Reactions of polyfluorinated chalcones with *o*-aminobenzenethiol and its zinc salt

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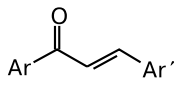
The reactions of polyfluorochalcones with *o*-aminothiophenol in methanol in the presence of HCl afford polyfluorine-substituted 2,3-dihydrobenzo[*b*][1,5]thiazepines. In some cases, the cyclization is accompanied by fluorine substitution in the perfluorophenyl ring. Probably, the formation of thiazepines proceeds through the Michael thia-adduct. The Zn salt of *o*-aminothiophenol reacts with chalcones in DMF exclusively *via* fluorine substitution.

Key words: polyfluorinated chalcones, polyfluorinated 2,4-diaryl-2,3-dihydrobenzo[*b*][1,5]-thiazepines, Michael thia-adducts.

Chalcones (benzalacetophenones, 1,3-diarylprop-2-en-1-ones) are highly reactive due to the presence of the carbonyl group conjugated with the double bond, which provides their interaction with nucleophiles at both the carbonyl group and double bond: Michael addition.[1] Polyfluorine-substituted chalcones have an additional reaction center: the perfluorophenyl ring in which the fluorine atoms are easily substituted by various nucleophilic groups.[2] Reactions of chalcones with binucleophiles leading to a diverse series of heterocyclic compounds are of special interest.[1] So, the interaction of chalcones with *o*-aminothiophenol serves as a method for synthesis of seven-membered heterocycles, 1,5-benzothiazepines, which are widely used pharmacophores.[3—8] In addition, 4-aryl-substituted thiazepines in which the aryl ring is conjugated with the azomethine group are structurally similar to 2-phenylpyridines and related heterocycles, whose complexes find use in phosphorescent organic photoemission diodes.[9]

The reactions of non-fluorinated chalcones and their derivatives mono- and disubstituted in aromatic rings with *o*-aminothiophenol were studied[3—6,10—15] in detail. The reaction is believed to proceed as a coupled addition of the SH group to the double bond of chalcone followed by the formation of the Michael thia-adduct and the subsequent intramolecular cyclization of the latter to benzothiazepine.[10,11]



1a—c

Ar = Ph, Ar´ = C_6F_5 (**a**), Ar = C_6F_5, Ar´ = Ph (**b**), Ar = Ar´ = C_6F_5 (**c**)

The purpose of this work is to study the reactions of polyfluorinated chalcones **1a—c**[16] with *o*-aminothiophenol (**2**) and its zinc salt (**3**).

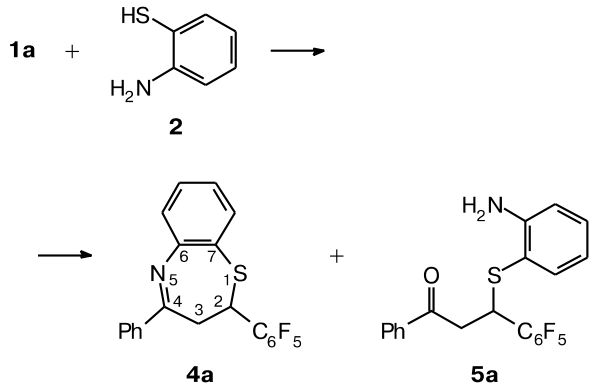
Results and Discussion

We have shown that reflux of polyfluorinated chalcones **1a—c** with an excess of *o*-aminothiophenol (**2**) in methanol in the presence of catalytic amounts of HCl (*cf.* Ref. 11) produces polyfluorosubstituted 1,5-benzothiazepines **4a—c**. It should be mentioned that the reactions proceed with some distinctions, depending on the structure of the starting chalcone. For instance, according to the ^1H and ^{19}F NMR spectral data, when perfluorobenzalacetophenone **1a** is refluxed with 2 moles of thiophenol **2**, the reaction mixture contains approximately equal amounts of 2-(perfluorophenyl)-4-phenyl-2,3-dihydrobenzo[*b*][1,5]thiazepine (**4a**) and the product of addition to the β-C atom, 3-(2-aminophenylthio)-3-(perfluorophenyl)-1-phenylpropan-1-ol (**5a**) (Scheme 1).

