-aryl-2-oxoethyl)hexahydropyrimidines **11a–e**

R	CH_3CH	CH_3 ax	CH_3 eq	CH_2–CO	CH_2	CH–CH_3	$(CH_3)_2C$
NO_2	23.0	24.1	33.2	46.2	46.4	47.1	50.0
Br	22.9	24.0	33.0	45.1	46.2	47.0	49.9
H	23.0	24.1	33.2	45.4	46.5	47.1	49.9
CH_3	23.0	24.1	33.2	45.3	46.5	47.1	49.9
OCH_3	23.0	24.1	33.2	45.0	46.5	47.0	49.9

R	C-2	C-2′,6′	C-3′,5′	C-4′	C-1′	CO	C_R
NO_2	62.7	123.9	129.9	144.7	n.d.	197.4	
Br	62.7	129.8	131.9	128.6	135.4	197.9	
H	62.8	128.0	128.6	133.4	136.8	199.0	—
CH_3	62.8	128.1	129.3	134.4	144.3	198.7	21.6
OMe	62.9	128.9	113.2	161.8	129.5	197.5	55.3

from CH_2), 3.46 (1H, m, CH–CH_3), 5.15 (1H, d, $J_{CH=CH}$=7.5, =CHCO), 6.80 (1H, dd, J_{CHNH}=12.8, $J_{CH=CH}$=8.0, =CHNH), 9.92 (1H, br s, NH). δ_C ($CDCl_3$): 24.8 (CH_3CH), 27.8 (C(CH_3)$_3$), 31.3 (2C, (CH_3)$_2$C), 44.2 (C(CH$_3$)$_3$), 49.4 (C(CH$_3$)$_2$), 51.7 (CH_2), 51.9 (CH–CH_3), 88.8 (=CHCO), 151.4 (=CHNH), 205.9 (CO). Compound *Z*-**12A** (minor chain), detected signals: δ_H ($CDCl_3$): 1.08 (3H, d, J_{CH_3CH}=6.5, CH_3–CH), 1.14 (9H, s, C(CH_3)$_3$), 1.31 (6H, s, C(CH_3)$_2$), 1.57 (2H, m, CH_2), 3.11 (1H, m, CH–CH_3), 5.19 (1H, d, $J_{CH=CH}$=8.0, =CHCO), 6.91 (1H, dd, J_{CHNH}=13.0, $J_{CH=CH}$=7.5, =CHNH), 10.27 (1H, d, J_{NHCH}=12.5, NH). δ_C ($CDCl_3$): 52.3 (CH_2), 53.9 (C(CH$_3$)$_2$), 89.0 (=CHCO), 205.8 (CO). Compound **12B** (cyclic): δ_H ($CDCl_3$): 0.92 (1H, t, $J_{5ax6ax}=J_{gem}$=12.5, H-5ax), 1.05 (3H, d, J_{CH_3CH}=6.0, CH_3–CH), 1.10 (3H, s, CH_3-eq), 1.14 (9H, s, C(CH_3)$_3$), 1.16 (3H, s, CH_3-ax), 1.49 (1H, dd, J_{5eq6ax}=3.0, J_{gem}=13.0, H-5eq), 2.71 (1H, dd, J_{H_aCH}=6.5, J_{gem}=18.0, H-a from CH_2–CO), 2.80 (1H, dd, J_{H_bCH}=4.5, J_{gem}=18.0, H-b from CH_2–CO), 2.97 (1H, m, CHCH$_3$), 4.02 (1H, dd, J_{CH-H_b}=4.7, J_{CH-H_a}=6.3, H-2). δ_C ($CDCl_3$): 23.0 (CH_3CH), 24.1 (CH_3-ax), 26.4 (C(CH_3)$_3$), 33.2 (CH_3-eq), 43.7 (CH_2CO), 44.2 (C(CH$_3$)$_3$), 46.5 (C-5), 47.0 (CH), 49.8 (C-4), 62.6 (C-2), 215.8 (CO).

