A study of tautomerism in *N*,*N*-dialkyl-4(5)-bromoalkanecarboxamides*

*A. V. Lozanova, A. V. Stepanov, and V. V. Veselovsky**

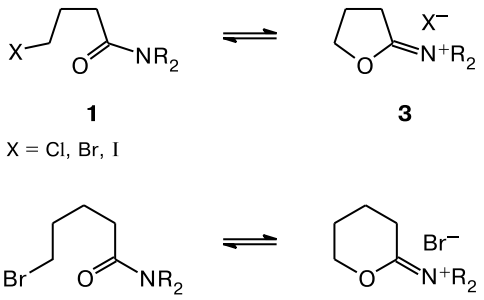
N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 119991 Moscow, Russian Federation.
Fax: +7 (499) 135 5328. E-mail: ves@ioc.ac.ru

N,*N*-Dialkyl-4-bromobutanamides exist in solution in tautomeric equilibrium with *N*,*N*-dialkyl-*N*-(tetrahydrofuran-2-ylidene)ammonium bromides, while related 4,5-dibromopentanamides show no similar interconversions with the corresponding iminium salts. A similar difference is observed when comparing the chemical behavior of their homologs, *viz.*, *N*,*N*-dialkyl-5-bromopentanamide and *N*,*N*-dialkyl-5,6-dibromohexanamide

Key words: *N*,*N*-dialkyl-4(5)-bromoalkanecarboxamides, *N*,*N*-dialkyl-*N*-(tetrahydrofuran-2-ylidene)ammonium bromides, *N*,*N*-dialkyl-*N*-(tetrahydropyran-2-ylidene)ammonium bromides, ring—chain tautomerism.

Earlier,[1] we have reported on ring—chain tautomerism of a novel type detected by ^{1}H NMR spectroscopy in solutions of *N*,*N*-dialkyl-4-halo- (**1**) and *N*,*N*-dialkyl-5-haloalkanecarboxamides (**2**) undergoing reversible interconversions into *N*,*N*-dialkyl-*N*-(tetrahydrofuran-2-ylidene)- (**3**) and *N*,*N*-dialkyl-*N*-(tetrahydropyran-2-ylidene)ammonium halides (**4**), respectively (Scheme 1). These systems show predictable thermal effects and are sensitive to the solvent polarity. The ratios of the tautomers in equilibrium mixtures (X = Br) under different conditions are given under Scheme 1.

Scheme 1



1 X = Cl, Br, I

3

2

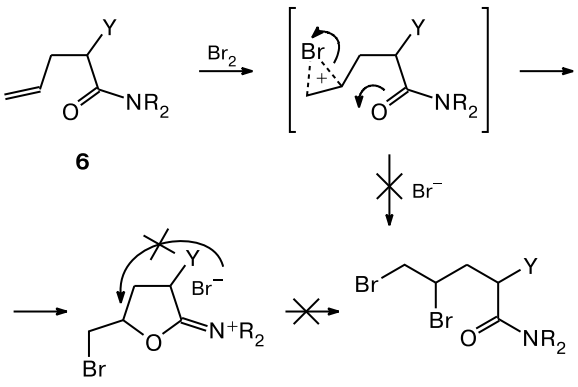
4

Solvent	*T*/K	**1** : **3**
$CDCl_3$	303	~2 : 3
$CDCl_3$	333	~9 : 1
DMSO-d_6	303	0 : 1

Solvent	*T*/K	**2** : **4**
$CDCl_3$	298	~97 : 3
DMSO-d_6	298	~1 : 1
DMSO-d_6	340	~6 : 5

Later,[2] we have found that *N*,*N*-dialkyl-*N*-(tetrahydrofuran-2-ylidene)ammonium bromides **5**, which are related to salts **3**, can be obtained by bromination of *N*,*N*-dialkylpent-4-enamides and their derivatives (**6**) (Scheme 2). Acyclic bromination products of the type **7**, whose formation is possible under these conditions, were not detected. Moreover, a ^{1}H NMR study of the behavior of iminium salts **5** in solutions revealed no signs of their possible transformations into the corresponding acyclic isomers **7**. Apparently, the observed pattern is due to (1) a substantial rate difference between an intramolecular interaction of the bromonium ion with the carbonyl group and an attack of the bromide anion and (2) the higher (than for unsubstituted salts **3**) energy of activation of the nucleophilic ring opening in compounds **5** at the secondary carbon atom.

Scheme 2



6

5

7

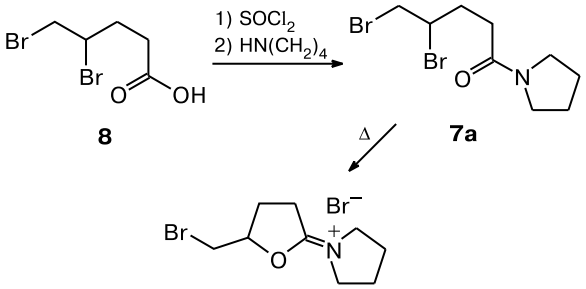
Y = H, SPh, SOPh, SO_2Ph

* Dedicated to Academician of the Russian Academy of Sciences I. L. Eremenko on the occasion of his 60th birthday.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 6, pp. 1211—1215, June, 2010.