The reaction of benzalperfluoroacetophenone **1b** with two moles of compound **2** affords 1,5-benzothiazepine **4b** substituted to the *para*-position of the C_6F_5 group by the *o*-aminothiophenol residue (Scheme 2). The higher mobility of the fluorine atom compared that in the previous reaction (see Scheme 1) is related, most likely, to the withdrawing influence of the azomethine group neighboring to the perfluorophenyl ring. A threefold excess of the reactant was used in the reaction of decafluorosubstituted chalcone **1c** with thiophenol **2**, taking into account that fluorine can be substituted in the both perfluorophenyl groups. However, the single product of this reaction is

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 2, pp. 353—358, February, 2011.
1066-5285/11/6002-361

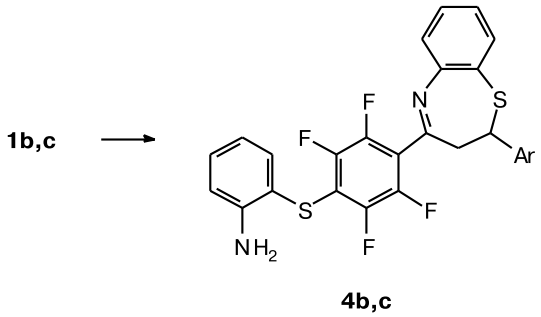
Scheme 1



Reagents and conditions: HCl, MeOH, reflux.

2-(perfluorophenyl)-4-[2,3,5,6-tetrafluoro-4-(2-aminophenylthio)phenyl]-2,3-dihydrobenzo[*b*][1,5]thiazepine (**4c**) (see Scheme 2). Fluorine atom substitution is observed in one of the C_6F_5 groups, namely, in position 4 of the thiazepine ring, and is due most likely to the aforementioned reason.

Scheme 2

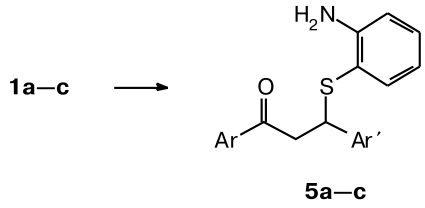


4: Ar = Ph (**b**), C_6F_5 (**c**)

Reagents and conditions: 2, HCl, MeOH, reflux.

To reveal the sequence of steps of formation of benzothiazepines, we synthesized thia-adducts **5a—c** by the reaction of chalcones **1a—c** with thiophenol **2** in methanol at 20 °C for 3—6 h (Scheme 3).

Scheme 3

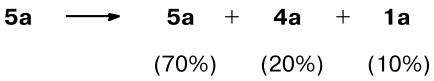


Ar = Ph, Ar′ = C_6F_5 (**a**), Ar = C_6F_5, Ar′ = Ph (**b**), Ar = Ar′ = C_6F_5 (**c**)

Reagents and conditions: 2, MeOH, 20 °C, 3—6 h.

Reflux of synthesized compounds **5a—c** in methanol in the presence of HCl for 3 h gives various mixtures of products. For instance, compound **5a** undergoes partial ring closure to form benzothiazepine **4a** and partially **5a** transforms into chalcone **1a**; however, the most part of **5a** remains unchanged under these conditions (Scheme 4).

Scheme 4

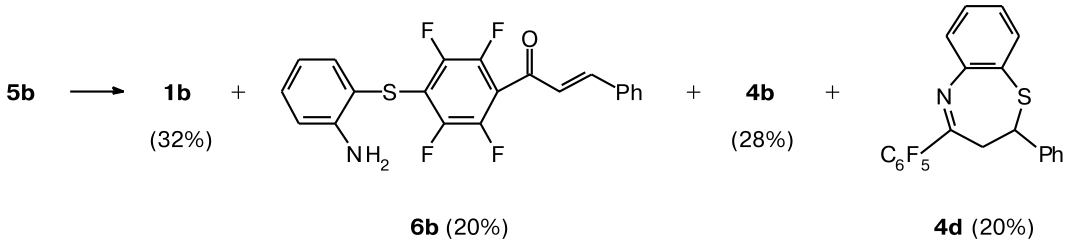


Reagents and conditions: HCl, MeOH, reflux.

On reflux under the same conditions, thia-adduct **5b** is completely consumed. The reaction mixture contains chalcones **1b** and **6b** substituted in the fluorinated ring, as well as benzothiazepines **4b** and **4d**, the former of which also contains the *o*-aminothiophenol residue in the *para*-position of the perfluorophenyl ring (Scheme 5).

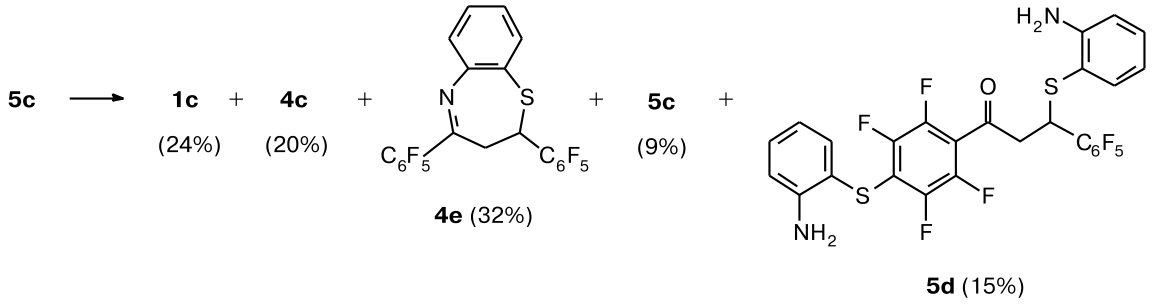
Under these conditions, compound **5c** also forms a complicated mixture of products containing chalcone **1c**, thia-adducts **5c** and **5d**, and benzothiazepines **4c** and **4e**, both substituted in the fluorinated ring and unsubstituted (Scheme 6).

