Alkyl 2-alkoxy(aryloxy)-2-isocyanato-3,3,3-trifluoropropionates

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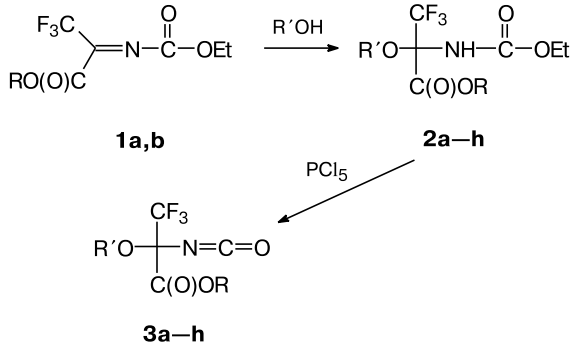
Previously unknown fluorinated α-alkoxy(aryloxy)alkylisocyanates, the esters of α-alkoxy- and α-aryloxy-2-isocyanato-3,3,3-trifluoropropionic acids, were obtained. The synthetic potential of these compounds were demonstrated in reactions with anilines leading to 2-substituted 3,3,3-trifluoroalanine derivatives.

Key words: methyl trifluoropyruvate alkoxycarbonylimines, carbamates, isocyanates, amino acids, aminals, alcohols, anilines, ureas, phosphorus pentachloride, fluoroorganic compounds.

Fluorinated α-substituted isocyanates are useful electrophilic reagents.[1] These highly reactive compounds can be regarded as synthones for the introduction of fluorinated carbamic groups into molecules of various organic nucleophiles.[2—4]

The aim of the present work is the synthesis of novel fluorinated α-alkoxy-α-aryloxyisocyanates. The 2-alkoxy- and 2-aryloxy-2-isocyanato-3,3,3-trifluoropropionates **3a—h** were obtained by alkoxylation (aryloxylation) of methyl trifluoropyruvate alkoxycarbonylimines **1a,b** with alcohols or phenols, followed by dealkoxylation of aminals **2a—h** (Scheme 1). The usefulness of compounds **3a—h** for the synthesis *N*-substituted 3,3,3-trifluoroalanine derivatives was estimated. In terms of seeking of novel biologically active substances, the presence of the pharmacophoric 3,3,3-trifluoroalanine fragment, which in some cases determines the high bacteriostatic activity of the related 3,3,3-trifluoroalanine derivatives,[5,6] is of undoubted interest.

Scheme 1



Compound	R	R′	Compound	R	R′
2a, **3a**	Et	Me	**2e**, **3e**	Me	Ph
2b, **3b**	Et	Et	**2f**, **3f**	Et	4-FC_6H_4
2c, **3c**	Et	Pr^i	**2g**, **3g**	Me	3-FC_6H_4
2d, **3d**	Et	Ph	**2h**, **3h**	Me	4-FC_6H_4

Ethoxycarbonylimines **1a,b** reacted exothermally with alcohols and phenols to give the corresponding aminals **2a—h**, which were isolated in 88—96% yield and characterized in the individual state. The compositions and the structures of **2a—h** were established based on the data from ^1H and ^{19}F NMR spectroscopy and elemental analysis. The characteristic signals in the ^{19}F NMR spectra of **2a—h** were observed in the range of δ 0—−1. The ^1H NMR spectra exhibited the singlet signals for the NH proton around δ 6 and 8 for aryloxyl- and alkoxyl-substituents, respectively. Subsequent dealkoxylation of aminals **2a—h** by refluxing with PCl_5 in $POCl_3$ for 2—3 h resulted in isocyanates **3a—h** in 68—71% yields.

Isocyanates **3a—h** are colorless light high-boiling liquids. The compositions and the structures of **3a—h** were determined based on the data from ^1H and ^{19}F NMR spectroscopy and confirmed by the data from elemental analysis, as well as by their chemical reactions with nucleophilic reagents. From our point of view, this allows us to estimate the synthetic potential of these novel fluorinated electrophiles for the synthesis of different 2-substituted 3,3,3-trifluoroalanine derivatives.

Thus isocyanates **3a—d,h** reacted exothermally with anilines **4a—i** in benzene at 20 °C giving ureas **5a—k** (Scheme 2).

Ureas **5a—k** are solid compounds obtained in 75—92% yields. The compositions and the structures of ureas **5a—k** were established based on the data from ^1H and ^{19}F NMR spectroscopy and elemental analysis. In the ^{19}F NMR of ureas **5a—k**, the characteristic singlet signals in the range of δ −0.5—0 were observed.

