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Synthesis and separation of stereoisomeric 2,4,6,8-tetrasubstituted 3,7-dithia-1,5-diazabicyclo[3.3.0]octanes

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Heterocyclization of hydrazine with aldehydes R—CHO (R = Me, Et, Pr^n, Bu^n, n-C_5H_{11}, Ph, 4-$MeOC_6H_4$, 3-Py) and H_2S leads to stereoisomeric 2,4,6,8-tetrasubstituted 3,7-dithia-1,5-diazabicyclo[3.3.0]octanes, which were separated by column chromatography. The *trans-transoid-trans*-configuration of tetramethyl(-ethyl,-propyl)-3,7-dithia-1,5-diazabicyclo-[3.3.0]octanes was inferred from the X-ray diffraction and ^1H and ^{13}C NMR spectroscopic data.

Key words: heterocyclization, hydrazine, aldehydes, hydrogen sulfide, 2,4,6,8-tetra-alkyl(aryl)-3,7-dithia-1,5-diazabicyclo[3.3.0]octanes, X-ray diffraction analysis.

Heterocycles[1,2] of thiadiazolidine series exhibit various biological activity. 3,7-Dithia-1,5-diazabicyclo[3.3.0]-octane containing fused thiadiazolidine rings was for the first time[3] synthesized from hydrazine, formaldehyde, and H_2S in 11% yield. Recently,[4,5] we have suggested improved methods for its preparation in 76 and 80% yields. We studied conformational features of this bicyclane in both the crystalline phase[6] and the solution.[4] In the crystal, molecules of this compound adopt the *cis*-conformation and retain the second order symmetry C_{2h}. In $CDCl_3$ solution at 24.5 °C, a conformational equilibrium between the *cis*-forms of 3,7-dithia-1,5-diazabicyclo[3.3.0]octane is observed due to the inversion of the nitrogen atoms.

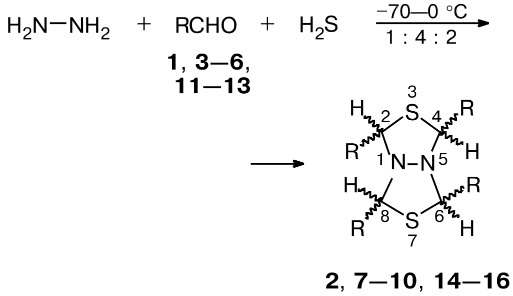
To develop efficient methods for the synthesis of alkyl- and aryl-substituted 3,7-dithia-1,5-diazabicyclo[3.3.0]-octanes, we studied a thiomethylation reaction of hydrazine with aliphatic and aromatic aldehydes and H_2S, as well as stereochemistry of the crystalline 2,4,6,8-tetrasubstituted 3,7-dithia-1,5-diazabicyclo[3.3.0]octanes.

Results and Discussion

Earlier, we have found that cyclothiomethylation of hydrazine with formaldehyde and H_2S, depending on the molar ratio of the starting reagents, temperature,[4] and medium pH[5] (in the case of acetic aldehyde, also on the order of mixing the starting reagents[7]) leads to heterocycles of 1,3,4-thiadiazolidine and 1,3,5-dithiazinane series.

In the present work, we show that a preliminary bubbling hydrogen sulfide through acetic aldehyde **1** with subsequent dropwise addition of hydrazine at temperatures below −10 °C regiospecifically leads to 2,4,6,8-tetramethyl-3,7-dithia-1,5-diazabicyclo[3.3.0]octane **2** (R = Me) in more than 64% yield. According to the ^1H and ^{13}C NMR spectroscopic data and GC-MS analysis, bicycle **2** is formed as a mixture of stereoisomers **2a—d** (Scheme 1, Table 1).

Scheme 1



R = Me (**1**, **2**); Et (**3**, **7**); Pr^n (**4**, **8**); Bu^n (**5**, **9**); n-C_5H_{11} (**6**, **10**); Ph (**11**, **14**); 4-$MeOC_6H_4$ (**12**, **15**); 3-Py (**13**, **16**)

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Table 1. Conditions of separation by column chromatography, physicochemical characteristics, and yields of stereoisomeric 2,4,6,8-tetraalkyl-3,7-dithia-1,5-diazabicyclo[3.3.0]octanes **2** and **7**—**10**

R^1	Separation conditions		Product	R_f	Physical state	Yield (%)
	Support	Eluent				
Me	SiO_2— —$AgNO_3$ (5%)	n-C_6H_{14}—EtOAc— —$CHCl_3$ (5 : 1 : 1)	**2a**	0.55	Crystal	31
			2b	0.59	Oil	18
			2c	0.61	Oil	7
			2d	0.63		7
Et	Activated charcoal (AG-5)	CH_2Cl_2— —$CHCl_3$ (2 : 1)	**7a**	0.58	Crystal	42
			7b	0.63	Oil	21
			7c	0.67	Oil	8
			7d	0.53		8
Pr^n	Activated charcoal (AG-5)	CH_2Cl_2— —$CHCl_3$ (2 : 1)	**8a**	0.53	Crystal	48
			8b	0.62	Oil	17
			8c	0.69	Oil	11
			8d	0.57		11
Bu^n	SiO_2— —$AgNO_3$ (5%)	Light petroleum —CH_2Cl_2 (5 : 3)	**9b**	0.56	Oil	52
			9c	0.66	Oil	20
			9d	0.78	Oil	22
n-C_5H_{11}	SiO_2— —$AgNO_3$ (5%)	n-C_6H_{14}—EtOAc— —$CHCl_3$ (5 : 1 : 1)	**10b**	0.57	Oil	54
			10c	0.68	Oil	34
			10d	0.75	Oil	12

Heterocyclization of hydrazine with other aliphatic aldehydes RCHO (R = Et (**3**), Pr^n (**4**), Bu^n (**5**), n-C_5H_{11} (**6**)) and H_2S similarly gave a series of the corresponding 2,4,6,8-tetraalkyl-3,7-dithia-1,5-diazabicyclo[3.3.0]octanes **7**—**10** as mixtures of stereoisomers. At the same time, the condensation of hydrazine with aromatic aldehydes RCHO **11**, **13** (R = Ph, 3-Py) and H_2S gave only one stereoisomer of 2,4,6,8-tetraaryl-3,7-dithia-1,5-diazabicyclo[3.3.0]octanes **14**, **16**, whereas in the case of anisaldehyde **12** (R = 4-$MeOC_6H_4$), stereoisomeric 2,4,6,8-tetrakis(4-methoxyphenyl)-3,7-dithia-1,5-diazabicyclo[3.3.0]octanes **15** were obtained.

