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Novel design of 3,8-diazabicyclo[3.2.1]octane framework in oxidative sulfonamidation of 1,5-hexadiene

Bagrat A. Shainyan [a,*], Mikhail Yu Moskalik [a], Vera V. Astakhova [a], Uwe Schilde [b]

[a] A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Division of Russian Academy of Science, 1 Favorsky Street, Irkutsk 664033, Russian Federation
[b] Institut für Chemie, Universität Potsdam, Karl-Liebknecht-Strasse 24-25, D-14476 Golm, Germany

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ABSTRACT

1,5-Hexadiene reacts with trifluoromethanesulfonamide in the oxidative system (*t*-BuOCl+NaI) to give *trans*-2,5-bis(iodomethyl)-1-(trifluoromethylsulfonyl)pyrrolidine **5** and 3,8-bis(trifluoromethylsulfonyl)-3,8-diazabicyclo[3.2.1]octane **6**. With arenesulfonamides $ArSO_2NH_2$ (Ar=Ph, Tol), the reaction stops at the formation of the trans and cis isomers of 2,5-bis(iodomethyl)-1-(arenesulfonyl)pyrrolidine **7** and **8** (1:1). The cis isomers of **7** and **8** do not undergo cyclization to the corresponding 3,8-disubstituted 3,8-diazabicyclo[3.2.1]octanes. The reaction with triflamide represents the first example of one-pot two-step route to 3,8-diazabicyclo[3.2.1]octane system.

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1. Introduction

N,N′-Disubstituted 3,8-diazabicyclo[3.2.1]octanes (aza-analogs of tropane) are actively investigated as substitutes for the piperazine-based biologically active compounds with analgesic, antiarrhythmic, antitussive, antitumor, and antiproliferative activity;[1–5] these results are partly summarized in the recent review.[6] However, since their first multi-step syntheses by Cignarella et al. in 1960–1961,[2–7] small progress has been made in the methodology of construction of the 3,8-diazabicyclo[3.2.1]octane framework.[8] For example, the recently achieved diastereoselective synthesis of 3,8-diazabicyclo[3.2.1]octane-2-carboxylic acid included cyclization of the separately prepared pyrrolidine derivative followed by the reduction of the formed bicyclic adduct to the target product in eight steps from pyroglutamic acid.[9] An alternative synthetic strategy for the preparation of 3,8-diazabicyclo[3.2.1]octane derivatives elaborated by Joule et al. and ascending to the pioneering works by Katrizky[10] is to react 3-oxidopyraziniums with methyl acrylate or methacrylate.[11] The formation of substituted 3,8-bis(tosyl)-3,8-diazabicyclo[3.2.1]octanes in extremely low yields from the properly substituted 2-benzoyl-1,4-bis(tosyl)piperazines upon irradiation was also reported.[12] The yields are moderate and the substrates must be prepared in advance from commercially available reagents. To the best of our knowledge only two examples have been reported for the formation of 3,8-diazabicyclo[3.2.1]octan-2-one derivatives by intramolecular cyclization reaction, namely, from *N,N′*-diprotected 5-allyl-2-piperazinone in nine steps with total yield of 23%[13] and from 3-allyl-2-piperazinone in five steps with total yield of 32%.[14]

2. Results and discussion

There are no examples of one-pot construction of 3,8-diazabicyclo[3.2.1]octanes; neither are there examples of the triflyl derivatives of 3,8-diazabicyclo[3.2.1]octanes. In continuation of our systematic studies of triflamides[15] and, in particular, of oxidative triflamidation of alkenes and dienes,[16] we report here the reactions of 1,5-hexadiene **1** with trifluoromethanesulfonamide (triflamide) **2**, toluenesulfonamide (tosylamide) **3a**, benzenesulfonamide **3b**, and methanesulfonamide **4** in the presence of an oxidant. The reaction was carried out under mild conditions (MeCN solution, cooling) in the oxidative system (*t*-BuOCl+NaI). Two products were formed in the total isolated yield of 91%, which were separated by column chromatography and assigned as 2,5-bis(iodomethyl)-1-(trifluoromethylsulfonyl)pyrrolidine **5** and 3,8-bis(trifluoromethylsulfonyl)-3,8-diazabicyclo[3.2.1]octane **6**.