We found it interesting to attempt an independent synthesis of dibromo amide of the type **7** and study its tendency toward cyclization into the corresponding iminium salt. It turned out that (±)-*N*-(4,5-dibromopentanoyl)pyrrolidine (**7a**) can be obtained in a conventional way from known 4,5-dibromopentanoic acid **8** and is a sufficiently stable crystalline solid (Scheme 3). However, melting of dibromide **7a** (~50 °C) resulted in its complete transformation into iminium salt **5a**: the ^{1}H NMR spectrum of the melt is identical with that reported[2b] for compound **5a**. The ~30% conversion of dibromide **7a** into salt **5a** was achieved when its solution in $CDCl_3$ was heated at 50 °C for 2 h.

Scheme 3

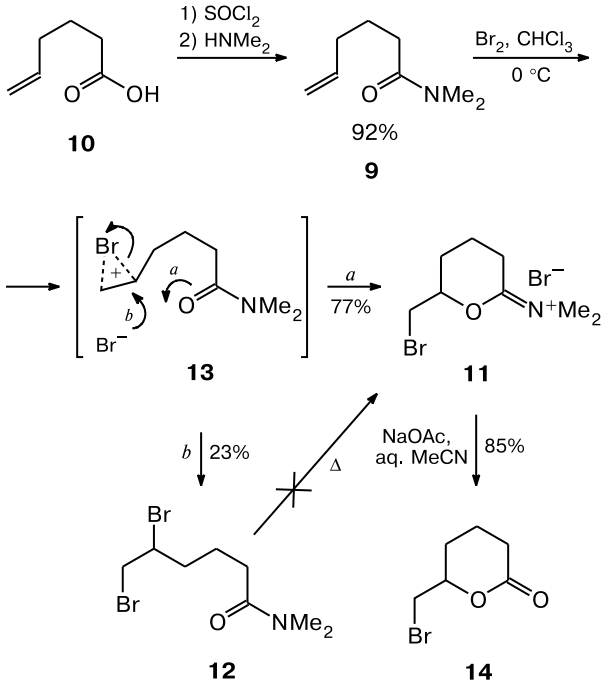


In contrast to the aforesaid reaction of unsaturated dialkylamides **6** with bromine, bromination of their homolog **9** (prepared from unsaturated acid **10**) gives a ~3 : 1 mixture of cyclic iminium salt **11** and vicinal dibromide **12** (Scheme 4). This reaction outcome probably results from an intramolecular attack (*a*) of the amide O atom on bromonium cation **13** and a competitive reaction (*b*) involving the bromide ion. The structure of iminium salt **11** was confirmed by its hydrolysis to known lactone **14**, as well as by elemental analysis and spectroscopic studies. Like its homologs **5** and in contrast to (tetrahydropyran-2-ylidene)ammonium salts **4**, salt **11** in solutions undergoes no transformation into the corresponding acyclic tautomer **12** (^{1}H NMR data). We also found that even prolonged heating of a solution of dibromide **12** (MeCN, 81—82 °C, 6 h) does not produce, in contrast to dibromo amide **7a**, appreciable amounts of the corresponding iminium bromide **11** (^{1}H NMR data).

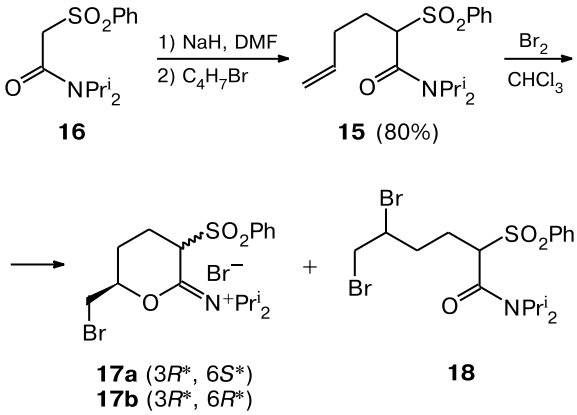
Similar results were obtained in bromination of unsaturated phenylsulfonyl derivative **15** prepared by alkylation of known sulfonyl amide **16** with 4-bromobutene (Scheme 5). Workup of the reaction mixture gave isomeric iminium salts **17a** and **17b** in a total yield of 60% (**17a**/**17b** = ~1.7 : 1) and a ~1 : 1* mixture of diastereomeric dibromides **18**.

* The plausible ratio of diastereomers **18** in the mixture, which cannot be separated by chromatography. In the ^{1}H NMR spectrum of the mixture, the signals for the identical protons of the isomers overlap completely.