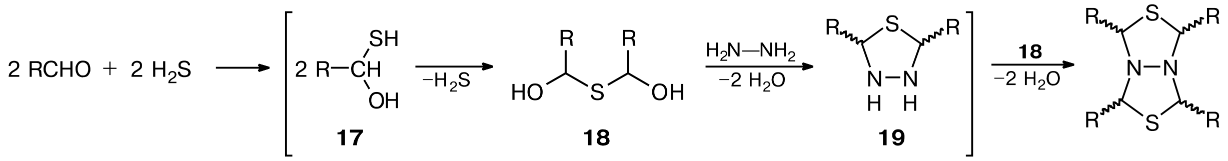
Obviously, formation of bicyclanes proceeds *via* the intermediacy of compounds **17**—**19** (Scheme 2). Cyclization of intermediates **18** and **19** is effected with elimination of water (see Scheme 2).

The stereoisomeric mixtures of compounds **2** and **7**—**10** were characterized by ^1H and ^{13}C NMR spectra and analyzed by gas chromato-mass spectrometry (GC-MS). Individual stereoisomers of the synthesized bicycles **2** and **7**—**10** were isolated by column chromatography (see Table 1) and characterized by ^1H and ^{13}C NMR spectroscopy. The crystalline compounds **2a** and **8a** were studied by X-ray diffraction, too (Figs 1 and 2).

The ^1H NMR spectrum of the unseparated stereoisomeric mixture of bicycle **2** at 20 °C exhibits two broad signals corresponding to the methyl (δ_H 1.13—1.82, $W_{1/2}$ = 60 Hz) and methine groups (δ_H 4.10—4.90, $W_{1/2}$ = 60 Hz) in the indicative regions, whereas in the relatively low-field, narrow region of the ^{13}C NMR spectrum δ 61.30—69.50, seven signals for the CH carbon atoms are observed, as well as seven resonances for the methyl groups (δ_C 18.10—25.90). The GC-MS data show that 2,4,6,8-tetraalkyl-3,7-dithia-1,5-diazabicyclo[3.3.0]octanes **2**, **7**, and **8** were obtained as mixtures of four isomers with different configuration of alkyl substituents, whereas **9** and **10**, as mixtures of three isomers. The mass spectra of stereoisomeric bicyclanes **2a**—**d** are identical, but differ in the Kovach indices.[8] Thus, for isomers **2a**, **2b**, and **2c**, the Kovach indices, determined experimentally (GC-MS), are 1500, 1550, and 1530, respectively.

For the isolation of individual stereoisomeric bicycles (**2** and **7**—**10**), we selected conditions for their efficient separation by column chromatography (see Table 1).

Scheme 2



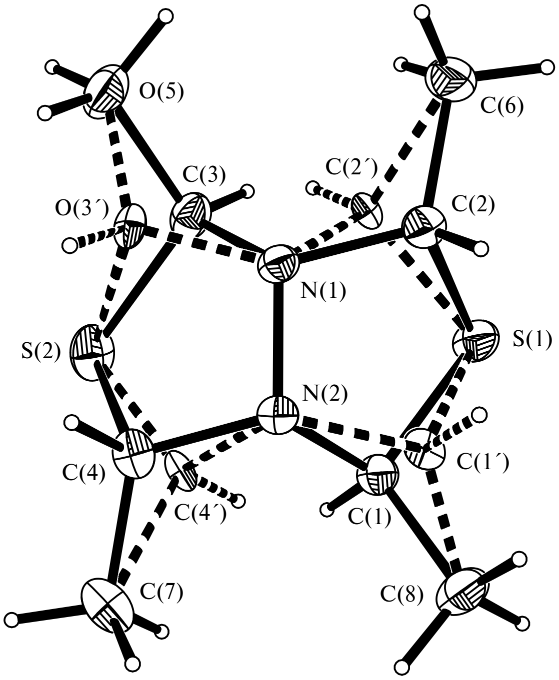


Fig. 1. Molecular structure of **2a**. The atoms are shown as thermal ellipsoids with $p = 50\%$, the minor disordered position are shown in the dashed lines.

Activated charcoal, Al_2O_3, SiO_2, as well as SiO_2 impregnated with $AgNO_3$—H_2O, were used as adsorbents. The best results in the separation of isomeric dithiadiazabicyclooctanes **2** were obtained with column chromatography on SiO_2 impregnated with $AgNO_3$—H_2O (5%).[9]

A gradual evaporation at room temperature of the eluent from the fraction with R_f 0.55 afforded crystals, which were studied by X-ray diffraction. The compound was determined to be the *trans-transoid-trans*-isomer (*TTT*) **2a**.

Bicycle **2a** is disordered, with the population of the major and the minor positions being 0.887 and 0.113, respectively. The two disordered fragments possess identical conformations and can be described as enantiomers with common of the sulfur and the nitrogen atoms and the methyl groups (see Fig. 1). In our further descriptions of the bicycle geometry, we will use the data for only the major fragment. Both five-membered rings are in the *twist-envelope* conformation, and the net conformation of the bicycle can be described as the *endo-endo* kind, with all the methyl groups being in the equatorial positions *TTT*.

