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Synthesis of new heteroatomic podands from ethyl 2-[(2-aminophenyl-amino)methylidene]-3-oxoalkanoates and thiophene-2,5-dicarboxaldehyde

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Experimental

General methods. IR diffuse reflectance spectra were recorded on a Perkin–Elmer Spectrum One FTIR spectrometer (400–4000 cm^{-1}). ^{1}H and ^{19}F NMR spectra were recorded on a Bruker DRX 400 instrument (^{1}H: 400 MHz, TMS as an internal standard; ^{19}F: 376 MHz, C_6F_6 as an internal standard) in $CDCl_3$. The elemental analyses were performed on a Perkin Elmer PE 2400 series II CHNS-O EA 1108 elemental analyzer. Melting points were measured in open capillaries with a Stuart SMP3 apparatus for melting temperature determination. Reactions were monitored by TLC with 0.20 mm Alugram Sil G/UV_{254} pre-coated silica gel plates (60 F254).

The IR spectrum of compound **3** contains three high-frequency absorption bands (1710, 1699, 1665 cm^{-1}) corresponding to the vibrations of three different carbonyl groups (CO_2Et, H-C=O and R^FC=O). Low-frequency shift of the R^FC=O absorption band is attributed to the involvement of this group in the formation of intramolecular hydrogen bond with the NH group. The absorption of NH group stretching vibrations is observed at 3091 cm^{-1}.

The correlation of the *Z* and *E* isomers (see Table 1S) in the ^{1}H NMR spectra was made based on the data obtained previously for esters of 2-alkyl(aryl, hetaryl)aminomethylidene-3-oxo-3-polyfluoroalkylpropionic acids,[1] according to which the

CH and NH protons of the *E* isomer are observed at lower field compared to the corresponding protons of the *Z* isomer.

A comparative analysis of the IR spectra of podands **4b-d** revealed no substantial differences between them. Thus, the IR spectra of these products show an absorption band at 1708−1695 cm^{-1} assigned to the vibrations of the free ethoxycarbonyl group. For diesters **4b,c** this band has a doublet form, obviously, due to the existence of the rotational *s-cis* and *s-trans*-isomers. The absorption bands of acyl and NH groups involved in hydrogen bonding are observed at 1642−1630 and 2992−2984 cm^{-1} respectively.

We have earlier found[1-4] that the tendency to undergo isomerization of the *E*-isomer to a mixture of *Z*- and *E*-isomers upon dissolution is general for ethyl esters of 2-(R-aminomethylidene)-3-oxo-3-polyfluoroalkylpropionic acids (R is alkyl, aryl, or hetaryl).

Thiophenedicarboxaldehyde **2** is available from Aldrich. All commercially available compounds were used as received unless stated otherwise. Diethyl 2-[(2-aminophenyl)aminomethylidene]malonate **1a**, ethyl 2-[(2-aminophenyl)aminomethylidene]-3-oxobutanoate **1b,** ethyl 2-[(2- aminophenyl)aminomethylidene]-3-oxo-3-polyfluoroalkylpropionates **1c,d** and tetraethyl 2,2'-[2,5-thienylbis(aminomethylidene-2-iminophenylene)] dimalonate **4a** were synthesized by the methods described earlier.[3,5,6]

Ethyl 2-[2-(5-formylthienyl)imino]phenylaminomethylidene-3-oxo-4,4,5,5-tetrafluoro-pentanoate **3.** A mixture of ester **1d** (1.34 g, 0.004 mol), thiophene-2,5-dicarboxaldehyde **2** (0.42 g, 0.003 mol) and glacial acetic acid (1 ml) in benzene (30 ml) was refluxed with the azeotropic distillation for 30 h. Then the reaction mixture was concentrated and chromatographed through silica gel with $CHCl_3$ as an eluent to provide product **3**. Yield 0.98 g (72 %), yellow powder, mp 119−120 °C. IR (DRA, ν/cm^{-1}): 3091 (NH), 2984 (CH), 1710 (CO_2Et), 1699 (C=O), 1665 (COR^F), 1631 (C=N), 1595, 1560 (C=C, NH), 1259-1078 (C-F). ^1H NMR ($CDCl_3$) δ: *E, Z*: 7.21-7.87 (m, 4H, C_6H_4), 10.00 (s, 1H, CO<u>H</u>); *E* (60%): 1.36 (t, 3H, $OCH_2\underline{CH_3}$, *J* 7.1 Hz), 4.31 (q, 2H, $O\underline{CH_2}CH_3$, *J* 7.1 Hz), 6.69 (tt, HCF_2, *J* 53.1, 5.9 Hz), 8.62 (d, 1H, =CH, *J* 14.4 Hz), 8.78 (s, 1H, <u>H</u>-C=N), 12.84 (br.d, 1H, NH, *J* 14.9 Hz); *Z* (40%): 1.35 (t, 3H, $OCH_2\underline{CH_3}$, *J* 7.1 Hz), 4.30 (q, 2H, $O\underline{CH_2}CH_3$, *J* 7.1 Hz), 6.38 (tt, HCF_2, *J*