Thus, we proposed a convenient preparative procedure for the synthesis of previously unknown polyfunctional

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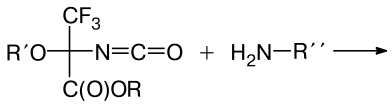
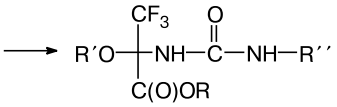
Scheme 2



3a—d,h **4a—i**



5a—k

Compound	R″	Compound	R″
4a	3-ClC_6H_4	**4f**	2,4-$Cl_2C_6H_3$
4b	2-$(CF_3)C_6H_4$	**4g**	4-$CF_3OC_6H_4$
4c	3-$(CF_3)C_6H_4$	**4h**	2-MeO-5-ClC_6H_3
4d	4-F-3-ClC_6H_3	**4i**	2-Cl-5-$CF_3C_6H_3$
4e	4-FC_6H_4		

Compound	R	R′	R′′
5a	Et	Me	3-ClC_6H_4
5b	Et	Me	2-$(CF_3)C_6H_4$
5c	Et	Me	3-$(CF_3)C_6H_4$
5d	Et	Et	3-ClC_6H_4
5e	Et	Et	4-F-3-ClC_6H_3
5f	Et	Pr^i	4-FC_6H_4
5g	Et	Pr^i	3-$(CF_3)C_6H_4$
5h	Et	Pr^i	2,4-$Cl_2C_6H_3$
5i	Et	OPh	4-$CF_3OC_6H_4$
5j	Et	OPh	2-MeO-5-ClC_6H_3
5k	Me	4-FC_6H_4	2-Cl-5-$CF_3C_6H_3$

α-substituted isocyanates — alkyl 2-alkoxy(2-aryloxy)-2-isocyanato-3,3,3-trifluoropropionates, which can be regarded as promising synthons for different 2-substituted 3,3,3-trifluoroalanine derivatives.

Experimental

^1H and ^{19}F NMR spectra were recorded on a Bruker DPX 200 instrument at 200.13 MHz and 188.29 MHz relative to tetramethylsilane (internal standard) and CF_3COOH (external standard), respectively. Melting points were determined in open capillaries. The starting ethoxycarbonylimines **1a,b** were synthesized according to the known procedure,[7] alcohols, phenols, and anilines **4a—i** were used as purchased (Aldrich).

Ethyl 2-ethoxycarbonylamino-3,3,3-trifluoro-2-methoxypropionate (2a), ethyl 2-ethoxy-2-ethoxycarbonylamino-3,3,3-trifluoropropionate (2b), ethyl 2-ethoxycarbonylamino-3,3,3-trifluoro-2-isopropoxypropionate (2c), ethyl 2-ethoxycarbonylamino-3,3,3-frifluoro-2-phenoxypropionate (2d), methyl 2-ethoxycarbonylamino-3,3,3-trifluoro-2-phenoxypropionate (2e), ethyl 2-ethoxycarbonylamino-3,3,3-trifluoro-2-(4-fluorophenoxy)propionate (2f), methyl 2-ethoxycarbonylamino-3,3,3-trifluoro-2-(3-fluorophenoxy)propionate (2g), methyl 2-ethoxycarbonylamino-3,3,3-trifluoro-2-(4-fluorophenoxy)propionate (2h) (general procedure). To a solution of the imine **1a,b** (0.1 mmol) in benzene (100 mL), the corresponding alcohol or phenol (0.1 mmol) was added. The reaction mixture was stirred for 2 h, the solvent was removed *in vacuo*, and the residue was redistilled or recrystallized from hexane. The yields, the melting points, the elemental analysis data and the spectral data of compounds **2a—h** are listed in Tables 1 and 2.