Scheme 4

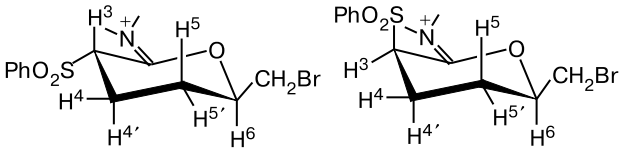


Scheme 5



Compounds **17** were isolated in the individual state using selective extraction and crystallization. The structures of these products and a mixture of diastereomers **18** were confirmed by physicochemical and elemental analyses. In particular, the relative configurations of the substituents in stereoisomers **17** were determined by comparing the experimental coupling constants of the protons in the ^{1}H NMR spectrum with the calculated ones. The calculations were performed with the MestrJ program (www.mestrec.com); the thermodynamically preferable conformations of stereoisomers **17** were found using the Gaussian program.[3] Characteristic were the coupling constants of the HC(3) and HC(6) protons, for which the experimental and calculated *J* values are in satisfactory

agreement (Table 1). Based on the data obtained, we assigned the 3*R**,6*S**- and 3*R**,6*R**-configurations to isomers **17a** and **17b**, respectively. Interestingly, in contrast to iminium salt **11** containing no phenylsulfonyl substituent, compounds **17** in solution undergo irreversible ring opening leading to the corresponding linear dibromides **18**. In this respect, major isomer **17a** is much more stable (half-conversion time ~20 days, $CDCl_3$, 20 °C, ^{1}H NMR), while minor isomer **17b** is transformed into compound **18** virtually completely within ~12 h ($CDCl_3$, 20 °C, ^{1}H NMR). This difference in chemical behavior between isomers **17** provides indirect evidence for their structural features, namely, the *pseudo*-equatorial arrangement of both substituents (at the C(3) and C(6) atoms) in the thermodynamically preferable conformation of the more stable isomer **17a**. In the less stable isomer **17b**, one substituent (SO_2Ph) is in the pseudoaxial position.



17a **17b**

Thus, our study revealed a dramatic influence of the position of the halogen atom in *N*,*N*-dialkylbromoalkanamides on their tendency toward ring—chain tautomerism.

Experimental

Melting points were measured on a Kofler hot stage. IR spectra were recorded on a Specord M-80 instrument. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-200, Bruker AM-300, and Bruker Avance 600 spectrometers at 298 K with reference to the solvent signals (δ 7.27 and 77.0 ($CDCl_3$) and δ 1.94 and 1.24 (CD_3CN), respectively). Mass spectra (EI, 70 eV) were measured on a Finnigan MAT ITD-700 instrument; an ESI mass spectrum was recorded on a Finnigan MAT LCQ spectrometer (capillary potential 4530 V). A solution of a sample in methanol was infused through a syringe into the ionization chamber at a rate of 10 μL min^{-1}; mass spectra (MS) (scan range from *m*/*z* 100 to *m*/*z* 2000) and tandem mass spectra (MS/MS) were recorded in the positive ion mode (helium was used as a gas for collisional activation). The interface capillary temperature was 213 °C, the main nitrogen flow was 19.4 conventional units, and the auxiliary nitrogen flow was 0.4 conventional units. The observation time of activation in MS/MS spectra was 30 ms. The activation energy was taken to be 40% of the relative maximum collision energy. Column chromatography was carried out on Silica gel 60 (0.04—0.06 mm, Fluka); R_f values were measured on Silufol plates. Solvents, including light petroleum (b.p. 40—70 °C), were purified and dried according to standard procedures. Pyrrolidine, *N*,*N*-diisopropylamine, hex-5-enoic acid, and thionyl chloride were the Acros Organics chemicals. (±)-4,5-Dibromopentanoic acid (**8**),[4] *N*,*N*-diisopropyl-2-phenylsulfonylacetamide (**16**),[2b] and 4-bromobutene[5] were prepared according to known procedures.

Table 1. Experimental and calculated coupling constants of selected protons in stereoisomers **17**

Compound	Assignment	δ	J_{exp}	J_{calc}
			Hz	
17a	HC(3)	5.33	2.4, 9.6	2.2, 7.8
	HC(6)	5.10	3.0, 11.3	2.2, 10.3
17b	HC(3)	5.8	5.0, 7.0	3.8, 5.2
	HC(6)	5.00	2.5, 12.0	2.7, 11.6