From ^{1}H NMR before separation the products **5** and **6** are formed in the ratio of 3:2. The ^{1}H NMR spectra of the two products have the

* Corresponding author. E-mail addresses: bagrat@irioch.irk.ru (B.A. Shainyan), us@chem.uni-potsdam.de (U. Schilde).

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same number of signals but differ in that the signals of **5** are broadened due to the flexibility of the five-membered ring, while for the rigid bicyclic structure of **6** they are more narrow and better resolved. The structure of product **6** was proved by the presence of the signals of two different CF_3 groups in the ^{13}C and ^{19}F NMR spectra and, finally, by X-ray analysis (Fig. 1).

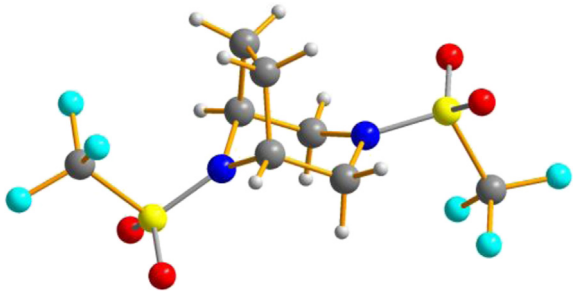


Fig. 1. X-ray structure of 3,8-bis(trifluoromethylsulfonyl)-3,8-diazabicyclo[3.2.1]octane **6**.

The formation of **6** is the first example of assembling the 3,8-diazabicyclo[3.2.1]octane framework in one-pot procedure. A priori, two mechanistic scenarios can be proposed for the formation of the product of bicyclization **6**, via the 2,5- (pathway A) or 1,6-cycloaddition (pathway B) to 1,5-hexadiene at the first step of the reaction (Scheme 2).

compound **5** to have the two iodomethyl groups trans to each other with respect to the heterocyclic ring (Fig. 2).

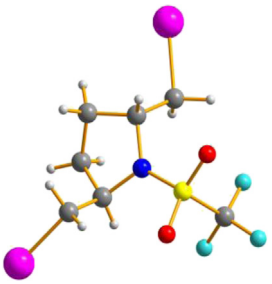
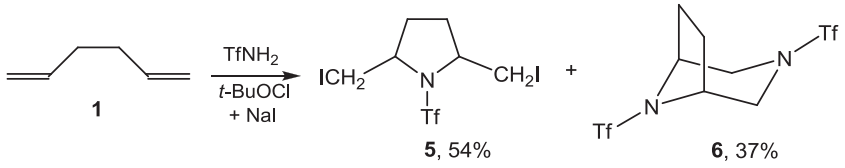
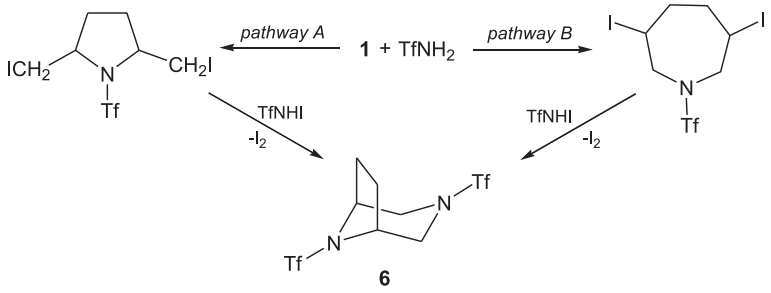


Fig. 2. X-ray structure of *trans*-2,5-bis(iodomethyl)-1-(trifluoromethylsulfonyl)pyrrolidine **5**. Beside the drawn 2*R*/5*R* enantiomer the 2*S*/5*S* enantiomer exists in the crystal.

