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From oxides of internal perfluoroolefins to fluorocontaining camphor thiazolinylhydrazones

Lyudmila V. Saloutina[a,*], Aleksandr Ya. Zapevalov[a], Mikhail I. Kodess[a], Konstantin A. Lyssenko[b], Mikhail Yu. Antipin[b], Victor I. Saloutin[a], Oleg N. Chupakhin[a]

[a]*Urals Branch of the Russian Academy of Sciences, Institute of Organic Synthesis, 20 S. Kovalevskoy, GSP-147, 620219 Ekaterinburg, Russia*

[b]*Russian Academy of Sciences, A.N. Nesmeyanov Institute of Organoelement Compounds, 28 Vavilova, 119991 Moscow, Russia*

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Abstract

The reaction of oxides of internal *trans*- and *cis*-perfluoroolefins with (*1S*, *4S*)- or racemic camphor thiosemicarbazone leads to the formation of *trans*- and *cis*-isomers of (*1S*, *4S*)- or racemic camphor 5′-fluoro-4′-hydroxy-4′,5′-di(perfluoroalkyl)-1′,3′-thiazolinyl-2′-hydrazones, respectively. Unsymmetrical dodecafluoro-2,3-epoxyhexane yields a mixture of regioisomeric hydrazones. The molecular structure of the *trans*-isomer of (*1S*, *4S*)-camphor 5′-fluoro-4′-hydroxy-4′,5′-bis(trifluoromethyl)-1′,3′-thiazolinyl-2′-hydrazone has been established by X-ray crystallography. The quite rare example of cocrystallization of two diastereomers of the latter in homochiral crystal (sp. group $P2_1$) has been revealed.

Keywords: Oxides of internal perfluoroolefins; Camphor thiosemicarbazone; Fluorocontaining camphor thiazolinylhydrazones

1. Introduction

Earlier we have shown that oxides of internal perfluoroolefins yield ring-opened compounds when they are treated with nucleophilic reagents (F^-, $LiAlH_4$, NH_3, NEt_3) [1–5]. At the same time, the former afford polyfluoroalkylated heterocycles, compounds with potential biological activity, when interacting with bifunctional nucleophiles such as ethylenediamine, 2-aminoethanol, thiourea and thiosemicarbazide [6,7]. Nothing has been reported on reactions of fluorooxiranes with carbonyl compounds, thiosemicarbazones containing chiral centers.

In the present work, we have studied the interaction of internal octafluoro-2,3-epoxybutane **1** [*trans*:*cis* ∼ 90:10], dodecafluoro-3,4-epoxyhexane **2** [*trans*:*cis* ∼ 90:10] and dodecafluoro-2,3-epoxyhexane **3** [*trans*:*cis* ∼ 90:10] [8,9] with (*1S*, *4S*) and racemic camphor thiosemicarbazone [(*1S*, *4S*)- and rac-CTSC] [10].

2. Results and discussion

We found the reaction of oxiranes **1**–**3** with (*1S*, *4S*)- or rac-CTSC to occur selectively in polar aprotic solvents (dioxane, acetonitrile) resulting in formation of (*1S*, *4S*)- or rac-camphor 5′-fluoro-4′-hydroxy-4′,5′-di(polyfluoroalkyl)-1′,3′-thiazolinyl-2′-hydrazones **4**–**7** in high yields. Treating oxiranes **1**, **2** with (*1S*, *4S*)-CTSC gave one regioisomer—(*1S*, *4S*)-camphor 5′-fluoro-4′-hydroxy-4′,5′-bis[trifluoromethyl (pentafluoroethyl)]-1′,3′-thiazolinyl-2′-hydrazones **4**, **5**. The final molar ratio of hydrazones with *trans*- and *cis*-arrangement of fluoroalkyl substitutions in thiazoline cycles **4**, **5** was determined by ^{19}F NMR to be approximately equal to the ratio *trans*:*cis* of starting oxiranes **1**, **2** when the reaction was carried out in dioxane or acetonitrile (Scheme 1) (similar to the reaction of internal perfluoroolefin oxides with thiourea in polar aprotic solvents [7]). This result can be explained by a considerable contribution of the S_N2 type of nucleophilic substitution both to the epoxide ring opening and to the thiazoline cyclization stages, that cause configuration inversion at both the epoxide carbon atoms [11]. As a result, the starting oxirane and the resulting thiazoline have the same (*trans*- or *cis*-) configuration.

* Corresponding author. Tel.: +7-3432-74-59-54; fax: +7-3432-74-59-54.
E-mail address: saloutin@ios.uran.ru (L.V. Saloutina).