(±)-*N*-(4,5-Dibromopentanoyl)pyrrolidine (7a). A stirred mixture of acid **8** (2.07 g, 8 mmol), $SOCl_2$ (9.1 g, 76.5 mmol), and DMF (0.3 mL) was heated at 50 °C (Ar) for 3 h and concentrated *in vacuo* to give 4,5-dibromopentanoyl chloride with the following ^{1}H NMR spectrum (200.13 MHz), δ: 2.08 (dddd, 1 H, HC(3), J = 5.6 Hz, J = 8.1 Hz, J = 10.0 Hz, J = 15.2 Hz); 2.66 (dddd, 1 H, H´C(3), J = 2.9 Hz, J = 6.9 Hz, J = 9.9 Hz, J = 15.2 Hz); 3.19 (m, 2 H, HC(2)); 3.61 (dd, 1 H, HC(5), J = 10.0 Hz, J = 10.1 Hz); 3.89 (dd, 1 H, H´C(5), J = 4.1 Hz, J = 10.1 Hz); 4.20 (dddd, 1 H, HC(4), J = 2.9 Hz, J = 4.1 Hz, J = 10.0 Hz, J = 10.0 Hz). This crude acid chloride was dissolved in CH_2Cl_2 (15 mL); a solution of pyrrolidine (1.14 g, 16 mmol) in CH_2Cl_2 (7 mL) was added with stirring at −10 °C (Ar) for 10 min. The reaction mixture was stirred at −10 °C for 1 h and concentrated *in vacuo*. The product was extracted with MeOBu^t and the extract was concentrated *in vacuo*. The resulting crude amide **7a** (1.9 g, 76%) was subjected to low-temperature (−20 °C) crystallization from light petroleum to give amide **7a** as colorless crystals, m.p. 45—49 °C*. Found (%): C, 34.38; H, 4.82; Br, 51.16; N, 4.41. $C_9H_{15}Br_2NO$. Calculated (%): C, 34.53; H, 4.83; Br, 51.05; N, 4.47. IR (KBr, ν/cm^{-1}): 644, 784, 872, 916, 988, 1036, 1164, 1192, 1224, 1256, 1340, 1364, 1444, 1632, 2868—3028. ^{1}H NMR (200.13 MHz), δ: 1.80—2.14 (m, 5 H, HC(3), 2 CH_2); 2.42—2.74 (m, 3 H, H´C(3), 2 HC(2)); 3.47 (m, 4 H, HCN); 3.65 (dd, 1 H, HC(5), J = 9.0 Hz, J = = 10.4 Hz); 3.86 (dd, 1 H, H´C(5), J = 4.5 Hz, J = 10.4 Hz); 4.33 (dddd, 1 H, HC(4), J = 2.5 Hz, J = 4.5 Hz, J = 9.9 Hz, J = 9.9 Hz).

***N*,*N*-Dimethylhex-5-enamide (9).** Thionyl chloride (11.9 g, 100 mmol) was added with stirring at 60 °C for 40 min to acid **10** (6.84 g, 60 mmol) and DMF (60 mg). The reaction mixture was stirred at 80—100 °C (Ar) for 5 h and concentrated *in vacuo*. The residue was distilled to give the corresponding acid chloride (6.92 g) with b.p. 53—55 °C (30 Torr), which was dissolved in THF (15 mL). The resulting solution was added at −10 °C (Ar) to a stirred solution of dimethylamine (6.75 g, 150.0 mmol) in THF (70 mL). The reaction mixture was stirred at 0 °C for 1 h, kept at 20 °C for an additional 15 h, and treated with water (30 mL). The organic layer was separated, washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was distilled to give amide **9** (6.77 g, 92%) with b.p. 53—55 °C (1.0 Torr). ^{1}H NMR (200.13 MHz), δ: 1.71 (m, 2 H, H_2C(3)); 2.08 (m, 2 H, H_2C(4)); 2.26 (m, 2 H, H_2C(2)); 2.91 and 2.97 (both s, 3 H each, 2 Me); 4.89—5.06 (m, 2 H, H_2C(6));

* The ^{1}H NMR spectrum of the melt is virtually identical with that of iminium salt **5a**.[2b]

5.77 (dddd, 1 H, HC(5), J = 6.9 Hz, J = 6.9 Hz, J = 10.1 Hz, J = 16.8 Hz) (*cf.* Ref. 6).

(±)-*N*-(6-Bromomethyltetrahydropyran-2-ylidene)-*N*,*N*-dimethylammonium bromide (11) and (±)-*N*,*N*-dimethyl-5,6-dibromohexanamide (12). A solution of Br_2 (1.39 g, 8.7 mmol) in $CHCl_3$ (25 mL) was added at 0 °C (Ar) for 1 h to a stirred solution of amide **9** (1.23 g, 8.7 mmol) in $CHCl_3$ (25 mL). The reaction mixture was kept at this temperature for 20 min and concentrated *in vacuo*. The residue was triturated with Et_2O (4×10 mL) until a homogeneous powdery product was formed, while decanting the ethereal solution. The product was crystallized from MeCN—Et_2O to give light yellow salt **11** (2.02 g, 77%), m.p. 85—89 °C (in a sealed capillary). Found (%): C, 31.31; H, 5.05; Br, 52.81; N, 4.70. $C_8H_{15}Br_2NO$. Calculated (%): C, 31.92; H, 5.02; Br, 53.09; N, 4.65. IR ($CHCl_3$, ν/cm^{-1}): 656, 824, 924, 960, 1032, 1080, 1242, 1304, 1336, 1400, 1416, 1424, 1432, 1460, 1656, 2448, 2752, 2936, 3368. MS, m/z (I_{rel} (%); scan range from m/z 60 to m/z 500): 303.9 (20), 302.0 (30), 299.9 (15), 223.1 (10), 222.1 (100), 221.1 (10), 220.1 (90), 140.0 (15). MS/MS (m/z 302; the activation energy was 50% of the relative maximum collision energy): 222.0 (25), 221.0 (5), 220.0 (85), 219.3 (5), 141.0 (10), 140.1 (100), 138.2.9 (5). MS/MS (m/z 221; the activation energy was 30% of the relative maximum collision energy): 222.1 (15), 220.1 (20), 140.1 (100). ^{1}H NMR (200.13 MHz), δ: 1.82—2.21 (m, 4 H, $H_2C(4)$, $H_2C(5)$); 2.94 (m, 2 H, $H_2C(3)$); 3.29 and 3.41 (both s, 3 H each, 2 Me); 3.69 (m, 2 H, H_2CBr); 5.06 (m, 1 H, HC(6)).