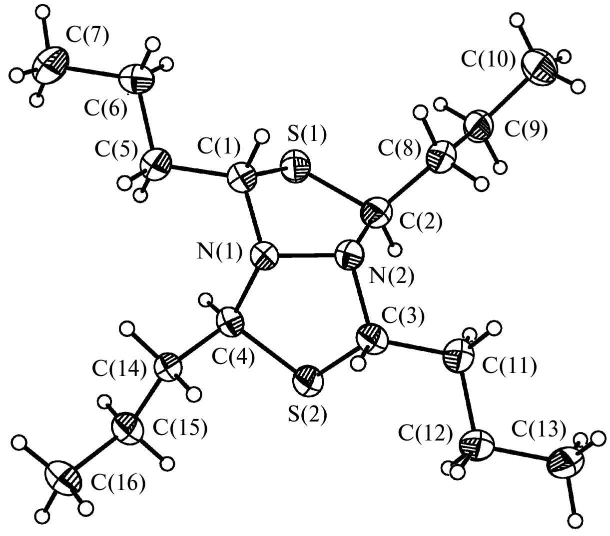
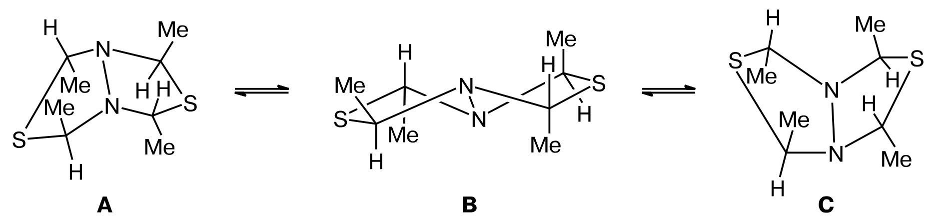


Fig. 2. Molecular structure of **8a**. The atoms are given as thermal ellipsoids with $p = 50\%$.

In the ^{1}H NMR spectrum of compound **2a**, the CH_3 and CH groups are found as four magnetically nonequivalent signals: two singlets at δ_H 1.40, 1.50 and two unsplited singlets at δ_H 4.50, 5.20, respectively. The ^{13}C NMR spectrum also contains two signals both in the high-field and both in the low-field regions at δ_C 18.50, 26.40 and 64.76, 66.30, respectively. The shape of the signals indicates a slow conformational exchange in the NMR time scale between conformers **A** and **B** (Scheme 3).[4] Quantum chemical calculations (B3LYP/6-31G(d,p), Gamess) show that conformer **A** predominates.

The ^{1}H and ^{13}C NMR spectra of the second stereoisomer **2b** (an oily product with R_f 0.59) exhibit two signals each: at δ_H 1.45 ($J = 4$ Hz), 4.52 ($^3J = 4$ Hz) and δ_C 29.80, 61.90. Taking into account molecular symmetry, it was suggested that two signals can be attributed to the *cis-cisoid-cis*-isomers (*CCC*) **2b**, with either equatorial or axial arrangement of the methyl groups.

Scheme 3



A ($\Delta G_{tot}{}^{298} = 0$ kcal mol^{-1})

B ($\Delta G_{tot}{}^{298} = 1.8$ kcal mol^{-1})

C ($\Delta G_{tot}{}^{298} = 0$ kcal mol^{-1})

In each of ^{1}H and ^{13}C NMR spectra of the third oily isomer **2c** (the fraction with R_f 0.61), three signals are observed: at δ_H 4.37, 4.39, 5.34 and δ_C 61.80, 67.30, 69.30. The signals for the methine carbon atoms of the ring are found in the low-field region of the spectrum, the signals at δ_C 17.60, 23.40, 25.86, and 28.10 due to the Me substituents are found, as well.

These conditions selected for the column chromatography separation did not allow us to isolate the fourth isomer **2d** in the individual state, therefore, the corresponding to it signals were obtained by subtraction of the signals assigned earlier for three other isomers **2a**—**c** from the spectrum of the unseparated mixture of isomers. In addition, we used homo- and heteronuclear experiments COSY and HSQC to reveal the H—H spin systems and the C—H interactions. Thus, the signals at δ_C 25.1 and 66.0 in the ^{13}C NMR spectrum and at δ_H 1.50 and 4.35 in the ^{1}H NMR spectrum were assigned to the fourth stereomer.

It should be noted that in the ^{1}H NMR spectra of stereoisomers **2b**—**d** recorded in the temperature interval 20—60 °C, a clear splitting of the signals for the methane and methyl protons is observed. It indicates that the conformational equilibrium is shifted toward the *endo*-*endo*-conformer **A** (see Scheme 3) already at room temperature.

To sum up, heterocyclization of hydrazine with acetic aldehyde and H_2S leads to four isomers of 2,4,6,8-tetramethyl-3,7-dithia-1,5-diazabicyclo[3.3.0]octane **2a**—**d** in the *endo*-*endo*-conformation with different configurations of the methyl groups, three of these isomers were isolated by column chromatography in the individual state (see Table 1).

Similar pattern is observed in the reaction of hydrazine with propionaldehyde (**3**) or butyraldehyde (**4**) and H_2S (see Scheme 1): four stereoisomeric 2,4,6,8-tetraethyl- and tetrapropyl-substituted bicyclanes **7** and **8** were synthesized, whose isolation was performed by column chromatography on AG-5 activated charcoal (see Table 1).

According to the X-ray diffraction data, the molecule of 2,4,6,8-tetrapropyl-3,7-dithia-1,5-diazabicyclo[3.3.0]-octane (**8a**), likewise the molecule of **2a**, is in the *endo*-*endo*-conformation with the *TTT*-configuration of the propyl groups (see Fig. 2).