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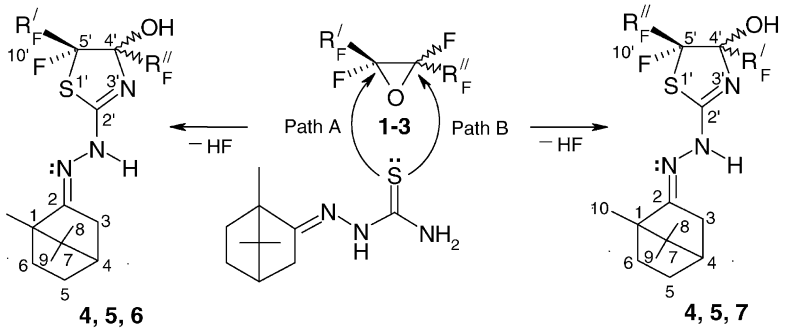


1, 4 $R_F^{/} = C\,F_3^{8'\,9'}$; $R_F^{//} = C\,F_3^{6'\,7'}$

2, 5 $R_F^{/} = CF_3^{9'}\,CF_2^{8'}$; $R_F^{//} = CF_2^{6'}\,C\,F_3^{7'}$

3, 6, 7 $R_F^{/} = CF_3^{9'}$; $R_F^{//} = CF_2^{6'}\,CF_2^{7'}\,CF_3^{8'}$

Scheme 1.

The ring opening of unsymmetrical dodecafluoro-2,3-epoxyhexane **3** with (*1S*, *4S*)-CTSC under the same conditions occurred in both possible directions (paths A and B, Scheme 1) to give regioisomeric (*1S*, *4S*)-camphor thiazolinylhydrazones **6**, **7** (**6**:**7** ∼ 44:56) consisting of mixtures of *trans*- and *cis*-isomers. *Trans*:*cis* ratios in thiazolines **6**, **7** were also nearly equal to corresponding value in the starting oxirane **3**. These results are in accordance with our data on regiodirectivity of reactions of unsymmetric polyfluorooxiranes with ethylenediamine, 2-aminoethanol and thiourea [6,7].

The structural assignment for *trans*- and *cis*-isomers of compounds **4**–**7** was made on the basis of their ^{19}F NMR spectra by comparison with those of *trans*- and *cis*-2-amino-5-fluoro-4-hydroxy-4,5-di(polyfluoroalkyl)-1,3-thiazolines as model compounds [7].

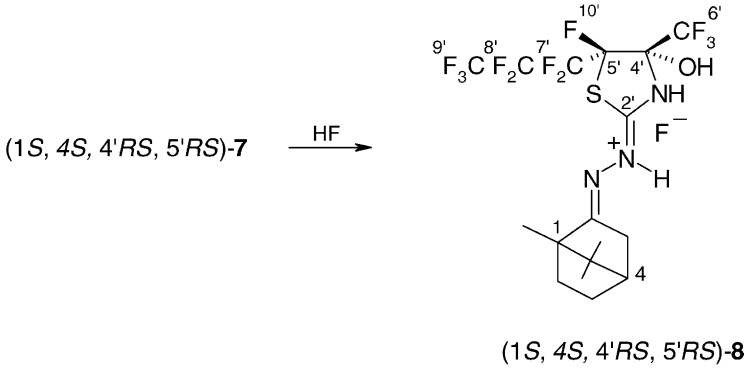
Hydrazones (*1S*, *4S*)-**4**, **5** with *trans*-orientation of fluoroalkyl groups of the thiazoline cycle were isolated by recrystallization of corresponding *trans*- and *cis*-isomer mixtures. Regioisomers (*1S*, *4S*)-**6** and (*1S*, *4S*)-**7** were not separated by crystallization; as a result, a mixture of *trans*-isomers of these compounds was obtained. Two groups of signals at a 1:1 ratio appeared in the ^{19}F NMR spectrum of (*1S*, *4S*)-camphor *trans*-thiazolinylhydrazone **4** [(*1S*, *4S*, *4′RS*, *5′RS*)-**4**] obtained in a solution of $CDCl_3$, probably, due to the existence of two diastereomers (*1S*, *4S*, *4′S*, *5′S*)-**4** and (*1S*, *4S*, *4′R*, *5′R*)-**4**. ^{1}H and ^{13}C NMR spectra of this compound also exhibited doubled resonance signals for most of the nuclei ^{1}H and ^{13}C, respectively.

By analogy with compound **4**, some signal doubling in ^{19}F NMR spectra of hydrazones **5**–**7** was ascribed to the existence of two diastereomers of these compounds in $CDCl_3$.

Rac-CTSC interacting with oxirane **1** also led to the formation of rac-**4** mainly in the *trans*-form [(*1RS*, *4RS*, *4′RS*, *5′RS*)-**4**] (the latter was isolated by crystallization). Doubled signals in ^{19}F, ^{1}H and ^{13}C NMR spectra of (*1RS*, *4RS*, *4′RS*, *5′RS*)-**4** as in the case of the *trans*-isomer of (*1S*, *4S*)-**4** could be attributed to the presence of two diastereomers consisting of two enantiomers: (*1S*, *4S*, *4′S*, *5′S*)-**4**, (*1R*, *4R*, *4′R*, *5′R*)-**4** and (*1S*, *4S*, *4′R*, *5′R*)-**4**, (*1R*, *4R*, *4′S*, *5′S*)-**4**.

