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SYNTHESIS AND SOME TRANSFORMATIONS OF γ-(*p*-FLUOROPHENYL)-γ-(2-FURYL)PROPYLAMINE

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Ethyl α-cyano-β-(p-fluorophenyl)-β-(2-furyl)propionate was obtained by the condensation of ethyl α-cyano-β-(2-furyl)acrylate with p-fluorophenylmagnesium bromide. Its deethoxycarbonylation led to β-(p-fluorophenyl)-β-(2-furyl)propionitrile. Reduction of the nitrile with lithium aluminum hydride gave γ-(p-fluorophenyl)-γ-(2-furyl)propylamine. Some transformations of the latter were studied.

Keywords: γ-(*p*-fluorophenyl)-γ-(2-furyl)propylamine, ethyl furfurylidenecyanoacetate, ethyl β-(*p*-fluorophenyl)-β-(2-furyl)propionate, reduction, deethoxycarbonylation.

Earlier we reported the synthesis and some transformations of γ-(2-furyl)-γ-phenylpropylamine [1]. In order to investigate the relation between the biological activity and structure in the present work we synthesized analogous derivatives containing a fluorine atom at the *p*-position of the benzene ring. Thus, in the reaction of *p*-fluorophenylmagnesium bromide with ethyl α-cyano-β-(2-furyl)acrylate (**1**) [2] we obtained ethyl α-cyano-β-(*p*-fluorophenyl)-β-(2-furyl)propionate (**2**), the deethoxycarbonylation of which led to the corresponding nitrile **3**. Reduction of the latter with lithium aluminum hydride gave the amine **4**. Reaction of the amine with substituted aromatic aldehydes or ketones **5a-h** led to the corresponding azomethines **6a-h**, which were reduced by sodium borohydride without isolation to the amines **7a-h** and transformed by treatment with various acid chlorides into the amides **8a-f**. From the amine **4** by reaction with succinic or phthalic anhydrides we obtained the N-substituted succinimide **9** and phthalimide **10** respectively (Scheme 1).

The compositions and structures of the synthesized compounds were confirmed by elemental analysis (Table 1) and ^{1}H NMR spectra (Table 2).

EXPERIMENTAL

The IR spectra were recorded in vaseline oil on a UR-20 spectrometer. The ^{1}H NMR spectra were recorded on a Varian Mercury-300 instrument (300 MHz) with TMS as internal standard.

Ethyl furfurylidenecyanoacetate **1** was obtained by the familiar procedure [2].

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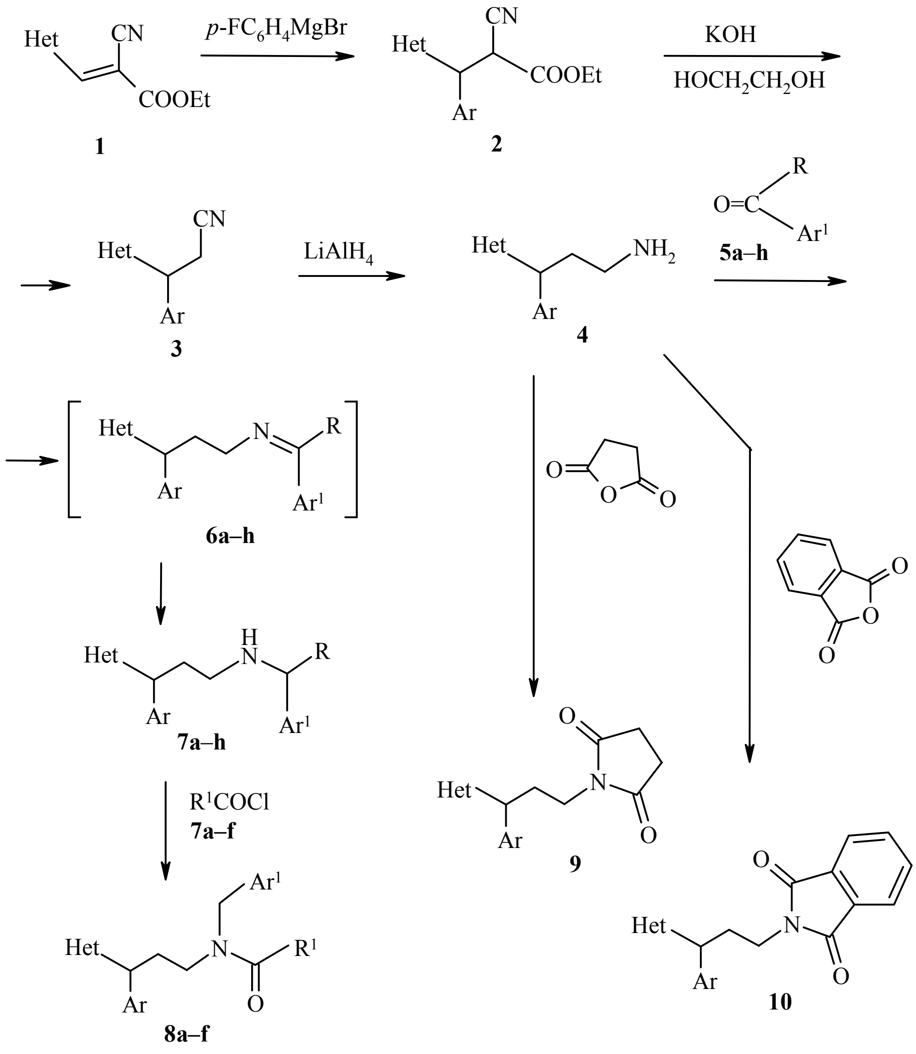
Scheme 1