Conformation and geometry of the bicyclic fragments in compounds **2a** and **8a** are similar to those in the unsubstituted 3,7-dithia-1,5-diazabicyclo[3.3.0]octane.[6] The distances of chemically equivalent C—S bonds are found to significantly differ: by 0.068 Å (the bonds S(1)—C(1) (1.800(1) Å) and S(1)—C(2) (1.868(1) Å)) and by 0.050 Å (the bonds S(2)—C(3) (1.802(2) Å) and S(2)—C(4) (1.851(2) Å)) in the molecule of **2a**; by 0.015 Å (the bonds C(1)—S(1) (1.836(7) Å) and C(2)—S(1) (1.821(6) Å)) and by 0.056 Å (the bonds C(4)—S(2) (1.799(6) Å) and C(3)—S(2) (1.855(6) Å)) in the molecule of **8a**. These values are close in the unsubstituted dithiadiazabicyclooctane, where the difference is[6] 0.0462 Å. The C—N bond distances considerably differ too: N(1)—C(2) (1.448(2) Å), N(1)—C(3) (1.514(2) Å) and N(2)—C(4) (1.451(1) Å), N(2)—C(1) (1.515(2) Å) in the molecule of **2a**, N(1)—C(1) (1.459(7) Å), N(1)—C(4) (1.507(7) Å) and N(2)—C(3) (1.471(7) Å), N(2)—C(2) (1.499(8) Å) in the molecule of **8a**. Therefore, the difference in the lengths of chemically equivalent C—N bonds is 0.066 and 0.064 Å in the molecule of **2a**, 0.048 and 0.028 Å in the molecule of **8a**. In the unsubstituted dithiadiazabicyclooctane, this difference is 0.0458 Å. The observed differences in the equivalent C—S and C—N bonds is accounted for by different stereoelectron interactions of the lone pair of electrons on the nitrogen atom lp-N—C—S.[7]

The crystal packing in the structures of interest is mainly determined by the van der Waals interactions between alkyl substituents, the shortest contacts are S...H 3.11 Å, N...H 2.58 Å (see Fig. 3).

The spectra of four individual isomers of tetraethyl- (**7a**—**d**) and tetrapropylbicyclanes (**8a**—**d**) resemble the spectra of configurational isomers of tetramethyl-substituted bicyclanes **2a**—**d**. A total yield of stereoisomeric tetraalkyl-substituted bicyclanes **7**—**10** increases from 80% to quantitative with the increase in the alkyl chain size in the starting aldehydes.

Note that in the case of valeraldehyde (**5**) and caproaldehyde (**6**), only three isomers **9b**—**d** and **10b**—**d**, respectively, are formed. These isomeric bicyclanes were also isolated in the individual state by column chromatography (see Table 1), in which case all three stereoisomeric fractions of tetrabutyl- and tetrapentyl-substituted bicyclanes are oily liquids. It is obvious that the bulky substituents (Bu^n, n-C_5H_{11}) hinder formation of the crystalline (*TTT*) 2,4,6,8-tetrabutyl- and 2,4,6,8-tetrapentyl-3,7-dithia-1,5-diazabicyclo[3.3.0]octanes **9a** and **10a** because of the transannular[10] strain.

The reactions of hydrazine and H_2S with aromatic benzaldehyde **11** and pyridine-3-carbaldehyde **13** were found to stereoselectively form the corresponding 2,4,6,8-tetraaryl-substituted 3,7-dithia-1,5-diazabicyclo[3.3.0]octanes **14** and **16**. Additional spectroscopic studies showed that in the temperature range –10—60 °C, positions of the signals for the methine protons of the thiadiazolidine ring in the molecules of **14** (δ_H 4.79) and **16** (δ_H 4.55) remain unchanged. Apparently, the configuration of the aryl substituents in compounds **14** and **16** is *CCC*, since in the ^{1}H and ^{13}C NMR spectra, like in the corresponding spectra of compound **2b**, the thiadiazolidine carbon and hydrogen atoms give one set of signals each. At the same time, the reaction with anisaldehyde **12** proceeds with the formation of three stereoisomeric bicyclooctanes **15a**—**c** (the ^{1}H, ^{13}C, HSQC and HPLC NMR spectroscopic data). The ratio of the signals for the endocyclic protons of the CH groups at δ_H 5.69, 5.99, and 5.31, corresponding to