Ethyl 3,3,3-trifluoro-2-isocyanato-2-methoxypropionate (3a), ethyl 2-ethoxy-3,3,3-trifluoro-2-isocyanatopropionate(3b),

Table 1. Yields, constants and elemental analysis data for compounds **2a—h, 3a—h,** and **5a—k**

Compound	Yield (%)	m.p./°C, b.p./(*p*/Torr)	Found / Calculated (%)			Molecular formula
			C	H	N	
2a	88	90—93 (3)	39.38 39.57	5.02 5.17	5.04 5.13	$C_9H_{14}F_3NO_5$
2b	91	87—89 (1)	41.69 41.82	5.42 5.61	4.99 4.88	$C_{10}H_{16}F_3NO_5$
2c	90	89—91 (1)	43.72 43.86	5.88 6.02	4.49 4.65	$C_{11}H_{18}F_3NO_5$
2d	89	Oil	50.33 50.15	4.98 4.81	4.32 4.18	$C_{14}H_{16}F_3NO_5$
2e	94	75—77	48.78 48.6	4.54 4.39	4.52 4.36	$C_{13}H_{14}F_3NO_5$
2f	96	Oil	47.51 47.6	4.11 4.28	3.73 3.96	$C_{14}H_{15}F_4NO_5$
2g	91	50—52	46.21 46.03	3.65 3.86	4.29 4.13	$C_{13}H_{13}F_4NO_5$
2h	91	63—65	46.29 46.03	3.71 3.86	4.01 4.13	$C_{13}H_{13}F_4NO_5$

(*to be continued*)

Table 1 (*continued*)

Compound	Yield (%)	M.p./°C, B.p./°C (*p*/Torr)	Found / Calculated (%)			Molecular formula
			C	H	N	
3a	77	60—62 (10)	37.21 37.02	3.68 3.55	6.31 6.17	$C_7H_8F_3NO_4$
3b	74	85—87 (25)	39.61 39.84	4.02 4.18	5.63 5.81	$C_8H_{10}F_3NO_4$
3c	81	78—82 (10)	42.16 42.36	4.59 4.74	5.28 5.49	$C_9H_{12}F_3NO_4$
3d	68	89—90 (2)	49.99 49.84	3.61 3.49	4.68 4.84	$C_{12}H_{10}F_3NO_4$
3e	73	80—82 (2)	48.22 48.01	3.11 2.93	5.22 5.09	$C_{11}H_8F_3NO_4$
3f	72	101—103 (2)	45.23 45.07	2.59 2.41	4.96 4.78	$C_{11}H_7F_4NO_4$
3g	77	84—85 (1)	46.71 46.92	3.12 2.95	4.77 4.56	$C_{12}H_9F_4NO_4$
3h	79	91—91 (1)	45.28 45.07	2.49 2.41	4.93 4.78	$C_{11}H_7F_4NO_4$
5a	88	126—128	44.21 44.02	4.11 3.98	8.09 7.9	$C_{13}H_{14}ClF_3N_2O_4$
5b	80	142—144	43.15 43.31	3.51 3.63	7.08 7.21	$C_{14}H_{14}F_6N_2O_4$
5c	75	141—142	43.48 43.31	3.51 3.63	7.38 7.21	$C_{14}H_{14}F_6N_2O_4$
5d	88	142—143	45.74 45.6	4.51 4.37	7.82 7.6	$C_{14}H_{16}ClF_3N_2O_4$
5e	83	162—164	43.65 43.48	4.12 3.91	7.42 7.24	$C_{14}H_{15}ClF_4N_2O_4$
5f	92	159—161	49.32 49.18	4.73 4.95	7.51 7.65	$C_{15}H_{18}F_4N_2O_4$
5g	79	149—150	46.33 46.16	4.48 4.36	6.95 6.73	$C_{16}H_{18}F_6N_2O_4$
5h	87	156—157	43.33 43.18	4.32 4.11	6.93 6.71	$C_{15}H_{17}Cl_2F_3N_2O_4$
5i	84	128—130	48.72 48.94	3.58 3.46	6.27 6.01	$C_{19}H_{16}F_6N_2O_5$
5j	78	112—114	49.33 49.1	3.79 3.69	6.19 6.03	$C_{19}H_{17}ClF_4N_2O_5$
5k	85	118—120	44.41 44.24	2.62 2.47	5.92 5.73	$C_{18}H_{12}ClF_7N_2O_4$

Table 2. ^1H and ^{19}F NMR spectra (δ (*J*/Hz)) of compounds **2a—h, 3a—h**, and **5a—k** in DMSO-d_6