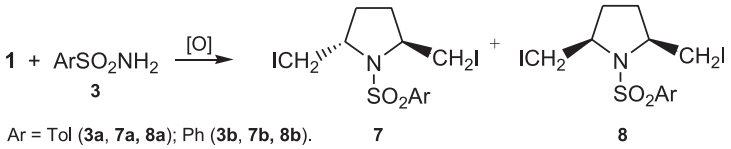
This explains why compound **5** does not react with triflamide to afford **6**, but leaves open the question whether the final product **6** is formed by pathway B or by pathway A via the transient cis isomer of **5**. Additional light was shed by the experiments with arenesulfonamides and methanesulfonamide. The reaction of **1** with arenesulfonamides **3a**,**b** proceeds in a different way than with triflamide. In both cases, two products were formed in approximately equal amounts (1:1.1 for **3a** and 1:1.2 for **3b**) and were identified as the trans and cis isomers of 2,5-bis(iodomethyl)-1-(arenesulfonyl) pyrrolidines **7** and **8** (Scheme 3).



Scheme 1. Mono and bicyclization in oxidative triflamidation of 1,5-hexadiene.



Scheme 2. Two possible routes to the product of bicyclization **6**.



Scheme 3. Formation of isomeric products of arenesulfonamidation of 1,5-hexadiene.

In pathway A, the formation of **6** is possible only for the cis arrangement of the two iodomethyl groups in 2,5-bis(iodomethyl)-1-(triflyl)pyrrolidine. Therefore, the structure of the isolated compound **5** (Scheme 1) was of particular interest. A special experiment showed that compound **5** does not react with triflamide under the conditions in Scheme 1. X-ray analysis showed

The mixture of diastereomers **7a** and **8a** was separated by column chromatography and the structure of **8a** was determined by X-ray analysis (Fig. 3). Note, that because of non-planarity of the pyrrolidine ring, the compound is not *meso* but exists in the crystal as a mixture of enantiomers (in solution, the ring is vibrationally averaged to planarity).

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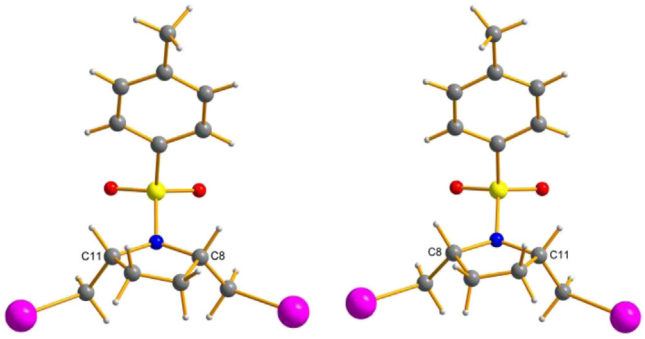
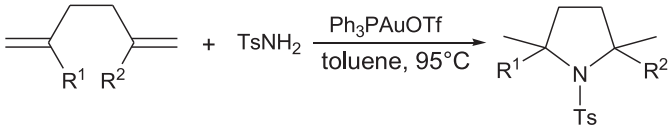


Fig. 3. X-ray structure of the two enantiomers of *cis*-2,5-bis(iodomethyl)-1-tosylpyrrolidine **8a**.

^{1}H NMR spectra of the cis and trans isomers **7** and **8** are similar in that they both show the ABX proton system but different in the relative position of the signals. In one isomer the signals are spaced by 1.2 ppm (4.1÷2.9 ppm), practically as they are in compound **5**, being shifted upfield with respect to **5** by ~0.2 ppm due to less electron withdrawing ability of the tosyl versus the triflyl group. This allowed us to assign the structure of this more abundant product to the trans isomer **7a**. The signals of the second (minor) product, cis isomer **8a**, are much closer to each other (3.7÷3.3 ppm). The signals of the CH_2CH_2 group of **8a** are well resolved and shifted upfield with respect to poorly resolved CH_2CH_2 signals of **7a**, which are closer to the corresponding non-resolved signals of the trans isomer **5**.

Diastereomers **7b** and **8b** could not be separated, so, the assignment was made based on the similarity of their ^{1}H NMR signals in the spectrum of the mixture of diastereomers to those of their analogs **7a** and **8a**. The signals of the major *trans*-diastereomer **7b** are also spaced by 1.2 ppm (4.2÷3.0 ppm) as in **7a**, whereas for the minor *cis*-diastereomer **8b** they almost coincide with the corresponding signals of **8a**.