4.3.1.5. 4-(2-Methyl-3-oxopent-1-enyl)amino-2-amino-2-methylpentane (13). Yield 34% (80 mg), colorless oil. HRMS: $C_{12}H_{24}N_2O$ $M^{+\bullet}$ calcd 212.1889; obsd 212.1898. Compound *E*-**13C** (major chain): δ_H (DMSO-d_6): 0.96 (3H, t, $J_{CH_3-CH_2}$=7.5, CH_3CH$_2$), 1.03 (1H, s, CH_3 from (CH$_3$)$_2$C), 1.05 (1H, s, CH_3 from (CH$_3$)$_2$C), 1.17 (3H, d, J_{CH_3-CH}=6.5, CH_3–CH), 1.40 (1H, dd, J_{gem}=14.0, J_{H_a-CH}=3.5, H-a from CH_2), 1.53 (3H, s, CH_3C=), 1.59 (1H, dd, J_{gem}=14.0, J_{H_b-CH}=9.5, H-b from CH_2), 2.44 (2H, q, $J_{CH_3-CH_2}$=7.5, CH_2CH$_3$), 3.57 (1H, m, CH–CH_3), 7.20 (1H, dd, $J_{NH-CH=}$=13.1, J_{NHCH}=5.1, NH), 7.48 (1H, d, J_{CH-NH}=13.0, =CH). δ_C (DMSO-d_6): 9.1 (CH_3C=), 10.5 (CH_3CH$_2$), 23.8 (CH_3CH), 28.2 (CH_2CH$_3$), 29.5 (CH_3 from (CH$_3$)$_2$C), 32.2 (CH_3 from (CH$_3$)$_2$C), 49.2 (C(CH$_3$)$_2$), 49.3 (CH_2), 50.2 (CH–CH_3), 103.7 (=CCH_3), 147.5 (=CH), 195.3 (CO). Compound *E*-**13A** (minor chain), detected signals: δ_H (DMSO-d_6): 0.96 (3H, t, $J_{CH_3-CH_2}$=7.5, CH_3CH$_2$), 1.06 (3H, overlap. d, CH_3CH), 1.24 (3H, s, from (CH$_3$)$_2$C), 1.27 (3H, s, from (CH$_3$)$_2$C), 1.45–1.55 (2H, m, CH_2), 1.54 (3H, s, CH_3–C=), 2.41 (2H, q, $J_{CH_3-CH_2}$=7.5, CH_2CH$_3$), 3.00 (1H, m, CH–CH_3), 7.52 (1H, d, J_{CH-NH}=13.5, =CH), 8.48 (1H, d, $J_{NH-CH=}$=14.0, NH). δ_C (DMSO-d_6): 9.2 (CH_3C=), 10.5 (CH_3CH$_2$), 27.6, 28.0 and 29.2 ((CH_3)$_2$C and CH_3CH), 28.3 (CH_2CH$_3$), 43.8 (CH–CH$_3$), 49.4 (CH_2), 53.9 (C(CH$_3$)$_2$), 103.9 (=C–CH_3), 144.5 (=CH), 195.2 (CO). Cyclic diastereomers **13B**: δ_H (DMSO-d_6): 0.70 (1H, t, $J_{5ax6ax}=J_{5ax5eq}$=12.0, H-5ax), 0.88–0.92 (6H, m, CH_3CH$_2$, CH_3–CH), 0.94–0.98 (3H, m, CH_3-4eq), 0.97–1.05 (6H, m, CH_3CH (side chain), CH_3-4ax), 1.35 (1H, m, H-5eq), 2.40–2.57 (3H, m, CH_2CH$_3$, CHCH$_3$, side chain), 2.70–2.80 (1H, m, H-6), 3.57 and 3.60 (1H, d, J_{H-2-CH}=8.0, H-2). δ_C (DMSO-d_6): 7.6 (2C, CH_3CH$_2$), 12.5 and 13.2 (CH_3CH, side chain), 22.8 and 22.9 (CH_3-6), 23.9 and 24.0 (CH_3-4ax), 32.8 and 32.9 (CH_3-4eq), 33.6 and 34.4 (CH_2–CH$_3$), 46.0 (C-5), 46.6 and 46.7 (C-6), 49.1 (2C, C-4), 51.0 and 51.6 (CO–CH–CH$_3$), 67.9 and 68.0 (C-2), 213.0 (2C, CO).

4.3.1.6. 4-(2-Oxocyclohexylidenyl)methylamino-2-amino-2-methylpentane (14). Yield 31% (170 mg), yellowish oil. HRMS: $C_{13}H_{24}N_2O$ $M^{+\bullet}$ calcd 224.1889; obsd 224.1882. Cyclohexane ring carbon signals are not assigned. Compound *E*-**14C** (major chain): δ_H ($CDCl_3$): 1.11–1.15 (3H, m, CH_3), 1.19 (3H, s, CH_3), 1.25 (3H, d, J_{CH_3-CH}=6.5, CH_3–CH), 1.45–1.50 (2H, m, CH_2), 1.60–1.75 (4H, m, 2H-4′, 2H-5′), 2.12–2.20 (2H, m, 2H-6′), 2.25–2.35 (2H, m, 2H-3′), 3.62 (1H, m, CHCH$_3$), 7.68 (1H, br m, NH), 7.78 (1H, d, $J_{=CH-NH}$=13.5, =CH). δ_C ($CDCl_3$): 22.9 (CH_3CH), 27.6 (CH_3), 33.3 (CH_3), 48.5 (CH_2), 49.6 ((CH$_3$)$_2$C), 49.8 (CH–CH_3), 104.5 (=C), 145.4 (=CH), 196.0 (CO). Compound *Z*-**14C** (major chain): δ_H ($CDCl_3$): 1.11–1.15 (6H, m, (CH$_3$)$_2$C), 1.25 (3H, d, J_{CH_3-CH}=6.5, CH_3–CH), 1.54 (1H, dd, J_{CH-CH_a}=3.5, J_{gem}=14.5, H-a from CH_2), 1.60–1.68 (1H, m, H-b from CH_2), 1.60–1.75 (4H, m, 2H-4′, 2H-5′), 2.25–2.35 (4H, m, 2H-3′,