It should be noted that a similar reaction of oxiranes **1**–**3** in MeOH gave complex product mixtures containing some amounts of the thiazolinylhydrazones **4**–**7** along with the corresponding thiazolinylhydrazonium fluorides and unidentified compounds (from ^{19}F NMR), probably due to side processes. In this case, only the hydrazonium fluorides could be isolated in individual form as insoluble compounds in $CHCl_3$ in low yields (∼10–15%). At the same time, only traces of the latters are formed in dioxane or acetonitrile. Probably, MeOH, in contrast to aprotic solvents, promotes hydrazone protonation and formation of the hydrazonium fluorides. Interestingly, when the interaction of compound **3** with (*1S*, *4S*)-CTSC was carried out in MeOH, the only regioisomeric hydrazone, namely, (*1S*, *4S*, *4′RS*, *5′RS*)-**7**, gave an insoluble hydrazonium fluoride (*1S*, *4S*, *4′RS*, *5′RS*)-**8** isolated as a monohydrate (*1S*, *4S*, *4′RS*, *5′RS*)-**8**·H_2O. The hydrazone protonation is likely to occur on the ring nitrogen atom, but the structure shown in the Scheme 2 seems to be realized, analogous to nonfluorinated thiazolil-2-hydrazones containing electron-attracting substituent at position 4 of the thiazoline cycle [12].

In order to obtain more precise information about the hydrazone's structure the X-ray investigation of (*1S*, *4S*, *4′RS*, *5′RS*)-**4** has been carried out. It has been revealed that upon the crystallization, instead of the expected resolution, the quite rare example of cocrystallization of two diastereomers (*1S*, *4S*, *4′R*, *5′R*) and (*1S*, *4S*, *4′S*, *5′S*) in homochiral crystal (sp. group $P2_1$) occurs (Fig. 1). Both the diastereomers have anti-configuration (substituent on the sp^2-nitrogen



Scheme 2.

is away from 10-CH_3) and crystallize in a 1:1 ratio with three solvate benzene molecules.

In the crystal, the diastereomers form intermolecular contacts which assemble them in an homochiral supramolecular helix structure with alternating diastereomers. In these helices, molecules are assembled not only by strong hydrogen bonds between the thiazoline nitrogen N(3) and hydroxy group (N . . . O ca. 2.730(5) Å) but also by unusual F . . . F_3C contacts (Figs. 1 and 2). While the latter F(4) . . . F(7A) and F(4A) . . . F(7) contacts (2.832(2), 2.840(2) Å) are comparable with sum of Van der Waals radii (2.88 Å) [13], they are characterized by the specific direction (FFC angles are ∼161°) and thus can be considered as secondary interactions. It is noteworthy that H-bonds and F . . . F contacts are formed only between the centers with opposite configuration in such a manner that, with the exception of the camphor residue, the crystal structure can be ideally described in $P2_1/c$ space group with two independent molecules. Thus the possible reason for diasteromers cocrystallization in (*1S*, *4S*, *4′RS*, *5′RS*)-**4** is the dominance of so stable homochiral supramolecular structure that persists even in the case of "chiral addend". The same was recently found for bicyclic dilactam for which highly stable heterochiral H-bonded structure also led to the diastereoisomers cocrystallization [14].

The principal geometry of two diastereomers is identical. The conformation of thiazoline ring is an envelope with the deviation of the C(5′) atom from the plane of S(1′),C(2′),N(3′),C(4′) atoms by 0.27 Å. The analysis of bond lengths in C(2)N(1)N(2)C(2′)N(3′) has revealed that C(2)=N(1) does not participate in electron density delocalization. If the N(2)–C(2′) bond length is significantly shortened up to 1.330(4) Å, the C(2)–N(1) is practically unperturbed, and C(2) atom deviates by 0.30 Å from the N(1)N(2)C(2′)N(3′)S(1′) plane.

It is noteworthy that an alternative synthetic route to hydrazones **4**–**7** may be the reaction of camphor with 5-fluoro-2-hydrazino-4-hydroxy-4,5-di(polyfluoroalkyl)-1,3-thiazolines [7]. So, we obtained hydrazone (*1S*, *4S*, *4′RS*, *5′RS*)-**4** by interaction of (*1S*, *4S*)-(−)-camphor with *trans*-5-fluoro-2-hydrazino-4-hydroxy-4,5-bis-(trifluoromethyl)-1,3-thiazoline in the presence of catalytic amounts of HCl (Scheme 3). However, this method has proved to be less successful compared with the above, because of the formation of by-products and low yields of the starting hydrazines.

