Synthesis of polyfluorochalcone acryloyl derivatives

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Reactions of pentafluorophenyl-containing chalcones with 4-hydroxypiperidine leads to the nitrogen atom substitution for the fluorine atom at position 4. Polyfluorinated hydroxypiperidinyl-substituted chalcones that obtained give the corresponding O-acrylates in the reactions with acryloyl chloride.

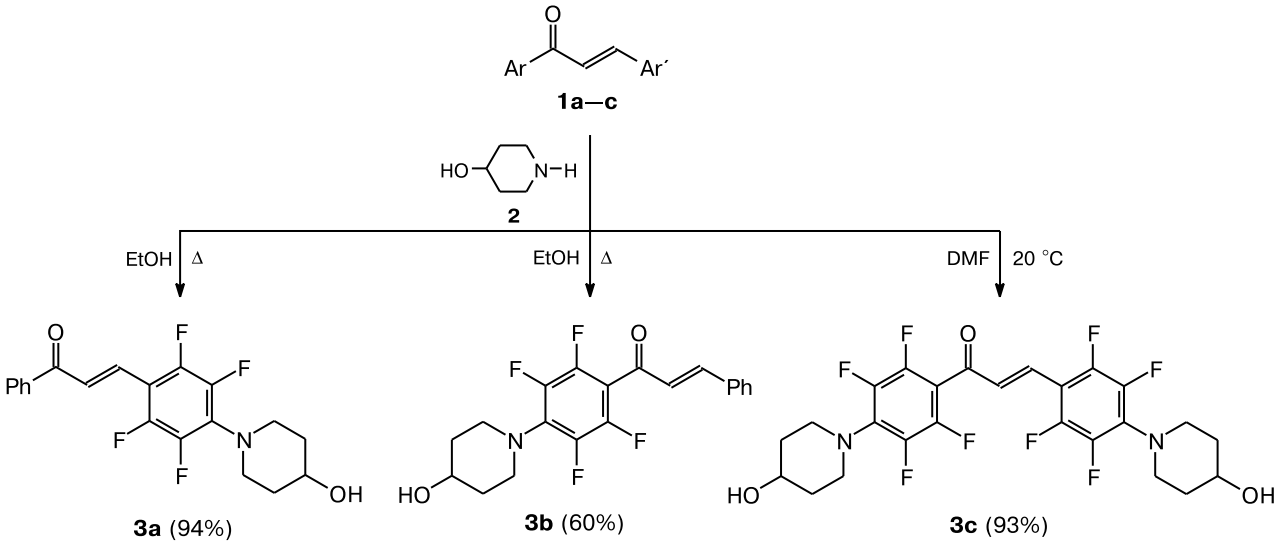
Key words: chalcones, 4-hydroxypiperidine, acrylates, organofluorine compounds.

Chalcones (benzylideneacetophenones) are photochemically active compounds, which can undergo photocyclization involving the double bond, that leads to the spatial cross-linking of molecules.[1—3] This property of chalcones is used in photochemical processes for preparation of photoresists.[4] Introduction of additional unsaturated photoactive group, in particular, acryloyl ones, into the chalcone molecules broadens their practical application as monomers.[5] The use of polyfluorinated chalcones creates additional possibilities for their functionalization because of high nucleofuge power of the fluorine atoms.

In the present work, acryloyl-substituted derivatives of polyfluorinated chalcones were obtained by a two-step synthesis, which includes introduction of a spacer (bridged) fragment containing hydroxy and amino groups into the perfluorophenyl ring, with subsequent acryloylation of the functional hydroxy group.

The reaction of polyfluorinated chalcones **1a—c** with 4-hydroxypiperidine (**2**) (Scheme 1) was carried out under the same conditions as with piperidine,[6] depending on the chalcone structure. For instance, in chalcone **1a**, the 4-hydroxypiperidine group substituted for the fluorine atom at *para*-position of the perfluorophenyl ring on reflux in ethanol to give high yield of chalcone **3a**. Formation of the *para*-isomer was unambiguously confirmed by the character of the ^{19}F NMR spectrum, which exhibits only two signals belonging to the four symmetrically arranged fluorine atoms in the *para*-disubstituted tetrafluorophenyl ring. Chalcone **1b** under these conditions also predominantly gives *para*-isomer with ~20% of *ortho*-isomer.

