ISSN 1070-4280, Russian Journal of Organic Chemistry, 2015, Vol. 51, No. 2, pp. 253–260. © Pleiades Publishing, Ltd., 2015.
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# Reactions of Polyfluorochalcones with *o*- and *p*-Phenylenediamines. Synthesis and Intramolecular Transformations of Polyfluorinated 2,4-Diaryl-2,3-dihydrobenzo-1*H*-1,5-diazepines

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Received October 15, 2014

**Abstract**—Polyfluorochalcones react with *o*-phenylenediamine in ethanol and 2-propanol in the presence of triethylamine or benzyltriethylammonium chloride (TEBAC) affording polyfluorinated 2,4-diaryl-2,3-dihydrobenzo-1*H*-1,5-diazepines. Along with the latter in the presence of triethylamine Michael aza-adducts presumably formed, and at the use of TEBAC in 2-propanol products of intramolecular cyclization and rearrangement of benzo-1,5-diazepines, dihydrobenzimidazo[1,2-*a*]quinolines were obtained. The reactions of polyfluorochalcones with *p*-phenylenediamine in ethanol or DMF proceed mostly with the substitution of the *para*-fluorine atom in the perfluorophenyl rings.

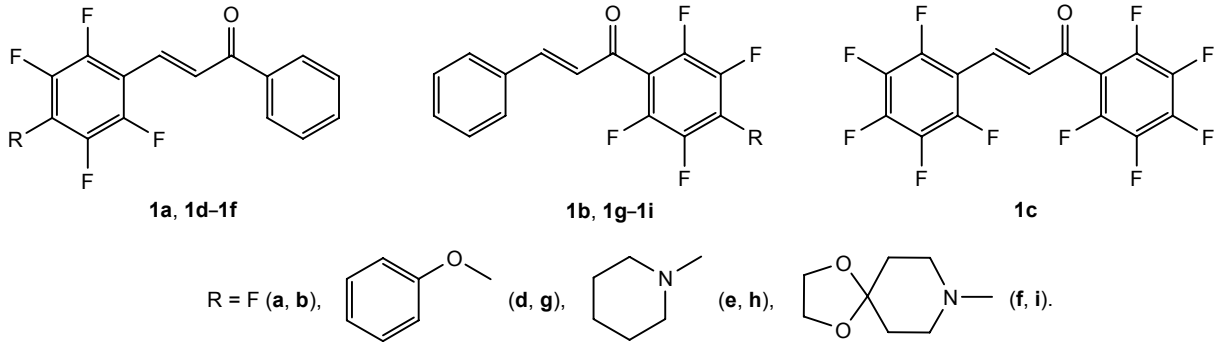
**DOI:** 10.1134/S1070428015020207

Chalcones reaction with *o*-phenylenediamine is one of the main procedures of the preparation of benzo-1*H*-1,5-diazepines [1], an important heterocycle class with versatile biological actions used as antidepressants, tranquilizing, antiphlogistic, anticonvulsant, antifeedant, antibacterial, and analgesic agents [2–5]. The synthesis of benzo-1,5-diazepines from chalcones and *o*-phenylenediamine is commonly carried out in the presence of bases, acids, or salts [1, 6–8]. It is expectable that fluorine atoms and polyfluorinated residues in the benzodiazepine molecule would significantly affect its biological properties [9, 10].

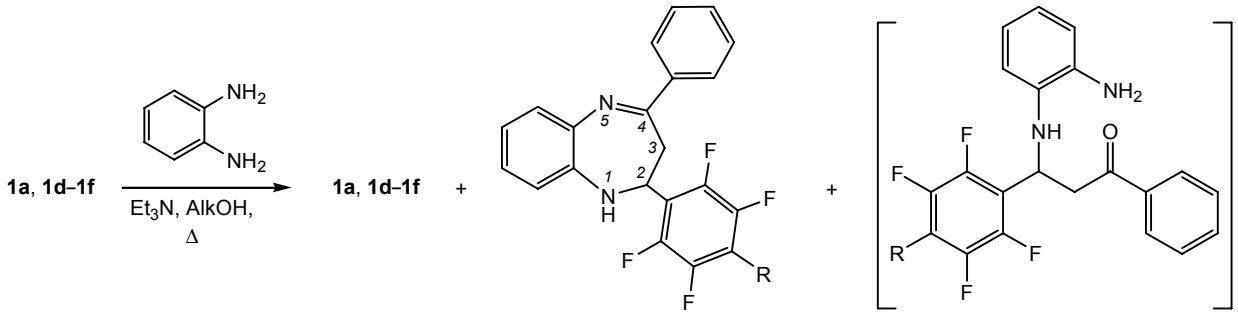
We formerly investigated reactions of polyfluorinated chalcones with nitrogen binucleophiles: hydrazine hydrate, phenylhydrazine [11], *o*-aminothiophenol [12] leading to the formation of various polyfluorinated azaheterocycles. The preliminary communication [13] contains the description of the first results of reactions between polyfluorochalcones **1a–1c** and *o*-phenylenediamine. In this study the number of substrates and reagents was extended and the optimization of the reaction conditions was attempted.

The reaction with *o*-phenylenediamine was performed for polyfluorinated chalcones **1a–1i**, with *p*-phenylenediamine, for compounds **1a–1c**.