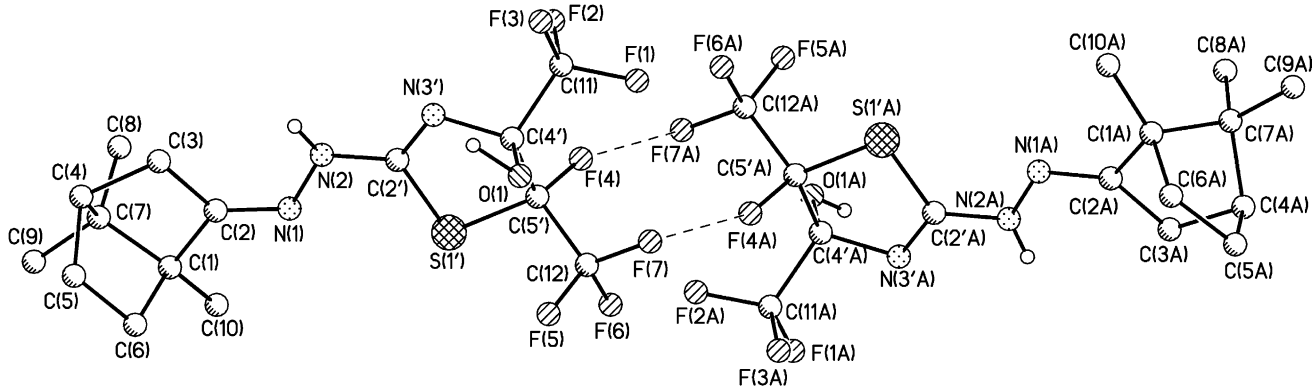


Fig. 1. The general view of the two diastereomers (1S, 4S, 4′R, 5′R)-4 and (1S, 4S, 4′S, 5′S)-4 forming the cocrystal. The important bond lengths (Å) for one of the diastereomers: S(1′)–C(2′) 1.758(4), S(1′)–C(5′) 1.817(4), O(1)–C(4′) 1.396(4), N(1)–C(2) 1.276(5), N(1)–N(2) 1.386(4), N(2)–C(2′) 1.331(5), C(2′)–N(3′) 1.298(5), N(3′)–C(4′) 1.438(5); bond angles (°): C(2′)–S(1′)–C(5′) 88.8(2), C(2)–N(1)–N(2) 115.5(3), C(2′)–N(2)–N(1) 117.7(3), N(3′)–C(2′)–N(2) 123.3(4), N(3′)–C(2′)–S(1′) 119.5(3), N(2)–C(2′)–S(1′) 117.2(3), N(1)–C(2)–C(3) 129.1(3), N(1)–C(2)–C(1) 123.2(3), C(3)–C(2)–C(1) 107.7(3), C(2′)–N(3′)–C(4′) 112.5(3).

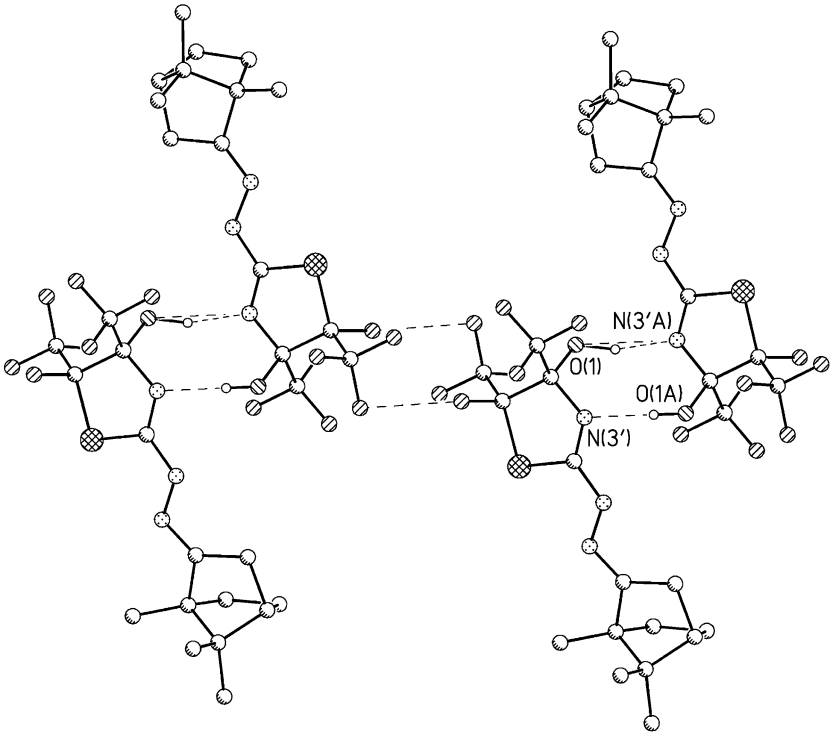
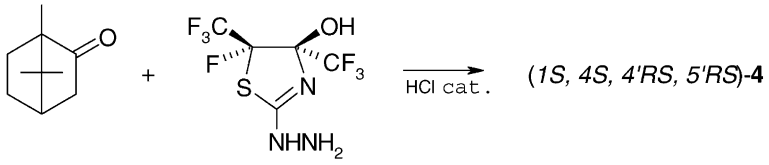


Fig. 2. The scheme illustrating the formation of the chiral helix directed along crystallographic axis ***b***.



Scheme 3.

3. Conclusion

We have developed an approach to the synthesis of unknown fluorocontaining camphor thiazolinylhydrazones, which may be of interest as biologically active compounds [15].