The combined ethereal supernatants were concentrated *in vacuo* and the residue was chromatographed on SiO_2 with light petroleum—MeOBu^t (1 : 3) as an eluent. The yield of dibromo amide **12** was 0.60 g (23%), colorless oil, R_f 0.32 (light petroleum—MeOBu^t, 1 : 4). Found (%): C, 31.70; H, 5.10; Br, 52.99; N, 4.95. $C_8H_{15}Br_2NO$. Calculated (%): C, 31.92; H, 5.02; Br, 53.09; N, 4.65. IR (thin film, ν/cm^{-1}): 568, 612, 648, 752, 804, 872, 936, 1056, 1148, 1232, 1264, 1336, 1400, 1480, 1496, 1552, 1644, 1692, 1728, 2936, 3176. MS, m/z (I_{rel} (%)): 300 $[M - 1]^+$ (2), 223 (11), 222 (74), 221 (5), 220 (75), 175 (5), 164 (2), 149 (19), 147 (18), 141 (26), 140 (89), 133 (4), 121 (13), 114 (24), 107 (8), 100 (21), 98 (20), 94 (19), 86 (69), 73 (22), 72 (100), 69 (28), 67 (47), 55 (73). ^{1}H NMR (200.13 MHz), δ: 1.65—2.41 (m, 6 H, 3 H_2C); 2.91 and 2.98 (both s, 3 H each, 2 Me); 3.62 (dd, 1 H, HC(6), J = 9.4 Hz, J = 10.3 Hz); 3.82 (dd, 1 H, H´C(6), J = 4.5 Hz, J = 10.3 Hz); 4.16 (dddd, 1 H, HC(5), J = 3.4 Hz, J = 4.5 Hz, J = 8.2 Hz, J = 9.3 Hz). ^{13}C NMR (50.03 MHz), δ: 22.4, 32.3, 35.7 and 36.3 (4 CH_2); 35.4 and 37.2 (2 Me); 52.6 (HCBr); 172.1 (C=O).

(±)-6-Bromomethyltetrahydropyran-2-one (14). A solution of salt **11** (0.9 g, 3 mmol) and $NaOAc \cdot 3H_2O$ (0.45 g, 3.3 mmol) in a mixture of MeCN (8 mL) and water (0.7 mL) was stirred at 20 °C for 5 h and concentrated *in vacuo*. The product was extracted from the residue with MeOBu^t. The extract was washed with water and brine, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on SiO_2 with light petroleum—MeOBu^t (1 : 3) as an eluent. The yield of lactone **14** was 0.49 g (85%), colorless oil, R_f 0.43 (light petroleum—MeOBu^t, 1 : 4). ^{1}H NMR (200.13 MHz), δ: 1.90 (m, 4 H, 2 H_2C); 2.53 (m, 2 H, H_2C); 3.58 (dd, 1 H, HCBr, J = 4.9 Hz, J = 9.8 Hz); 3.58 (dd, 1 H, H´CBr, J = 3.7 Hz, J = 9.8 Hz); 4.51 (dddd, 1 H, HC(6), J = 3.5 Hz, J = 4.7 Hz, J = 5.8 Hz, J = 10.3 Hz) (*cf.* Ref. 7).