Compound	^1H	^{19}F
2a	1.15 (t, 3 H, $\underline{CH_3}CH_2O$, *J* = 7.6); 1.25 (t, 3 H, $\underline{CH_3}CH_2O$, *J* = 7.9); 3.51 (s, 3 H, MeO); 4.12 (q, 2 H, $CH_3\underline{CH_2}O$, *J* = 7.9); 4.32 (q, 2 H, $CH_3\underline{CH_2}O$, *J* = 7.6); 7.91 (s, 1 H, NH)	−0.03 (s, CF_3)
2b	1.20 (t, 3 H, $\underline{CH_3}CH_2O$, *J* = 7.6); 1.32 (m, 6 H, $\underline{CH_3}CH_2O$); 4.02 (m, 2 H, $CH_3\underline{CH_2}O$); 4.12—4.32 (m, 4 H, $CH_3\underline{CH_2}O$); 8.12 (s, 1 H, NH)	−1.38 (s, CF_3)
2c	1.20 (d, 6 H, Me, *J* = 8.2); 1.32 (m, 6 H, $\underline{CH_3}CH_2O$); 4.02 (m, 1 H, $Me_2\underline{CH}O$); 4.11—4.35 (m, 4 H, $CH_3\underline{CH_2}O$); 8.09 (s, 1 H, NH)	−1.38 (s, CF_3)

(*to be continued*)

Table 2 (*continued*)