4. Experimental

^{1}H NMR spectra were recorded on Bruker DRX-400 and Tesla BS-567 A spectrometers operating at 400 and 100 MHz, respectively. ^{13}C and ^{19}F NMR spectra were recorded on Bruker DRX-400 instrument operating at 100 and 376 MHz, respectively. Chemical shifts are reported in ppm (δ) downfield from internal tetramethylsilane (TMS) for hydrogen and carbon and internal C_6F_6 for fluorine. Mass spectra were obtained on Varian MAT-311 mass spectrometer at 70 eV. Infrared spectra were obtained on Specord 75 IR spectrometer. The frequencies are reported per centimeter. Melting points were measured in open capillaries and are reported uncorrected. Oxiranes **1–3** [8,9] were prepared according to reported procedures.

*4.1. Crystallographic data for (1S, 4S, 4′R, 5′R)-(**4**) and (1S, 4S, 4′S, 5′S)-(**4**) cocrystal*

$C_{48}H_{54}F_{14}N_6O_2S_2$ cocrystal at 110 K is monoclinic, space group $P2_1$, $a = 11.765(3)$ Å, $b = 11.172(2)$ Å, $c = 19.830(4)$ Å, $\beta = 99.307(4)^\circ$, $V = 2572.0(9)$ Å^3, $Z = 2$, $M = 230.32$, $d_{calc} = 1.391$ g cm^{-3}, μ(Mo Kα) = 1.99 cm^{-1}, $F(0\,0\,0) = 1116$. Intensities of 20,537 reflections were measured with a Smart 1000 CCD diffractometer at 110 K (λ(Mo Kα) = 0.71073 Å, ω-scans with 0.3° step in ω and 10 s per frame exposure, $2\theta < 60^\circ$), and 12,511 (R(int) = 0.0309) independent reflections were used in further refinement. The structure was solved by direct methods and refined by the full-matrix least-squares technique against F^2 in the anisotropic–isotropic approximation. Hydrogen atoms were located from the Fourier synthesis and refined in the riding model. The absolute configuration has been determined by means of the Flack parameter the value of which in the case of (*1S*, *4S*, *4′S*, *5′S*) and (*1S*, *4S*, *4′R′*, *5′R*) configurations for two diastereomers was 0.00(9). The refinement converged to wR2 = 0.1239 and GOF = 0.958 for all independent reflections (R1 = 0.0528 was calculated

against F for 7108 observed reflections with $I > 2(\sigma(I))$. All calculations were performed using SHELXTL PLUS 5.1 on IBM PC AT.

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary no. CCDC–CCDC 184325. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223/336-033; e-mail: deposit@ccdc.cam.ac.uk.

*4.2. Trans-isomer of (1S, 4S)-camphor 5′-fluoro-4′-hydroxy-4′,5′-bis-(trifluoromethyl)-1′,3′-thiazolinyl-2′-hydrazone (1S, 4S, 4′RS, 5′RS)-(**4**) (new compound)*

4.2.1. Method 1

A mixture of oxirane (**1**) (3 g, 13.9 mmol), (*1S*, *4S*)-CTSC (0.5 g, 2.2 mmol) and dioxane (10 ml) was heated in a sealed tube in a boiling water bath for 2 h, with intermittent shaking. After cooling (−70 °C), the tube was opened and the residual oxirane condensed into cooled trap (−70 °C). The precipitate (HF salt of hydrazone, 0.05 g) was filtered off, filtrate was poured into water (150 ml) and allowed to stand for crystallization of the reaction product for 12 h. The resulting precipitate was collected by filtration, washed with water, dried (50–60 °C) and recrystallized from benzene–hexane (∼5:1), then from benzene to afford 0.4 g (0.95 mmol) (43%) of colorless crystals of (*1S*, *4S*, *4′RS*, *5′RS*)-(**4**), mp 149–153 °C; IR (vaseline oil); ν 1608 (s) and 1635 (s) (C=N), 3070 (broad, m) (OH, NH), 3320 (m) cm^{-1} (NH); ^1H NMR ($CDCl_3$): 0.76 (3H, s, CH_3), 0.95 (3H, s, CH_3), 0.98 (s) and 1.19 (s) (1:1, 3H, CH_3), 1.23 (1H, m), 1.40 (1H, m), 1.71–1.95 (3H, m), 2.04 (1H, m), 2.36 (1H, dm, $J = 16.9$ Hz) (hydrogens of bicycloheptane skeleton), 7.18 (2H, broad s, OH, NH); ^{13}H NMR ($CDCl_3$): 10.71 (s) and 10.75 (s) (1:1, C-10), 18.48 (s) and 18.49 (s) (1:1, C-8), 19.34 (s) and 19.45 (s) (1:1, C-9), 27.11 (s, C-5), 32.36 (s) and 32.39 (s) (1:1, C-6), 33.72 (s) and 33.83 (s) (1:1, C-3), 44.03 (s) and 44.05 (s) (1:1, C-4), 48.19 (s) and 48.25 (s) (1:1, C-7), 53.22 (s) and 53.25 (s) (1:1, C-1), 100.19 (dq) and 100.55 (dq) (1:1, $^2J_{CF}$= 32.0 Hz, $^2J_{CF} = 24.6$ Hz, C-4′), 110.72 (dq) and 110.86 (dq) (1:1, $^1J_{CF} = 243.6$ Hz, $^2J_{CF} = 32.5$ Hz, C-5′), 121.28 (qd) and 121.29 (qd) (1:1, $^1J_{CF}$= 284.2 Hz, $^2J_{CF} = 33.9$ Hz, C-8′), 122.09 (q, $^1J_{CF} = 287.4$, C-6′), 165.68 (s) and 165.83 (s) (1:1, C-2′), 170.81 (s) and 171.26 (s) (1:1, C-2); ^{19}F NMR ($CDCl_3$): 14.29 (qq) and 14.49 (qq) (1:1, 1F, $^3J_{FF} = 10.0$ Hz, $^4J_{FF} = 20.8$ Hz, $CF^{10'}$), 83.66 (dq) and 83.69 (dq) (1:1, 3F, $^4J_{FF} = 20.8$, $^5J_{FF} = 4.8$, $CF_3^{7'}$), 90.26 (dq) and 90.30 (dq) (1:1, $^3J_{FF} = 10.0$ Hz, $^5J_{FF} = 4.8$ Hz, $CF_3^{9'}$). Anal. calcd. for $C_{15}H_{18}F_7N_3OS$: C, 42.8; H, 4.3; F, 31.6; N, 10.0; S, 7.6. Found: C, 42.9; H, 4.3; F, 31.7; N, 10.0; S, 7.7.