2H-6), 3.46 (1H, m, CH_3–C*H*), 6.67 (1H, d, $J_{=CH-NH}$= 12.5, =CH), 10.28 (1H, br s, NH). δ_C ($CDCl_3$): 24.9 (*C*H_3–CH), 31.2 (CH_3), 31.5 (CH_3), 49.3 (*C*$(CH_3)_2$), 51.6 (CH_2), 51.7 (*C*H–CH_3), 101.2 (=C), 151.2 (=CH), 196.9 (CO). Compound *E*-**14A** (minor chain): δ_H ($CDCl_3$): 1.16 (3H, d, J_{CH_3-CH}=6.0, C*H*$_3$CH), 1.29 (3H, s, CH_3), 1.33 (3H, s, CH_3), 1.45–1.50 (2H, m, CH_2), 1.60–1.75 (4H, m, 2H-4′, 2H-5′), 2.12–2.20 (2H, m, 2H-6′), 2.25–2.35 (2H, m, 2H-3′), 3.10–3.19 (1H, m, C*H*–CH_3), 7.87 (1H, d, $J_{=CH-NH}$=14.5, =CH), 8.39 (1H, d, $J_{=CH-NH}$=14.5, NH). δ_C ($CDCl_3$): 28.3 (CH_3), 28.6 (CH_3), 29.8 (CH_3), 44.5 (*C*H–CH_3), 49.9 (CH_2), 54.6 (*C*$(CH_3)_2$), 104.2 (=C), 143.8 (=CH), 195.6 (CO). Compound *Z*-**14A** (minor chain): δ_H ($CDCl_3$): 1.11–1.15 (3H, m, C*H*$_3$–CH), 1.31 (6H, s, $(CH_3)_2$C), 1.57 (2H, m, CH_2), 1.60–1.75 (4H, m, 2H-4′, 2H-5′), 2.25–2.35 (4H, m, 2H-3′, 2H-6), 3.10–3.19 (1H, m, C*H*–CH_3), 6.77 (1H, d, $J_{=CH-NH}$=13.0, =CH), 10.74 (1H, d, $J_{=CH-NH}$=12.5, NH). δ_C ($CDCl_3$): 26.5 (*C*H_3–CH), 28.4 (CH_3), 29.1 (CH_3), 43.6 (*C*H–CH_3), 52.3 (CH_2), 53.8 (*C*$(CH_3)_2$), 101.2 (=C), 148.7 (=CH), 196.7 (CO). Cyclic diastereomers **14B**, detected signals: δ_H ($CDCl_3$): 0.84 (1H, t, J_{5ax6ax}=J_{5ax5eq}=12.5, H-5ax), 1.03 and 1.04 (3H, d, J_{CH_3-CH}=6.5, C*H*$_3$CH), 1.10 and 1.12 (3H, s, CH_3-eq), 1.45–1.50 (1H, m, H-5eq), 2.42–2.51 (1H, m, H-1′), 2.89 (1H, m, H-6), 3.72 and 3.81 (1H, d, $J_{H\text{-}2\text{–}H\text{-}1'}$=5.0, H-2). δ_C ($CDCl_3$): 23.1 (2C, *C*H_3CH), 23.9 and 24.0 (CH_3-4ax), 35.3 (CH_3-4eq), 47.0 (2C, C-5), 47.1 and 47.4 (C-6), 49.0 and 49.2 (C-4), 55.9 and 56.1 (C-1′), 66.1 and 66.7 (C-2), 213.4 and 213.8 (CO).