Scheme 5



Reagents and conditions: HCl, MeOH, reflux.

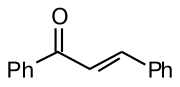
Scheme 6



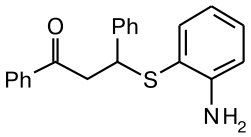
Reagents and conditions: HCl, MeOH, reflux.

The presence of chalcones **1a—c** in the reaction mixtures indicates that the addition to the β-C atom is reversible. It is most likely that the formation of chalcone **6b** and thiazepines **4b**,**c** substituted in the perfluorophenyl rings is the result of interaction of compounds **1b** and **4d**,**e** with *o*-aminophenol evolved upon the decomposition of β-adducts **5b**,**c**. Reversibility of the formation of Michael thia-adducts from non-fluorinated chalcones and *o*-aminothiophenol was not observed earlier; however, it was shown[17] that the cyclization of the thia-adducts to benzothiazepines is reversible and can also contribute to the complicated composition of reaction mixtures formed upon cyclization of thia-adducts **5a—c**.

To explain the lower stability of polyfluorine-substituted thia-adducts **5a—c** compared to that of non-fluorinated compound **5e** (see Ref. 17), we performed the PBE/3z calculations for compounds **1a—c** and **5a—c** and non-fluorinated compounds **1e** and **5e** (Table 1).



1e



5e

Table 1. Total energies (E^{tot}) of compounds **1a—c**,**e** and **5a—c**,**e** and the relative differences of total energies ($\Delta\Delta E$)* according to the data of DFT/PBE/3z calculations

Chalcone	$-E^{tot}_{1}$ /a.u.	Thia-adduct	$-E^{tot}_{5}$ /a.u.	$\Delta\Delta E$ /kcal mol^{-1}
1a	1149.38284	**5a**	1834.79842	3.42
1b	1149.37662	**5b**	1834.78911	5.35
1c	1645.31596	**5c**	2330.72938	4.78
1e	653.43613	**5e**	1338.85716	0

* The relative difference of total energies ($\Delta\Delta E$) were determined with respect to the difference of total energies of compounds **1e** and **5e** ($E^{tot}_{5e} - E^{tot}_{1e}$).

The relative differences in total energies determined with respect to the value of ($E^{tot}_{5e} - E^{tot}_{1e}$) indicate how the thermal effect of the reaction **1a—c** + $H_2NC_6H_4SH \rightarrow$ **5a—c** is smaller than that for the reaction **1e** + $H_2NC_6H_4SH \rightarrow$ **5e**. It seems natural to assume that a decrease in the thermal effect of the direct reaction would favor the occurrence of the backward reaction. The calculated values of relative differences of total energies correlate with the content of products of the backward reactions (chalcones) in the reaction mixtures.

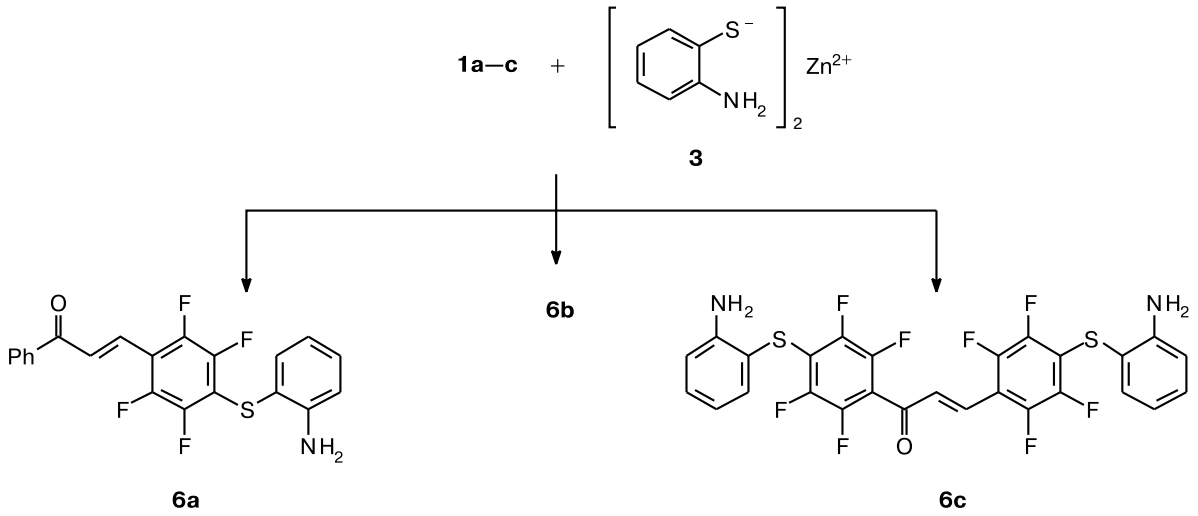
Chalcone **6b** and *para*-substituted chalcones **6a** and **6c** were synthesized by the reaction of chalcones **1a—c** with *o*-aminothiophenol zinc salt (**3**) in DMF at room temperatures. In all cases, the reaction proceeds only *via* nucleophilic substitution of the fluorine atom in the *para*-position of the perfluorophenyl ring (Scheme 7).