(±)-*N*,*N*-Diisopropyl-2-phenylsulfonylhex-5-enamide (15). A ~55% suspension (142 mg) of NaH (~3.3 mmol) in mineral oil was added in portions at 10 °C (Ar) for 5 min to a stirred solution of *N*,*N*-diisopropyl-2-phenylsulfonylacetamide (**16**) (849 mg, 3.0 mmol) in DMF (4 mL). After 30 min, 4-bromobutene (446 mg, 3.3 mmol) was added. The reaction mixture was warmed to 20 °C, kept at this temperature for 15 h, and decomposed with water (15 mL). The organic material was extracted with Bu^{t}OMe. The organic layer was separated, washed with water and brine, dried with Na_2SO_4, and concentrated *in vacuo*. The residue was chromatographed on SiO_2. Gradient elution with light petroleum—Bu^{t}OMe from 2 : 1 to 1 : 1 gave amide **15** (0.8 g, 80%) as colorless crystals, m.p. 66—68 °C (from light petroleum). Found (%): C, 64.43; H, 7.97; N, 4.20; S, 9.53. $C_{18}H_{27}NO_3S$. Calculated (%): C, 64.06; H, 8.06; N, 4.15; S, 9.50. IR (KBr, ν/cm^{-1}): 528, 568, 688, 712, 760, 848, 920, 1040, 1080, 1136, 1184, 1208, 1300, 1368, 1448, 1480, 1584, 1640, 2960—3032. MS, m/z (I_{rel} (%)): 337 $[M]^+$ (4), 322 (9), 280 (2), 273 (3), 254 (2), 241 (2), 232 (17), 230 (8), 219 (2), 213 (2), 197 (16), 196 (69), 169 (5), 154 (17), 144 (44), 143 (66), 142 (70), 141 (34), 128 (15), 125 (46), 118 (12), 111 (21), 100 (54), 95 (58), 85 (100), 76 (50), 69 (74), 55 (55). ^{1}H NMR (200.13 MHz), δ: 1.17, 1.33 and 1.42 (all d, 3 H each, 3 Me, J = 6.8 Hz); 1.42 (d, 3 H, Me, J = 6.5 Hz); 1.83—2.16 (m, 4 H, 2 CH_2); 3.46 (quint, 1 H, HC(Me)$_2$, J = 6.8 Hz); 4.25—4.40 (m, 2 H, HC(Me)$_2$, HCS); 4.98 and 5.03 (both m, 1 H each, H_2C=); 5.70 (m, 1 H, HC=); 7.47—7.85 (m, 5 H, H_{arom}).

(3*R,6*S**)- and (3*R**,6*R**)-*N*-(6-Bromomethyl-3-phenylsulfonyltetrahydropyran-2-ylidene)-*N*,*N*-diisopropylammonium bromides (17a,b) and *N*,*N*-diisopropyl-5,6-dibromo-2-phenylsulfonylhexanamides (18).** A solution of Br_2 (0.48 g, 3.0 mmol) in $CHCl_3$ (60 mL) was added at −10 °C (Ar) for 30 min to a stirred solution of amide **15** (1.01 g, 3.0 mmol) in $CHCl_3$ (50 mL). The reaction mixture was kept at this temperature for 30 min and concentrated *in vacuo* at 20 °C. The organic material was extracted from the residue (1.49 g) with Et_2O (3×15 mL) and dried *in vacuo* (2 Torr) to give a ~1.7 : 1 mixture of isomers **17a**/**17b** (0.9 g, 60%) (^{1}H NMR) as a yellow powder. Isomer **17a** was isolated by extraction with chloroform followed by precipitation with Et_2O (20 → −20 °C). The purity of compound **17a** was ~90% (^{1}H NMR). Crystallization of this product and the chloroform-insoluble residue containing the minor component gave analytically pure isomers **17a** and **17b**.

Bromide **17a**: colorless crystals, m.p. 145—151 °C (decomp.). Found (%): C, 43.73; H, 5.29; Br, 32.35; N, 2.75; S, 6.49. $C_{18}H_{27}Br_2NO_3S$. Calculated (%): C, 43.47; H, 5.47; Br, 32.14; N, 2.82; S, 6.45. IR (KBr, ν/cm^{-1}): 648, 688, 720, 760, 800, 856, 896, 940, 1040, 1068, 1088, 1104, 1120, 1152, 1224, 1288, 1296, 1312, 1328, 1340, 1376, 1392, 1412, 1448, 1520, 1568, 1616, 2936—3800. MS, m/z (I_{rel} (%); scan range from m/z 100 to m/z 510): 498.9 (10), 497.9 (50), 495.9 (100), 495.1 (20), 493.9 (50), 456.0 (15), 454.0 (30), 452.0 (15), 418.2 (40), 416.0 (35), 374.2 (5), 313.1 (15), 276.3 (25), 274.0 (20); MS/MS (m/z 496; the activation energy was 30% of the relative maximum collision energy): 455.8 (55), 453.8 (100), 451.8 (50), 373.9 (5), 355.9 (5), 353.9 (15), 314.8 (10), 312.8 (20), 290.0 (15), 276.0 (35), 274.0 (40). ^{1}H NMR (600.13 MHz, CD_3CN), δ: 1.39 and 1.48 (both d, 3 H each, 2 Me, J = 6.5 Hz); 1.53 and 1.58 (both d, 3 H each, 2 Me, J = 6.8 Hz); 1.87 (dddd, 1 H, $H_{ax}C(5)$, J = 8.0 Hz, J = 10.4 Hz, J = 11.25 Hz, J = 14.4 Hz); 2.26 (dddd, 1 H, $H_{eq}C(5)$, J = 2.5 Hz, J = 3.0 Hz, J = 10.3 Hz, J = 14.4 Hz); 2.29 (dddd, 1 H, $H_{ax}C(4)$, J = 2.5 Hz, J = 9.6 Hz, J = 11.3 Hz, J = 15.2 Hz); 2.40 (dddd, 1 H, $H_{eq}C(4)$, J = 2.4 Hz, J = 8.0 Hz,