There are only two examples of the reaction of sulfonamides with compounds containing the 1,5-diene motif. The first is the gold(I) catalyzed hydroamination of 1,5-hexadienes leading to ~1:1.7 mixture of the cis and trans adducts (Scheme 4).[17]



Scheme 4. Au(I)-catalyzed heterocyclization of 1,5-dienes with tosylamide.

The second is the formation of 2,5-diiodo-9-(trifluoromethylsulfonyl)-9-azabicyclo[4.2.1]nonane containing the pyrrolidine motif by the reaction of oxidative triflamidation of 1,5-cyclooctadiene (the cyclic analog of compound **1**) (Scheme 5).[16c]

Scheme 5. Oxidative heterocyclization of 1,5-cyclooctadiene with triflamide.

Usually, 2,5-disubstituted pyrrolidines are prepared by heterocyclization by substitution of Br[7] or OTs[18] groups in the −CX−C−C−CX− motif by amines. What is important to our study is that the cis and trans isomers are formed in comparable yields,[7c,18b] unless the substrate, which is involved in heterocyclization, is enantiomerically pure. For optically active substrate, the reaction is enantioselective due to the presence of a chiral center.[18b]

No bicyclic products analogous to **6** are formed with arenesulfonamides. Moreover, neither isomer of 2,5-bis(iodomethyl)-1-(tosyl)pyrrolidine **7a**, **8a** reacts with triflamide under the oxidative conditions employed. ^{1}H NMR analysis showed the presence of unreacted triflamide and the isomers **7a**, **8a** in the same ratio as in their mixture taken for the reaction. Formally, it can be considered as an argument against pathway A and in favor of an alternative route, e.g., pathway B in Scheme 2 as a route to compound **6**. However, the formation of both isomers **7** and **8** with arenesulfonamides **3** makes extremely improbable any mechanism of formation of **6** avoiding the formation of the cis isomer of **5**. Rather, the absence of the products of bicyclization of the type **6** with arenesulfonamides should be considered as a manifestation of the difference between triflamide and other sulfonamides. Note also that no reaction occurred with methanesulfonamide. As was emphasized,[15] even a small difference in electron-acceptor ability of R may result in principal changes in reactivity of RSO_2NH_2, in particular, in different courses of the reactions with alkenes in the same oxidative system.[16a,19] It was suggested that a strong acceptor effect of the sulfonyl group brings sulfonamides to such a threshold of reactivity after which even a moderate effect of the CF_3 group may cause the observed drastic changes.[15] With this in mind, we propose mechanism A to be operative, which can be detalized for the formation of the products of mono and bicyclization as shown in Scheme 6.

The inertness of methanesulfonamide **4** under the conditions employed is, apparently, the result of its less electrophilic character than sulfonamides **2**, **3**. Note that alkanesulfonamides are more rarely than arenesulfonamides used as N_1 sulfonamidation units[19–21] and usually show lower yields.[20] The absence of bicyclic products in the reaction with arenesulfonamides **3** and inactivity of compounds **7** and **8** with respect to triflamide suggest that the iodine substitution reaction is very sensitive to the electron-acceptor ability of the RSO_2 group in the molecule of bis(iodomethyl)-1-(organylsulfonyl)pyrrolidine. Finally, the aforementioned inertness of *N*-triflylpyrrolidine **5** to triflamide is indicative that the last two steps of the iodine substitution and cyclization in Scheme 6 are somehow interdependent, otherwise we should see the products of mono or disubstitution of iodine in **5** by triflamide.