The exclusive formation of *para*-substituted chalcones **6a—c** is due to the use of an aprotic polar solvent DMF. For instance, we showed that in DMF at 20 °C *o*-aminothiophenol (**2**) with chalcone **1a** forms predominantly *para*-substituted chalcone **6a** with a minor admixture of β-thia-adduct **5a**; according to the data of ^{1}H and ^{19}F NMR spectroscopy, the ratio **6a** : **5a** is 9 : 1.

The structures of the synthesized compounds were determined by the IR and ^{1}H and ^{19}F NMR spectral data and confirmed by elemental analysis. The yields, melting points, and elemental analysis data are presented in Table 2. The spectral data are given in Table 3.

Thus, in the present work we studied the reactions of three polyfluorinated chalcones, *viz.*, perfluorobenzalacetophenone (**1a**), benzalperfluoroacetophenone (**1b**), and decafluorobenzalacetophenone (**1c**), with *o*-aminothiophenol and its zinc salt. It was shown that the reactions of polyfluorochalcones with *o*-aminothiophenol in methanol in the presence of HCl afforded polyfluoroaryl-substituted 2,3-dihydrobenzo[*b*][1,5]thiazepines and, in several cases, was accompanied by the substitution of the fluorine atom in the *para*-position of the perfluorophenyl ring by the *o*-aminothiophenol residue. It is most likely that the first step is the addition of the thiol group of the reactant

Scheme 7



Reagents and conditions: DMF, 20 °C.

to the β-C atom of chalcone, and the reaction is reversible. The reactions of polyfluorochalcones with *o*-aminothiophenol zinc salt (**3**) in DMF at 20 °C proceed exclusively *via* nucleophilic substitution of the fluorine atom in the *para*-position of the perfluorophenyl rings.

Experimental

NMR spectra were recorded on a Bruker AV-300 instrument at the frequencies 300.13 (^{1}H) and 282.37 (^{19}F) MHz in $CDCl_3$ relative to the signals of residual protons of $CDCl_3$ (^{1}H, δ_H = = 7.24) and C_6F_6 (^{19}F). IR spectra were obtained on a Vector 22 instrument in $CDCl_3$.

GL-MS analysis was carried out on an Agilent Technologies instrument including an Agilent 6890N gas chromatograph and an Agilent 5973N GL-MS system (EI, 70 eV). Conditions: capillary column 30 000×0.25 mm, stationary phase HP-5MS (0.25 μm), helium as a carrier gas (1 mL min^{-1}); temperature programming: 2 min at 50 °C, heating from 50 to 280 °C with a rate of 10 °C min^{-1}, 5 min at 280 °C; temperature of the evaporator 280 °C, temperature of the ion source 230 °C, scan rate 1.2 scan s^{-1} in the mass region 30—800 a.u.

Quantum chemical calculations with full geometry optimization were performed by the DFT/PBE/3z method using the PRIRODA program.[18]

Starting chalcones **1a—c** were synthesized according to the known procedures.[16]

Commercially available *o*-aminothiophenol (98%) (Acros) was used. Dimethylformamide was pre-dried over calcined sieves 3 Å and 9 Å.