J = 10.3 Hz, J = 15.2 Hz); 3.70 (dd, 1 H, HCBr, J = 7.2 Hz, J = 12.2 Hz); 3.85 (dd, 1 H, H´CBr, J = 3.0 Hz, J = 12.2 Hz); 4.22 (sept, 1 H, HCN, J = 6.8 Hz); 4.61 (sept, 1 H, HC´N, J = 6.5 Hz); 5.10 (dddd, 1 H, HC(6), J = 3.0 Hz, J = 3.0 Hz, J = 7.2 Hz, J = 11.3 Hz); 5.36 (dd, 1 H, HC(3), J = 2.4 Hz, J = 9.6 Hz); 7.51 (t, 1 H, J = 7.5 Hz); 7.78 (dd, 2 H, HC_{arom}, J = 7.5 Hz, J = 7.8 Hz); 8.04 (d, 1 H, HC_{arom}, J = 7.8 Hz). ^{13}C NMR (150.03 MHz, CD_3CN), δ: 19.6, 20.3 20.2, 20.8 (4 Me); 20.9 (C(4)), 25.0 (C(5)), 33.3 (C—Br); 54.7 (HCN) 58.6 (HC´N); 60.0 (HCS); 86.3 (C(6)); 130.5, 131.4, 132.1, 137.2 (C—Ar); 166.3 (C=N).

Bromide **17b**: light yellow crystals, m.p. 95—107 °C (decomp.). Found (%): C, 43.69; H, 5.13; Br, 32.51; N, 2.75; S, 6.55. $C_{18}H_{27}Br_2NO_3S$. Calculated (%): C, 43.47; H, 5.47; Br, 32.14; N, 2.82; S, 6.45. IR (KBr, ν/cm^{-1}): 456, 512, 584, 648, 696, 720, 768, 792, 856, 896, 952, 1048, 1080, 1104, 1128, 1152, 1256, 1284, 1300, 1312, 1380, 1400, 1420, 1448, 1544, 1612, 2864—3800. MS, m/z (I_{rel} (%); scan range from m/z 100 to m/z 2000): 498.1 (15), 496.1 (30), 494.1 (20), 454.1 (10), 419.3 (20), 418.2 (100), 417.0 (20), 416.2 (90), 376.2 (15), 336.3 (20), 313.1 (10), 277.2 (10), 276.0 (20); MS/MS (m/z 496; the activation energy was 30% of the relative maximum collision energy): 377.6 (5), 371.9 (10), 356.0 (15), 353.9 (35), 352.0 (15), 314.9 (15), 312.8 (40), 289.9 (25), 276.0 (90), 275.0 (20), 274.0 (100), 250.0 (15), 232.1 (10), 223.7 (5), 178.9 (5), 142.9 (5); MS/MS (m/z 418; the activation energy was 30% of the relative maximum collision energy): 419.1 (5), 417.9 (15), 416.0 (10), 377.9 (5), 376.9 (15), 375.9 (95), 373.9 (100), 333.9 (5), 295.0 (5), 294.0 (25), 292.0 (35), 291.0 (30), 276.9 (70), 275.9 (40), 274.9 (70), 274.2 (40), 249.8 (8), 234.0 (45), 232.0 (45), 197.1 (5), 196.1 (40), 152.0 (5). ^{1}H NMR (600.13 MHz, $CDCl_3$), δ: 1.57 and 1.58 (both d, 3 H each, 2 Me, J = 6.5 Hz); 1.75 and 1.77 (both d, 3 H each, 2 Me, J = 6.8 Hz); 2.10—2.20 (m, 3 H, HC(4), $H_2C(5)$); 2.70—2.80 (m, 1 H, H´C(4)); 3.57 (dd, 1 H, HCBr, J = 7.3 Hz, J = 12.1 Hz); 3.82 (td, 1 H, H´CBr, J = 2.5 Hz, J = 12.1 Hz); 4.15 (m, 1 H, HCN); 5.2 (m, 1 H, HC´N); 5.3 (m, 1 H, HC(6), J = 2.5 Hz, J = 12.0 Hz); 6.9 (dd, 1 H, HC(3), J = 5.0 Hz, J = 7.0 Hz); 7.7 (t, 1 H, HC_{arom}, J = 7.7 Hz); 7.8 (t, 1 H, HC_{arom}, J = 7.5 Hz); 8.1 (d, 1 H, HC_{arom}, J = 7.9 Hz). ^{13}C NMR (150.03 MHz, $CDCl_3$), δ: 19.8, 20.0, 20.1 and 21.5 (4 Me); 21.8 (C(4)), 26.0 (C(5)), 35.8 (C—Br); 53.4 (HCN) 58.2 (HCN); 59.3 (HCS); 84.2 (C(6)); 128.6 (C—Ar); 129.8(C—Ar); 134.2(C—Ar); 136.1(C—Ar); 166.9 (C=N).