Scheme 1



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

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The same picture is observed in the reaction of chalcone **1c**. The results obtained agree with the data in the work[6] on the direction of the amino group attack during nucleophilic substitution in perfluorinated chalcone rings. To avoid *ortho*-substitution, the reaction of chalcone **1c** with 4-hydroxypiperidine (**2**) was carried out in DMF at room temperature. The structures of compounds **3a—c** were established based on the ^{1}H and ^{19}F NMR spectral data and confirmed by the results of elemental analysis (Tables 1 and 2).

The hydroxy group of compounds **3a—c** were further subjected to acylation with acryloyl chloride in the presence of triethylamine in dichloromethane at room temperature (Scheme 2). Acrylates **4a—c** were obtained in good yields, but because of their disposition to polymerization, they were stored as solutions in dichloromethane at reduced temperature and were not isolated in the individual state. The structures of compounds **4a—c** were inferred only from the NMR spectral data (see Table 2).

Thus, the ^{1}H NMR spectrum of chalcone **4b** exhibits multiplets for eight protons of the substituted piperidine ring at δ 1.91, 2.07, 3.23, and 3.53, a complex multiplet for the proton at position 4 of the piperidine ring at δ 5.09, and characteristic signals at δ 5.89, 6.18, and 6.49 belonging to the three protons of the acryloyl group and forming an ABX system. In addition, the spectrum exhibits signals for five protons of the phenyl ring and two methine protons at the double bond of chalcone as a multiplet in the region δ 7.44—7.61. The ^{19}F NMR spectrum exhibits two signals for two *ortho*- (δ 19.31) and two *meta*-fluorine atoms (δ 11.15) in the *para*-disubstituted tetrafluorophenyl ring. The yields of compounds **4a—c** were calculated from the NMR spectra.

The acrylates **4a—c** obtained can be of interest as monomers for photoresists and holographic materials.

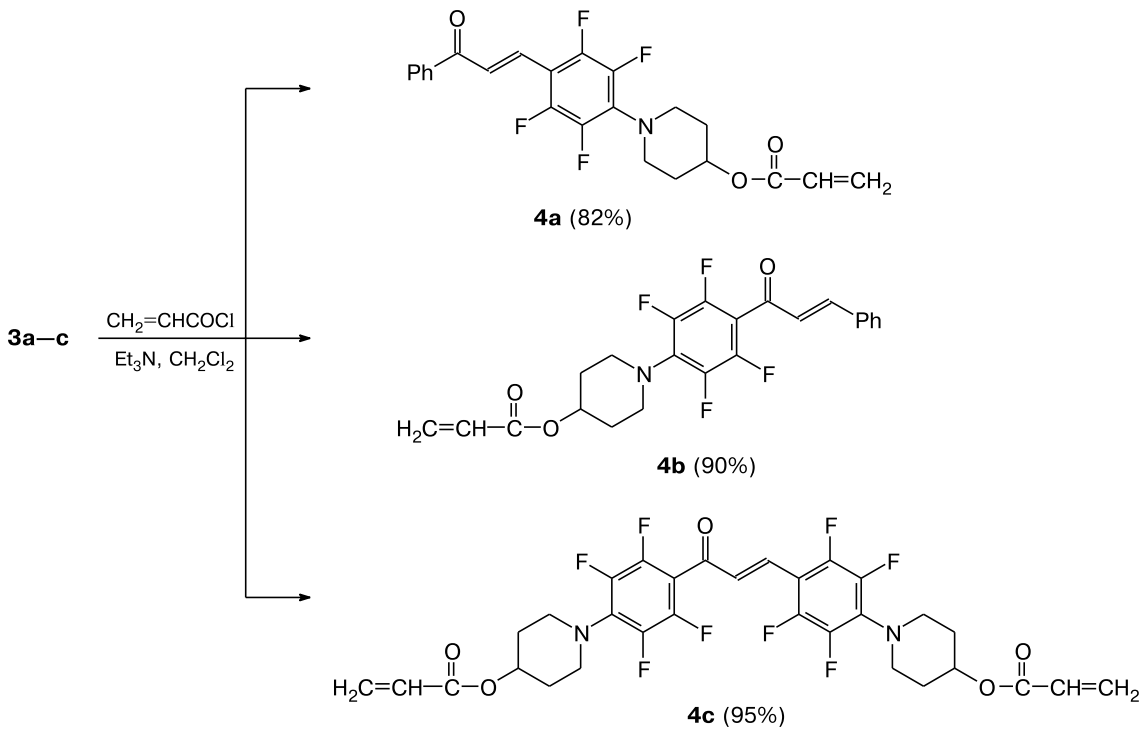
Table 1. Yields, melting points, and elemental analysis data for compounds **3a—c**