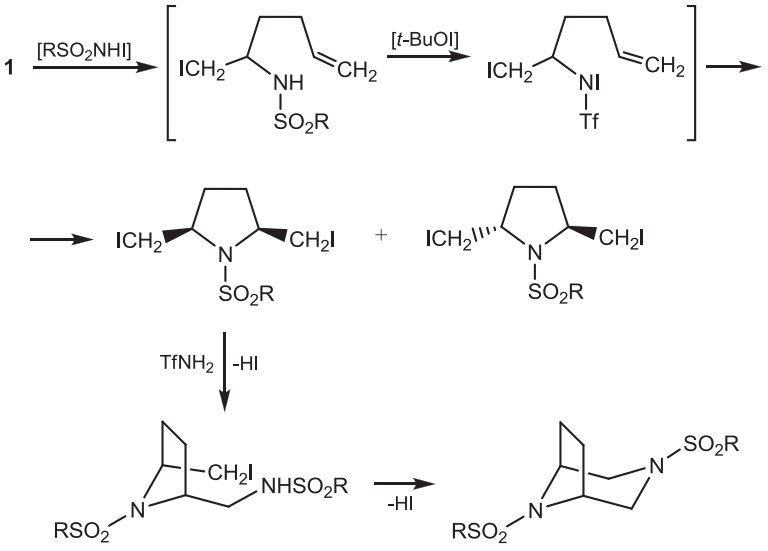
3. Conclusions

In summary, the reaction of 1,5-hexadiene with triflamide under oxidative conditions affords *trans*-2,5-bis(iodomethyl)-1-(trifluoromethylsulfonyl)pyrrolidine and 3,8-bis(trifluoromethylsulfonyl)-3,8-diazabicyclo[3.2.1]octane, whereas with less electrophilic arenesulfonamides the reaction stops at the isomeric 2,5-bis(iodomethyl)-1-(arenesulfonyl)pyrrolidines. The proposed mechanism includes the formation of cis and trans isomers of 2,5-bis(iodomethyl)-1-(organylsulfonyl)pyrrolidines. The trans isomer is the final product both for triflamide and arenesulfonamides, while the fate of the cis isomer depends on the substituent in the sulfonyl group. The reaction with triflamide provides the first example of one-pot assembling of the 3,8-diazabicyclo[3.2.1]octane framework.

4. Experimental section

4.1. General

IR spectra were taken on a Bruker Vertex 70 spectrophotometer in KBr. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker DPX 400 spectrometer at working frequencies 400 (^{1}H), 100 (^{13}C), and 376 (^{19}F) MHz; ^{1}H and ^{13}C NMR chemical shifts are reported in parts



Scheme 6. A tentative mechanism of mono and bicyclization during oxidative sulfamidation of 1,5-hexadiene.

per million downfield to TMS, and ^{19}F NMR in ppm downfield to $CFCl_3$. The HRMS ESI spectra were recorded using a Micromass Q-TOFmicro mass spectrometer in positive electrospray mode with an electron energy of 70 eV. Elemental compositions were determined by accurate mass measurement with standard deviation <5 ppm. H_3PO_4 was used as reference compound. Elemental analysis on C, H, and N was carried out on an elemental analyzer from Thermo-Finnigan (Milan, Italy) model Flash EA. X-ray crystal structure determinations were performed on an Imaging Plate Diffraction System IPDS-2 (Stoe) at 210 K using graphite monochromatized Mo Kα radiation.

4.2. Synthesis

*4.2.1. Reaction of 1,5-hexadiene with triflamide **2**.* *t*-BuOCl (9.2 mL, 81 mmol) was added dropwise to a solution of triflamide **2** (4 g, 27 mmol), NaI (12.1 g, 81 mmol), and 1,5-hexadiene (3.2 mL, 27 mmol) in MeCN (120 mL) at 4°C. The mixture was stirred for 24 h in argon atmosphere in the dark, then concentrated on a rotary evaporator, the residue treated with aqueous $Na_2S_2O_3$ (80 mL), extracted with ether (80 mL), the extract dried over $CaCl_2$, the solvent removed to give ~9 g of dark brown residue, which was eluted on a silica column (hexane, hexane/Et_2O 1:1) to afford *trans*-2,5-bis(iodomethyl)-1-(trifluoromethylsulfonyl)pyrrolidine **5** (7.02 g, 54%) and 3,8-bis(trifluoromethylsulfonyl)-3,8-diazabicyclo[3.2.1]octane **6** (1.88 g, 37% with respect to triflamide, taking into account the presence of two triflamide residues in the molecule). Analytically pure samples were obtained by crystallization from hexane.