Het = 2-furyl, Ar = *p*-fluorophenyl; **5a-f** – **7a-f** R = H, **a** Ar^1 = Ph, **b** Ar^1 = *p*-$Me_2NC_6H_4$;
c Ar^1 = *p*-*i*-$C_3H_7OC_6H_4$, **d** Ar^1 = *p*-$MeOC_6H_4$, **e** Ar^1 = *m*,*p*-$(MeO)_2C_6H_3$, **f** Ar^1 = *o*-FC_6H_4, **5g-h** – **7g-h** R = Me,
g Ar^1 = *p* -ClC_6H_4, **h** Ar^1 = Ph; **8 a-b** R^1 = Me, **a** Ar^1 = Ph, **b** Ar^1 = *p*-$MeOC_6H_4$,
c-f R^1 = Et, **c** Ar^1 = Ph, **d** Ar^1 = *p*-$MeOC_6H_4$, **e** Ar^1 = *m*,*p*-$(MeO)_2C_6H_3$, **f** Ar^1 = *p*-FC_6H_4

TABLE 1. The Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, % C	H	N	bp, °C (mm Hg)	Yield, %
1	2	3	4	5	6	7
2	$C_{16}H_{14}FNO_3$	66.83 66.89	4.85 4.91	4.91 4.87	160-162 (1)	81
3	$C_{13}H_{10}FNO$	72.60 72.55	4.62 4.68	6.45 6.50	138-141 (1)	54
4	$C_{13}H_{14}FNO$	71.27 71.21	6.48 6.43	6.32 6.38	118 (2)	87

TABLE 1 (continued)

1	2	3	4	5	6	7
7a	$C_{20}H_{20}FNO$	$\frac{77.68}{77.64}$	$\frac{6.48}{6.51}$	$\frac{4.50}{4.52}$	182-184 (2)	90
7b	$C_{22}H_{25}FN_2O$	$\frac{75.02}{74.97}$	$\frac{7.17}{7.14}$	$\frac{8.00}{7.94}$	220-221 (1)	78
7c	$C_{23}H_{26}FNO_2$	$\frac{75.15}{75.17}$	$\frac{7.11}{7.15}$	$\frac{3.80}{3.81}$	226-229 (1)	90
7d	$C_{21}H_{22}FNO_2$	$\frac{75.15}{75.19}$	$\frac{6.50}{6.53}$	$\frac{4.16}{4.12}$	195-198 (1)	93
7e	$C_{22}H_{24}FNO_3$	$\frac{71.55}{71.52}$	$\frac{6.50}{6.54}$	$\frac{3.82}{3.79}$	220-224 (1)	86
7f	$C_{20}H_{19}F_2NO$	$\frac{73.33}{73.37}$	$\frac{5.88}{5.84}$	$\frac{4.23}{4.27}$	189-191 (2.5)	87
7g	$C_{21}H_{21}ClFNO$	$\frac{70.52}{70.48}$	$\frac{6.00}{5.97}$	$\frac{3.86}{3.91}$	215-217 (2)	76
7h	$C_{21}H_{22}FNO$	$\frac{77.95}{77.99}$	$\frac{6.81}{6.85}$	$\frac{4.30}{4.33}$	200-201 (2)	74
8a	$C_{22}H_{22}FNO_2$	$\frac{75.24}{75.19}$	$\frac{6.33}{6.30}$	$\frac{4.02}{3.98}$	210-213 (1.5)	69
8b	$C_{23}H_{24}FNO_3$	$\frac{72.40}{72.42}$	$\frac{6.30}{6.34}$	$\frac{3.63}{3.67}$	245-248 (2)	71
8c	$C_{23}H_{24}FNO_2$	$\frac{75.63}{75.59}$	$\frac{6.66}{6.61}$	$\frac{3.80}{3.83}$	225-228 (1.5)	66
8d	$C_{24}H_{26}FNO_3$	$\frac{72.72}{72.70}$	$\frac{6.62}{6.60}$	$\frac{3.52}{3.53}$	240-244 (1)	67
8e	$C_{25}H_{28}FNO_4$	$\frac{70.60}{70.56}$	$\frac{6.60}{6.63}$	$\frac{3.25}{3.29}$	253-256 (2)	64
8f	$C_{23}H_{23}F_2NO_2$	$\frac{75.76}{72.04}$	$\frac{6.32}{6.04}$	$\frac{3.80}{3.65}$	215-219 (1)	70
9	$C_{17}H_{16}FNO_3$	$\frac{67.80}{67.76}$	$\frac{5.39}{5.35}$	$\frac{4.60}{4.64}$	190-193 (1)	68
10	$C_{21}H_{16}FNO_3$	$\frac{72.33}{72.19}$	$\frac{4.56}{4.61}$	$\frac{4.05}{4.00}$	210-214 (1)	72