Taking into consideration the easy substitution of fluorine in the perfluorophenyl rings of chalcones at



**Scheme 1.**




**1a–2a–3a** 29 : 6 : 65 (EtOH, 5 h) **1e–2e–3e** 37 : 34 : 29 (EtOH, 21 h)

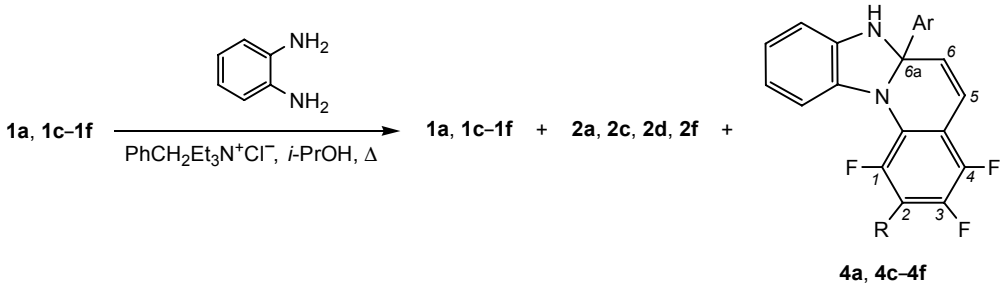
**1d–2d–3d** 26 : 13 : 61 (EtOH, 5 h) **1f–2f–3f** 38 : 41 : 21 (*i*-PrOH, 28 h)

the treatment with nucleophiles [14] we used a large excess of *o*-phenylenediamine (7 mol) to avoid "coupling" of two and more chalcone molecules through a reagent molecule linker. The reactions were carried out in alcohols (ethanol and 2-propanol) in the presence of triethylamine or triethylbenzyl ammonium chloride (TEBAC), which also were used in excess.

The direction of the reaction is governed both by the structure of the initial chalcone and the reaction conditions. At boiling pentafluorobenzalacetophenone **1a** and its derivatives **1d–1f** with *o*-phenylenediamine in ethanol in the presence of triethylamine for 4–5 h, regardless of a large excess of the reagent, the complete conversion of the initial chalcones was not attained. Reaction mixtures alongside the chalcones contained 2,3-dihydro-1*H*-benzo-1,5-diazepines **2a** and **2d–2f** and compounds which we suggested to be Michael aza-adducts **3a** and **3d–3f** and which apparently were the benzodiazepine precursors (Scheme 1). The latter is confirmed by a virtually total conversion of β-adduct **3a** in diazepine **2a** at prolonging the reaction to 22 h. However chalcones **1e** and **1f** were not completely consumed even in 21–28 h, apparently due to the lower electron-acceptor influence of the piperidine-substituted polyfluorophenyl ring on the electrophilicity of the contiguous β-carbon atom. The TLC monitoring of the reaction shows that at increasing the reaction time the content of the β-adducts **3** in the reaction mixture decreases, and that of benzodiazepines **2** grows.

Aza-adducts **3a** and **3d–3f** were not isolated; evidently, they are not sufficiently stable at chromatographing on aluminum oxide. The presumable structures of compounds **3** were established from the NMR data on the reaction mixtures, same as the structures of compounds obtained in the reactions of polyfluorochalcones with piperazine [15] and *o*-amino-thiophenol [12]. For instance, in the $^1$H NMR spectrum of the mixture obtained from chalcone **1a** characterictic signals are observed of the *ABX* system of β-aza-adduct **3a**: 5.54 d.t [$J_1$ 11 Hz (CHNH), $J_2$ = $J_3$ = 7 Hz (C<u>H</u>-$CH_2$)] and 3.58, 3.80 d.d ($CH_2$, $J_1$ 17, $J_2$ = $J_3$ = 7 Hz). Besides a doublet from the NH group at 3.96 ppm, $J$ 11 Hz, a broadened singlet of the $NH_2$ group at 3.36 ppm, and multiplets of aromatic protons at 6.69, 7.43, and 7.95 ppm also correspond to compound **3a**. $^{19}$F NMR

**Scheme 2.**




**1a–2a–4a** 10 : 23 : 67 **1d–2d–4d** 7 : 44 : 49 **1f–2f–4f** 28 : 13 : 59

**1c–2c–4c** 22 : 57 : 21 **1e–2e–4e** 7 : 0 : 93

spectrum contains three signals of fluorine atoms from the pentafluorophenyl group at 0.22, 6.63, and 18.50 ppm.

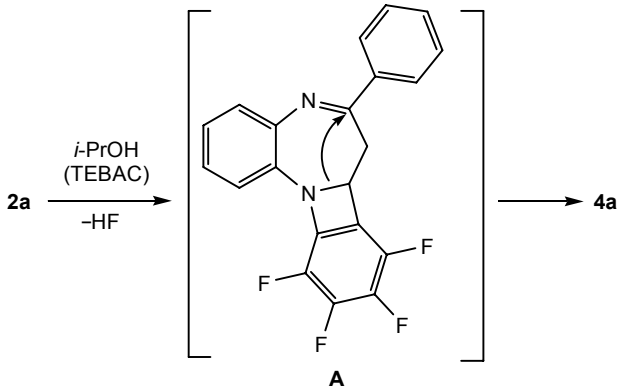
Isomeric to chalcone **1a** benzalpentafluoroacetophenone **1b** and its derivatives **1g–1i** do not react under these conditions with *o*-phenylenediamine, and the decafluoro-substituted chalcone **1c** provided an intractable complex mixture.

Boiling of polyfluorobenzalacetophenones **1a** and **1c**–**1f** with excess *o*-phenylenediamine in 2-propanol in the presence of TEBAC led to the formation of a mixture of benzodiazepines **2** and polyfluoro-6a-phenyl-6a,7-dihydrobenzimidazo[1,2-*a*]-quinolines **4** (Scheme 2); the ratios of compounds given in the Scheme were obtained from $^{19}$F NMR data.

The structures of compounds **2a** and **4a** were established in [13] from the data of X-ray diffraction analysis and $^{1}$H, $^{19}$F NMR spectra. NMR spectra of compounds **2c–2f** and **4c–4f** have similar appearance, are in agreement with their structures, and are confirmed by the high resolution mass spectra.