*4.2.2. trans-2,5-Bis(iodomethyl)-1-(trifluoromethylsulfonyl)pyrrolidine, **5**.* Colorless crystals, mp 96 °C; ν_{max} (KBr) 2985, 1384, 1225, 1202, 1190, 1146 cm^{-1}; δ_H ($CDCl_3$) 4.33 (2H, br s, NC*H*), 3.70 (2H, m, CH^AI), 3.10 (2H, m, CH^BI), 2.28 (4H, m, CH_2); δ_H (C_6D_6) 3.91 (2H, br s, NCH), 3.46 (4H, m, CH^{A}I), 2.50 (2H, d, *J* 10.3 Hz, CH^BI), 1.53 (2H, m, CH^A in CH_2), 1.42 (2H, m, CH^B in CH_2); δ_C ($CDCl_3$) 119.5 (q, *J* 323.6 Hz, *C*F_3), 63.5 (N*C*), 29.0 (br, *C*H_2), 5.8 (br, *C*H_2I); δ_F ($CDCl_3$) −74.88; HRMS calcd for $C_7H_{10}F_3I_2NO_2S$ (M^+) 482.8474. Found: 482.8476; Anal. Calcd: C, 17.41; H, 2.09; N, 2.90; S, 6.64. Found: C, 17.56; H, 2.12; N, 2.98; S, 6.98.

*4.2.3. 3,8-Bis(trifluoromethylsulfonyl)-3,8-diazabicyclo[3.2.1]octane, **6**.* Colorless crystals, mp 153 °C; ν_{max} (KBr) 2967, 1388, 1229, 1191, 1103; δ_H ($CDCl_3$) 4.43 (2H, s, NC*H*), 3.82 (2H, d, *J* 12.4 Hz, CH^AI), 3.41 (2H, d, *J* 12.4 Hz, CH^BI), 2.18 (2H, m, CH^A in CH_2), 2.09 (2H, m, CH^B in CH_2); δ_C (CD_2Cl_2) 120.2 (q, *J* 321.0 Hz, *C*F_3), 119.8 (q, *J* 319.5 Hz, *C*F_3), 58.4 ($C^{1,5}$), 53.3 ($C^{2,4}$), 27.8 ($C^{6,7}$); δ_F ($CDCl_3$) −75.71, −78.21; HRMS calcd for $C_8H_{10}F_6N_2O_4S_2$ (M^+) 375.9986. Found: 395.9983.

*4.2.4. Reaction of 1,5-hexadiene with tosylamide **3a**.* *t*-BuOCl (4 mL, 35 mmol) was added dropwise to a solution of tosylamide **3a** (2 g, 12 mmol), NaI (5.85 g, 35 mmol), and 1,5-hexadiene (1.4 mL, 12 mmol) in MeCN (80 mL) upon stirring in argon atmosphere in the dark at −6°C in the course of 6 h. Then the solvent was removed under vacuum, the residue was dissolved in $CHCl_3$, washed with aqueous $Na_2S_2O_3$, and dried over $CaCl_2$. The solvent was removed and the residue was purified from tarry admixtures by eluting on a silica column (hexane/Et_2O 2:1). The crude product (4.8 g, 81%) consisted of the trans and cis isomers of 2,5-bis(iodomethyl)-1-(tolylsulfonyl)pyrrolidine **7a** and **8a** in ~2:1 ratio, which were separated on a silica column to give fractions enriched with each isomer, from which the analytically pure isomers (0.4 g of (*R*,*R*+*S*,*S*)-2,5-bis(iodomethyl)-1-(tolylsulfonyl)pyrrolidine, **7a**, and 0.28 g of (*R*,*S*)-2,5-bis(iodomethyl)-1-(tolylsulfonyl)pyrrolidine, **8a**) were isolated by crystallization from ethyl acetate.

