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SYNTHESIS OF AMINES OF THE DI- AND TRIFURYLMETHANE SERIES

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Methods are proposed for the synthesis of amines of the di- and trifurylmethane series – prospective compounds for the production of polymers and macrocyclic molecules – on the basis of 2-(2-furylmethyl)-1,3-isoindolinedione.

Keywords: di- and trifurylmethanes, 2-(2-furylmethyl)-1,3-isoindolinedione, carbonyl compounds, hydrazinolysis, acid-catalyzed condensation.

On account of the unique properties of the furan ring furan compounds have found application in many fields of chemistry – for the production of various carbo- and heterocyclic systems, in the synthesis of polymeric materials and macromolecules. Difurylmethanes occupy a significant place among furan derivatives. Difurylmethane structures have attracted the attention of investigators engaged in the chemistry of polymeric compounds since they are readily obtainable replacements for the diphenylmethanes employed in the synthesis of polymers [1-4]. Diamines of the difurylmethane series have found use in the production of epoxide resins [5], while the difurfuryl diisocyanates synthesized from them are used in the production of polyurethane systems [6-8].

A traditional method for the synthesis of difurylmethane structures is the acid-catalyzed condensation of carbonyl compounds with furan derivatives; the use of concentrated sulfuric acid [9, 10], ion-exchange resins [11, 12], acidic zeolites [13], phosphoric acid [14], and concentrated perchloric acid [15] has been described. However, the ease of reaction of the amino group in furfurylamine with carbonyl compounds presupposes certain features of the condensation. In order to prevent side transformations it is necessary to protect the amino function.

The original method for the synthesis of diamines of the difurylmethane series, which makes it possible to avoid the introduction of a protecting group, involves condensation of furfurylamine and carbonyl compounds in hydrochloric acid [16-19]. The latter in this case acts as catalyst and solvent and also deactivates the amino group, thereby preventing the occurrence of undesirable side reactions at the amino group. A significant disadvantage of this method is the fact that the process takes place without a solvent, which prevents the use of crystalline substances in the reaction.

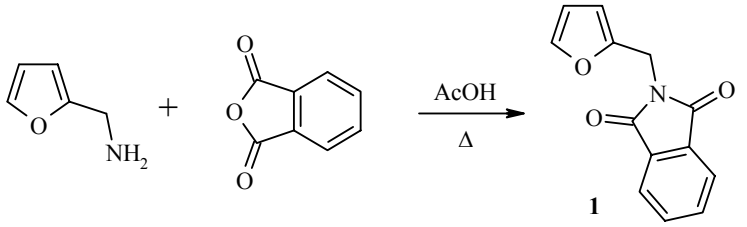

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TABLE 1. Physicochemical Characteristics of Compounds **2a–g**

Compound	Ar	Empirical formula	Found, % / Calculated, %				mp, °C	Yield, %
			C	H	N	Hal		
2a	C_6H_5	$C_{33}H_{22}N_2O_6$	73.08 / 73.06	4.03 / 4.09	5.19 / 5.16		180-181	56
2b	4-BrC_6H_4	$C_{33}H_{21}BrN_2O_6$	63.75 / 63.78	3.45 / 3.41	4.47 / 4.51	12.89 / 12.86	204-205	63
2c	4-ClC_6H_4	$C_{33}H_{21}ClN_2O_6$	68.72 / 68.69	3.61 / 3.67	4.85 / 4.86	6.17 / 6.14	187-188	58
2d	4-$O_2NC_6H_4$	$C_{33}H_{21}N_3O_8$	67.50 / 67.46	3.62 / 3.60	7.12 / 7.15		167-168	67
2e	4- $Me_2NC_6H_4$	$C_{35}H_{27}N_3O_6$	71.74 / 71.79	4.66 / 4.65	7.21 / 7.18		236-237	21
2f	3-$O_2NC_6H_4$	$C_{33}H_{21}N_3O_8$	67.49 / 67.46	3.58 / 3.60	7.17 / 7.15		156-157	67
2g	3,4-$(MeO)_2C_6H_3$	$C_{35}H_{26}N_2O_8$	69.80 / 69.76	4.37 / 4.35	4.59 / 4.65		187-188	65

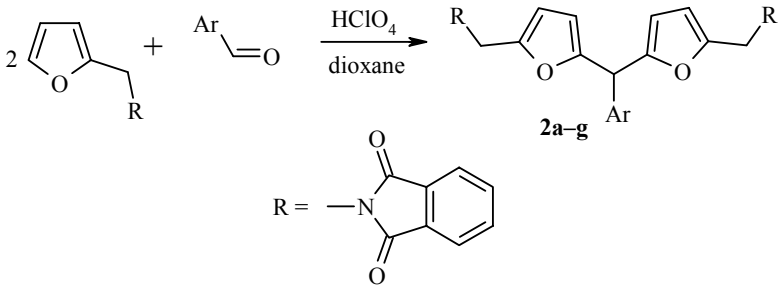
TABLE 2. ^{1}H NMR Spectra of Compounds **2a–g**