TABLE 2. The ^1H NMR Spectra of Compounds **2-4**, **7-10**

Compound*	Chemical shifts, δ, ppm (SSCC, J, Hz)*^{2}
1	2
2	1.18 (1.5H, t, J = 7.1) and 1.20 (1.5H, t, J = 7.1, CH_3); 4.15 (1H, q, J = 7.1) and 4.15 (1H, q, J = 7.1, CH_2); 4.61 (0.5H, d, J = 7.4) and 4.71 (0.5H, d, J = 7.4, CHCN); 4.77 (0.5H, d, J = 7.4) and 4.82 (0.5H, d, J = 7.4, CHAr); 6.27 (0.5H, d, J = 3.4, H_{Het}-3); 6.34-6.42 (1.5H, m, H_{Het}-3,4); 7.06 (1H, t, J = 8.5) and 7.09 (1H, t, J = 8.5, H_{Ar}-3,5); 7.36-7.46 (3H, m, H_{Ar}-2,6, H_{Het}-5)
3	3.05 (1H, dd, J_1 = 16.9, J_2 = 7.4) and 3.11 (1H, dd, J_1 = 16.9, J_2 = 7.4, $CH\underline{CH_2}$); 4.45 (1H, t, J = 7.4, CH); 6.24 (1H, d, J = 3.2, H_{Het}-3); 6.34 (1H, dd, J_1 = 3.2, J_2 = 2.0, H_{Het}-4); 7.05 (2H, t, J = 8.7, H_{Ar}-3,5); 7.31 (2H, dd, J_1 = 8.7, J_2 = 5.4, H_{Ar}-2,6); 7.42 (1H, d, J = 2.0, H_{Het}-5)
4	1.92 (1H, m) and 2.13 (1H, dq, J_1 = 13.5, J_2 = 7.0, $CH\underline{CH_2}$); 1.97 (2H, br, NH_2); 2.53 (2H, m, NCH_2); 4.14 (1H, t, J = 7.7, CH); 6.06 (1H, d, J = 3.2, H_{Het}-3); 6.26 (1H, dd, J_1 = 3.2, J_2 = 1.8, H_{Het}-4); 6.98 (2H, t, J = 8.7, H_{Ar}-3,5); 7.22 (2H, dd, J_1 = 8.7, J_2 = 5.4, H_{Ar}-2,6); 7.32 (1H, d, J = 1.8, H_{Het}-5)
7a	1.75 (1H, br, NH); 1.89 (1H, dtd, J = 13.7, J = 8.2 and J = 6.5) and 2.22 (1H, dq, J_1 = 13.7, J_2 = 7.1, $CH\underline{CH_2}$); 2.47 (1H, dt, J_1 = 11.5, J_2 = 6.8) and 2.51 (1H, dt, J_1 = 11.5, J_2 = 6.8, NCH_2); 3.66 (1H, d, J = 13.4) and 3.69 (1H, d, J = 13.4, $CH_2C_6H_5$); 4.17 (1H, dd, J_1 = 8.2, J_2 = 7.1, CH); 6.04 (1H, d, J = 3.3, H_{Het}-3); 6.25 (1H, dd, J_1 = 3.3, J_2 = 1.8, H_{Het}-4); 6.96 (2H, t, J = 8.7, H_{Ar}-3,5); 7.14-7.27 (7H, m, H_{Ar}-2,6 and C_6H_5); 7.31 (1H, d, J = 1.8, H_{Het}-5)

TABLE 2 (continued)