*4.2.5. (R,R+S,S)-2,5-Bis(iodomethyl)-1-(tolylsulfonyl)pyrrolidine, **7a**.* Colorless crystals, mp 133 °C. IR spectrum of **7a** is similar to that of **8a**; δ_H ($CDCl_3$) 7.69 (2H, d, *J* 8.2 Hz, CH_o), 7.29 (2H, d, *J* 8.2 Hz, CH_m), 4.13 (2H, m, CH), 3.67 (2H, dd, *J* 9.7, 2.7 Hz, CH^{A}I), 2.94 (2H, t, *J* 9.7 Hz, CH^{B}I), 2.45 (3H, s, CH_3), 2.11 (2H, m, CH^A in CH_2), 2.04 (2H, m, CH^B in CH_2). δ_C ($CDCl_3$) 143.8 (C_p), 138.4 (C-1), 129.9 (C_m), 126.8 (C_o), 62.1 (CH), 28.9 (CH_2), 21.5 (CH_3), 8.3 (CH_2I). Anal. Calcd: C, 30.91; H, 3.39; N, 2.77. Found: C, 30.86; H, 3.41; N, 3.17.

*4.2.6. (R,S)-2,5-Bis(iodomethyl)-1-(tolylsulfonyl)pyrrolidine, **8a**.* Colorless crystals, mp 145 °C. ν_{max} 3039, 2944, 1599, 1447, 1343, 1206, 1164, 1091, 1026, 971, 817, 770, 706, 665, 580, 553; δ_H ($CDCl_3$) 7.70 (2H, d, *J* 8.1 Hz, CH_o), 7.33 (2H, d, *J* 8.1 Hz, CH_m), 3.71 (2H, m, *C*H), 3.56 (2H, dd, *J* 9.9, 3.0 Hz, CH^AI), 3.27 (2H, t, *J* 9.9 Hz, CH^BI), 2.42 (3H, s, CH_3), 1.86 (2H, m, CH^A in CH_2), 1.69 (2H, m, CH^B in CH_2). δ_C ($CDCl_3$) 144.4 (C_p), 133.8 (*C*-1), 130.1 (C_m), 127.6 (C_o), 63.1 (*C*H), 30.0 (CH_2), 21.6 (CH_3), 11.14 (CH_2I); Anal. Calcd: C, 30.91; H, 3.39; N, 2.77. Found: C, 30.41; H, 3.19; N, 3.19.

*4.2.7. Reaction of 1,5-hexadiene with phenylsulfonamide **3b**.* To the solution of 1 g (6.4 mmol) of benzenesulfonamide **3b**, 0.75 mL

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(6.4 mmol) of 1,5-hexadiene and 2.9 g (19 mmol) of dry NaI in MeCN (40 mL) 2.2 mL (19 mmol) of *t*-BuOCl was added dropwise in argon atmosphere in the dark with cooling. The mixture was stirred for 1 day, then treated with aqueous $Na_2S_2O_3$ (80 mL), extracted with ethyl acetate (80 mL), and dried over $CaCl_2$. The solvent was removed in vacuum to afford 2.5 g (80%) of dark residue, which was purified on a silica column (0.063–0.200 mm) by gradual elution with hexane, ether/hexane 1:1, ether. Triflamide (~0.2 g) was recovered and 1.5 g of **7b**/**8b** was obtained. All trials to separate the obtained mixture to pure diastereomers by column separation or fractional crystallization failed. Mp 106.6°C; ν_{max} 3044, 2942, 1584, 1445, 1349, 1207, 1159, 1093, 1021, 979, 832, 775, 719, 667, 582, 569; Anal. Calcd, %: C, 29.35; H, 3.08; N, 2.85; S, 6.53. Found, %: C, 29.74; H, 3.03; N, 2.79; S, 6.54.

4.2.8. (R,S)-2,5-Bis(iodomethyl)-1-(benzenesulfonyl)pyrrolidine, ***7b****.* δ_H ($CDCl_3$) 7.86 (2H, d, *J* 7.3 Hz, CH_o), 7.57 (3H, m, CH_{m+p}), 4.20 (2H, m, CH), 3.70 (2H, dd, *J* 9.8, 2.5 Hz, CH^AI), 3.00 (2H, t, *J* 10.0 Hz, CH^BI), 2.19 (2H, m, CH^A in CH_2), 2.07 (2H, m, CH^B in CH_2); δ_C ($CDCl_3$) 136.9 (C_p), 133.6 (C-1), 129.6 (C_m), 127.8 (C_o), 62.3 (CH), 29.2 (CH_2), 8.5 (CH_2I).