The formation of benzimidazoquinolines **4** we ascribed in [13] to an intramolecular substitution of the *ortho*-fluorine atom in the polyfluorophenyl group of benzodiazepines **2** formed in the first stage of the reaction followed by their skeleton rearrangement into compounds **4** via unstable intermediate structure **A** (Scheme 3). This Scheme was confirmed by the conversion of benzodiazepine **2a** into compound **4a** under the reaction conditions, and also in the absence of TEBAC, i.e., the latter was not the catalyst of the rearrangement.

**Scheme 3.**

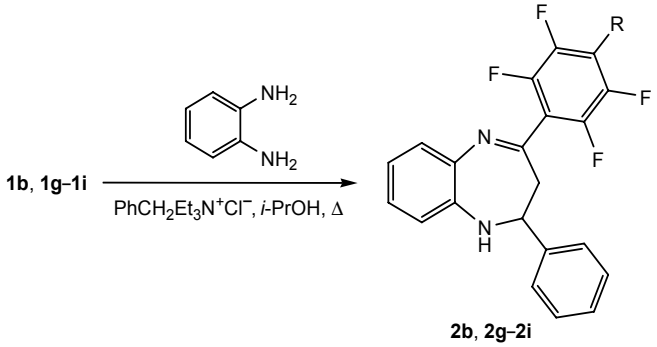



We considered in [13] an alternative reaction mechanism of benzimidazoquinolines **4** formation consisting in the primary reaction of the reagent at the carbonyl group of the chalcone giving a cyclic aminal followed by its intramolecular cyclization involving the substitution of the *ortho*-fluorine atom in the pentafluorophenyl ring. However this mechanism appears less probable since the common amine reactions with chalcones proceed at the β-C atom to form Michael adducts [16]; rare examples of 1,2-addition have been observed in chalcones reactions with *p*-phenylenediamine in acid or strongly alkaline environment [17, 18].

Piperidine and triethylamine inhibit the conversion of benzodiazepine **2a** in benzimidazoquinoline **4a**. We cannot yet understand this fact since usually the presence of amines favors the nucleophilic substitution of fluorine.

Benzalpentafluoroacetophenone **1b** and its *para*-derivatives **1g–1i** at boiling with excess *o*-phenylenediamine in 2-propanol in the presence of TEBAC afford the corresponding benzodiazepines **2b** and **2g–2i** (Scheme 4), where the possibility of the *ortho*-cylization is excluded. The yields of isolated compounds are low, yet they are the principal products. Along with benzodiazepines **2** small amounts (up to 25%) of initial chalcones are present, and also the impurity of nonidentified products having according to NMR data close structure for all initial chalcones. We failed to isolate these products from either of the reaction mixtures.

**Scheme 4.**



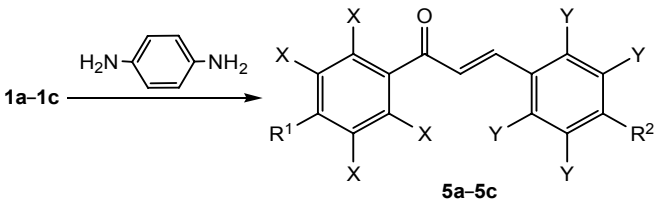

42% (**b**), 31% (**g**), 26% (**f**), 19% (**i**)

We also investigated the reaction of chalcones **1a–1c** with *p*-phenylenediamine. These reactions with nonfluorinated chalcones remain poorly studied, and the known data show the prevailing formation of Schiff's bases [17, 18].

The reaction of chalcone **1a** was carried out in the same conditions as with *o*-phenylenediamine: in ethanol in the presence of triethylamine. The only compound isolated from the reaction mixture was 3-[4-(4–aminophenylamino)-2,3,5,6-tetrafluorophenyl]-1-

phenylprop-2-en-1-one **5a** (Scheme 5). Reactions of chalcones **1b** and **1c** with *p*-phenylenediamine were performed in DMF to avoid the formation of the products of the *ortho*-substitution [14]. In the presence of $Et_3N$ we obtained in low yields chalcones **5b** and **5c** substituted with a (4-amino)phenylamino group in the *para*-position of the fluorinated rings (Scheme 5).

**Scheme 5.**




Reagents and conditions: EtOH–$Et_3N$, Δ, 7 h, X = $R^1$ = H, Y = F, $R^2$ = $HNC_6H_4NH_2$-*p*, 72% (**a**); DMF–$Et_3N$, 20°C, 4 h, Y = $R^2$ = H, X = F, $R^1$ = $HNC_6H_4NH_2$-*p*, 18% (**b**); DMF–$Et_3N$, 20°C, 4 h, X = Y = F, $R^1$ = $R^2$ = $HNC_6H_4NH_2$-*p*, 28% (**c**).

The low yield of the disubstituted chalcone **5c** may be due to the formation of β-aza-adducts. Same as in the reaction with *o*-phenylenediamine we failed to isolate the β-adduct from the reaction mixture, therefore the structure of bis-aza-adduct **6c** is presumable [15].