Benzothiazepines 4a—c (general procedure). Chalcone **1a—c** (1 mmol) was added to a solution of *o*-aminothiophenol (**2**) (2 mmol for **1a,b**, 3 mmol for **1c**) in MeOH (15 mL), and then 3 droplets of concentrated HCl were added with magnetic stirring. The reaction was refluxed for 3 h and cooled down. To isolate thiazepines **4a,b**, the reaction mixture was poured onto ice and the precipitate that formed was filtered off, washed with water, and dried in air. To isolate thiazepine **4c**, the reaction mixture was evaporated and the oily residue was triturated with hexane—diethyl ether (1 : 1). The products obtained were analyzed by ^{1}H and ^{19}F NMR methods. Pure compounds were isolated by recrystallization from EtOH. Thiazepine **4a** was prepurified by chromatography on a column with Al_2O_3 (hexane—benzene (1 : 1) as eluent). 2-(Perfluorophenyl)-4-phenyl-2,3-dihydrobenzo[*b*][1,5]thiazepine (**4a**), 2-(phenyl)-4-[2,3,5,6-tetrafluoro-4-(2-aminophenylthio)phenyl]-2,3-dihydrobenzo[*b*]-[1,5]thiazepine (**4b**), and 2-(perfluorophenyl)-4-[2,3,5,6-tetrafluoro-4-(2-aminophenylthio)phenyl]-2,3-dihydrobenzo[*b*]-[1,5]thiazepine (**4c**) were obtained.

β-Thia-adducts 5a—d (general procedure). *o*-Aminothiophenol (**2**) (138 mg, 1.1 mmol) was added to a suspension of chalcone **1a—c** (1 mmol) in MeOH (15 mL). The reaction mixture was magnetically stirred at room temperature (for 6 h in the case of **1a**, for 3 h in the case of **1b—c**). To isolate compounds **5a** and **5c**, the reaction mixture was poured onto ice, the precipitate that formed was filtered off, washed, and dried in air, and 3-(2-aminophenylthio)-3-(perfluorophenyl)-1-phenylpropan-1-one (**5a**), and 3-(2-aminophenylthio)-1,3-bis(perfluorophenyl)propan-1-one (**5c**) were obtained. To isolate 3-(2-aminophenylthio)-1-(perfluorophenyl)-3-phenylpropan-1-one (**5b**), the precipitate formed in the reaction mixture was filtered off, washed, and dried in air; an additional amount of compound **5b** was precipitate with water from the filtrate. Under the above described conditions, the reaction of chalcone **1c** with *o*-aminothiophenol (**2**) (2 mol) afforded a mixture of compound **5c** and 3-(2-aminophenylthio)-1-[4-(2-aminophenylthio)-2,3,5,6-tetrafluorophenyl]-3-(perfluorophenyl)propan-1-one (**5d**) in the ratio 2 : 1. *para*-Substituted thia-adduct **5d** was isolated from this mixture by recrystallization from EtOH.

Reaction of chlacone 1a with *o*-aminothiophenol (2) in DMF. Thiophenol **2** (0.25 g, 2 mmol) was added to a suspension of chalcone **1a** (0.3 g, 1 mmol) in DMF (15 mL). The reaction mixture was magnetically stirred at room temperature for 4 h

Table 2. Conditions of synthesis, yields, melting points, and elemental analysis data for compounds **4a—c**, **5a—d**, and **6a—c**

Starting chalcone	Ratio **1** : **2**	Product	Yield (%)	M.p./°C (solvent)	Found / Calculated (%)					Molecular formula
					C	H	F	N	S	
1a	1 : 2	**4a**	50	145—147 (ethanol)	62.26 62.22	2.98 2.98	23.10 23.43	3.59 3.46	8.40 7.91	$C_{21}H_{12}NSF_5$
1b	1 : 2	**4b**	88	120—123 (ethanol)	63.40 63.51	3.40 3.55	14.94 14.88	5.75 5.50	12.40 12.56	$C_{27}H_{18}N_2S_2F_4$
1c	1 : 3	**4c**	80	172—175 (ethanol)	54.10 54.00	2.31 2.18	27.93 28.47	4.89 4.67	10.62 10.68	$C_{27}H_{13}N_2S_2F_9$
1a	1 : 1	**5a**	69	96—99 (hexane)	58.81 59.57	3.31 3.33	22.48 22.44	3.36 3.31	7.43 7.57	$C_{21}H_{14}NOSF_5$
1b	1 : 1	**5b**	81	116—118 (hexane)	59.83 59.57	3.35 3.33	22.49 22.44	3.26 3.31	7.76 7.57	$C_{21}H_{14}NOSF_5$
1c	1 : 1	**5c**[a]	68	109—112[b]	49.07 49.13	1.90 1.77	37.08 37.01	2.66 2.73	6.26 6.25	$C_{21}H_9NOSF_{10}$
1c	1 : 2	**5d**	65[c]	119—122 (hexane)	52.18 52.43	2.43 2.44	27.64 27.64	4.46 4.53	10.32 10.37	$C_{27}H_{15}N_2OS_2F_9$
1a	1 : 2	**6a**	55	134—137[d]	62.69 62.68	3.43 3.26	18.80 18.64	3.28 3.48	8.33 7.97	$C_{21}H_{13}NOSF_4$
1b	1 : 2	**6b**	73	104—107[d]	62.64 62.68	3.36 3.26	18.90 18.64	3.39 3.48	7.71 7.97	$C_{21}H_{13}NOSF_4$
1c	1 : 2	**6c**[e]	98	—	—	—	—	—	—	$C_{27}H_{14}N_2OS_2F_8$