53.1, 5.9 Hz), 8.50 (d, 1H, =CH, *J* 14.4 Hz), 8.74 (s, 1H, H-C=N), 12.02 (br.d, 1H, NH, *J* 14.9 Hz). ^{19}F NMR ($CDCl_3$) δ: *E* (60%): 23.26 (dm, 2F, α-CF_2, *J* 53.1 Hz), 39.61 (m, 2F, 2 β-CF_2); *Z* (40%): 23.66 (dm, 2F, α-CF_2, *J* 53.1 Hz), 41.12 (m, 4F, 2 β-CF_2). Found (%): C, 52.40; H, 3.64; F 16.63; N, 6.26; S, 6.99. Calc. for $C_{20}H_{16}F_4N_2O_4S$ (%): C, 52.63; H, 3.53; F, 16.65; N, 6.14; S, 7.02.

Diethyl 2,2'-[2,5-thienylbis(aminomethylidene-2-iminophenylene)]bis(3-oxo-butanoate) **4b**. A mixture of ester **1b** (1.74 g, 0.007 mol), thiophene-2,5-dicarboxaldehyde **2** (0.42 g, 0.003 mol) and glacial acetic acid (2 ml) in benzene (40 ml) was refluxed with the azeotropic distillation for 21 h. Then the reaction mixture was concentrated to dryness. The resulting precipitate of **4b** was crystallized from ethanol. Yield 1.35 g (74 %), yellow powder, mp 198−199 °C. IR (DRA, ν/cm^{-1}): 3092 (NH), 2981 (CH), 1695 (CO_2Et), 1630 (C=O), 1600, 1584, 1556 (NH, C=N, C=C). ^{1}H NMR ($CDCl_3$) δ: *EE, ZZ*: 7.17-7.21, 7.28-7.40 (m, 8H, 2 C_6H_4); *EE* (90%): 1.35 (t, 6H, 2 $OCH_2\underline{CH_3}$, *J* 7.1 Hz), 2.57 (s, 6H, 2 Me), 4.27 (q, 4H, 2 $O\underline{CH_2}CH_3$, *J* 7.1 Hz), 7.91 (s, 2H, thiophene), 8.60 (d, 2H, 2 =CH, *J* 13.6 Hz), 8.72 (s, 2H, 2 H-C=N), 13.17 (br.d, 2H, 2 NH, *J* 13.7 Hz); *ZZ* (10%): 1.33 (t, 6H, 2 $OCH_2\underline{CH_3}$, *J* 7.3 Hz), 2.51 (s, 6H, 2 Me), 4.38 (q, 4H, 2 $O\underline{CH_2}CH_3$, *J* 7.3 Hz), 7.80 (s, 2H, thiophene), 8.58 (d, 2H, 2 =CH, *J* 13.5 Hz), 8.70 (s, 2H, 2 H-C=N), 11.65 (br.d, 2H, 2 NH, *J* 13.4 Hz). Found (%): C, 63.52; H, 4.96; N, 9.03; S 5.10. Calc. for $C_{32}H_{32}N_4O_6S$ (%): C, 63.78; H, 5.27; N, 9.33; S, 5.34.

Diethyl 2,2'-[2,5-thienylbis(aminomethylidene-2-iminophenylene)]bis(3-oxo-4,4,4-trifluorobutanoate) **4c**. A mixture of ester **1c** (2.12 g, 0.007 mol), thiophene-2,5-dicarboxaldehyde **2** (0.42 g, 0.003 mol) and glacial acetic acid (2 ml) in toluene (40 ml) was refluxed with the azeotropic distillation for 25 h. Then the reaction mixture was concentrated to dryness and the residue was dissolved in diethyl ether (10 ml). The resulting precipitate of **4c** was filtered off and crystallized from ethanol. Yield 1.36 g (64 %), yellow powder, mp 149−150 °C. IR (DRA, ν/cm^{-1}): 3174 (NH), 2984 (CH), 1701 (CO_2Et), 1738 (COR^F), 1600, 1580, 1563 (NH, C=N, C=C), 1238-1150 (C-F). ^{1}H NMR ($CDCl_3$) δ: *EE, ZZ*: 7.28-7.47 (m,