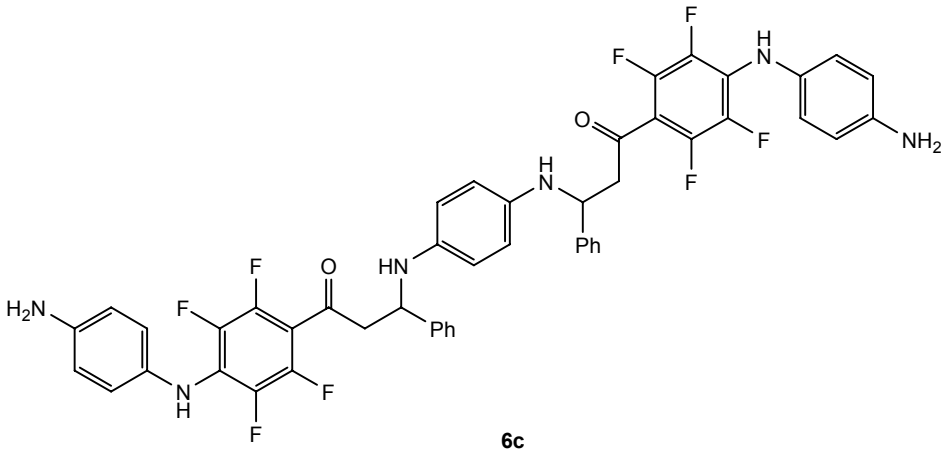
## EXPERIMENTAL

Chalcones **1a–1c** were synthesized by procedure [19], compounds **1d**, **1e**, **1g**, and **1h**, by method [14]. Spectral and analytical measurements were performed in the Chemical service center of joint usage of the Siberian Branch of the Russian Academy of Sciences. $^1H$ and $^{19}F$ NMR spectra were registered on a spectrometer Bruker AC-300 (300.13 and 282.37 MHz respectively). In the $^1H$ NMR spectra the residual protons of solvents $CHCl_3$ ($\delta_H$ 7.24 ppm) and DMSO ($\delta_H$ 2.50 ppm) served as internal reference, in $^{19}F$ NMR spectrum internal reference was $C_6F_6$. High-resolution mass spectra were measured on a DFS instrument at a direct admission of the sample, ionizing electrons energy 70eV. The molecular mass and the composition of compounds was determined from the precise value of the mass of the molecular ion.

The products ratios in the reaction mixtures (Schemes 1, 2) were calculated from the $^{19}F$ NMR data. The yields of all isolated compounds are reported with respect to the amount of chalcone brought into the reaction.

**1-Phenyl-3-[2,3,5,6-tetrafluoro-4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)phenyl]prop-2-en-1-one (1f)**. To a solution of 3.0 g (10.0 mmol) of chalcone **1a** in 20 mL of DMF was added 2.56 mL (20.0 mmol) of 1,4-dioxa-8-azaspiro[4.5]decene. The mixture was stirred by a magnetic stirrer at room temperature for 8 h, poured on crushed ice, the precipitate was filtered off, washed with $H_2O$, and dried in air. Yield 3.71 g (88%), yellow powder, mp 104–106°C (from EtOH). $^1H$ NMR spectrum ($CHCl_3$), δ, ppm: 1.83 m (4H, $2CH_{2piperidine}$), 3.42 m (4H, $2CH_{2piperidine}$), 3.99 br.s (4H, $2CH_2$, $OCH_2CH_2O$), 7.45–7.43 m ($2H_{Ar}$), 7.53–7.62 m ($1H_{Ar}$), 7.75, 7.78 (*AB*, 2H, CH=CH, *J* 16.0 Hz), 7.96–8.05 m ($2H_{Ar}$). $^{19}F$ NMR spectrum ($CHCl_3$), δ, ppm: 9.98 (2F, $F^{3,5}$), 20.66 (2F, $F^{2,6}$). Found $[M]^+$ 421.1287. $C_{22}H_{19}F_4NO_3$. Calculated *M* 421.1296.

**3-Phenyl-1-[2,3,5,6-tetrafluoro-4-(1,4-dioxa-8-aza-spiro[4.5]dec-8-yl)phenyl]prop-2-en-1-one (1i)**. To a solution of 3.0 g (10.0 mmol) of chalcone **1b** in 20 mL of DMF was added 1.84 mL (14.4 mmol) of 1,4-dioxa-8-aza-spiro[4.5]decane. The mixture was stirred by a magnetic stirrer at room temperature for




**6c**

3 h, poured on crushed ice, the precipitate was filtered off, washed with $H_2O$, and dried in air. Yield 3.98 g (94%), yellow powder, mp 98–101°C (from EtOH). $^1$H NMR spectrum ($CHCl_3$), δ, ppm: 1.87 m (4H, $2CH_{2piperidine}$), 3.46 m (4H, $2CH_{2piperidine}$), 4.03 s (4H, $2CH_2$, $OCH_2CH_2O$), 7.08 d (1H, CH=, *J* 15.9 Hz), 7.40–7.47 m ($3H_{Ar}$), 7.56–7.63 m (3H, $2H_{Ar}$, CH=). $^{19}$F NMR spectrum ($CHCl_3$), δ, ppm: 10.99 (2F, $F^{3,5}$), 19.22 (2F, $F^{2,6}$). Found $[M]^+$ 421.1289. $C_{22}H_{19}F_4NO_3$. Calculated *M* 421.1296.

**Reaction of 1-phenyl-3-(2,3,5,6-tetrafluoro-4-phenoxyphenyl)prop-2-en-1-one (1d) with *o*-phenylenediamine**. *a* (Scheme 1). To a solution of 1.27 g (11.8 mmol) of *o*-phenylenediamine and 1.62 mL (11.8 mmol) of triethylamine in 10 mL of ethanol was added 0.62 g (1.7 mmol) of chalcone **1d**. The mixture was boiled at stirring with a magnetic stirrer for 5 h, cooled to room temperature and poured on ice, the viscous reaction product was extracted with ethyl ether, the extract was washed with water, dried with $MgSO_4$, the solvent was distilled off in a vacuum on a rotary evaporator, the residue (0.71 g) was analyzed by $^1$H and $^{19}$F NMR spectroscopy.