Com-pound	Chemical shifts, δ, ppm., SSCC (*J*, Hz)					
	CH (1H, s)	CH_2 (4H, s)	H_{Fur}-3 (2H, d)	H_{Fur}-4 (2H, d)	Ar	Phthal (8H, m)
2a	5.47	4.70	5.97 (*J* = 3.1)	6.24 (*J* = 3.1)	7.18 (5H, s)	7.83-7.92
2b	5.50	4.70	5.99 (*J* = 3.2)	6.24 (*J* = 3.2)	7.11 (2H, d, *J* = 8.4, 2,6-H_{Ar}) 7.37 (2H, d, *J* = 8.4, 3,5-H_{Ar})	7.84-7.91
2c	5.53	4.70	5.98 (*J* = 3.1)	6.25 (*J* = 3.1)	7.17 (2H, d, *J* = 8.6, 2,6-H_{Ar}), 7.25 (2H, d, *J* = 8.6, 3,5-H_{Ar})	7.81-7.90
2d	5.75	4.71	6.07 (*J* = 3.1)	6.28 (*J* = 3.1)	7.42 (2H, d, *J* = 8.7, 2,6-H_{Ar}), 8.03 (2H, d, *J* = 8.7, 3,5-H_{Ar})	7.80-7.90
2e	5.28	4.70	5.92 (*J* = 3.2)	6.21 (*J* = 3.2)	6.52 (2H, d, *J* = 8.7, 2,6-H_{Ar}), 6.97 (2H, d, *J* = 8.7, 3,5-H_{Ar})	7.83-7.88
2f	5.80	4.70	6.06 (*J* = 3.1)	6.29 (*J* = 3.1)	7.51-7.64 (2H, m, 2,6-H_{Ar}), 7.98-8.05 (2H, m, 4,5-H_{Ar})	7.81-7.88
2g	5.80	4.70	5.96 (*J* = 3.1)	6.24 (*J* = 3.1)	3.59 (3H, s, CH_3O), 3.67 (3H, s, CH_3O), 6.64-6.77 (3H, m, 2,5,6-H_{Ar})	7.80-7.91

Thus, the acid-catalyzed condensation of carbonyl compounds with N-substituted furfurylamine provides the most convenient and universal method for the synthesis of diamines of the difurylmethane series since any reagents can be used irrespective of their state of aggregation.

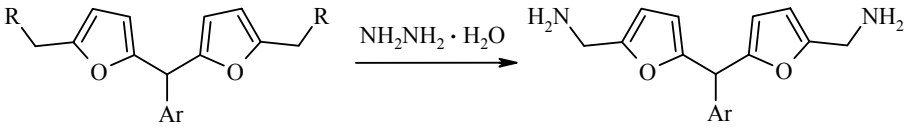
For the synthesis of difurylarylmethanes based on furfurylamine we used 2-(2-furylmethyl)-1,3-isoindolinedione – the product from reaction of furfurylamine with phthalic anhydride.

This compound enters readily into reaction with various aromatic aldehydes in dioxane at 40-50°C in the presence of catalytic amounts of 70% perchloric acid (Tables 1 and 2).



2 a Ar = Ph, **b** Ar = 4-BrC_6H_4, **c** Ar = 4-ClC_6H_4, **d** Ar = 4-$O_2NC_6H_4$, **e** Ar = 4-$Me_2NC_6H_4$, **f** Ar = 3-$O_2NC_6H_4$, **g** Ar = 3,4-$(MeO)_2C_6H_3$

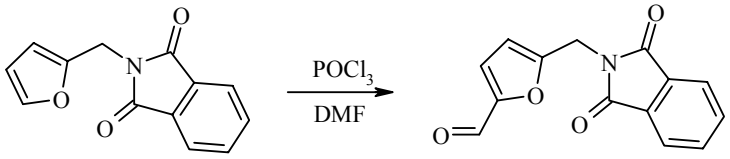
Since the aim of the difurylmethane synthesis was to produce the diamines, we removed the protecting groups by reaction of the methanes **2a-d** with hydrazine hydrate.



2a–d **3a–d**

The synthesized amines **3a-d** were viscous oily liquids (Tables 3 and 4).

For the synthesis of the symmetrical triamine the furfural **4** was prepared by the formylation of 2-(2-furylmethyl)-1,3-isoindolinedione (**1**).



1 **4**

Condensation of the obtained aldehyde with the furan **1** in dioxane in the presence of perchloric acid as catalyst leads to the trifluoromethane **5** with a yield of 49%.

We developed [20] a convenient single-stage method for the production of symmetrical trifluoromethanes by the reaction of 5-R-furfural with ethylene glycol in the presence of the ion-exchange resin Amberlyst 15. By the reaction of the aldehyde **4** with ethylene glycol in benzene, catalyzed by Amberlyst 15 (50% of the mass of the furfural), it is possible to synthesize the symmetrical trifluoromethane **5** with a yield of 80%. When boiled with hydrazine hydrate compound **5** gives the triamine **6**.