Concentration of the above ethereal supernatant *in vacuo* gave a mixture of diastereomers **18** (0.59 g, 40%) as colorless crystals, m.p. 108—110 °C (light petroleum—MeOBu^t). Found (%): C, 43.67; H, 5.52; Br, 31.77; N, 2.81; S, 6.38. $C_{18}H_{27}Br_2NO_3S$. Calculated (%): C, 43.47; H, 5.47; Br, 32.14; N, 2.82; S, 6.45. IR (KBr, ν/cm^{-1}): 480, 536, 568, 688, 720, 756, 800, 824, 872, 920, 1044, 1088, 1132, 1212, 1272, 1280, 1300, 1336, 1368, 1448, 1512, 1644, 2968—3800. MS, m/z (I_{rel} (%)): 497 $[M]^+$ (2), 484 (7), 483 (5), 482 (18), 481 (11), 454 (2), 440 (5), 433 (11), 418 (22), 415 (12), 390 (4), 377 (5), 376 (26), 374 (19), 358 (67), 356 (89), 354 (44), 338 (9), 323 (13), 316 (14), 294 (5), 276 (12), 274 (16), 254 (6), 241 (13), 234 (15), 232 (39), 197 (37), 196 (75), 185 (20), 175 (23), 167 (18), 154 (23), 153 (61), 151 (25), 143 (89), 142 (91), 141 (62), 128 (54), 125 (62), 119 (58), 110 (46), 100 (82), 94 (74), 85 (100), 76 (75), 70 (60), 67 (75), 57 (61). ^{1}H NMR (600.13 MHz, $CDCl_3$), δ: 1.20 and 1.41 (both d, 3 H each, 2 Me, J = 6.8 Hz); 1.29 and 1.30 (both d, 3 H each, 2 Me, J = 6.4 Hz); 1.41 (d, 3 H, Me, J = 6.7 Hz); 1.56—2.41 (m, 4 H, 2 CH_2); 3.50 (m, 2 H, $\underline{H}C(Me)_2$, HC(6)); 3.81 (m, 1 H, H´C(6)); 4.04 (m, 1 H, HC(5)); 4.33 (m, 2 H, $\underline{H}$´$C(Me)_2$, $\underline{H}CS$); 7.51—7.85 (m, 5 H, H_{arom}). ^{13}C NMR (50.03 MHz, $CDCl_3$), δ: 20.0, 20.1, 20.3, and 21.2 (4 Me); 26.1, 26.9, 32.8, 33.4, 35.5, and 35.9 (3 CH_2); 46.9, 50.0, 50.5, and 51.4 (3 CH); 65.9, 66.4 (HCS); 172.1 (C=O).

References

1. (a) M. V. Zlokazov, A. V. Lozanova, V. V. Veselovsky, *Mendeleev Commun.*, 2003, 242; (b) M. V. Zlokazov, A. V. Lozanova, V. V. Veselovsky, *Izv. Akad. Nauk, Ser. Khim.*, 2004, 521 [*Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 547].
2. (a) A. V. Lozanova, T. M. Ugurchieva, M. V. Zlokazov, A. V. Stepanov, V. V. Veselovsky, *Mendeleev Commun.*, 2006, 15; (b) A. V. Lozanova, T. M. Ugurchieva, V. V. Veselovsky, *Izv. Akad. Nauk, Ser. Khim.*, 2007, 124 [*Russ. Chem. Bull., Int. Ed.*, 2007, **56**, 130]; (c) T. M. Ugurchieva, A. V. Lozanova, M. V. Zlokazov, V. V. Veselovsky, *Izv. Akad. Nauk*, *Ser. Khim.*, 2007, 1485 [*Russ. Chem. Bull., Int. Ed.*, 2007, **56**, 1544]; (d) T. M. Ugurchieva, A. V. Lozanova, M. V. Zlokazov, V. V. Veselovsky, *Izv. Akad. Nauk, Ser. Khim.*, 2008, 644 [*Russ. Chem. Bull., Int. Ed.*, 2008, **57**, 657].
3. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, *Gaussian 03, Revision B.02*, Gaussian, Inc.; Pittsburgh PA: 2003.
4. E. K. Starostin, A. V. Ignatenko, M. A. Lapitskaya, K. K. Pivnitskii, G. I. Nikishin, *Izv. Akad. Nauk, Ser. Khim.*, 2001, 797 [*Russ. Chem. Bull., Int. Ed.*, 2001, **50**, 833].
5. E. F. Witucki, G. L. Rowley, M. Warner, M. B. Frankel, *J. Org. Chem.*, 1972, **37**, 192.
6. J. T. Gupton, D. Baran, R. Bennett, G. R. Hertel, *Synth. Commun.*, 1984, **14**, 1001.
7. D. Ch. Braddock, G. Cansell, S. A. Hermitage, *Chem. Commun.*, 2006, 2483.

Received October 15, 2009;
in revised form March 1, 2010