4.2.9. (R,S)-2,5-Bis(iodomethyl)-1-(benzenesulfonyl)pyrrolidine, ***8b****.* δ_H ($CDCl_3$) 7.86 (2H, d, *J* 7.3 Hz, CH_o), 7.57 (3H, m, CH_{m+p}), 3.75 (2H, m, CH), 3.60 (2H, dd, *J* 9.9, 2.9 Hz, CH^AI), 3.33 (2H, t, *J* 9.9 Hz, CH^BI), 1.90 (2H, m, CH^A in CH_2), 1.72 (2H, m, CH^B in CH_2); δ_C ($CDCl_3$) 141.7 (C_p), 133.2 (C-1), 129.7 (C_m), 127.0 (C_o), 63.3 (CH), 30.2 (CH_2), 11.2 (CH_2I).

4.2.10. Reaction of 1,5-hexadiene with methanesulfonamide ***4****.* Methanesulfonamide **4** (3 g, 32 mmol) and 14.2 g (95 mmol) of NaI were dissolved in 120 mL of MeCN, the mixture was cooled upon stirring to −35 °C and 3.7 mL (32 mmol) of 1,5-hexadiene was added. Then 11 mL (95 mmol) of *t*-BuOCl was added dropwise under argon in the dark in the course of 10 min and the mixture was stirred with TLC monitoring for 24 h. The spot of $MeSO_2NH_2$ did not disappear. The mixture was treated as above and the residue analyzed by NMR, which revealed the presence of mainly the starting material.

4.3. X-ray measurements

Crystal data for **5**: $C_7H_{10}F_3I_2NO_2S$, M_r=483.02 g mol^{-1}, crystal dimensions 0.50×0.45×0.40 mm, orthorhombic, space group *Pbca*, *a*=9.0384(4), *b*=13.1528(6), *c*=22.3699(8) Å, *V*=2659.3(2) Å^3, *Z*=8, ρ_{calcd}=2.413 g cm^{-1}; μ(Mo Kα)=4.91 mm^{-1} (λ=0.71073 Å), *T*=210 K; $2\Theta_{max}$=49.16°, 15,171 reflections measured, 2226 unique (R_{int}=0.0582), *R*=0.0439, *wR*=0.1125 ($I>2\sigma(I)$).

Crystal data for **6**: $C_8H_{10}F_6N_2O_4S_2$, M_r=376.30 g mol^{-1}, crystal dimensions 1.0×1.5×0.05 mm, triclinic, space group $P\bar{1}$, *a*=6.5267(5), *b*=11.0005(9), *c*=11.1688(10) Å, α=116.385(6)°, β=91.289(7)°, γ=95.530(6)°, *V*=713.1(1) Å^3, *Z*=2, ρ_{calcd}=1.753 g cm^{-1}; μ(Mo Kα)=0.460 mm^{-1} (λ=0.71073 Å), *T*=150 K; $2\Theta_{max}$=49.99°, 4612 reflections measured, 2356 unique (R_{int}=0.0646), *R*=0.0457, *wR*=0.1230 ($I>2\sigma(I)$).

Crystal data for **8a**: $C_{13}H_{17}I_2NO_2S$, M_r=505.14 g mol^{-1}, crystal dimensions 0.8×0.7×0.4 mm, monoclinic, space group $P2_1/n$, *a*=7.8509(6), *b*=11.2192(5), *c*=18.9203(12) Å, β=98.076(5)°, *V*=1649.99(18) Å^3, *Z*=4, ρ_{calcd}=2.033 g cm^{-1}; μ(Mo Kα)=3.936 mm^{-1} (λ=0.71073 Å), *T*=210 K; $2\Theta_{max}$=50.00°, 10,389 reflections measured, 2826 unique (R_{int}=0.1288), *R*=0.0661, *wR*=0.1774 ($I>2\sigma(I)$).

For details of the data collection and the structure solution and refinement, see Supplementary data. CCDC 931587 (**5**), CCDC 931588 (**6**), and CCDC 980000 (**8a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Supplementary data

Experimental details, spectroscopic data, and X-ray structural information for new compounds (CCDC 931587 (**5**), 931588 (**6**), 980000 (**8a**)). Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2014.04.095.

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