1	2
7b	1.90 (1H, br, NH); 1.99 (1H, dtd, $J_1 = 13.5$, $J_2 = 8.3$, $J_3 = 6.6$) and 2.24 (1H, dq, $J_1 = 13.5$, $J_2 = 7.0$, $\mathrm{CH\underline{CH_2}}$); 2.49 (1H, dt, $J_1 = 11.6$, $J_2 = 6.6$) and 2.53 (1H, dt, $J_1 = 11.6$, $J_2 = 6.6$, $\mathrm{NCH_2}$); 2.93 (6H, s, $\mathrm{N(CH_3)_2}$); 3.57 (1H, d, $J = 12.8$) and 3.61 (1H, d, $J = 12.8$, $\mathrm{CH_2Ar^1}$); 4.18 (1H, dd, $J_1 = 8.3$, $J_2 = 7.0$, CH); 6.08 (1H, d, $J = 3.2$, $\mathrm{H_{Het}}$-3); 6.28 (1H, dd, $J_1 = 3.2$, $J_2 = 1.9$, $\mathrm{H_{Het}}$-4); 6.64 (2H, d, $J = 8.7$, $\mathrm{H_{Ar1}}$-3,5); 6.98 (2H, t, $J = 8.7$, $\mathrm{H_{Ar}}$-3,5); 7.11 (2H, d, $J = 8.7$, $\mathrm{H_{Ar1}}$-2,6); 7.22 (2H, dd, $J_1 = 8.7$, $J_2 = 5.4$, $\mathrm{H_{Ar}}$-2,6); 7.34 (1H, d, $J = 1.9$, $\mathrm{H_{Het}}$-5)
7c	1.33 (6 H, d, $J = 6.0$, $\mathrm{(CH_3)_2}$); 1.91 (1H, br, NH); 1.98 (1H, dtd, $J_1 = 13.5$, $J_2 = 8.2$, $J_3 = 6.4$) and 2.23 (1H, dq, $J_1 = 13.5$, $J_2 = 7.0$, $\mathrm{CH\underline{CH_2}}$); 2.47 (1H, dt, $J_1 = 11.6$, $J_2 = 6.7$) and 2.51 (1H, dt, $J_1 = 11.6$, $J_2 = 6.7$, $\mathrm{NCH_2}$); 3.59 (1H, d, $J = 13.0$) and 3.62 (1H, d, $J = 13.0$, $\mathrm{CH_2Ar^1}$); 4.17 (1H, dd, $J_1 = 8.2$, $J_2 = 7.0$, CH); 4.52 (1H, c. п, $J = 6.0$, OCH); 6.05 (1H, d, $J = 3.2$, $\mathrm{H_{Het}}$-3); 6.27 (1H, dd, $J_1 = 3.2$, $J_2 = 1.8$, $\mathrm{H_{Het}}$-4); 6.76 (2H, d, $J = 8.6$, $\mathrm{H_{Ar1}}$3,5); 6.97 (2H, t, $J = 8.6$, $\mathrm{H_{Ar1}}$-3,5); 7.15 (2H, d, $J = 8.6$, $\mathrm{H_{Ar1}}$2,6); 7.21 (2H, dd, $J_1 = 8.6$, $J_2 = 5.5$, $\mathrm{H_{Ar1}}$-2,6); 7.32 (1H, d, $J = 1.8$, $\mathrm{H_{Het}}$-5)
7d	1.47 (1H, br, NH); 1.97 (1H, dtd, $J_1 = 13.6$, $J_2 = 8.4$, $J_3 = 6.8$) and 2.21 (1H, dq, $J_1 = 13.6$, $J_2 = 6.8$, $\mathrm{CH\underline{CH_2}}$); 2.40-2.54 (2H, m, $\mathrm{NCH_2}$); 3.58 (1H, d, $J = 13.1$) and 3.62 (1H, d, $J = 13.1$, $\mathrm{CH_2Ar^1}$); 3.76 (3H, s, $\mathrm{OCH_3}$); 4.16 (1H, dd, $J_1 = 8.4$, $J_2 = 6.8$, CH); 6.04 (1H, d, $J = 3.2$, $\mathrm{H_{Het}}$-3); 6.26 (1H, dd, $J_1 = 3.2$, $J_2 = 1.8$, $\mathrm{H_{Het}}$-4); 6.78 (2H, d, $J = 8.7$, $\mathrm{H_{Ar1}}$-3,5); 6.96 (2H, t, $J = 8.7$, $\mathrm{H_{Ar}}$-3,5); 7.16 (2H, d, $J = 8.7$, $\mathrm{H_{Ar1}}$-2,6); 7.20 (2H, dd, $J_1 = 8.7$, $J_2 = 5.6$, $\mathrm{H_{Ar}}$-2,6); 7.31 (1H, d, $J = 1.8$, $\mathrm{H_{Het}}$-5)