[a] MS, *m/z*: $[M]^+$, found 513.0235, calculated 513.0240, $C_{21}H_9NOSF_{10}$.
[b] The product was purified by washing with pentane.
[c] The content of the compound **5d** in the reaction mixture according to the ^{19}F NMR spectral data is presented.
[d] The compound was isolated in the pure form by column chromatography on Al_2O_3 (benzene as eluent).
[e] MS, *m/z*: $[M]^+$, found 598.0423, calculated 598.0414, $C_{27}H_{14}N_2OS_2F_8$.

Table 3. ^1H and ^{19}F NMR ($CDCl_3$) and IR spectra ($CHCl_3$) of compounds **4a—d**, **5a—d**, and **6a—c**

Compound	^1H NMR, δ_H (*J*/Hz)	^{19}F NMR*, δ_F	IR, ν/cm^{-1}
4a	3.24 (dd, 1 H, $H_a(3)$, $J_1 = 13.0$, $J_2 = 5.0$); 3.31 (t, 1 H, $H_b(3)$, $J_1 = J_2 = 13.0$); 5.40 (dd, 1 H, H(2), $J_1 = 13.0$, $J_2 = 5.0$); 7.16 (td, 1 H_{arom}, $J_1 = J_2 = 7.5$, $J_3 = 1.5$); 7.32 (dd, 1 H_{arom}, $J_1 = 7.5$, $J_2 = 1.5$); 7.46—7.56 (m, 4 H_{arom}); 7.61 (br.d, 1 H_{arom}, $J = 7.5$); 8.06 (m, 2 H_{arom})	0.53, 6.81, 22.27 (2 : 1 : 2)	1525 (C—F); 1613 (C=N)
4b	2.91 (dd, 1 H, $H_a(3)$, $J_1 = 13.0$, $J_2 = 5.0$); 3.12 (t, 1 H, $H_b(3)$, $J_1 = J_2 = 13.0$); 4.48 (br.s, 2 H, NH_2); 5.03 (dd, 1 H, H(2), $J_1 = 13.0$, $J_2 = 5.0$); 6.71 (m, 2 H_{arom}); 7.13—7.29 (m, 8 H_{apom}); 7.47 (td, 1 H_{arom}, $J_1 = J_2 = 7.5$, $J_3 = 1.5$); 7.57 (br.d, 1 H_{arom}, $J = 7.5$); 7.64 (dd, 1 H_{arom}, $J_1 = 7.5$, $J_2 = 1.5$)	21.37, 28.74 (1 : 1)	1487 (C—F); 1612 (C=N); 3393, 3490 (NH_2)
4c	2.82 (dd, 1 H, $H_a(3)$, $J_1 = 13.0$, $J_2 = 5.0$); 3.41 (t, 1 H, $H_b(3)$, $J_1 = J_2 = 13.0$); 4.44 (br.s, 2 H, NH_2); 5.45 (dd, 1 H, H(2), $J_1 = 13.0$, $J_2 = 5.0$); 6.69—6.74 (m, 2 H_{arom}); 7.16—7.64 (m, 6 H_{arom})	0.69, 7.35, 21.15, 22.54, 29.00 (2 : 1 : 2 : 2 : 2)	1468, 1523 (C—F); 1612 (C=N); 3393, 3490 (NH_2)
4d	2.91 (dd, 1 H, $H_a(3)$, $J_1 = 13.0$, $J_2 = 5.0$); 3.15 (t, 1 H, $H_b(3)$, $J_1 = J_2 = 13.0$); 5.04 (dd, 1 H, H(2), $J_1 = 13.0$, $J_2 = 5.0$); 6.95—7.67 (m, 9 H, H_{arom})	0.96, 9.71, 21.31 (2 : 1 : 2)	
5a	3.78 (d, 2 H, CH_2, $J = 7.0$); 4.53 (br.s, 2 H, NH_2); 5.10 (t, 1 H, CH, $J_1 = J_2 = 7.0$); 6.55 (t, 1 H_{arom}, $J_1 = J_2 = 7.5$); 6.70 (d, 1 H_{arom}, $J = 7.5$); 7.05—7.17 (m, 2 H_{arom}); 7.42—7.63 (m, 3 H_{arom}); 7.91 (d, 2 H_{arom}, $J = 7.5$)	–0.62, 6.00, 20.45 (2 : 1 : 2)	1501, 1519 (C—F); 1687 (C=O); 3373, 3485 (NH_2)