*b* (Scheme 2). To a solution of 1.01 g (9.4 mmol) of *o*-phenylenediamine and 2.09 g (9.4 mmol) of TEBAC in 10 mL of 2-propanol was added 0.5 g (1.3 mmol) of chalcone **1d**. The mixture was boiled at stirring with a magnetic stirrer for 6 h, cooled to room temperature and poured on crushed ice, the viscous reaction product was extracted with $CH_2Cl_2$, the extract was washed with water, dried with $CaCl_2$, the solvent was distilled off in a vacuum on a rotary evaporator, the residue (1.04 g) was analyzed by $^1$H and $^{19}$F NMR spectroscopy. By preparative TLC on $Al_2O_3$ (eluent benzene–hexane, 1 : 1) two compounds were isolated. The first fraction contained **1,3,4-trifluoro-2-phenoxy-6a-phenyl-6a,7-dihydrobenzimidazo[1,2-*a*]-quinoline (4d)**. Yield 0.2 g (33%), yellow oily substance. $^1$H NMR spectrum ($CHCl_3$), δ, ppm: 4.41 br.s (1H, NH), 6.43 d.d (1H, CH=, *J* 9.8, 0.8 Hz), 6.58–6.71 m ($2H_{Ar}$), 6.76–6.86 m (3H, $2H_{Ar}$, CH=), 7.01–7.08 m ($2H_{Ar}$), 7.11–7.18 m ($1H_{Ar}$), 7.29–7.41 m ($5H_{Ar}$), 7.51–7.57 m ($2H_{Ar}$). $^{19}$F NMR spectrum ($CHCl_3$), δ, ppm: 6.66 br.d (1F, $F^4$, *J* 21.6 Hz), 13.87 d.d (1F, $F^3$, *J* 21.6, 12.3 Hz), 24.24 br.d (1F, $F^1$, *J* 12.3 Hz). Found $[M]^+$ 442.1285. $C_{27}H_{17}F_3N_2O$. Calculated *M* 442.1288. The second fraction contained **4-phenyl-2-(2,3,5,6-tetrafluoro-4-phenoxyphenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (2d)**. Yield 0.2 g (33%), yellow powder, mp 112–115°C (from EtOH). UV spectrum ($CHCl_3$), $\lambda_{max}$, nm (log ε): 261 (4.34), 359 (3.78). $^1$H NMR spectrum ($CHCl_3$), δ, ppm: 3.27, 3.36, 5.69 (1H each, $CH_2CH$, *ABX*, *J* 12.7, 10.4, 3.8 Hz), 3.74 br.s (1H, NH), 6.77–6.82 m ($1H_{Ar}$), 6.94–6.99 m ($2H_{Ar}$), 7.01–7.11 m ($2H_{Ar}$), 7.11–7.17 m ($1H_{Ar}$), 7.31–7.40 m ($3H_{Ar}$), 7.44–7.50 m ($3H_{Ar}$), 7.95–8.03 m ($2H_{Ar}$). $^{19}$F NMR spectrum ($CHCl_3$), δ, ppm: 8.46 m (2F, $F^{3,5}$), 19.45 m (2F, $F^{2,6}$). Found $[M]^+$ 462.1350. $C_{27}H_{18}F_4N_2O$. Calculated *M* 462.1345.

**Reaction 1-phenyl-3-[2,3,5,6-tetrafluoro-4-(piperidin-1-yl)phenyl]prop-2-en-1-one (1e) with *o*-phenylenediamine**. *a* (Scheme 1). To a solution of 2.08 g (19.3 mmol) of *o*-phenylenediamine and 2.68 mL (19.3 mmol) of triethylamine in 20 mL of ethanol was added 1.0 g (2.8 mmol) of chalcone **1e**. The mixture was boiled at stirring for 20 h, cooled to room tempera-ture and poured on ice, the residue was filtered off, washed with $H_2O$, and dried in air. The reaction pro-duct (1.64 g) was analyzed by $^1$H and $^{19}$F NMR spectros-copy. By column chromatography on $Al_2O_3$ (eluent benzene–hexane, 1 : 4) we isolated **4-phenyl-2-[2,3,5,6-tetrafluoro-4-(piperidin-1-yl)-phenyl]-2,3-dihydro-1*H*-1,5-benzodiazepine (2e)**. Yield 0.28 g (22%), yellow powder, mp 108–110°C (from EtOH). UV spectrum ($CHCl_3$), $\lambda_{max}$, nm (log ε): 266 (4.43), 345 (3.83). $^1$H NMR spectrum ($CHCl_3$), δ, ppm: 1.54–1.73 m (6H, $3CH_2$), 3.15–3.32 m (6H, $3CH_2$), 3.59 br.s (1H, NH), 5.55 d.d (1H, CH, *J* 10.3, 4.4 Hz), 6.71–6.77 m ($1H_{Ar}$), 6.97–7.08 m ($2H_{Ar}$), 7.31–7.38 m ($1H_{Ar}$), 7.42–7.48 m ($3H_{Ar}$), 7.95–8.01 m ($2H_{Ar}$). $^{19}$F NMR spectrum ($CHCl_3$), δ, ppm: 11.12 m (2F, $F^{3,5}$), 17.14 m (2F, $F^{2,6}$). Found $[M]^+$ 453.1830. $C_{26}H_{23}F_4N_3$. Calculated *M* 453.1823.