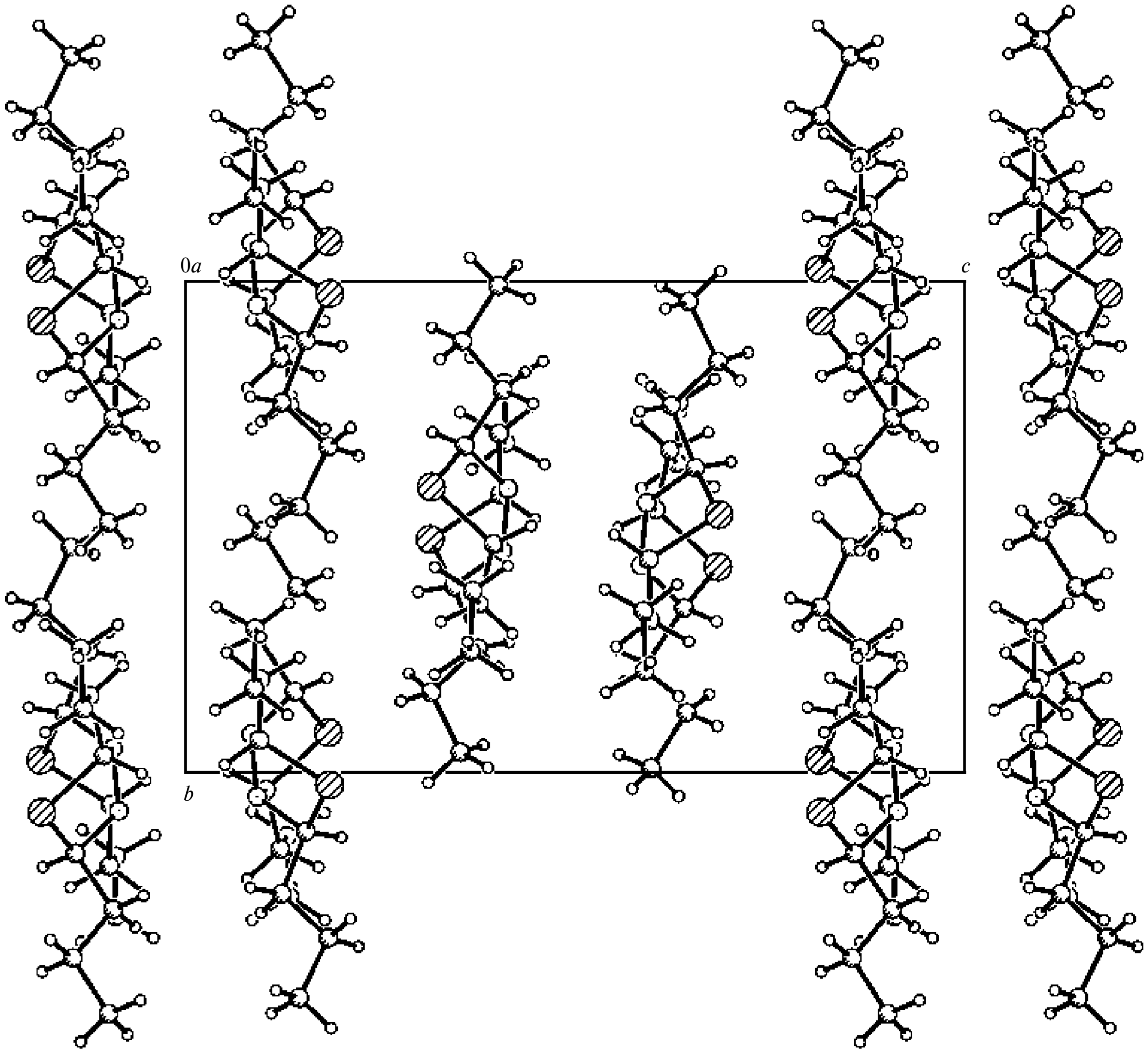


Fig. 3. Packing of molecules in crystal of **8a**.

isomers **15a**, **15b**, and **15c**, is ~1 : 2 : 1. The heteronuclear correlation HSQC-experiments revealed the following correlations (δ): $\delta_H(5.69) \leftrightarrow \delta_C(55.56)$, $\delta_H(5.99) \leftrightarrow \delta_C(51.00)$, and $\delta_H(5.31) \leftrightarrow \delta_C(58.41)$.

Note that because a decrease in the reactivity of the aromatic aldehydes (the conversion of 40%) as compared to the aliphatic counterparts (the conversion of up to 100%), a total yield of 2,4,6,8-tetraaryl-substituted 3,7-dithia-1,5-diazabicyclo[3.3.0]octanes **14—16** did not exceed 30%.

In conclusion, a series of stereoisomeric 2,4,6,8-tetraalkyl(aryl)-3,7-dithia-1,5-diazabicyclo[3.3.0]octanes **2**, **7—10** and **14—16** was synthesized for the first time; conditions for the separation of 2,4,6,8-tetraalkyl-substituted stereoisomers **2** and **7—10** by column chromatography were developed.

Experimental

Products were analyzed by GLC on a Chrom-5 chromatograph with a flame-ionizing detector and a 2400×3 mm packed steel column, an SE-30 (5%) stationary phase on a Chromaton N-AW-HMDS support, 50—270 °C at 8 °C min^{-1} temperature programming, helium carrier gas. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer (^{13}C, 100.62; ^{1}H, 400.13 MHz) in $CDCl_3$. Homo- (H—H COSY) and heteronuclear (H—C: HSQC, HMBC) experiments were performed using standard Bruker programs. IR spectra were recorded on a Specord 75 IR spectrophotometer (KBr pellets). GLC-MS spectral analysis of compounds **2b—d** was performed on a Finigan model 4021 instrument (a 50000×0.25 mm glass capillary column, HP-5 stationary phase, helium carrier gas, 50 to 300 °C at 5 °C min^{-1} temperature programming, 280 °C injector temperature, 250 °C temperature of the source of ions, 70 eV), whereas analysis of compound **2a** was carried out on a Shimadzu LCMS-2010EV instrument. Elemental analysis of the samples was performed on a Karlo Erba elemental analyzer (model No. 1106). Isomeric mixtures of **15a—c** were analyzed by HPLC on a Shimadzu QP-2010Plus chromatograph, a Supelco PTE-5 capillary column (30 m × 0.25 mm). Column chromatography was conducted on KSKG silica gel impregnated with solution of $AgNO_3$.[9] TLC was performed on Silufol W-254 plates, visualizing in iodine vapors.