8H, 2 C_6H_4); *EE* (78%): 1.35 (t, 6H, 2 $OCH_2\underline{CH_3}$, *J* 7.1 Hz), 4.31 (q, 4H, 2 $O\underline{CH_2}CH_3$, *J* 7.1 Hz), 7.93 (s, 2H, thiophene), 8.71 (d, 2H, 2 =CH, *J* 14.4 Hz), 8.77 (s, 2H, 2 H-C=N), 12.87 (br.d, 2H, 2 NH, *J* 14.4); *ZZ* (22%): 1.31 (t, 6H, 2 $OCH_2\underline{CH_3}$, *J* 7.1 Hz), 4.32 (q, 4H, 2 $O\underline{CH_2}CH_3$, *J* 7.1 Hz), 7.88 (s, 2H, thiophene), 8.59 (d, 2H, 2 =CH, *J* 14.4 Hz), 8.75 (s, 2H, 2 H-C=N), 12.19 (br.d, 2H, 2 NH, *J* 14.4 Hz). ^{19}F NMR ($CDCl_3$) δ: *E* (78%): 89.11 (s, 6F, 2 CF_3); *Z* (22%): 89.99 (s, 6F, 2 CF_3). Found (%): C, 54.11; H, 3.37; F 15.51; N, 7.67; S, 4.35. Calc. for $C_{32}H_{26}F_6N_4O_6S$ (%): C, 54.24; H, 3.70; F, 16.09; N, 7.91; S, 4.52.

Diethyl 2,2'-[2,5-thienylbis(aminomethylidene-2-iminophenylene)]bis(3-oxo-4,4,5,5-tetrafluoropentanoate) **4d** was synthesized similarly to compound **4c** from ester **1d** (2.34 g, 0.007 mol). Yield 1.44 g (62 %), orange powder, mp 187−188 °C. IR (DRA, ν/cm^{-1}): 3172 (NH), 2993 (CH), 1708 (CO_2Et), 1642 (COR^F), 1600, 1563, 1558 (NH, C=N, C=C), 1284-1206 (C-F). ^{1}H NMR ($CDCl_3$) δ: *EE, ZZ*: 7.28-7.44 (m, 8H, 2 C_6H_4); *EE* (88%): 1.36 (t, 6H, 2 $OCH_2\underline{CH_3}$, *J* 7.1 Hz), 4.30 (q, 4H, 2 $O\underline{CH_2}CH_3$, *J* 7.1 Hz), 6.69 (tt, 2H, 2 HCF_2, *J* 52.9, 5.8 Hz), 7.88 (s, 2H, thiophene), 8.62 (d, 2H, 2 =CH, *J* 14.4 Hz), 8.75 (s, 2H, 2 H-C=N), 12.89 (br.d, 2H, 2 NH, *J* 14.4 Hz); *ZZ* (12%): 1.31 (t, 6H, 2 $OCH_2\underline{CH_3}$, *J* 7.1 Hz), 4.35 (q, 4H, 2 $O\underline{CH_2}CH_3$, *J* 7.1 Hz), 6.39 (tt, 2H, 2 HCF_2, *J* 52.9, 5.8 Hz), 7.84 (s, 2H, thiophene), 8.52 (d, 2H, 2 =CH, *J* 14.4 Hz), 8.74 (s, 2H, 2 H-C=N), 11.99 (br.d, 2H, 2 NH, *J* 14.4 Hz). ^{19}F NMR ($CDCl_3$) δ: *EE* (88%): 23.64 (dt, 4F, 2 α-CF_2, *J* 53.1, 8.1 Hz), 39.61 (m, 4F, 2 β-CF_2); *ZZ* (12%): 22.22 (dt, 4F, 2 α-CF_2, *J* 53.1, 8.1 Hz), 41.11 (m, 4F, 2 β-CF_2). Found (%): C, 52.91; H, 3.22; F 19.53; N, 7.16; S, 4.35. Calc. for $C_{34}H_{28}F_8N_4O_6S$ (%): C, 52.85; H, 3.64; F, 19.67; N, 7.25; S, 4.15.

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Table 1S Chemical shifts (δ) of the NH- and CH-protons for compounds **3** and **4b-d** in ^{1}H NMR spectra

No.	R^F	Isomer	=CH- signals, δ, ppm	HC=N- signals, δ, ppm	NH-signals, δ, ppm	Contetnt, %
3	$H(CF_2)_2$	*E*	8.62	8.78	12.84	60
		Z	8.50	8.74	12.02	40
4b	Me	*EE*	8.60	8.72	13.17	90
		ZZ	8.58	8.70	11.65	10
4c	CF_3	*EE*	8.71	8.77	12.87	78
		ZZ	8.59	8.75	12.19	22
4d	$H(CF_2)_2$	*EE*	8.62	8.75	12.89	88
		ZZ	8.52	8.74	11.99	12