Compound	^{1}H	^{19}F
2d	1.11 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 1.31 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.7); 4.03 (m, 2 H, $CH_3\underline{CH_2}O$); 4.29 (m, 2 H, $CH_3\underline{CH_2}O$); 6.01 (s, 1 H, NH); 7.12 (m, 3 H, CH_{Ar}); 7.28 (m, 2 H, CH_{Ar});	−0.81 (s, CF_3)
2e	1.10 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 3.95 (s, 3 H, MeO); 4.00 (m, 2 H, $CH_3\underline{CH_2}O$); 5.90 (s, 1 H, NH); 7.10 (m, 3 H, CH_{Ar}); 7.25 (m, 2 H, CH_{Ar});	−0.93 (s, CF_3)
2f	1.10 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 1.30 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.6); 4.0 (m, 2 H, $CH_3\underline{CH_2}O$); 4.38 (m, 2 H, $CH_3\underline{CH_2}O$); 6.15 (s, 1 H, NH); 6.95 (m, 2 H, CH_{Ar}); 7.11 (m, 2 H, CH_{Ar});	−0.89 (s, 3 F, CF_3); −40.43 (m, 1 F, CF_{Ar})
2g	1.15 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 3.91 (s, 3 H, MeO); 4.02 (m, 2 H, $CH_3\underline{CH_2}O$); 6.01 (s, 1 H, NH); 6.93 (m, 3 H, CH_{Ar}); 7.21 (m, 1 H, CH_{Ar});	−1.01 (s, 3 F, CF_3); −33.90 (m, 1 F, CF_{Ar})
2h	1.12 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 3.96 (s, 3 H, MeO); 4.05 (m, 2 H, $CH_3\underline{CH_2}O$); 5.93 (s, 1 H, NH); 6.95 (m, 2 H, CH_{Ar}); 7.11 (m, 2 H, CH_{Ar});	−1.03 (s, 3 F, CF_3); −40.08 (m, 1 F, CF_{Ar})
3a	1.35 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.6); 3.50 (s, 3 H, MeO); 4.45 (q, 2 H, J = 7.6)	−2.30 (s, CF_3)
3b	1.35 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.6); 1.35 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.9); 4.05 (q, 2 H, $CH_3\underline{CH_2}O$, J = 7.5) 4.50 (q, 2 H, $CH_3\underline{CH_2}O$, J = 7.9)	−2.08 (s, CF_3)
3c	1.20 (d, 6 H, Me_2CHO, J = 8.1); 1.41 35 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.7); 4.02 (m, 1 H, $Me_2\underline{CH}O$); 4505 (q, 2 H, $CH_3\underline{CH_2}O$, J = 7.5)	−1.92 (s, CF_3)
3d	1.25 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.8); 4.40 (q, 2 H, $CH_3\underline{CH_2}O$, J = 7.8); 7.02 (m, 2 H, CH_{Ar}); 7.32 (m, 3 H, CH_{Ar})	3.11 (s, CF_3)
3e	3.86 (s, 3 H, MeO); 7.02 (d, 2 H, CH_{Ar}, J = 8.1); 7.12 (m, 1 H, CH_{Ar}); 7.31 (m, 2 H, CH_{Ar})	−3.05 (s, CF_3)
3f	3.95 (s, 3 H, MeO); 7.05 (m, 2 H, CH_{Ar}); 7.33 (m, 2 H, CH_{Ar})	−2.91 (s, 3 F, CF_3); −39.09 (m, 1 F, CF_{Ar})
3g	1.30 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.7); 4.35 (q, 2 H, $CH_3\underline{CH_2}O$, J = 7.7); 7.12—7.31 (m, 4 H, CH_{Ar})	−2.94 (s, 3 F, CF_3); −39.28 (m, 1 F, CF_{Ar})
3h	3.91 (s, 3 H, MeO); 6.85 (m, 2 H, CH_{Ar}); 6.95 (m, 1 H, CH_{Ar}); 7.30 (m, 1 H, CH_{Ar})	−3.12 (s, 3 F, CF_3); −32.62 (m, 1 F, CF_{Ar})
5a	1.32 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 3.56 (s, 3 H, MeO); 4.28 (m, 2 H, $CH_3\underline{CH_2}O$); 7.02 (m, 1 H, CH_{Ar}); 7.26 (m, 2 H, CH_{Ar}); 7.62 (m, 2 H, CH_{Ar} + NH); 7.34 (s, 1 H, NH)	−0.11 (s, CF_3)
5b	1.28 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 3.58 (s, 3 H, MeO); 4.26 (m, 2 H, $CH_3\underline{CH_2}O$); 7.34 (t, 1 H, CH_{Ar}, J = 8.8); 7.68 (m, 3 H, CH_{Ar}); 7.88 (s, 1 H, NH); 7.94 (s, 1 H, NH)	17.33 (s, CF_3); 0.08 (s, CF_3)
5c	1.32 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 3.57 (s, 3 H, MeO); 4.31 (m, 2 H, $CH_3\underline{CH_2}O$); 7.36 (m, 3 H, CH_{Ar}); 7.49 (t, 1 H, CH_{Ar}, J = 8.8); 7.66 (m, 3 H, CH_{Ar}); 7.88—8.08 (m, 3 H, CH_{Ar} + NH + NH)	15.36 (s, CF_3); −0.15 (s, CF_3)
5d	1.26 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 1.32 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 3.72—3.94 (m, 2 H, $CH_3\underline{CH_2}O$); 4.31 (m, 2 H, $CH_3\underline{CH_2}O$); 6.64 (s, 1 H, CH_{Ar}); 7.12 (m, 1 H, CH_{Ar}); 7.28 (m, 2 H, CH_{Ar}); 7.56 (s, 1 H, NH); 7.68 (s, 1 H, NH)	−0.24 (s, CF_3)
5e	1.18 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 1.22 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.5); 3.72 (m, 1 H, $CH_3\underline{CH_2}O$); 3.98 (m, 1 H, $CH_3\underline{CH_2}O$); 4.28 (m, 2 H, $CH_3\underline{CH_2}O$); 7.23 (m, 2 H, CH_{Ar}); 7.37 (s, 1 H, CH_{Ar}); 7.81 (s, 1 H, NH); 8.53 (s, 1 H, NH)	−0.46 (s, 3 F, CF_3); −46.61 (m, 1 F, CF_{Ar})
5f	1.18—1.34 (m, 9 H, Me_2CHO + $\underline{CH_3}CH_2O$); 4.28 (m, 2 H, $CH_3\underline{CH_2}O$); 4.48 (m, 1 H, $Me_2\underline{CH}O$); 6.56 (s, 1 H, NH); 7.06 (m, 2 H, CH_{Ar}); 7.39 (m, 2 H, CH_{Ar}); 7.52 (s, 1 H, NH)	−0.49 (s, 3 F, CF_3); −42.70 (m, 1 F, CF_{Ar})
5g	1.17 (d, 3 H, Me_2CHO, J = 6.8); 1.26 (m, 6 H, Me_2CHO + $\underline{CH_3}CH_2O$); 4.27 (m, 2 H, $CH_3\underline{CH_2}O$); 4.55 (m, 1 H, $Me_2\underline{CH}O$); 7.37 (m, 2 H, CH_{Ar}); 7.53 (m, 1 H, CH_{Ar}); 7.62 (m, 1 H, CH_{Ar}); 7.98 (s, 1 H, NH); 8.60 (s, 1 H, NH)	15.50 (s, CF_3); −0.40 (s, CF_3)
5h	1.18—1.32, 1.18—1.34 (m, 9 H, Me_2CHO + $\underline{CH_3}CH_2O$); 4.20 (m, 2 H, $CH_3\underline{CH_2}O$); 4.56 (m, 1 H, $Me_2\underline{CH}O$); 7.34 (d, 1 H, CH_{Ar}, J = 8.1); 7.48 (m, 2 H, CH_{Ar}); 7.82 (s, 1 H, NH); 7.94 (s, 1 H, NH)	−0.57 (s, CF_3)
5i	1.29 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.2); 4.34 (m, 2 H, $CH_3\underline{CH_2}O$); 7.08—7.29 (m, 8 H, CH_{Ar}); 7.38 (s, 1 H, NH); 7.46 (s, 1 H, NH)	19.78 (s, CF_3); 0.34 (s, CF_3)
5j	1.32 (t, 3 H, $\underline{CH_3}CH_2O$, J = 7.2); 3.88 (s, 3 H, MeO); 4.36 (m, 2 H, $CH_3\underline{CH_2}O$); 6.96 (s, 1 H, CH_{Ar}); 7.06 (m, 3 H, CH_{Ar}); 7.31 (m, 3 H, CH_{Ar} + NH); 7.49 (s, 1 H, NH)	0.24 (s, 3 F, CF_3); −40.58 (m, 1 F, CF_{Ar})
5k	3.84 (s, 3 H, MeO); 7.05 (m, 2 H, CH_{Ar}); 7.22 (m, 3 H, CH_{Ar}); 7.38 (s, 1 H, NH); 7.51 (m, 2 H, CH_{Ar}); 8.01 (s, 1 H, NH)	15.46 (s, 3 F, CF_3); 0.27 (s, 3 F, CF_3); −40.18 (m, 1F, CF_{Ar})