X-ray diffraction analysis of compounds 2a and 8a. The measurements were performed on Bruker APEX2 CCD at 100 K (**2a**) and Bruker SMART 1000 CCD at 120 K (**8a**) diffractometers (λ(Mo-Kα) = 0.71073 Å, ω-scan technique). For crystals of **2a**, preliminary data are given in the work.[7] Crystals of **8a** are colorless, $C_{16}H_{32}N_2S_2$ (FW = 316.56), monoclinic, space group $P2_1/c$, at 120 K a = 9.905(4), b = 10.748(4), c = 17.344(6) Å, β = 99.834 (8)°, V = 1819.3 (11) $Å^3$, Z = 4, d_{calc} = 1.156 g cm^3, μ(Mo-Kα) = 0.287 cm^{-1}, F(000) = 696. Experimental set of 15462 reflections (2θ < 52°) was obtained from a very small single crystal 0.10×0.10×0.05 mm in size; 3577 independent reflections (R_{int} = 0,1439) were used for the structure solution and refinement. The structure was solved by direct method, non-hydrogen atoms were refined in anisotropic approximation, hydrogen atoms were placed in the geometrically calculated positions and made allowance for in isotropic approximation in the strictly fixed model. The final R-factors are: wR_2 = 0.1385 for all the independent reflections, R_1 = 0.0696 for 1029 observed reflections with $I > 2\sigma(I)$, 185 refined parameters, GOF = 0.889, the residual electron density 0.428 and –0.373 e $Å^{-3}$.

All the calculations were performed using the SHELXTL-Plus 5.0 program.[11]

Cyclothiomethylation of $N_2H_4 \cdot H_2O$ with aldehydes RCHO (R = Me, Et, Pr^n, Bu^n, n-C_5H_{11}, Ph, 4-$MeOC_6H_4$, 3-Py) (general procedure). An aldehyde (0.2 mol) was saturated with hydrogen sulfide (0.2 mol) at temperature ≤ –10 °C over 15—20 min, then hydrazine hydrate (0.05 mol) was added dropwise. The reaction mixture was stirred for 3 h at a given temperature, then extracted with chloroform (3×50 mL), the extract was concentrated on a rotary evaporator. The obtained products **2** and **7—10** were purified by column chromatography.

2,4,6,8-Tetramethyl-3,7-dithia-1,5-diazabicyclo[3.3.0]-octane (2a), the yield was 31%. The spectral characteristics are identical to those reported in the work,[7] I_k = 1500.

Compound 2b. Light yellow oil, the yield was 18%, R_f 0.59, SiO_2—$AgNO_3$, n-C_6H_{14}—EtOAc—$CHCl_3$ (5 : 1 : 1). IR, ν/cm^{-1}: 670, 740, 880, 1120, 1450, 2972. ^1H NMR (20 °C), δ: 1.45 (d, 12 H, Me, J = 4 Hz)); 4.52 (q, 4 H, CH, J = 4 Hz). ^{13}C NMR, δ: 29.80, 61.90. I_k = 1550. MS, m/z (I_{rel} (%)): 204 $[M]^+$ (90), 119 $[N_2H_3CHMeSCMe]^+$ (98), 74 $[NCHMeS]^+$ (8), 57 $[N_2CHMe]^+$ (97). Found (%): C, 46.93; H, 7.52; N, 13.63; S, 31.18. $C_8H_{16}N_2S_2$. Calculated (%): C, 47.02; H, 7.89; N, 13.71; S, 31.38.

Compound 2c. Light yellow oil, the yield was 7%. R_f 0.61, SiO_2—$AgNO_3$, n-C_6H_{14}—EtOAc—$CHCl_3$ (5 : 1 : 1). ^1H NMR (20 °C), δ: 1.41 (m, 3 H, Me); 1.48 (s, 3 H, Me); 1.41 (s, 3 H, Me); 1.66 (s, 3 H, Me); 4.38 (br.s, 1 H, CH); 4.39 (br.s, 2 H, CH); 5.34 (br.s, 1 H, CH). ^{13}C NMR, δ: 17.6, 23.4, 25.86, 28.1, 61.80, 67.30, 69.30. I_k = 1530. MS, m/z (I_{rel} (%)): 204 $[M]^+$ (90), 119 $[N_2H_3CH(Me)SC(Me)]^+$ (98), 74 $[NCH(Me)S]^+$ (8), 57 $[N_2CH(Me)]^+$ (97).

Compound 2d. Light yellow oil, the yield was 7%, R_f 0.63, SiO_2—$AgNO_3$, n-C_6H_{14}—EtOAc—$CHCl_3$ (5 : 1 : 1). ^1H NMR (20 °C), δ: 1.50 (d, 12 H, Me); 4.35 (s, 4 H, CH). ^{13}C NMR, δ: 25.10, 66.00. MS, m/z (I_{rel} (%)): 204 $[M]^+$ (90), 119 $[N_2H_3CH(Me)SCMe]^+$ (98), 74 $[NCH(Me)S]^+$ (8), 57 $[N_2CH(Me)]^+$ (97).

2,4,6,8-Tetraethyl-3,7-dithia-1,5-diazabicyclo[3.3.0]octane (7a). Colorless crystals, the yield was 42%, m.p. 58—59 °C, R_f 0.58, C_{act} (AG-5), CH_2Cl_2—$CHCl_3$ (2 : 1). IR, ν/cm^{-1}: 690, 750, 885, 1120, 1380, 2940. ^1H NMR ($CDCl_3$), δ: 0.95 (m, 12 H, Me); 1.56 (d, 8 H, CH_2, J = 6.58 Hz); 4.79 (br.s, 4 H, CH, $W_{1/2}$ = 18 Hz). ^{13}C NMR, δ: 11.39, 11.75, 25.54, 31.44, 69.71, 72.4. Found (%): C, 55.27; H, 9.18; N, 10.63; S, 24.54. $C_{12}H_{24}N_2S_2$. Calculated (%): C, 55.34; H, 9.29; N, 10.76; S, 24.68.

Compound 7b. Light yellow oil, the yield was 8%, R_f 0.67, C_{act} (AG-5), CH_2Cl_2—$CHCl_3$ (2 : 1). ^1H NMR ($CDCl_3$), δ: 0.94 (t, 12 H, Me, J = 7.2 Hz); 1.72—1.67 (m, 8 H, CH_2); 4.57 (q, 4 H, CH, J = 5.8 Hz). ^{13}C NMR, δ: 13.99, 28.52, 72.80.