4.3.1.7. 4-(2-Oxocyclopentylidenyl)methylamino-2-amino-2-methylpentane (15). Yield 27% (150 mg), yellow oil. HRMS: $C_{12}H_{22}N_2O$ $M^{+\bullet}$ calcd 210.1732; obsd 210.1730. Compound *E*-**15C** (major chain): δ_H ($CDCl_3$): 1.11–1.15 (3H, m, CH_3), 1.19 (3H, s, CH_3), 1.24 (3H, d, J_{CH_3-CH}=6.5, C*H*$_3$–CH), 1.45–1.50 (2H, m, CH_2), 1.84–1.93 (2H, m, 2H-4′), 2.25–2.30 (2H, m, 2H-3′), 2.35–2.42 (2H, m, 2H-5′), 3.60 (1H, m, C*H*CH_3), 7.43 (1H, d, $J_{=CH-NH}$=14.0, =CH), 7.60 (1H, br m, NH). δ_C ($CDCl_3$): 19.9 (C-4′), 22.7 (*C*H_3CH), 25.9 (C-5′), 27.7 (CH_3), 35.3 (CH_3), 39.3 (C-3′), 48.5 (CH_2), 49.7 (*C*H–CH_3), 50.0 ($(CH_3)_2$*C*), 105.9 (=C), 141.1 (=CH), 203.5 (CO). Compound *Z*-**15C** (major chain): δ_H ($CDCl_3$): 1.11–1.15 (6H, m, $(CH_3)_2$C), 1.24 (3H, d, J_{CH_3-CH}=6.5, C*H*$_3$–CH), 1.54 (1H, dd, J_{CH-CH_a}=3.5, J_{gem}=14.5, H-a from CH_2), 1.63 (1H, dd, J_{CH-CH_b}=8.8, J_{gem}=14.7, H-b from CH_2), 1.84–1.93 (2H, m, 2H-4′), 2.25–2.30 (2H, m, 2H-3′), 2.48–2.54 (2H, m, 2H-5′), 3.46 (1H, m, CH_3–C*H*), 6.69 (1H, d, $J_{=CH-NH}$=12.5, =CH), 9.07 (1H, br s, NH). δ_C ($CDCl_3$): 22.0 (C-4′), 24.8 (*C*H_3–CH), 27.6 (C-5′), 31.2 (CH_3), 31.5 (CH_3), 38.8 (C-3′), 49.4 (*C*$(CH_3)_2$), 51.4 (CH_2), 51.6 (*C*H–CH_3), 103.1 (=C), 145.4 (=CH), 204.7 (CO). Compound *E*-**15A** (minor chain): δ_H ($CDCl_3$): 1.16 (3H, d, J_{CH_3-CH}=6.5, C*H*$_3$CH), 1.29 (3H, s, CH_3), 1.31 (3H, s, CH_3), 1.45–1.50 (2H, m, CH_2), 1.84–1.93 (2H, m, 2H-4′), 2.25–2.30 (2H, m, 2H-3′), 2.34–2.39 (2H, m, 2H-5′), 3.09–3.19 (1H, m, C*H*–CH_3), 7.52 (1H, d, $J_{=CH-NH}$=14.5, =CH), 8.34 (1H, d, $J_{=CH-NH}$=14.5, NH). δ_C ($CDCl_3$): 19.9 (C-4′), 26.0 (C-5′), 28.3 (CH_3), 28.6 (CH_3), 29.7 (CH_3), 38.9 (C-3′), 44.6 (*C*H–CH_3), 49.8 (CH_2), 54.6 (*C*$(CH_3)_2$), 105.6 (=C), 139.5 (=CH), 204.0 (CO). Compound *Z*-**15A** (minor chain): δ_H ($CDCl_3$): 1.11–1.15 (3H, m, C*H*$_3$–CH), 1.30 (6H, s, $(CH_3)_2$C), 1.56 (2H, m, CH_2), 1.84–1.93 (2H, m, 2H-4′), 2.25–2.30 (2H, m, 2H-3′), 2.48–2.54 (2H, m, 2H-5′), 3.09–3.19 (1H, m, C*H*–CH_3), 6.80 (1H, d, $J_{=CH-NH}$=13.0, =CH), 9.50 (1H, d, $J_{=CH-NH}$=13.0, NH). δ_C ($CDCl_3$): 22.0 (C-4′), 26.5 (*C*H_3–CH), 27.8 (C-5′), 28.2 (CH_3), 29.1 (CH_3), 39.8 (C-3′), 43.7 (*C*H–CH_3), 52.1 (CH_2), 53.9 (*C*$(CH_3)_2$), 103.1 (=C), 142.9 (=CH), 204.5 (CO). Cyclic diastereomers **15B**, detected signals: δ_H ($CDCl_3$): 0.80–0.90 (1H, m, H-5ax), 1.04 and 1.05 (3H, d, J_{CH_3-CH}=6.5, C*H*$_3$CH), 1.09 and 1.10 (3H, s, CH_3-eq), 1.45–1.50 and 1.52–1.56 (1H, m, H-5eq), 1.84–1.93 (2H, m, 2H-4′), 2.27 and 2.32 (1H, m, H-1′), 2.25–2.30 (2H, m, 2H-3′), 2.35–2.42 (2H, m, 2H-5′), 2.89 (1H, m, H-6), 3.78 and 3.91 (1H, d, $J_{H\text{-}2\text{–}H\text{-}1'}$= 5.3, H-2). δ_C ($CDCl_3$): 20.5 and 20.6 (C-4′), 23.0 (2C, *C*H_3CH), 24.0 and 24.1 (CH_3-4ax), 22.5 and 26.4 (C-5′), 33.1 and 33.2 (CH_3-4eq), 39.2 and 39.3 (C-3′), 46.6 and 46.7 (C-5), 47.0 and 47.3 (C-6), 49.7 (2C, C-4), 53.9 and 54.4 (C-1′), 65.9 and 66.5 (C-2), 220.8 and 220.9 (CO).