*b* (Scheme 2). To a solution of 2.08 g (19.3 mmol) of *o*-phenylenediamine and 4.29 g (19.3 mmol) of TEBAC in 15 mL of 2-propanol was added 1.0 g (2.8 mmol) of chalcone **1e**. The mixture was boiled at stirring for 25 h, cooled to room temperature and poured on ice, the product was extracted with ethyl ether, the extract was washed with water, dried with $MgSO_4$, the solvent was distilled off in a vacuum on a rotary evaporator, the residue (1.6 g) was analyzed by $^1$H and $^{19}$F NMR spectroscopy. By column chromatography on $Al_2O_3$ (eluent benzene) we isolated **1,3,4-trifluoro-6a-phenyl-2-piperidin-1-yl-6a,7-dihydrobenzimidazo[1,2-*a*]quinoline (4e)**. Yield 1.04 g (87%), yellow oily substance. $^1$H NMR spectrum ($CHCl_3$), δ, ppm: 1.58–1.75 m (6H, $3CH_2$), 3.15–3.35 m (4H, $2CH_2$), 4.34 br.s (1H, NH), 6.25 d.d (1H, CH=, *J* 9.8, 0.6 Hz), 6.50–6.55 m ($1H_{Ar}$), 6.64–6.68 m ($1H_{Ar}$), 6.69–6.80 m (3H, $2H_{Ar}$, CH=), 7.28–7.33 m ($3H_{Ar}$),

7.52–7.58 m (2$H_{Ar}$). $^{19}$F NMR spectrum ($CHCl_3$), δ, ppm: 10.05 d (1F, $F^4$, *J* 21.1 Hz), 11.33 d.d (1F, $F^3$, *J* 21.1, 11.3 Hz), 28.59 m (1F, $F^1$). Found $[M]^+$ 433.1830. $C_{26}H_{22}F_3N_3$. Calculated *M* 433.1825.

**Reaction of 1-phenyl-3-[2,3,5,6-tetrafluoro-4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)phenyl]-prop-2-en-1-one (1f) with *o*-phenylenediamine**. *a* (Scheme 1). To a solution of 1.8 g (16.6 mmol) of *o*-phenylenediamine and 2.31 mL (16.6 mmol) of triethylamine in 20 mL of 2-propanol was added 1.0 g (2.4 mmol) of chalcone **1f**. The mixture was boiled at stirring for 22 h, cooled to room temperature, and poured on ice, the precipitate was filtered off, washed with $H_2O$, and dried in air. The reaction product (1.07 g) was analyzed by $^1$H and $^{19}$F NMR spectroscopy. By column chromatography on $Al_2O_3$ (eluent benzene) we isolated **2-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-2,3,5,6-tetrafluorophenyl]-4-phenyl-2,3-dihydro-1*H*-1,5-benzodiazepine (2f)**. Yield 0.34 g (28%), yellow powder, mp 153–155°C (from EtOH). UV spectrum ($CHCl_3$), $\lambda_{max}$, nm (log ε): 266 (4.48). $^1$H NMR spectrum ($CHCl_3$), δ, ppm: 1.82 br.t (4H, 2$CH_2$, *J* 5.4 Hz), 3.21, 3.27, 5.56 (1H each, $CH_2CH$, *ABX*, *J* 13.6, 10.9, 3.5 Hz), 3.31–3.37 m (4H, 2$CH_2$), 3.59 br.s (1H, NH), 3.98 br.s (4H, 2$CH_2$, $OCH_2CH_2O$), 6.74 br.d (1$H_{Ar}$, *J* 7.7 Hz), 6.97–7.07 m (2$H_{Ar}$), 7.31–7.37 m (1$H_{Ar}$), 7.41–7.47 m (3$H_{Ar}$), 7.94–7.99 m (2$H_{Ar}$). $^{19}$F NMR spectrum ($CHCl_3$), δ, ppm: 11.39 m (2F, $F^{3,5}$), 17.46 m (2F, $F^{2,6}$). Found $[M]^+$ 511.1873. $C_{28}H_{25}F_4N_3O_2$. Calculated *M* 511.1877.

*b*. To a solution of 0.9 g (8.3 mmol) of *o*-phenylenediamine and 1.86 g (8.3 mmol) of TEBAC in 15 mL of 2-propanol was added 0.5 g (1.2 mmol) of chalcone **1f**. The mixture was boiled at stirring for 20 h, cooled to room temperature, and poured on ice, the precipitate was filtered off, washed with $H_2O$, and dried in air. The reaction product (0.52 g) was analyzed by $^1$H and $^{19}$F NMR spectroscopy. By preparative TLC on $Al_2O_3$ (eluent benzene–hexane, 1 : 2) we isolated **2-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-1,3,4-trifluoro-6a-phenyl-6a,7-dihydrobenzimidazo-[1,2-*a*]quinoline (4f)**. Yield 0.28 g (47%), yellow powder, mp 110–113°C (from EtOH). UV spectrum ($CHCl_3$), $\lambda_{max}$, nm (log ε): 304 (4.24), 365 (3.46), 455 (3.49). $^1$H NMR spectrum ($CHCl_3$), δ, ppm: 1.78–1.97 m (4H, 2$CH_2$), 3.39–3.48 m (4H, 2$CH_2$), 3.99 br.s (4H, 2$CH_2$, $OCH_2CH_2O$), 4.38 br.s (1H, NH), 6.26 d.d (1H, CH=, *J* 9.9, 0.8 Hz), 6.49–6.56 m (1$H_{Ar}$), 6.62–6.68 m (1$H_{Ar}$), 6.71 d.d (1H, CH=, *J* 9.9, 1.3 Hz), 6.74–6.81 m (2$H_{Ar}$), 7.26–7.35 m (3$H_{Ar}$), 7.46–7.54 m (2$H_{Ar}$). $^{19}$F NMR spectrum ($CHCl_3$), δ, ppm: 10.41 d (1F, $F^4$, *J* 21.0 Hz), 11.64 d.d (1F, $F^3$, *J* 21.0, 11.9 Hz), 28.74 br.d (1F, $F^1$, *J* 11.9 Hz). Found $[M]^+$ 491.1813. $C_{28}H_{24}F_3N_3O_2$. Calculated *M* 491.1815.