7e	1.54 (1H, br, NH); 1.97 (1H, dtd, $J_1 = 13.5$, $J_2 = 8.2$, $J_3 = 6.4$) and 2.22 (1H, dq, $J_1 = 13.5$, $J_2 = 7.0$, $\mathrm{CH\underline{CH_2}}$); 2.45 (1H, dt, $J_1 = 11.8$, $J_2 = 6.7$) and 2.49 (1H, dt, $J_1 = 11.8$, $J_2 = 6.7$, $\mathrm{NCH_2}$); 3.58 (1H, d, $J = 13.2$) and 3.60 (1H, d, $J = 13.2$, $\mathrm{CH_2Ar^1}$); 3.78 (3H, s, $\mathrm{OCH_3}$); 3.80 (3H, s, $\mathrm{OCH_3}$); 4.15 (1H, dd, $J_1 = 8.2$, $J_2 = 7.0$, CH); 6.05 (1H, d, $J = 3.2$, $\mathrm{H_{Het}}$-3); 6.26 (1H, dd, $J_1 = 3.2$, $J_2 = 1.9$, $\mathrm{H_{Het}}$-4); 6.73 (2H, br.. s, $\mathrm{H_{Ar1}}$-5,6); 6.84 (1H, br.. s, $\mathrm{H_{Ar1}}$-2); 6.96 (2H, t, $J = 8.7$, $\mathrm{H_{Ar}}$-3,5); 7.20 (2H, dd, $J_1 = 8.7$, $J_2 = 5.5$, $\mathrm{H_{Ar}}$-2,6); 7.31 (1H, d, $J = 1.9$, $\mathrm{H_{Het}}$-5)
7f	1.78 (1H, br, NH); 2.02 (1H, dtd, $J_1 = 13.6$, $J_2 = 8.2$, $J_3 = 6.4$) and 2.26 (1H, dq, $J_1 = 13.6$, $J_2 = 6.9$, $\mathrm{CH\underline{CH_2}}$); 2.51 (1H, dt, $J_1 = 11.5$, $J_2 = 6.7$) and 2.55 (1H, dt, $J_1 = 11.5$, $J_2 = 6.7$, $\mathrm{NCH_2}$); 3.76 (2H, $\mathrm{CH_2Ar^1}$); 4.21 (1H, dd, $J_1 = 8.2$, $J_2 = 6.9$, CH); 6.08 (1H, d, $J = 3.3$, $\mathrm{H_{Het}}$-3); 6.28 (1H, dd, $J_1 = 3.3$, $J_2 = 1.8$, $\mathrm{H_{Het}}$-4); 6.99 (2H, t, $J = 8.7$, $\mathrm{H_{Ar}}$-3,5); 7.03 (1H, m); 7.09 (1H, t, $J = 7.5$); 7.21 (1H, m) and 7.38 (1H, td, $J_1 = 7.5$, $J_2 = 1.7$, $\mathrm{H_{Ar1}}$-3,4,5,6); 7.23 (2H, dd, $J_1 = 8.7$, $J_2 = 5.5$, $\mathrm{H_{Ar}}$-2,6); 7.33 (1H, d, $J = 1.8$, $\mathrm{H_{Het}}$-5)
7g	1.25 (1.5H, d, $J = 6.6$) and 1.26 (1.5H, d, $J = 6.6$, $\mathrm{CH_3}$); 1.74 (1H, br, NH); 1.86–2.03 (1H, m) and 2.09-2.25 (1H, m, $\mathrm{CH\underline{CH_2}}$); 2.23–2.41 (2H, m, $\mathrm{NCH_2}$); 3.63 (0.5H, q, $J = 6.6$) and 3.64 (0.5H, q, $J = 6.6$, $\mathrm{CHAr^1}$); 4.10 (0.5H, dd, $J_1 = 8.6$, $J_2 = 6.0$) and 4.15 (0.5H, t, $J = 7.7$, CH); 6.01 (0.5H, d, $J = 3.1$) and 6.02 (0.5H, d, $J = 3.1$, $\mathrm{H_{Het}}$-3); 6.24 (1H, br, $\mathrm{H_{Het}}$-4); 6.94 (1H, t, $J = 8.6$) and 6.97 (1H, t, $J = 8.6$, $\mathrm{H_{Ar}}$-3,5); 7.14 (1H, dd, $J_1 = 8.6$, $J_2 = 5.4$) and 7.20 (1H, dd, $J_1 = 8.6$, $J_2 = 5.4$, $\mathrm{H_{Ar}}$-2,6); 7.22 (2H, s) and 7.23 (2H, s, $\mathrm{H_{Ar1}}$-2,3,5,6); 7.30 (1H, br, $\mathrm{H_{Het}}$-5)