4.3.2. Preparation of the bis-condensation product 16 (procedure B). To a solution of β-keto aldehyde (2 mmol) in 10 mL of ether, a solution of diamine **1** in 10 mL of ether was added dropwise. The mixture was left standing overnight, dried over Na_2SO_4, filtered, and concentrated in vacuo.

4.3.2.1. 1,3-Bis[(4,4-dimethyl-3-oxopent-1-enyl)amino]-butane (16). Yield 85% (520 mg), yellow oil. HRMS: $C_{18}H_{32}N_2O_2$ $M^{+\bullet}$ calcd 308.2464; obsd 308.2467. δ_H ($CDCl_3$): 1.14 (18H, s+s, 2×(C*H*$_3$)$_3$C), 1.24 (6H, d, J_{CH_3CH}=6.80, CH_3), 1.73 (2H, m, C*H*$_2$–CH), 3.15–3.35 (3H, m, C*H*CH_3, CH_2NH), 5.18 (2H, d+d, $J_{CH=CH}$=8.0, 2× =CH–CO), 6.70 (1H, dd, $J_{CH=CH}$=7.5, J_{CH-NH}=12.5, =C*H*–NH), 6.75 (1H, dd, $J_{CH=CH}$=7.5, J_{CH-NH}=12.5, =C*H*–NH), 9.79 (2H, br s, NH). δ_C ($CDCl_3$): 22.5 (CH_3), 26.2 (CH_3), 27.7 ((*C*H_3)$_3$C), 38.7 (*C*H_2CH), 41.6 ((CH$_3$)$_3$*C*), 45.5 (CH_2–NH), 52.0 (*C*H–CH_3), 89.3 (*C*H–CO), 89.5 (*C*H–CO), 151.8 (CHNH), 153.2 (CHNH), 206.5 (CO), 206.6 (CO).

4.3.3. Reaction of 1,3-diamines with β-diketones, β-keto esters, and β-keto amides (procedure C, substances 24, 26–28). A dicarbonyl compound (2–3 mmol) was added to an equimolar amount of diamine without solvent. The mixture was stirred in the presence of HCl vapor (trace amounts) until the reaction was complete (monitoring by TLC), and the product precipitated from hexane solution by freezing to −65 °C.

4.3.3.1. 1-(1-Methyl-3-phenyl-3-oxoprop-1-enylamino)-3-aminobutane, 22 and 23 (unseparated mixture). Yield 30% (140 mg) (procedure A), colorless oil. HRMS: $C_{14}H_{20}N_2O$ $M^{+\bullet}$ calcd 232.1576; obsd 232.1576. Major chain (**22**, 83%): δ_H ($CDCl_3$): 1.14 (3H, d, J_{CH_3-CH}=6.5, C*H*$_3$–CH), 1.60–1.75 (2H, m, C*H*$_2$–CH), 2.07 (3H, s, C*H*$_3$C=), 3.09 (1H, m, C*H*–CH_3), 3.41 (2H, m, CH_2–NH), 5.66 (1H, s, =CH), 7.35–7.41 (3H, m, H-3′, H-4′, H-5′), 7.84 (2H, dd, J_{23}=8.0, J_{24}=1.7, H-2′, H-6′), 11.45 (1H, br m, NH). δ_C ($CDCl_3$): 19.3 (*C*H_3C=), 24.3 (*C*H_3–CH), 39.3 (*C*H_2–CH), 40.4 (CH_2–NH), 44.5 (*C*H–CH_3), 91.9 (=CH), 126.7 (C-2′, C-6′), 128.0 (C-3′, C-5′), 130.2 (C-4′), 140.3 (C-1′), 164.9 (=*C*–CH_3), 187.4 (CO). Minor chain (**23**, 17%): δ_H ($CDCl_3$): 1.26 (3H, d, J_{CH_3-CH}=6.5,