**Reaction of 3-phenyl-1-(2,3,5,6-tetrafluoro-4-phenoxyphenyl)prop-2-en-1-one (1g) with *o*-phenylenediamine**. To a solution of 2.03 g (18.8 mmol) of *o*-phenylenediamine and 4.18 g (18.8 mmol) of TEBAC in 20 mL of 2-propanol was added 1.0 g (2.7 mmol) of chalcone **1g**. The mixture was boiled at stirring for 20 h, cooled to room temperature, and poured on ice, the viscous reaction product was extracted with $CH_2Cl_2$, the extract was washed with water, dried with $CaCl_2$, the solvent was distilled off in a vacuum on a rotary evaporator, the residue (2.11 g) was dissolved in benzene and chromatographed on a column packed with $Al_2O_3$ (eluent benzene) to obtain **2-phenyl-4-(2,3,5,6-tetrafluoro-4-phenoxyphenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (2g)**. Yield 0.38 g (31%), yellow oily substance. $^1$H NMR spectrum ($CHCl_3$), δ, ppm: 3.07, 3.17, 5.14 (1H each, $CH_2CH$, *ABX*, *J* 14.0, 8.9, 3.2 Hz), 4.08 br.s (1H, NH), 6.80 m (1$H_{Ar}$), 6.94–7.01 m (3$H_{Ar}$), 7.09–7.16 m (2$H_{Ar}$), 7.29–7.42 m (8$H_{Ar}$). $^{19}$F NMR spectrum ($CHCl_3$), δ, ppm: 7.85 m (2F, $F^{3,5}$), 19.66 m (2F, $F^{2,6}$). Found $[M]^+$ 462.1352. $C_{27}H_{18}F_4N_2O$. Calculated *M* 462.1345.

**Reaction of 3-phenyl-1-[2,3,5,6-tetrafluoro-4-(piperidin-1-yl)phenyl]prop-2-en-1-one (1h) with *o*-phenylenediamine**. To a solution of 2.08 g (19.3 mmol) of *o*-phenylenediamine and 4.28 g (19.3 mmol) of TEBAC in 15 mL of 2-propanol was added 1.0 g (2.8 mmol) of chalcone **1h**. The mixture was boiled at stirring for 20 h, cooled to room temperature, and poured on ice, the viscous reaction product was extracted with $CH_2Cl_2$, the extract was washed with water, dried with $CaCl_2$, the solvent was distilled off in a vacuum on a rotary evaporator, the residue (1.82 g) was chromatographed on a column packed with $Al_2O_3$ (eluent benzene). We obtained **2-phenyl-4-(2,3,5,6-tetrafluoro-4-piperidin-1-ylphenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (2h)**. Yield 0.32 g (26%), yellow oily substance. $^1$H NMR spectrum ($CHCl_3$), δ, ppm: 1.45–1.63 m (6H, 3$CH_2$), 2.88, 2.99, 5.01 (1H each, $CH_2CH$, *ABX*, *J* 14.3, 9.4, 3.3 Hz), 3.11 m (4H, 2$CH_2$), 3.89 br.s (1H, NH), 6.66 d.d (1$H_{Ar}$, *J* 8.2, 1.5 Hz), 6.84 d.d.d (1$H_{Ar}$, *J* 8.2, 7.7, 1.5 Hz), 7.07 d.d.d (1$H_{Ar}$, *J* 8.2, 7.7, 1.5 Hz), 7.12–7.30 m (6$H_{Ar}$). $^{19}$F NMR spectrum ($CHCl_3$), δ, ppm: 10.36 m (2F, $F^{3,5}$), 17.51 m (2F, $F^{2,6}$). Found $[M]^+$ 453.1817. $C_{26}H_{23}F_4N_3$. Calculated *M* 453.1823.

**Reaction of 3-phenyl-1-[2,3,5,6-tetrafluoro-4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)phenyl]-prop-2-en-1-one (1i) with *o*-phenylenediamine**. To a solution of 0.9 g (8.3 mmol) of *o*-phenylenediamine and 1.86 g (8.3 mmol) of TEBAC in 15 mL of 2-propanol was added 0.5 g (1.2 mmol) of chalcone **1i**. The mixture was boiled at stirring for 20 h, cooled to room temperature, and poured on ice, the reaction product was extracted with $CH_2Cl_2$, the extract was washed with water, dried with $CaCl_2$, the solvent was distilled off in a vacuum, the residue (0.84 g) was subjected to preparative TLC on $Al_2O_3$ (eluent benzene–hexane, 1 : 2) to obtain **4-[4-(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)-2,3,5,6-tetrafluorophenyl]-2-phenyl-2,3-dihydro-1*H*-1,5-benzodiazepine (2i)**. Yield 0.12 g (19%), yellow powder, mp 135–138°C (from EtOH). UV spectrum ($CHCl_3$), $\lambda_{max}$, nm (log ε): 269 (4.13), 303 (4.14), 369 (3.9). $^1$H NMR spectrum ($CHCl_3$), δ, ppm: 1.83 m (4H, $2CH_2$), 2.97, 3.09, 5.11 (1H each, $CH_2CH$, *J* 14.3, 9.2, 2.9 Hz), 3.34 m (4H, $2CH_2$), 3.98 br.s (5H, NH, $2CH_2$), 6.77 d.d (1$H_{Ar}$, *J* 7.6, 1.5 Hz), 6.94 t.d (1$H_{Ar}$, *J* 8.4, 7.6, 1.5 Hz), 7.07 t.d (1$H_{Ar}$, *J* 8.4, 7.6, 1.5 Hz), 7.26–7.38 m (6$H_{Ar}$). $^{19}$F NMR spectrum ($CHCl_3$), δ, ppm: 10.63 m (2F, $F^{3,5}$), 17.76 m (2F, $F^{2,6}$). Found $[M]^+$ 511.1868. $C_{28}H_{25}F_4N_3O_2$. Calculated *M* 511.1877.