(*to be continued*)

Table 3 (*continued*)

Compound	^{1}H NMR, δ_H (J/Hz)	^{19}F NMR*, δ_F	IR, ν/cm^{-1}
5b	3.49 (d, 2 H, CH_2, J = 7.0); 4.31 (br.s, 2 H, NH_2); 4.60 (t, 1 H, CH, $J_1 = J_2$ = 7.0); 6.54 (td, 1 H_{arom}, $J_1 = J_2$ = 8.0, J_3 = 1.5); 6.67 (dd, 1 H_{arom}, J_1 = 8.0, J_2 = 1.5); 7.04—7.27 (m, 7 H_{arom})	1.93, 13.12, 21.38 (2 : 1 : 2)	1495, 1522 (C—F); 1711 (C=O); 3374, 3480 (NH_2)
5c	3.67 (d, 2 H, CH_2, J = 7.0); 4.44 (br.s, 2 H, NH_2); 5.03 (t, 1 H, CH, $J_1 = J_2$ = 7.0); 6.56 (t, 1 H_{arom}, $J_1 = J_2$ = 8.0); 6.70 (d, 1 H_{arom}, J = 8.0); 7.06 (d, 1 H_{arom}, J = 8.0); 7.14 (t, 1 H_{arom}, $J_1 = J_2$ = 8.0)	–0.14, 2.46, 6.69, 14.20, 20.47, 21.59 (2 : 2 : 1 : 1 : 2 : 2)	
5d	3.64 (d, 2 H, CH_2, J = 7.0); 4.40 (br.s, 4 H, 2 NH_2); 5.00 (t, 1 H, CH, $J_1 = J_2$ = 7.0); 6.55 (t, 1 H_{arom}, $J_1 = J_2$ = 8.0); 6.70 (m, 3 H_{arom}); 7.01—7.21 (m, 3 H_{arom}); 7.54 (d, 1 H_{arom}, J = 8.0)	–0.23, 6.79, 20.46, 21.06, 29.36 (2 : 1 : 2 : 2 : 2)	
6a	4.43 (c, 2 H, NH_2); 6.63—6.75 (m, 2 H_{arom}); 7.17 (t, 1 H_{arom}, $J_1 = J_2$ = 8.0); 7.44—7.66 (m, 4 H_{arom}); 7.99 (d, 2 H_{arom}, J = 8.0); 7.77, 7.83 (AB system, 2 H, CH=CH)	22.84, 27.75 (1 : 1)	1477 (C—F); 1671 (C=O); 3394, 3481 (NH_2)
6b	4.45 (br.s, 2 H, NH_2); 6.55—7.65 (m, 11 H, CH=CH, 9 H_{arom})	21.15, 29.25 (1 : 1)	1469 (C—F); 1657 (C=O); 3393, 3491 (NH_2)
6c	4.40 (br.s, 4 H, 2 NH_2); 6.55—7.68 (m, 10 H, CH=CH, 8 H_{arom})	21.36, 23.28, 27.62, 29.29 (1 : 1 : 1 : 1)	1469 (C—F); 1635(C=O); 3383, 3473 (NH_2)

* The intensity ratio is given in parentheses.

and poured onto ice. The precipitate that formed was filtered off, washed with water, and dried in air. According to the data of ^{1}H and ^{19}F NMR spectroscopy, the isolated precipitate (0.39 g) contained a mixture of compounds **6a** and **5a** in the ratio 9 : 1.

Conversion of thia-adducts 5a—c. Three droplets of concentrated HCl were added to a solution of compound **5a—c** (0.3 g) in MeOH (15 mL) and the mixture was refluxed for 3 h, cooled, and poured onto ice. In the case of the starting compound **5a**, the precipitate that formed was filtered off, washed with water, and dried in air. Oily residues that formed from thia-adducts **5b—c** were extracted with diethyl ether and the extract was dried with $CaCl_2$ and evaporated. The reaction products were analyzed by ^{1}H and ^{19}F NMR methods.

The reaction mixture obtained in the case of compound **5b** was separated by chromatography on Al_2O_3: at first, column chromatography (hexane as eluent) and then preparative TLC (benzene—hexane (1 : 1) mixture as eluent) were used. Two fractions were obtained, which contained according to the ^{1}H and ^{19}F NMR spectral data 3-(perfluorophenyl)-1-phenylprop-2-en-1-one (**1b**) and 4-(perfluorophenyl)-2-phenyl-2,3-dihydrobenzo[*b*][1,5]thiazepine (**4d**) (fraction 1) and substituted in the fluorinated ring benzothiazepine **4b** and 1-[4-(2-aminophenylthio)-2,3,5,6-tetrafluorophenyl]-3-phenylprop-2-en-1-one (**6b**) (fraction 2). Compounds **1b**, **4b**, and **6b** were identified in mixtures by the ^{1}H and ^{19}F NMR spectral data and by comparison with the spectra of authentic samples. We failed to isolate thiazepine **4d** in the pure form from the reaction mixture. Two products, whose molecular weights corresponded to compounds **1b** and **4d**, were found in the sample of fraction 1 by the LC-MS method.