C*H*$_3$CH), 1.60–1.75 (2H, m, C*H*$_2$–CH), 2.09 (3H, s, C*H*$_3$C=), 2.80 (2H, m, C*H*$_2$–NH$_2$), 3.80 (C*H*–CH$_3$), 5.62 (1H, s, =CH), 7.35–7.41 (3H, m, H-3′, H-4′, H-5′), 7.84 (2H, dd, J_{23}=8.0, J_{24}=1.7, H-2′, H-6′), 11.45 (1H, br m, NH). δ_C ($CDCl_3$): 19.3 (*C*H$_3$C=), 22.1 (*C*H$_3$–CH), 38.5 (CH$_2$–NH$_2$), 40.8 (*C*H$_2$–CH), 46.9 (*C*H–CH$_3$), 91.8 (=CH), 126.7 (C-2′, C-6′), 128.0 (C-3′, C-5′), 130.2 (C-4′), 140.3 (C-1′), 164.0 (=*C*–CH$_3$), 187.3 (CO).

4.3.3.2. 4-(1-Methyl-3-oxobut-1-enyl)amino-2-amino-2-methylpentane (24). Yield 85% (330 mg), colorless oil. HRMS: $C_{11}H_{22}N_2O$ $M^{+\bullet}$ calcd 198.1732; obsd 198.1740. δ_H ($CDCl_3$): 1.02 (3H, s, CH_3), 1.03 (3H, s, CH_3), 1.11 (3H, d, J_{CH-CH_3}=6.4, C*H*$_3$–CH), 1.46 (1H, dd, J_{CH-H_a}=3.4, J_{gem}=14.5, H-a from CH_2), 1.56 (1H, dd, J_{CH-H_b}=8.3, J_{gem}=14.5, H-b from CH_2), 1.87 (6H, s, C*H*$_3$C=CH, CH$_3$–CO), 3.60 (1H, m, C*H*–CH$_3$), 4.80 (1H, s, =CH), 10.81 (1H, br d, $J_{NH-CH(CH_3)}$=7.7). δ_C ($CDCl_3$): 18.6 (*C*H$_3$C=), 24.5 (C*H*$_3$–CH), 28.5 (*C*H$_3$–CO), 30.7 (CH_3), 31.7 (CH_3), 45.8 (*C*H–CH$_3$), 49.0 (*C*(CH$_3$)$_2$), 51.6 (CH_2), 94.8 (=CH), 161.3 (=*C*–CH$_3$), 194.1 (CO).

4.3.3.3. 4-(1-Methyl-3-phenyl-3-oxoprop-1-enyl)amino-2-amino-2-methylpentane (25). Yield 37% (190 mg) (procedure A), colorless oil. HRMS: $C_{16}H_{24}N_2O$ $M^{+\bullet}$ calcd 260.1889; obsd 260.1900. δ_H ($CDCl_3$): 1.28 (3H, d, J_{CH_3-CH}=6.0, C*H*$_3$–CH), 1.41 (3H, s, CH_3), 1.44 (3H, s, CH_3), 1.98 (1H, dd, J_{CH-CH_a}=9.3, J_{gem}=15.0, H-a from CH_2), 2.07 (1H, dd, J_{CH-H_b}=2.5, H-b from CH_2), 2.19 (3H, s, C*H*$_3$C=), 4.06 (1H, m, C*H*CH$_3$), 5.64 (1H, s, =CH), 7.35–7.42 (3H, m, H-3′, H-4′, H-5′), 7.81 (2H, dd, J_{23}=8.0, J_{24}=1.5, H-2′, H-6′), 11.49 (1H, d, $J_{NH-CH(CH_3)}$=9.0, NH). δ_C ($CDCl_3$): 19.6 (*C*H$_3$C=), 24.6 (*C*H$_3$–CH), 25.8 (CH_3), 28.0 (CH_3), 45.6 (*C*H–CH$_3$), 47.9 (CH_2), 54.3 (*C*(CH$_3$)$_2$), 92.6 (=CH), 126.9 (C-2′, C-6′), 128.2 (C-3′, C-5′), 130.6 (C-4′), 140.3 (C-1′), 163.9 (=*C*–CH$_3$), 187.8 (CO).