Crude product obtained by Method A contained *cis*-isomer of (*1S*, *4S*)-camphor 5′-fluoro-4′-hydroxy-4′,5′-bis-(trifluoromethyl)-1′,3′-thiazolinyl-2′-hydrazone (*1S*, *4S*, *4′RS*, *5′SR*)-(**4**) (∼12%) (from ^{19}F NMR data).

^{19}F NMR ($CDCl_3$): 19.53 (m, 1F,), 82.68 (qd) and 82.72 (qd) (1:1, 3F, $^4J_{F,F}$ 3.7 Hz, $^5J_{F,F} = 10.7$ Hz, $CF_3^{7'}$), 88.81 (dq) and 88.83 (dq) (1:1, 3F, $^3J_{F,F} = {}^5J_{F,F} = 10.7$ Hz, $CF_3^{9'}$).

4.2.2. Method 2

Into a stirred solution of hydrazine (**9**) (0.6 g, 2.0 mmol) in 6 ml of H_2O and 10 ml MeOH was added drop-wise 10% solution of HCl (0.5 ml), then a solution of (*1S*)-(−)-camphor (0.4 g, 2.0 mmol) in 4 ml of MeOH. After 0.5 h of heating at reflux the reaction mixture was allowed to stand for 24 h at room temperature for partial evaporation and crystallization of the reaction product. The resulting precipitate was collected by filtration, dried at ∼40 °C and recrystallized from hexane–benzene (1:1) to give 0.2 g (0.5 mmol) (25%) of (*1S*, *4S*, *4′RS*, *5′RS*)-(**4**).

*4.3. Trans-isomer of rac-camphor 5′-fluoro-4′-hydroxy-4′,5′-bis-(trifluoromethyl)-1′,3′-thiazolinyl-2′-hydrazone (1RS, 4RS, 4′RS, 5′RS)-(**4**) (new compound)*

In a similar manner to Method 1, oxirane (**1**) (2.0 g, 9.3 mmol) was treated with rac-CTSC (0.5 g, 2.2 mmol). Recrystallization of crude product from benzene gave 0.6 g (1.4 mmol) (64%) of colorless crystals of (*1RS*, *4RS*, *4′RS*, *5′RS*)-(**4**), mp 149.5–153 °C; IR (vaseline oil); ν 1610 (s) and 1640 (s) (C=N), 3100 (broad, m), (OH, NH), 3320 (m) cm^{-1} (NH); ^1H, ^{19}F and ^{13}C NMR spectra are identical to those of *trans*-isomer of (*1S*, *4S*, *4′RS*, *5′RS*)-(**4**). Anal. calcd. for $C_{15}H_{18}F_7N_3OS$: C, 42.8; H, 4.3; F, 31.6; N, 10.0; S, 7.6. Found: C, 42.7; H, 4.2; F, 31.5; N, 10.0; S, 7.5.