Compound 7c. Light yellow oil, the yield was 21%, R_f 0.63, C_{act} (AG-5), CH_2Cl_2—$CHCl_3$ (2 : 1). ^1H NMR ($CDCl_3$), δ: 0.79 (m, 12 H, Me); 1.52 (m, 8 H, CH_2); 4.00 (s, 1 H, CH); 4.78 (s, 1 H, CH); 4.90 (s, 2 H, CH). ^{13}C NMR, δ: 15.03, 15.46, 16.60, 29.26, 33.82, 35.13, 70.84, 73.29, 76.02.

Compound 7d. Light yellow oil, the yield was 8%, R_f 0.53, C_{act} (AG-5), CH_2Cl_2—$CHCl_3$ (2 : 1). ^1H NMR (20 °C), δ: 1.04 (t, 12 H, Me, J = 7.2 Hz); 1.72—1.67 (m, 8 H, CH_2); 4.50 (q, 4 H, CH, J = 5.8 Hz). ^{13}C NMR, δ: 12.99, 27.50, 72.80.

2,4,6,8-Tetrapropyl-3,7-dithia-1,5-diazabicyclo[3.3.0]-octane (8a). Colorless crystals, the yield was 48%, m.p. 61—62 °C, R_f 0.53, C_{act} (AG-5), CH_2Cl_2—$CHCl_3$ (2 : 1). IR, ν/cm^{-1}: 650, 780, 870, 1150, 1460, 2840. ^1H NMR (20 °C), δ: 0.83 (m, 12 H, Me); 1.41 (m, 8 H, CH_2); 2.25 (s, 8 H, CH_2); 4.17 (dd, 2 H, CH, J = 4.8 Hz, J = 8.4 Hz); 4.74 (q, 2 H, CH, J = 4.8 Hz). ^{13}C NMR, δ: 13.93, 21.38, 21.94, 41.54, 42.91, 69.49, 72.77. Found (%): C, 60.27; H, 10.15; N, 8.53; S, 20.24. $C_{16}H_{32}N_2S_2$. Calculated (%): C, 60.70; H, 10.19; N, 8.85; S, 20.26.

Compound 8b. Light green oil, the yield was 17%, R_f 0.62, C_{act} (AG-5), CH_2Cl_2—$CHCl_3$ (2 : 1). ^1H NMR (20 °C, $CDCl_3$), δ: 0.96 (m, 12 H, Me); 2.36—2.44 (m, 16 H, CH_2); 4.83 (d, 4 H, CH, J = 4 Hz). ^{13}C NMR, δ: 13.80, 20.83, 41.18, 68.31.

Compound 8c. Light green oil, the yield was 11%, R_f 0.69, C_{act} (AG-5), CH_2Cl_2—$CHCl_3$ (2 : 1). ^1H NMR (20 °C, $CDCl_3$), δ: 0.96 (m, 12 H, Me); 2.36—2.44 (m, 16 H, CH_2); 4.83 (dd, 4 H, CH, J_1 = 5.2 Hz, J_2 = 5.6 Hz). ^{13}C NMR, δ: 13.80, 20.83, 41.18, 72.53, 72.99, 73.89.

Compound 8d. Light green oil, the yield was 11%, R_f 0.57, C_{act} (AG-5), CH_2Cl_2—$CHCl_3$ (2 : 1). ^1H NMR (20 °C, $CDCl_3$), δ: 0.84 (m, 12 H, Me); 2.48—3.20 (m, 16 H, CH_2); 4.53 (d, 4 H, CH, J = 4.6 Hz). ^{13}C NMR, δ: 13.80, 23.80, 42.01, 71.20.

2,4,6,8-Tetrabutyl-3,7-dithia-1,5-diazabicyclo[3.3.0]octane (9b). Red oil, the yield was 52%, R_f 0.56, SiO_2—$AgNO_3$, light petroleum—CH_2Cl_2 (5 : 3). ^1H NMR (20 °C), δ: 0.81 (m, 6 H, Me); 0.82 (s, 6 H, Me); 1.31 (br.s, 24 H, CH_2, $W_{1/2}$ = 90 Hz); 4.42 (s, 2 H, CH); 4.80 (s, 2 H, CH). ^{13}C NMR, δ: 13.67, 13.76, 22.16, 22.26, 26.82, 28.02, 34.47, 35.45, 72.86, 73.74. Found (%): C, 64.27; H, 10.28; N, 7.50; S, 17.19. $C_{20}H_{40}N_2S_2$. Calculated (%): C, 64.46; H, 10.82; N, 7.52; S, 17.24. IR, ν/cm^{-1}: 670, 740, 880, 1120, 1450, 2972.

Compound 9c. Red oil, the yield was 20%, R_f 0.66, SiO_2—$AgNO_3$, light petroleum—CH_2Cl_2 (5 : 3). ^1H NMR (20 °C), δ: 0.74 (m, 3 H, Me); 0.88 (q, 3 H, Me, J = 5.61 Hz); 0.94 (m, 6 H, Me); 1.22 (m, 2 H, CH_2); 1.51 (m, 2 H, CH_2); 1.88 (m, 4 H,

CH_2); 2.25 (br.s, 16 H, CH_2); 4.67 (s, 1 H, CH); 4.76 (t, 1 H, CH, J = 5.13 Hz); 4.87 (s, 2 H, CH). ^{13}C NMR, δ: 13.69, 13.70, 13.73, 22.17, 22.19, 22.26, 25.45, 25.54, 25.71, 33.36, 33.67, 33.95, 68.17, 71.11, 72.37.