**Transformations of 2-perfluorophenyl-4-phenyl-2,3-dihydro-1*H*-benzo-1,5-diazepine (2a)**. *a*. A mixture of 0.04 g (0.1 mmol) of benzodiazepine **2a** and 0.07 g (0.3 mmol) of TEBAC in 3 mL of 2-propanol was boiled at stirring with a magnetic stirrer for 2 h, cooled, and poured on crushed ice. The separated precipitate was filtered off, washed with water, and dried in air. According to $^{19}$F NMR data the reaction product contained 78% of benzimidazoquinoline **4a** and 22% of benzodiazepine **2a**.

*b*. A solution of 0.03 g of benzodiazepine **2a** in 2 mL of 2-propanol was boiled at stirring for 2 h, poured on ice, the reaction product was extracted with chloroform. The extract was washed with water, dried with $CaCl_2$, the solvent was evaporated. According to $^{19}$F NMR data the reaction product contained 81% of benzimidazoquinoline **4a** and 19% of benzodiazepine **2a**.

*c*. To a solution of 0.02 g of benzodiazepine **2a** in 4 mL of 2-propanol was added 2 drops of piperidine, and the mixture was boiled at stirring for 2 h. After workup of the reaction mixture as in experiment *a* the isolated precipitate contained only benzodiazepine **2a**.

*d*. To a solution of 0.03 mg of benzodiazepine **2a** in 3 mL of 2-propanol was added 3 drops of triethylamine, and the mixture was boiled at stirring for 2 h. After workup of the reaction mixture as in experiment *a* the isolated precipitate contained only compound **2a**.

**Reaction of 3-(perfluorophenyl)-1-phenylprop-2-en-1-one (1a) with *p*-phenylenediamine**. To a solution of 0.3 g (1.0 mmol) of chalcone **1a** in 10 mL of ethanol was added 0.28 mL (2.0 mmol) of triethylamine and 0.54 g (5.0 mmol) of *p*-phenylenediamine. The mixture was boiled at stirring for 7 h, cooled to room temperature, and poured on ice. The precipitate was filtered off, washed with $H_2O$, and dried in air to obtain **3-{4-[(4-aminophenyl)amino]-2,3,5,6-tetrafluorophenyl}-1-phenylprop-2-en-1-one (5a)**. Yield 0.28 g (72%), yellow powder, mp 215–218°C (from EtOH). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 4.95 br.s (2H, $NH_2$), 6.52 m (2$H_{Ar}$), 6.82 m (2$H_{Ar}$), 7.53–7.79 m (5H, 3$H_{Ar}$, CH=CH, *J* 16.0 Hz), 8.03 m (2$H_{Ar}$), 8.51 br.s (1H, NH). $^{19}$F NMR spectrum (DMSO-$d_6$), δ, ppm: 8.17 m (2F, $F^{3,5}$), 20.13 m (2F, $F^{2,6}$). Found $[M]^+$ 386.1034. $C_{21}H_{14}F_4N_2O$. Calculated *M* 386.1037.

**Reaction of 1-(perfluorophenyl)-3-phenylprop-2-en-1-one (1b) with *p*-phenylenediamine**. To a solution of 0.5 g (1.7 mmol) of chalcone **1b** in 10 mL of DMF was added 0.47 mL (3.4 mmol) of triethylamine and 0.92 g (8.5 mmol) of *p*-phenylenediamine. The mixture was stirred at room temperature for 4 h, poured on ice and left overnight in a refrigerator. The precipitate was filtered off, washed with $H_2O$, and dried in air. The product (0.7 g) was subjected to column chromatography on $Al_2O_3$ (eluent benzene–dichloromethane, 1 : 1). We isolated **1-{4-[(4-aminophenyl)amino]-2,3,5,6-tetrafluorophenyl}-3-phenylprop-2-en-1-one (5b)**. Yield 0.12 g (18%), orange powder, mp 62–65°C (from MeOH). $^1$H NMR spectrum ($CHCl_3$), δ, ppm: 3.64 br.s (2H, $NH_2$), 5.81 br.s (1H, NH), 6.64 m (2$H_{Ar}$), 6.91 m (2$H_{Ar}$), 7.09 d (1H, CH=, *J* 16.0 Hz), 7.40 m (3$H_{Ar}$), 7.53–7.71 m (3H, 2$H_{Ar}$, CH=). $^{19}$F NMR spectrum ($CHCl_3$), δ, ppm: 7.27 m (2F, $F^{3,5}$), 19.50 m (2F, $F^{2,6}$). Found $[M]^+$ 386.1034. $C_{21}H_{14}F_4N_2O$. Calculated *M* 386.1037.

**Reaction of 1,3-bis(perfluorophenyl)prop-2-en-1-one (1c) with *p*-phenylenediamine**. To a solution of 0.3 g (0.77 mmol) of chalcone **1c** in 10 mL of DMF was added 0.44 mL (3.1 mmol) of triethylamine and 0.83 g (7.7 mmol) of *p*-phenylenediamine. The mixture was stirred at room temperature for 4 h, poured on ice, the precipitate was filtered off, washed with $H_2O$, dried

in air, and twice recrystallized from ethanol to obtain **1,3-bis{4-[(4-aminophenylamino)-2,3,5,6-tetrafluorophenyl]}prop-2-en-1-one (5c)**. Yield 0.12 g (28%), red-brown powder, mp 198–200°C (from EtOH). $^1$H NMR spectrum, δ, ppm: 3.64 br.s (4H, $2NH_2$), 5.81 br.s (2H, 2NH), 6.64 m ($4H_{Ar}$), 6.90 m ($4H_{Ar}$), 7.28 d (*AB*, 1H, CH=, *J* 16.0 Hz), 7.69 d (*AB*, 1H, CH=, *J* 16.0 Hz). $^{19}$F NMR spectrum , δ, ppm: 6.30 m (2F), 7.12 m (2F), 19.66 m (2F), 21.12 m (2F). Found $[M]^+$ 564.1187. $C_{27}H_{16}F_8N_4O$. Calculated *M* 564.1196.

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