*4.4. Trans-isomer of (1S, 4S)-camphor 5′-fluoro-4′-heptafluoropropyl-4′-hydroxy-5′-trifluoromethyl-1′,3′-thiazolinyl-2′-hydrazone (1S, 4S, 4′RS, 5′RS)-(**6**) (new compound) and trans-isomer of (1S, 4S)-camphor 5′-fluoro-5′-heptafluoropropyl-4′-hydroxy-4′-trifluoromethyl-1′,3′-thiazolinyl-2′-hydrazone (1S, 4S, 4′RS, 5′RS)-(**7**) (new compound)*

In a similar manner, compound (**3**) (2.5 g, 7.9 mmol) was treated with (*1S*, *4S*)-CTSC (1.0 g, 4.4 mmol) in 15 ml of dioxane for 4.5 h. After cooling, the tube was opened and the reaction mixture was poured into water (100 ml). The lower organic layer was separated, washed with water and allowed to stand under a new portion of water for 24 h. The resulting crystals were collected by filtration, dried at 50–60 °C and recrystallized from benzene to give 1.6 g (3.1 mmol) (69.1%) of colorless crystals of (*1S*, *4S*, *4′RS*, *5′RS*)-(**6**) and (*1S*, *4S*, *4′RS*, *5′RS*)-(**7**) (∼39:61), mp 129–158 °C; IR (vaseline oil); ν 1630 (s) and 1650 (s) and 1675 (m) (C=N), 3160 (broad, m) (OH, NH), 3350 (m) cm^{-1} (NH). Anal. calcd. for $C_{17}H_{18}F_{11}N_3OS$: C, 39.2; H, 3.5; F, 40.1; N, 8.1; S, 6.1. Found: C, 39.2; H 3.4; F, 40.1; N, 8.0; S, 6.1; ^1H NMR ($CDCl_3$): 0.762 (s) and 0.773 (s) (1:1, 3H, CH_3), 0.95 (3H, s, CH_3), 0.981 (s) and 0.985 (s) (1:1, 3H, CH_3), 1.22 (1H, m),

1.40 (1H, m), 1.70–1.97 (3H, m), 2.05 (1H, m), 2.35 (1H, d, $J = 16.6$ Hz) (hydrogens of bicycloheptane skeleton), 6.70 (2H, broad s, OH, NH).

(*1S*, *4S*, *4′RS*, *5′RS*)-(**6**): ^{19}F NMR ($CDCl_3$): 13.92 (m, 1F, $CF^{10'}$), 39.23 (2F, $CF_2^{7'}$-AB system, $J_{7'A,7'B} = 286.6$ Hz), 37.99 (m, 1F, $CF_B^{7'}$), 40.49 (t, 1F, $J = 11.7$ Hz, $CF_A^{7'}$), 45.04 (2F, $CF_2^{6'}$-AB system, $J_{6'A,6'B} = 288.5$ Hz), 43.99 (m, 1F, $CF_B^{6'}$), 46.11 (m, 1F, $CF_A^{6'}$), 80.66 (t) and 80.88 (t) (1:1, 3F, $J = 11$ Hz, $CF_3^{8'}$), 90.22 (t) and 90.24 (t) (1:1, 3F, $J = 9.5$ Hz, $CF_3^{9'}$).

(*1S*, *4S*, *4′RS*, *5′RS*)-(**7**): ^{19}F NMR ($CDCl_3$): 15.12 (m) and 15.38 (m) (1F, $C^{10'}$), 38.96 (2F, $CF_2^{7'}$-AB system, $J_{7'A,7'B} = 290.5$ Hz), 37.69 (m, 1F, $CF_B^{7'}$), 40.23 (m, 1F, $CF_A^{7'}$), 48.65 (2F, $CF_2^{6'}$-AB system, $J_{6'A,6'B} = 289.0$ Hz), 43.13 (m, 1F, $CF_B^{6'}$), 54.17 (tq, 1F, $^3J_{F,F} = 8.3$ Hz, $^4J_{F,F} = 13.4$ Hz, $CF_A^{6'}$), 81.20 (dd, 3F, $^4J_{F,F} = 8.3$ Hz, $^4J_{F,F} = 13.4$ Hz, $CF_3^{8'}$), 84.33 (t) and 84.35 (t) (1:1, 3F, $^4J_{FF} = {}^5J_{FF} = 20.9$ Hz, $CF_3^{9'}$).

*4.5. Trans-isomer of (1S, 4S)-camphor 5′-fluoro-4′-hydroxy-4′,5′-bis(pentafluoroethyl)-1′,3′-thiazolinyl-2′-hydrazone (1S, 4S, 4′RS, 5′RS)-(**5**) (new compound)*