4.3.3.4. 3-((4-Methyl-4-aminopent-2-yl)amino)but-2-enoic acid, ethyl ester (26). Yield 68% (150 mg), transparent colorless oil. HRMS: $C_{12}H_{24}N_2O_2$ $M^{+\bullet}$ calcd 228.1838; obsd 228.1829. Compound *Z*-**26** (major chain, 83%): δ_H (DMSO-d_6): 0.97 (3H, s, CH_3), 1.01 (3H, s, CH_3), 1.09–1.14 (6H, m, C*H*$_3$–CH, C*H*$_3$CH$_2$), 1.47 (2H, d, *J*=5.8, CH_2), 1.93 (3H, s, CH$_3$C=), 3.75 (1H, m, CH$_3$–C*H*), 3.85–3.95 (2H, m, C*H*$_2$CH$_3$), 4.27 (1H, s, =CH), 8.43 (1H, d, $J_{NH-CH(CH_3)}$=9.5, NH). δ_C (DMSO-d_6): 14.5 (*C*H$_3$CH$_2$), 19.0 (*C*H$_3$C=), 24.7 (*C*H$_3$CH), 30.3 (CH_3), 32.1 (CH_3), 45.2 (CH$_3$*C*H), 48.7 (*C*(CH$_3$)$_2$), 51.8 (CH_2), 57.3 (*C*H$_2$CH$_3$), 80.9 (=CH), 160.7 (=*C*CH$_3$), 169.4 (CO). Compound *E*-**26** (minor chain, 17%): δ_H (DMSO-d_6): 0.98 (3H, s, CH_3), 0.99 (3H, s, CH_3), 1.04 (3H, m, C*H*$_3$–CH), 1.09–1.14 (3H, m, C*H*$_3$CH$_2$), 1.35 (1H, dd, J_{CH-H_a}=3.9, J_{gem}=14.2, H-a from CH_2), 1.58 (1H, m, H-b from CH_2), 2.14 (3H, s, CH$_3$C=), 3.46 (1H, m, C*H*CH$_3$), 3.85–3.95 (2H, m, C*H*$_2$CH$_3$), 4.43 (1H, s, =CH), 6.85 (1H, d, J_{NH-CH}=6.8, NH). δ_C (DMSO-d_6): 14.7 (*C*H$_3$CH$_2$), 21.7 (*C*H$_3$C=), 22.7 (*C*H$_3$CH), 29.6 (CH_3), 31.2 (CH_3), 45.0 (CH$_3$*C*H), 49.0 (*C*(CH$_3$)$_2$), 49.3 (CH_2), 57.0 (*C*H$_2$CH$_3$), 79.6 (=CH), 158.5 (=*C*CH$_3$), 168.1 (CO).

4.3.3.5. 2-((4-Methyl-4-aminopent-2-yl)amino)cyclohex-1-enic acid, ethyl ester (27). Yield 60% (220 mg), colorless oil. HRMS: $C_{15}H_{28}N_2O_2$ $M^{+\bullet}$ calcd 268.2151; obsd 268.2156. δ_H ($CDCl_3$): 1.13 (3H, s, CH_3), 1.14 (3H, s, CH_3), 1.15 (3H, d, J_{CH-CH_3}=6.0, C*H*$_3$CH), 1.27 (3H, t, $J_{CH_2-CH_3}$=7.2, C*H*$_3$CH$_2$), 1.55–1.59 (3H, m, 2H-4′, H-a from CH_2 amin), 1.63 (1H, dd, J_{CH-H_b}=9.0, J_{gem}=14.4, H-b from CH_2 amin), 1.65–1.69 (2H, m, 2H-5′), 2.27 (2H, t, *J*=6.3, 2H-6′), 2.35 (2H, m, H-6′), 3.74 (1H, m, C*H*–CH$_3$), 4.09 (2H, q, $J_{CH_2-CH_3}$=7.5, C*H*$_2$–CH$_3$), 8.89 (1H, d, J_{CH-NH}=9.6, NH). δ_C ($CDCl_3$): 14.6 (*C*H$_3$CH$_2$), 22.3 (C-5′), 22.7 (C-4′), 23.8 (C-3′), 25.1 (*C*H$_3$CH), 26.4 (C-6′), 30.9 (2C, 2×CH$_3$), 44.6 (*C*HCH$_3$), 49.6 (*C*(CH$_3$)$_2$), 51.9 (CH$_2$-amin), 58.6 (*C*H$_2$CH$_3$), 89.8 (C-2′), 158.2 (C-1′), 170.9 (CO).

4.3.3.6. 3-((4-Methyl-4-aminopent-2-yl)amino)but-2-enic acid, diethylamid (28). Yield 52% (100 mg), colorless oil. HRMS: $C_{14}H_{29}N_3O$ $M^{+\bullet}$ calcd 255.2311; obsd 255.2319. δ_H (DMSO-d_6): 0.95–1.05 (12H, m, (CH$_3$)$_2$C, 2C*H*$_3$CH$_2$), 1.08 (3H, d, J_{CH_3-CH}=6.6, C*H*$_3$–CH), 1.44 (2H, d, J_{CH-CH_2}=5.4, CH_2), 1.91 (3H, s, CH$_3$–C=), 3.20 (4H, m, C*H*$_2$CH$_3$), 3.68 (1H, m, C*H*CH$_3$), 4.47 (1H, s, =CH), 9.48 (1H, d, J_{NHCH}=9.6, NH). δ_C (DMSO-d_6): 14.0 (*C*H$_3$CH$_2$), 19.5 (CH$_3$C=), 25.1 (*C*H$_3$CH), 30.5 (CH_3), 31.9 (CH_3), 41.9 (*C*H$_2$CH$_3$), 44.7 (*C*H–CH$_3$), 48.8 (*C*(CH$_3$)$_2$), 52.1 (CH_2), 81.0 (=CH), 157.3 (=*C*–CH$_3$), 169.0 (CO).