Compound	Yield (%)	M.p./°C (solvent for recrystallization)	Found / Calculated (%)				Molecular formula
			C	H	F	N	
3a	94	106—109.5 (50% aq. ethanol)	63.16 / 63.49	4.72 / 4.53	20.09 / 19.82	3.74 / 3.70	$C_{20}H_{17}F_4NO_2$
3b	60	105—107 (benzene—hexane, 1 : 1)	63.52 / 63.49	4.50 / 4.53	20.05 / 19.82	3.74 / 3.70	$C_{20}H_{17}F_4NO_2$
3c	93	167.5—170.5 (50% aq. ethanol)	54.69 / 54.55	4.02 / 4.03	27.70 / 27.61	4.91 / 5.10	$C_{25}H_{22}F_8N_2O_3$

Table 2. ^{1}H and ^{19}F NMR spectral data for compounds **3a—c** and **4a—c**

Compound	δ (*J*/Hz)	
	^{19}F	^{1}H
3a	9.77, 20.33 (both 2 F each)	1.68 (m, 2 H, CH_2); 1.99 (m, 3 H, CH_2, OH); 3.18, 3.51 (both m, 2 H each, CH_2); 3.88 (m, 1 H, CH); 7.44—8.00 (m, 7 H, Ph, —CH=CH—)
3b	11.03, 19.25 (both 2 F each)	1.59—1.78 (m, 3 H, CH_2, OH); 1.99, 3.20, 3.51 (all m, 2 H each, CH_2); 3.89 (m, 1 H, CH); 7.06, 7.57 (AB-system, 2 H, —CH=CH—, J = 16.0); 7.35—7.60 (m, 5 H, Ph)
3c	9.76, 10.89, 19.45, 20.93 (all 2 F each)	1.49—1.78 (m, 6 H, CH_2, OH); 1.98, 3.20, 3.53 (all m, 4 H each, CH_2); 3.89 (m, 2 H, CH); 7.26, 7.63 (AB-system, 2 H, —CH=CH—, J = 16.0)
4a	9.84, 20.43 (both 2 F each)	1.86, 2.02, 3.28, 3.48 (all m, 2 H each, CH_2 in N(C_5H_9)); 5.05 (m, 1 H, CH in N(C_5H_9)); 5.84 (br.d, ABX-system, 1 H, COCH=CH_2, J = 10.0); 6.14 (dd, ABX-system, 1 H, COCH=CH_2, J_1 = 17.0, J_2 = 10.0); 6.43 (br.d, ABX-system, 1 H, COCH=CH_2, J = 17.0); 7.42—8.03 (m, 7 H, Ph, —CH=CH—)
4b	11.15, 19.31 (both 2 F each)	1.91, 2.07, 3.23, 3.53 (all m, 2 H each, CH_2 in N(C_5H_9)); 5.09 (m, 1 H, CH in N(C_5H_9)); 5.89 (dd, ABX-system, 1 H, COCH=CH_2, J_1 = 10.5, J_2 = 1.2); 6.18 (dd, ABX-system, 1 H, COCH=CH_2, J_1 = 17.5, J_2 = 10.5); 6.49 (dd, ABX-system, 1 H, COCH=CH_2, J_1 = 17.5, J_2 = 1.2); 7.02—7.61 (m, 7 H, Ph, —CH=CH—)
4c	9.83, 10.94, 19.56, 21.03 (all 2 F each)	1.85, 2.05, 3.28, 3.50 (all m, 4 H each, CH_2 in N(C_5H_9)); 5.05 (m, 2 H, CH in N(C_5H_9)); 5.84 (dd, ABX-system, 2 H, COCH=CH_2, J_1 = 10.0, J_2 = 1.5); 6.11 (ddd, ABX-system, 2 H, COCH=CH_2, J_1 = 17.5, J_2 = 10.0, J_3 = 1.5); 6.39 (dt, ABX-system, 2 H, COCH=CH_2, J_1 = 17.5, J_2 = J_3 = 1.5); 7.25, 7.62 (AB-system, 2 H, —CH=CH—, J = 16.5)