In a similar manner, oxirane (**2**) (2.0 g, 6.3 mmol) was treated with (*1S*, *4S*)-CTSC (0.5 g, 2.2 mmol) in 10 ml of dioxane or in 12 ml of CH_3CN. Recrystallization of crude product from benzene gave 0.6 g (1.2 mmol) (52%) (dioxan) or 0.5 g (1.0 mmol) (43%) (CH_3CN) of colorless crystals of (*1S*, *4S*, *4′RS*, *5′RS*)-(5), mp 152–154.5 °C; IR (vaseline oil); ν 1625 (s) and 1650 (m) (C=N), 3200 (broad, m) and 3540 (broad, m) (OH, NH), 3320 (m) cm^{-1} (NH); ^{1}H NMR ($CDCl_3$): 0.77 (3H, s, CH_3), 0.96 (3H, s, CH_3), 1.00 (3H, s, CH_3), 1.92–2.55 (7H, m, hydrogens of bicycloheptane skeleton), 3.63 (2H, broad s, OH, NH); ^{19}F NMR ($CDCl_3$): 17.22 (m, 1F, $CF^{10'}$), 42.23 (2F, $CF_2^{6'}$-AB system, $J_{6'A,6'B} = 292$ Hz), 40.35 (m, 1F, $CF_B^{6'}$), 44.12 (m, 1F, $CF_A^{6'}$), 46.60 (2F, $CF_2^{8'}$-AB system, $J_{8'A,8'B} = 292.0$ Hz), 39.82 (1F, m, $CF_B^{8'}$), 53.39 (1F, m, $CF_A^{8'}$), 82.00 (3F, d, $J = 13.7$ Hz, $CF_3^{7'}$), 83.34 (d) and 83.47 (d) (1:1, 3F, $J = 2.4$ Hz, $CF_3^{9'}$); MS, *m/z* (rel int.): 522 $[M + 1]^+$ (17.6), 520 $[M - 1]^+$ (1.1), 402 $[M–C_2F_5]^+$ (98.5), 373 $[M–C_{10}H_{14}N]^+$ (10.0), 150 $[C_{10}H_{16}N]^+$ (33.5), 119 $[C_2F_5]^+$ (7.7), 69 $[CF_3]^+$(31.6). Anal. calcd. for $C_{17}H_{18}F_{11}N_3OS$: C, 39.2; H, 3.5; F, 40.1; N, 8.1; S, 6.1. Found: C, 39.2; H, 3.5; F, 39.9; N, 8.1; S, 6.1.

*4.6. Hydrate of trans-isomer of (1S, 4S)-camphor 5′-fluoro-5′-heptafluoropropyl-4′-hydroxy-4′-trifluoromethyl-1′,3′-thiazolinyl-2′-hydrazonium fluoride (1S, 4S, 4′RS, 5′RS)-(**8**)·H₂O (new compound)*

In a similar manner, oxirane (**3**) (3.0 g, 9.5 mmol) was treated with (*1S*, *4S*)-CTSC (1.0 g, 4.4 mmol) in 35 ml of MeOH for 4 h. After cooling, the tube was opened, and the reaction mixture was concentrated under reduced pressure. The solid residue was washed with hot $CHCl_3$ and dried at ~80 °C to afford 0.4 g (0.7 mmol) (15%) of salt (*1S*, *4S*, *4′RS*, *5′RS*)-(**8**)·H_2O, white powder, mp 162–163 °C; IR (vazeline oil); ν 1515 (m) and 1630 (m) and 1680 (s) (C=N), 2400–2800 (broad, m) $(NH)^+$, 3140 (broad, m) cm^{-1} (OH, NH); ^{1}H NMR (Me_2SO): 0.69 (s) and 0.72 (s) (1:1, 3H, CH_3), 0.91 (6H, s, $2CH_3$), 1.14–2.36 (7H, m, bicycloheptane skeleton), 7.52 (5H, br.s, OH, NH, HF, H_2O); ^{19}F NMR (Me_2SO): 17.60 (1F, m, $CF^{10'}$), 23.17 (1F, broad s, HF), 40.15 (2F, $CF_2^{8'}$-AB system, $J_{8'A,8'B} = 285.6$ Hz), 38.91 (t, 1F, $J_{FF} = 11.0$ Hz; $F_B^{8'}$), 41.39 (1F, dd, $^3J_{FF} = 9.8$ Hz; $^4J_{F,F} = 25.0$ Hz, $F_A^{8'}$), 50.02 (2F, $CF_2^{7'}$-AB system, $J_{7'A,7'B} = 288.1$ Hz), 43.97 (1F, m, $CF_B^{7'}$), 56.07 (1F, tq, $^3J_{FF} = {}^4J_{F,F} = 11.0$ Hz, $F_A^{7'}$), 82.54 (t, 3F, $^4J_{F,F} = 11.0$ Hz, $CF_3^{9'}$), 86.71 (3F, t, $^4J_{F,F} = {}^5J_{F,F} = 21.4$ Hz, $CF_3^{6'}$); MS, *m/z*, (rel. int.): 523 $[M–OH–F]^+$ (11.9), 521 $[M–H_2O–HF]^+$ (50.0), 452 $[M–H_2O–HF–CF_3]^+$ (45.7), 373 $[M–OH–F–C_{10}H_{16}N]^+$ (27.9), 150 $[C_{10}H_{16}N]^+$ (40.80), 136 $[C_{10}H_{16}]^+$ (14.0), 134 $[C_{10}H_{14}]^+$ (74.4), 69 $[CF_3]^+$ (42.8). Anal. calcd. for $C_{17}H_{21}F_{12}N_3O_2S$: C, 36.5; H, 3.8; F, 40.8; N, 7.5; S, 5.7. Found: C, 36.5; H, 3.5; F, 40.9; N, 7.4; S, 5.7.

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