4.3.3.7. 2,4,4,6-Tetramethyl-3,4,5,6-tetrahydropyrimidine (29). Yield 80% (220 mg), white powder, mp 135 °C. HRMS: $C_8H_{16}N_2$ $M^{+\bullet}$ calcd 140.1313; obsd 140.1314. δ_H (DMSO-d_6): 1.08 (1H, t, J_{5ax6ax}=J_{gem}=13.0, H-5ax), 1.11 (3H, s, CH_3), 1.14 (3H, d, J_{CH_3-CH}=6.5, C*H*$_3$–CH), 1.18 (3H, s, CH_3), 1.74 (1H, dd, J_{5eq6ax}=3.5, J_{gem}=13.0, H-5eq), 1.90 (3H, s, C*H*$_3$–C=), 3.38 (1H, m, CH$_3$–C*H*). δ_C (DMSO-d_6): 20.1 (*C*H$_3$C=), 21.4 (*C*H$_3$CH), 29.1 (CH_3), 29.9 (CH_3), 41.0 (CH_2), 43.4 (CH), 49.3 (*C*(CH$_3$)$_2$), 154.5 (=C).

Acknowledgements

We thank Dr. V. Ovcharenko from University of Turku, Finland, for help, fruitful discussions and HRMS spectra. We also thank Dr. S. I. Yakimovich from University of St. Petersburg, Russia, for fruitful discussions.

References and notes

1. Zelenin, K. N.; Alekseyev, V. V.; Pihlaja, K.; Ovcharenko, V. V. *Russ. Chem. Bull.* **2002**, *51*, 205–221.
2. Lázár, L.; Fülöp, F. *Eur. J. Org. Chem.* **2003**, 3025–3042 and references therein.
3. Valters, R. E.; Fülöp, F.; Korbonits, D. *Adv. Heterocycl. Chem.* **1996**, *66*, 1–71.
4. Göblyös, A.; Lásár, L.; Fülöp, F. *Tetrahedron* **2002**, *58*, 1011–1016.
5. Lázár, L.; Göblyös, A.; Martinek, T. A.; Fülöp, F. *J. Org. Chem.* **2002**, *67*, 4734–4741.
6. Zelenin, K. N.; Alekseyev, V. V.; Ukraintsev, I. V.; Tselinsky, I. V. *Org. Prep. Proced. Int.* **1998**, *30*, 53–61.
7. Sinkkonen, J.; Zelenin, K. N.; Potapov, A.-K. A.; Lagoda, I. V.; Alekseyev, V. V.; Pihlaja, K. *Tetrahedron* **2003**, *59*, 1939–1950.

8. Maloshitskaya, O.; Sinkkonen, J.; Ovcharenko, V. V.; Zelenin, K. N.; Pihlaja, K. *Tetrahedron* **2004**, *60*, 6913–6921.
9. Hetényi, A.; Szakonyi, Z.; Klika, K. D.; Pihlaja, K.; Fülöp, F. *J. Org. Chem.* **2003**, *68*, 2175–2182.
10. Yakimovich, S. I.; Zelenin, K. N. *Zh. Obshch. Khim.* **1995**, *65*, 705–727.
11. Maloshitskaya, O.; Sinkkonen, J.; Alekseyev, V. V.; Zelenin, K. N.; Pihlaja, K. *Tetrahedron* **2005**, *61*, 7294–7303.
12. Maloshitskaya, O.; Alekseyev, V. V.; Pihlaja, K. *Khim. Geterotsikl. Soedin.* **2006**, *42*, 280–281.
13. Zelenin, K. N.; Potapov, A.-K. A.; Alekseyev, V. V.; Lagoda, I. V. *Chem. Heterocycl. Comp.* **2004**, *40*, 903–910.
14. Valters, R. E.; Flitch, W. *Ring–Chain Tautomerism*; Plenum: New York, NY, London, 1985.
15. Kozerski, L.; Kamienska-Trela, K.; Kania, L.; von Philipsborn, W. *Helv. Chim. Acta* **1983**, *66*, 2113–2128.
16. Zhuo, J.-C. *Magn. Reson. Chem.* **1998**, *36*, 565–572.
17. Hauser, C. R.; Swamer, F. W.; Adams, J. T. *Organic Reactions*; Adams, R., Ed.; Wiley: New York, NY, 1954; Vol. 8, pp 59–196.