The components of the reaction mixture obtained from compound **5c** were identified by comparison of the ^{1}H and ^{19}F NMR spectra with the spectra of authentic samples (for compounds **1c**, **4c**, **5c**, and **5d**). The product, whose molecular weight corresponded to benzothiazepine **4e**, was found in the reaction mixture by the LC-MS method.

Reactions of chalcones 1a—c with *o*-aminothiophenol zinc salt (general procedure). *o*-Aminothiophenol zinc salt (**3**) (380 mg, 2 mmol) was added to a suspension of chalcone **1a—c** (1 mmol) in DMF (20 mL). The mixture was magnetically stirred at room temperature for 5 h and poured onto ice. The precipitate that formed was filtered off and dissolved in diethyl ether. A residue of the zinc salt was filtered off and the filtrate was dried with $MgSO_4$ and evaporated. The products were isolated by chromatography on a column with Al_2O_3 (benzene as eluent). 3-[4-(2-Aminophenylthio)-2,3,5,6-tetrafluorophenyl]-1-phenylprop-2-en-1-one (**6a**), 1-[4-(2-aminophenylthio)-2,3,5,6-tetrafluorophenyl]-3-phenylprop-2-en-1-one (**6b**), and 1,3-bis[4-(2-aminophenylthio)-2,3,5,6-tetrafluorophenyl]prop-2-en-1-one (**6c**) were obtained.

References

1. D. N. Dhar, *The Chemistry of Chalcones and Related Compounds*, Wiley-Interscience, New York—Chichester—Brisbane—Toronto, 1981, 285 pp.
2. N. A. Orlova, E. F. Maior, T. N. Gerasimova, *Izv. Sib. Otd. Akad. Nauk SSSR*, *Ser. Khim. Nauk,* 1989, **3**, 117 [*Izv. Sib. Otd. Akad. Nauk SSSR*, *Ser. Khim. Nauk*, 1989, **3**, 117 (in Russian)].
3. A. Lévai, *Chem. Heterocycl. Comp.*, 1986, **22**, 1161.
4. M. Kodomari, T. Noguchi, T. Aoyama, *Synth. Commun.*, 2004, **10**, 1783.
5. G. L. Khatik, R. Kumar, A. K. Chakraborti, *Synthesis*, 2007, **4**, 541.

6. S. Pant, B. Singhal, M. Upreti, U. C. Pant, *Molecules*, 1998, **3**, 159.
7. A. Yadav, A. Awasthi, N. K. Rao, *Eur. J. Med. Chem.*, 2009, **44**, 1.
8. D. Cai, J. G. Mulle, D. T. Yue, *Mol. Pharm.*, 1997, **51**, 872.
9. K. Świderek, P. Paneth, *J. Phys. Org. Chem.*, 2009, **22**, 845.
10. W. D. Stephens, L. Field, *J. Org. Chem.*, 1959, **24**, 1576.
11. A. K. Gupta, V. K. Singh, U. C. Pant, *Indian J. Chem., Sect. B*, 1983, **22**, 1057.
12. M. Zahouily, Y. Abrouki, A. Rayadh, S. Sebti, H. Dhimane, M. David, *Tetrahedron Lett.*, 2003, **44**, 2463.
13. M. Zahouily, Y. Abrouki, A. Rayadh, *Tetrahedron Lett.*, 2002, **43**, 7729.
14. Y. Abrouki, M. Zahouily, A. Rayadh, B. Bahlaouan, S. Sebti, *Tetrahedron Lett.*, 2002, **43**, 8951.
15. M. S. Khanna, D. Kumar, C. P. Garg, R. P. Kapoor, *Indian J. Chem., Sect. B*, 1995, **34**, 333.
16. R. Filler, V. D. Beaucaire, H. H. Kang, *J. Org. Chem.*, 1975, **40**, 935.
17. V. D. Orlov, N. N. Kolos, N. N. Ruzhitskaya, *Khim. Geterotsikl. Soedin.*, 1983, 1638 [*Chem. Heterocycl. Compd.* (*Engl. Transl.*), 1983, **19**, 1293].
18. D. N. Laikov, *Chem. Phys. Lett.*, 1997, **281**, 151.

Received June 30, 2010;
in revised form November 12, 2010