7h	1.28 (1.5H, d, $J = 6.6$) and 1.29 (1.5H, d, $J = 6.6$, $\mathrm{CH_3}$); 1.52 (1H, br, NH); 1.87-2.00 (1H, m) and 2.11-2.24 (1H, m, $\mathrm{CH\underline{CH_2}}$); 2.24-2.44 (2H, m, $\mathrm{NCH_2}$); 3.64 (0.5H, q, $J = 6.6$) and 3.65 (0.5H, q, $J = 6.6$, $\mathrm{CHAr^1}$); 4.12 (0.5H, dd, $J_1 = 8.9$, $J_2 = 6.3$) and 4.16 (0.5H, t, $J = 7.7$, CH); 6.00 (0.5H, d, $J = 3.2$) and 6.02 (0.5H, d, $J = 3.2$, $\mathrm{H_{Het}}$-3); 6.23 (0.5H, dd, $J_1 = 3.2$, $J_2 = 1.9$) and 6.25 (0.5H, dd, $J_1 = 3.2$, $J_2 = 1.9$, $\mathrm{H_{Het}}$-4); 6.92 (1H, t, $J = 8.7$) and 6.97 (1H, t, $J = 8.7$, $\mathrm{H_{Ar}}$-3,5); 7.14 (1H, dd, $J_1 = 8.7$, $J_2 = 5.4$) and 7.18 (1H, dd, $J_1 = 8.7$, $J_2 = 5.4$, $\mathrm{H_{Ar}}$-2,6); 7.17-7.25 (5H, m, $\mathrm{C_6H_5}$); 7.29 (0.5H, d, $J = 1.9$) and 7.30 (0.5H, d, $J = 1.9$, $\mathrm{H_{Het}}$-5)
8a	1.93 (1.5H, s) and 2.00 (1.5H, s, Ac); 2.02-2.14 (1H, m) and 2.20-2.36 (1H, m, $\mathrm{CH\underline{CH_2}}$); 3.03-3.22 (1.5H, m) and 3.31 (0.5H, ddd, $J_1 = 13.3$, $J_2 = 9.7$, $J_3 = 5.7$, $\mathrm{NCH_2}$); 3.93 (0.5H, t, $J = 7.6$) and 3.94 (0.5H, t, $J = 7.6$, CH); 4.45 (1H, s) and 4.45 (0.5H, d, $J = 14.8$) and 4.49 (0.5H, d, $J = 14.8$, $\mathrm{CH_2Ar^1}$); 6.06 (0.5H, d, $J = 3.2$) and 6.08 (0.5H, d, $J = 3.2$, $\mathrm{H_{Het}}$-3); 6.25 (0.5H, dd, $J_1 = 3.2$, $J_2 = 2.0$) and 6.28 (0.5H, dd, $J_1 = 3.2$, $J_2 = 2.0$, $\mathrm{H_{Het}}$-4); 6.96 (1H, t, $J = 8.7$) and 6.98 (1H, t, $J = 8.7$, $\mathrm{H_{Ar}}$-3,5); 7.09-7.33 (7H, m, $\mathrm{H_{Ar}}$-2,6, $\mathrm{C_6H_5}$); 7.30 (0.5H, d, $J = 2.0$) and 7.34 (0.5H, d, $J = 2.0$, $\mathrm{H_{Het}}$-5)
8b	1.91 (1.5H, s) and 2.02 (1.5H, s, Ac); 2.00-2.14 (1H, m) and 2.19-2.36 (1H, m, $\mathrm{CH\underline{CH_2}}$); 3.00-3.20 (1.5H, m) and 3.28 (0.5H, ddd, $J_1 = 13.5$, $J_2 = 9.5$, $J_3 = 5.7$, $\mathrm{NCH_2}$); 3.76 (1.5H, s) and 3.77 (1.5H, s, $\mathrm{OCH_3}$); 3.93 (1H, t, $J = 7.7$, CH); 4.37 (1H, s) and 4.38 (0.5H, d, $J = 14.5$) and 4.43 (0.5H, d, $J = 14.5$, $\mathrm{CH_2Ar^1}$); 6.07 (0.5H, d, $J = 3.1$) and 6.09 (0.5H, d, $J = 3.1$, $\mathrm{H_{Het}}$-3); 6.26 (0.5H, dd, $J_1 = 3.1$, $J_2 = 1.9$) and 6.29 (0.5H, dd, $J_1 = 3.1$, $J_2 = 1.9$, $\mathrm{H_{Het}}$-4); 6.77 (1H, d, $J = 8.6$) and 6.82 (1H, d, $J = 8.6$, $\mathrm{H_{Ar1}}$-3,5); 6.97 (2H, t, $J = 8.6$, $\mathrm{H_{Ar}}$-3,5); 7.01 (1H, d, $J = 8.6$) and 7.05 (1H, d, $J = 8.6$, $\mathrm{H_{Ar1}}$-2,6); 7.20 (2H, dd, $J_1 = 8.6$, $J_2 = 5.4$, $\mathrm{H_{Ar}}$-2,6); 7.31 (0.5H, d, $J = 1.9$) and 7.35 (0.5H, d, $J = 1.9$, $\mathrm{H_{Het}}$-5)