ethyl 3,3,3-trifluoro-2-isocyanato-2-isopropoxypropionate (3c), ethyl 3,3,3-trifluoro-2-isocyanato-2-phenoxypropionate (3d), methyl 3,3,3-trifluoro-2-isocyanato-2-phenoxypropionate (3e), ethyl 3,3,3-trifluoro-2-(4-fluorophenoxy)-2-isocyanatopropionate (3f), methyl 3,3,3-trifluoro-2-(3-fluorophenoxy)-2-isocyanatopropionate (3g), methyl 3,3,3-trifluoro-2-(4-fluorophenoxy)-2-isocyanatopropionate (3h) (general procedure). A mixture of **2a—h** (0.05 mmol) and PCl_5 (10.4 g, 0.05 mmol) in $POCl_3$ (30 mL) was refluxed for 2 h and concentrated *in vacuo*. The products were purified by fractional distillation to give **3a—h**. The yields, melting points, elemental analysis data, and the spectral data of compounds **3a—h** are listed in Tables 1 and 2.

Ethyl 2-[3-(3-chlorophenyl)ureido]-3,3,3-trifluoro-2-methoxypropionate (5a), ethyl 3,3,3-trifluoro-2-[3-(2-trifluoromethylphenyl)ureido]-2-methoxypropionate (5b), ethyl 3,3,3-trifluoro-2-[3-(3-trifluoromethylphenyl)ureido]-2-methoxypropionate (5c), ethyl 2-[3-(3-chlorophenyl)ureido]-2-ethoxy-3,3,3-trifluoropropionate (5d), ethyl 2-[3-(3-chloro-4-fluorophenyl)-ureido]-2-ethoxy-3,3,3-trifluoropropionate (5e), ethyl 3,3,3-trifluoro-2-[3-(4-fluorophenyl)ureido]-2-isopropoxypropionate (5f), ethyl 3,3,3-trifluoro-2-[3-(3-trifluoromethylphenyl)ureido]-2-isopropoxypropionate (5g), ethyl 2-[3-(2,4-dichlorophenyl)-ureido]-2-ethoxy-3,3,3-trifluoropropionate (5h), ethyl 3,3,3-trifluoro-2-[3-(4-trifluoromethoxyphenyl)ureido]-2-phenoxypropionate (5i), ethyl 2-[3-(5-chloro-2-methoxyphenyl)ureido]-3,3,3-trifluoro-2-phenoxypropionate (5j), ethyl 2-[3-(2-chloro-5-trifluoromethylphenyl)ureido]-3,3,3-trifluoro-2-(4-fluorophenoxy)propionate (5k) (general procedure). To a solution of isocyanates **3a—d,h** (0.01 mmol) in benzene (20 mL) the corresponding aniline **4a—j** (0.01 mmol) was added. After the exothermic reaction was finished, the mixture was stirred for 2 h, the solvent was removed *in vacuo*, and the residue was recrystallized from hexane. The yields, melting points, elemental analysis data, and the spectral data of compounds **5a—k** are listed in Tables 1 and 2.

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