Compound 9d. Dark orange oil, the yield was 22%, R_f 0.78, $SiO_2—AgNO_3$, light petroleum—CH_2Cl_2 (5 : 3). ^{1}H NMR (20 °C), δ: 0.84 (m, 12 H, Me); 1.29 (m, 24 H, CH_2); 4.23 (br.s, 4 H, CH). ^{13}C NMR, δ: 13.67, 22.36, 26.66, 27.08, 27.63, 31.12, 31.41, 31.40, 37.76, 38.50, 38.80, 71.10.

2,4,6,8-Tetrapentyl-3,7-dithia-1,5-diazabicyclo[3.3.0]octane (10b). Dark orange oil, the yield was 54%, R_f 0.57, $SiO_2—AgNO_3$, n-C_6H_{14}—EtOAc—$CHCl_3$ (5 : 1 : 1). ^{1}H NMR (20 °C), δ: 0.84 (m, 12 H, Me); 1.10—1.50 (m, 16 H, CH_2); 1.50—2.00 (m, 16 H, CH_2); 4.24 (br.s, 4 H, CH). ^{13}C NMR, δ: 13.80, 22.43, 27.22, 31.51, 38.91, 71.21. Found (%): C, 67.16; H, 11.22; N, 6.52; S, 14.24. $C_{24}H_{48}N_2S_2$. Calculated (%): C, 67.23; H, 11.28; N, 6.53; S, 14.96.

Compound 10c. Dark orange oil, the yield was 34%, R_f 0.68, $SiO_2—AgNO_3$, n-C_6H_{14}—EtOAc—$CHCl_3$ (5 : 1 : 1). ^{1}H NMR (20 °C), δ: 0.84 (br.s, 12 H, Me); 1.29 (m, 32 H, CH_2); 4.23 (m, 3 H, CH); 5.15 (s, 1 H, CH). ^{13}C NMR, δ: 13.67, 22.36, 26.66, 27.08, 27.63, 31.12, 31.41, 31.40, 37.76, 38.50, 38.80, 68.17, 71.10, 72.37.

Compound 10d. Dark orange oil, the yield was 12%, R_f 0.75, $SiO_2—AgNO_3$, n-C_6H_{14}—EtOAc—$CHCl_3$ (5 : 1 : 1). ^{1}H NMR (20 °C), δ: 0.84 (m, 12 H, Me); 1.10—1.50 (m, 16 H, CH_2); 1.50—2.00 (m, 16 H, CH_2); 4.24 (br.s, 4 H, CH). ^{13}C NMR, δ: 13.80, 22.43, 27.22, 31.51, 38.91, 71.21.

2,4,6,8-Tetraphenyl-3,7-dithia-1,5-diazabicyclo[3.3.0]octane (14). Orange crystals, the yield was 19%, m.p. 88—89 °C. IR, ν/cm^{-1}: 690, 750, 1620, 2900. ^{1}H NMR (20 °C), δ: 4.79 (br.s, 4 H, CH, $W_{1/2}$ = 17.9 Hz); 7.41 (m, 4 H, CH_{Ar}); 7.51 (d, 4 H, CH_{Ar}, J = 2.29 Hz); 7.90 (s, 12 H, CH_{Ar}). ^{13}C NMR, δ: 53.39, 128.09, 128.41, 128.74, 131.18, 140.00. Found (%): C, 74.14; H, 5.21; N, 6.05; S, 14.10. $C_{28}H_{24}N_2S_2$. Calculated (%): C, 74.30; H, 5.34; N, 6.19; S, 14.17.

2,4,6,8-Tetrakis(4-methoxyphenyl)-3,7-dithia-1,5-diazabicyclo[3.3.0]octanes (15a—c). Orange crystals, the yield was 22%, the ratio **15a** : **15b** : **15c** = 1 : 2 : 1. ^{1}H NMR (20 °C), δ: 3.85 (s, 12 H, OMe) for **15a**; 3.83 (s, 12 H, OMe) for **15b**; and 3.76 (s, 12 H, OMe) for **15c**; 5.69 (br.s, 4 H, CH) for **15a**; 5.99 (br.s, 4 H, CH) for **15b**; and 5.31 (br.s, 4 H, CH) for **15c**; 6.85 (d, 8 H, CH_{Ar}, J = 7.2 Hz) for **15a**; 6.95 (d, 8 H, CH, J = 8.8 Hz) for **15b**; and 6.99 (d, 8 H, CH_{Ar}, J = 7.81 Hz) for **15c**; 7.27—7.83 (m, 8 H, CH_{Ar}). ^{13}C NMR, δ: 52.73, 55.56 for **15a**; 51.00 for **15b**; and 58.41 for **15c**; 114.30 for **15a**; 114.25 for **15b**; and 116.25 for **15c**; 129.19 for **15a** and **15c**; 129.50 for **15b**; 130.46 for **15a**; 130.30 for **15b**; and 130.20 for **15c**; 131.99 for **15a**; 132.30 for **15b**; and 132.00 for **15c**; 162.14 for **15a**; 161.12 for **15b**; and 159.86 for **15c**.

2,4,6,8-Tetra(pyridin-3-yl)-3,7-dithia-1,5-diazabicyclo-[3.3.0]octane (16). Orange crystals, the yield was 24%, m.p. 79—80 °C. ^{1}H NMR (20 °C), δ: 4.55 (br.s, 4 H, CH, $W_{1/2}$ = = 17.9 Hz); 7.12 (br.s, 4 H, CH); 7.30 (d, 4 H, CH, J = 7.6 Hz); 8.42 (br.s, 4 H, CH); 8.58 (s, 4 H, CH). ^{13}C NMR, δ: 51.17, 123.78, 129.65, 134.88, 150.30, 151.91. Found (%): C, 63.06; H, 4. 12; N, 18.30; S, 14.01. $C_{24}H_{20}N_6S_2$. Calculated (%): C, 63.13; H, 4.42; N, 18.41; S, 14.05.

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