TABLE 2 (continued)

1	2
8c	1.06 (1.5H, t, J = 7.2) and 1.07 (1.5H, t, J = 7.2, CH_3); 2.01–2.14 (1H, m) and 2.22-2.36 (1H, m, $CH\underline{CH_2}$); 2.19 (1H, q, J = 7.2) and 2.27 (1H, q, J = 7.2, $\underline{CH_2}CH_3$); 3.03-3.23 (1.5H, m) and 3.34 (0.5H, ddd, J_1 = 13.4, J_2 = 9.6, J_3 = 5.6, NCH_2); 3.93 (0.5H, t, J = 7.7) and 3.95 (0.5H, t, J = 7.7, CH); 4.47 (1H, s) and 4.48 (0.5H, d, J = 14.7) and 4.53 (0.5H, d, J = 14.7, $CH_2C_6H_5$); 6.06 (0.5H, d, J = 3.2) and 6.11 (0.5H, d, J = 3.2, H_{Het}-3); 6.26 (0.5H, dd, J_1 = 3.2, J_2 = 1.9) and 6.28 (0.5H, dd, J_1 = 3.2, J_2 = 1.9, H_{Het}-4); 6.97 (1H, t, J = 8.7) and 6.99 (1H, t, J = 8.7, H_{Ar}-3,5); 7.11-7.35 (8H, m, H_{Ar}-2,6, C_6H_5, H_{Het}-5)
8d	1.04 (3H, t, J = 7.3, $CH_2\underline{CH_3}$); 1.97-2.11 (1H, m) and 2.19-2.31 (1H, m, $CH\underline{CH_2}$); 2.14 (1H, q, J = 7.3) and 2.27 (1H, q, J = 7.3, $\underline{CH_2}CH_3$); 2.96-3.18 (1.5H, m) and 3.28 (0.5H, ddd, J_1 = 13.4, J_2 = 9.6, J_3 = 5.5, NCH_2); 3.76 (3H, s, OCH_3); 3.91 (1H, br. t, J = 7.7, CH); 4.37 (1H, s) and 4.37 (0.5H, d, J = 14.5) and 4.42 (0.5H, d, J = 14.5, CH_2Ar^1); 6.05 (0.5H, d, J = 3.2) and 6.08 (0.5H, d, J = 3.2, H_{Het}-3); 6.25 (0.5H, dd, J_1 = 3.2, J_2 = 1.9) and 6.27 (0.5H, dd, J_1 = 3.2, J_2 = 1.9, H_{Het}-4); 6.75 (1H, d, J = 8.6) and 6.80 (1H, d, J = 8.6, H_{Ar1}-3,5); 6.93-7.03 (4H, m, H_{Ar}-3,5, H_{Ar1}-2,6); 7.19 (2H, dd, J_1 = 8.7, J_2 = 5.4, H_{Ar}-2,6); 7.30 (0.5H, d, J = 1.9) and 7.34 (0.5H, d, J = 1.9, H_{Het}-5)
8e	1.05 (3H, t, J = 7.3, $CH_2\underline{CH_3}$); 1.99-2.12 (1H, m) and 2.19-2.36 (1H, m, $CH\underline{CH_2}$); 2.16 (1H, q, J = 7.3) and 2.28 (1H, q, J = 7.3, $\underline{CH_2}CH_3$); 3.00-3.19 (1.5H, m) and 3.30 (0.5H, ddd, J_1 = 13.5, J_2 = 9.7, J_3 = 5.5, NCH_2); 3.74 (1.5H, s) and 3.76 (1.5H, s, OCH_3); 3.77 (3H, s, OCH_3); 3.93 (1H, br. t, J = 7.7, CH); 4.37 (1H, s) and 4.37 (0.5H, d, J = 14.5) and 4.41 (0.5H, d, J = 14.5, CH_2Ar^1); 6.07 (0.5H, d, J = 3.2) and 6.10 (0.5H, d, J = 3.2, H_{Het}-3); 6.26 (0.5H, dd, J_1 = 3.2, J_2 = 1.8) and 6.28 (0.5H, dd, J_1 = 3.2, J_2 = 1.8, H_{Het}-4); 6.55–6.61 (1H, m, H_{Ar1}-6); 6.62-6.70 (1H, m, H_{Ar1}-2); 6.72 (0.5H, d, J = 8.1, H_{Ar1}-5); 6.97 (1H, t, J = 8.7) and 6.99 (1H, t, J = 8.7, H_{Ar}-3,5); 7.20 (2H, dd, J_1 = 8.7, J_2 = 5.5, H_{Ar}-2,6); 7.31 (0.5H, d, J = 1.8) and 7.35 (0.5H, d, J = 1.8, H_{Het}-5)
8f	1.05 (3H, t, J = 7.3, $CH_2\underline{CH_3}$); 1.98-2.13 (1H, m) and 2.21-2.38 (1H, m, $CH\underline{CH_2}$); 2.18 (1H, q, J = 7.3) and 2.28 (1H, q, J = 7.3, $\underline{CH_2}CH_3$); 3.07-3.23 (1.5H, m) and 3.32 (0.5H, ddd, J_1 = 13.5, J_2 = 9.7, J_3 = 5.6, NCH_2); 3.95 (1H, t, J = 7.7, CH); 4.50 (1H, s) and 4.56 (1H, s, CH_2Ar^1); 6.07 (0.5H, d, J = 3.2) and 6.10 (0.5H, d, J = 3.2, H_{Het}-3); 6.26 (0.5H, dd, J_1 = 3.2, J_2 = 1.9) and 6.27 (0.5H, dd, J_1 = 3.2, J_2 =1.9, H_{Het}-4); 6.94-7.29 (6H, m, H_{Ar}-3,5, H_{Ar1}-3,4,5,6); 7.20 (2H, dd, J_1 = 8.7, J_2 = 5.4, H_{Ar}-2,6); 7.31 (0.5H, d, J = 1.9) and 7.34 (0.5H, d, J = 1.9, H_{Het}-5)
9	2.10 (1H, dtd, J_1 = 13.8, J_2 = 7.9, J = 6.3) and 2.30 (1H, dtd, J_1 = 13.8, J_2 = 7.7, J = 6.7, $CH\underline{CH_2}$); 2.53 (4H, s, $C(O)CH_2$); 3.37 (1H, ddd, J_1 = 13.3, J_2 = 7.9, J_3 = 6.3) and 3.42 (1H, ddd, J_1 = 13.3, J_2 = 7.9, J_3 = 6.3, NCH_2); 4.01 (1H, br. t, J = 7.6, CH); 6.10 (1H, d, J = 3.2, H_{Het}-3); 6.27 (1H, dd, J_1 = 3.2, J_2 = 1.9, H_{Het}-4); 7.00 (2H, t, J = 8.7, H_{Ar}-3,5); 7.24 (2H, dd, J_1 = 8.7, J_2 = 5.4, H_{Ar}-2,6); 7.34 (1H, d, J = 1.9, H_{Het}-5)
10	2.23 (1H, dtd, J_1 = 13.6, J_2 = 8.1, J = 6.5) and 2.41 (1H, dq, J_1 = 13.6, J_2 = 6.8, $CH\underline{CH_2}$); 3.60 (1H, ddd, J_1 = 13.7, J_2 = 7.8, J_3 = 6.4) and 3.63 (1H, ddd, J_1 = 13.7, J_2 = 7.8, J_3 = 6.4, NCH_2); 4.06 (1H, br. t, J = 7.6, CH); 6.10 (1H, d, J = 3.2, H_{Het}-3); 6.23 (1H, dd, J_1 = 3.2, J_2 = 1.9, H_{Het}-4); 6.96 (2H, t, J = 8.7, H_{Ar}-3,5); 7.25 (2H, dd, J_1 = 8.7, J_2 = 5.4, H_{Ar}-2,6); 7.30 (1H, d, J = 1.9, H_{Het}-5); 7.73-7.81 (4H, m, Ar^1)