Scheme 2



Experimental

^{1}H and ^{19}F NMR spectra were recorded on a Bruker AC-200 spectrometer (200.13 and 188.2 MHz, respectively) in $CDCl_3$, residual signals for the $CHCl_3$ protons (δ 7.24) and C_6F_6 were used as references.

Compounds **1a—c** were synthesized according to the known procedure.[7]

Reaction of chalcones 1a—c with 4-hydroxypiperidine (2) (general procedure). 4-Hydroxypiperidine (**2**) (1.5—2.0 mmol (2.5 mmol for **1c**)) was added to a solution of chalcone **1a—c** (1 mmol) in ethanol (DMF for **1c**) (15 mL). The reaction mixture was refluxed for 2.5—3.5 h (in the case of chalcone **1c**, the mixture was magnetically stirred for 4 h at 20 °C), then poured on ice, a precipitate that formed was filtered off and dried in air. The following pure forms of compounds **3a—c** were isolated by recrystallization: 3-[2,3,5,6-tetrafluoro-4-(4-hydroxypiperidin-1-yl)phenyl]-1-phenylprop-2-en-1-one (**3a**), 1-[2,3,5,6-tetrafluoro-4-(4-hydroxypiperidin-1-yl)phenyl]-3-phenylprop-2-en-1-one (**3b**), and 1,3-bis[2,3,5,6-tetrafluoro-4-(4-hydroxypiperidin-1-yl)phenyl]prop-2-en-1-one (**3c**).

Reaction of chalcones 3a—c with acryloyl chloride (general procedure). A solution of acryloyl chloride (3 mmol) in dichloromethane (5 mL) was added dropwise to a solution of chalcone **3a—c** (1 mmol) and triethylamine (3 mmol) in dried with $CaCl_2$ dichloromethane (20 mL) at 0—5 °C. The reaction mixture was stirred for 2 h at 20 °C, diluted with dichloromethane (25 mL), washed with water, and dried with $CaCl_2$. The solvent was evaporated *in vacuo* without heating, the residue was analyzed by ^{1}H and ^{19}F NMR. The following compounds were obtained: 3-[4-(4-acryloyloxypiperidin-1-yl)-2,3,5,6-tetrafluorophenyl]-1-phenylprop-2-en-1-one (**4a**) (82%), 1-[4-(4-acryloyloxypiperidin-1-yl)-2,3,5,6-tetrafluorophenyl]-3-phenylprop-2-en-1-one (**4b**) (90%), and 1,3-bis[4-(4-acryloyloxypiperidin-1-yl)-2,3,5,6-tetrafluorophenyl]prop-2-en-1-one (**4c**) (95%). The yields were calculated from the ^{19}F NMR spectral data. Compounds **4a—c** were dissolved in dichloromethane (2 mL) and stored at −18 °C.

The yields, melting points, and elemental analysis data for compounds **3a—c** are given in Table 1, the ^{1}H and ^{19}F NMR spectral data for all the synthesized compounds, in Table 2.

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