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*Compounds **2**, **7g**,**h**, and **8a-f** were in the form of mixtures of two diastereoisomers in approximately equal amounts.

*[2] The ^{1}H NMR spectra were recorded in a 1:3 mixture of DMSO-d_6 and carbon tetrachloride.

Ethyl α-Cyano-β-(*p*-fluorophenyl)-β-(2-furyl)propionate (2). To an ether solution of the Grignard reagent prepared from magnesium (8.4 g, 0.33 mol) in absolute ether (50 ml) and *p*-fluorobromobenzene (59.5 g, 0.34 mol) in ether (200 ml) we added with gentle boiling and stirring a solution of the ester **1** (53.5 g, 0.27 mol) in benzene (50 ml). The reaction mixture was stirred at 42-44°C for 1.5 h, kept at room temperature for 16-20 h, acidified with 10% hydrochloric acid, and extracted with ether. The extract was washed with water and dried. The residue after distillation of the solvents was distilled under vacuum. We obtained 65.0 g (81.2%) of the ester **2**. IR spectrum, ν, cm^{-1}: 1590, 1610 (C=C arom.), 1720 (C=O), 2225 (CN).

β-(*p*-Fluorophenyl)-β-(2-furyl)propionitrile (3). Potassium hydroxide (25.2 g, 0.45 mol) was dissolved by heating in ethylene glycol (135 ml). The obtained solution was added to the ester **2** (65 g, 0.22 mol). The mixture was boiled with a reflux condenser for 3 h and was then cooled, water (135 ml) was added, and the product was extracted with ether. The extract was washed with water and dried, and the residue after distillation of the ether was distilled under vacuum. We obtained 48.7 g of the nitrile **3**. IR spectrum, ν, cm^{-1}: 1585, 1615 (C=C arom.), 2225 (CN).

γ-(*p*-Fluorophenyl)-γ-(2-furyl)propylamine (4). To a cooled solution of lithium aluminum hydride (10.6 g, 0.28 mol) in dry ether (200 ml) we added dropwise an ether solution of the nitrile **3** (30 g, 0.14 mol) while keeping the temperature of the reaction mass in the range of 0±2°C. Stirring was continued for a further 1 h at the same temperature, the mixture was cooled to -10°C (in a bath of ice and salt), and water (10 ml), 15% sodium hydroxide solution (10 ml), and water (31 ml) were added dropwise in succession. The reaction mass was filtered, the inorganic precipitate was washed with ether, and the ether was then combined with the organic layer of the filtrate. The ether solution was dried, and the residue after removal of the ether was distilled under vacuum. We obtained 26.5 g of the amine **4**. IR spectrum, ν, cm^{-1}: 1590, 1610 (C=C arom.), 3300 (NH_2).

Ar^1(R)-Methyl[γ-(*p*-fluorophenyl)-γ-(2-furyl)propyl]amines (7a-h). A mixture of equimolar amounts of the amine **4** and the aromatic aldehyde **5a-f** or ketone **5g**,**h** in benzene or xylene (in the case of **5g**,**h**) was boiled for 4 h with a Dean–Stark tube until the water had completely separated. The solvent was then distilled, the residue was dissolved in methanol, and an equimolar amount of $NaBH_4$ was added to the obtained solution in portions with stirring and cooling in water so that the temperature of the mixture did not exceed 20°C. The reaction mass was stirred for a further 1 h at room temperature, and the methanol was then distilled. The residue was made alkaline with 20% sodium hydroxide solution and extracted with ether. The extract was dried, the ether was distilled from the residue, and the amines **7a-h** were isolated by distillation.

N-(R^1CO)[Ar^1(R)-Methyl][γ-(*p*-fluorophenyl)-γ-(2-furyl)propyl]amines (8a-f). To a solution of the amine **7a-f** (0.03 mol) and triethylamine (3 g, 0.032 mol) in absolute benzene (30 ml) we added an equimolar amount of acetyl chloride (in the case of **7a**,**b**) or propionyl chloride (**7c-f**). The mixture was boiled with a reflux condenser for 4 h, cooled, washed with water, and extracted with benzene. The extract was dried, and the amides **8a-f** were isolated from the residue after distillation of the benzene.

N-[γ-(*p*-Fluorophenyl)-γ-(2-furyl)propyl]maleimide (9). A mixture of the amine **4** (7 g, 0.032 mol) and succinic anhydride (3.2 g, 0.02 mol) in benzene (50 ml) was boiled for 10 h with a Dean–Stark tube until the water had been completely separated. The benzene was then evaporated, and 6.3 g of the product **9** was isolated from the residue by vacuum distillation. IR spectrum, ν, cm^{-1}: 1590, 1610 (C=C arom.), 1690 (C=O).

N-[γ-(*p*-Fluorophenyl)-γ-(2-furyl)]propylphthalimide (10). From the amine **4** (7 g, 0.032 mol) and phthalic anhydride (4.8 g, 0.032 mol) by the procedure described above for the product **9** we obtained 6.6 g of the phthalimide **10**. IR spectrum, ν, cm^{-1}: 1590, 1610 (C=C arom.), 1690 (C=O).

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