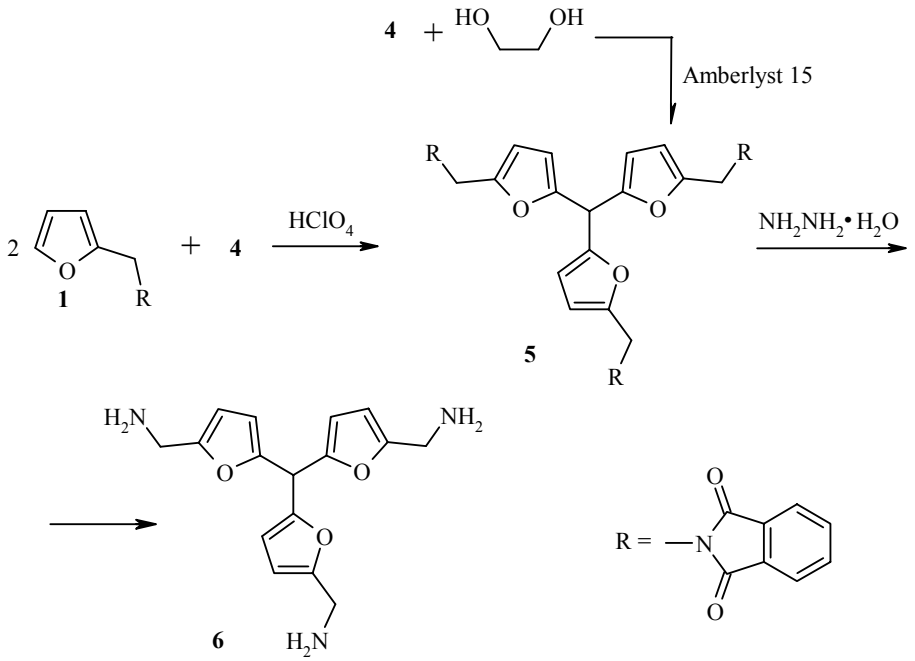
TABLE 3. Physicochemical Chercteristics of Compounds **3a–d**

Com-pound	Empirical formula	Found, % / Calculated, %				Yield, %	mp, °C, oxalate
		C	H	N	Hal		
3a	$C_{17}H_{18}N_2O_2$	72.35 / 72.32	6.47 / 6.43	9.96 / 9.92		47	164-165
3b	$C_{17}H_{17}BrN_2O_2$	56.48 / 56.52	4.79 / 4.74	7.77 / 7.75	22.08 / 22.12	57	198-199
3c	$C_{17}H_{17}ClN_2O_2$	64.43 / 64.46	5.43 / 5.41	8.88 / 8.84	11.12 / 11.19	53	160-161
3d	$C_{17}H_{17}N_3O_4$	62.42 / 62.38	5.26 / 5.23	12.80 / 12.84		57	154-155

TABLE 4. ^{1}H NMR Spectra of Compounds **3a–d**

Com-pound	Chemical shifts, δ, ppm, SSCC (*J*, Hz)					
	CH (1H, s)	CH_2 (4H, s)	H_{Fur}-3 (2H, d)	H_{Fur}-4 (2H, d)	Ar	others (8H, br. s)
3a	5.59	4.02	6.21 (*J* = 2.6)	6.47 (*J* = 2.6)	7.22-7.28 (5H, m)	7.09 (NH_3^+ + HOOCCOO$^-$)
3b	5.60	4.04	6.22 (*J* = 2.5)	6.47 (*J* = 2.5)	7.29 (2H, d, *J* = 8.3, H_{Ar}-2,6), 7.54 (2H, d, *J* = 8.3, H_{Ar}-3,5)	5.29 (NH_3^+ + HOOCCOO$^-$)
3c	5.62	4.03	6.21 (*J* = 2.5)	6.46 (*J* = 2.5)	7.30-7.38 (4H, m)	7.24 (NH_3^+ + HOOCCOO$^-$)
3d	5.60	4.03	6.22 (*J* = 2.6)	6.47 (*J* = 2.6)	7.29 (2H, d, *J* = 8.3, H_{Ar}-2,6), 7.54 (2H, d, *J* = 8.3, H_{Ar}-3,5)	5.37 (NH_3^+ + HOOCCOO$^-$)

We have thus proposed methods for the synthesis of difurylmethane diamines and a symmetrical trifurylmethane triamine – prospective compounds for use in the chemistry of polymeric materials and macrocycles.



EXPERIMENTAL

The ^{1}H NMR spectra were recorded in DMSO on a Bruker AC-200 spectrometer (200 MHz) with HMDS as internal standard (δ 0.055 ppm). Thin-layer chromatography was performed on Silufol and SORBFIL plates with iodine, bromine, and a solution of 2,4-DNPH as developers.

Synthesis of 2-(5-{Aryl[5-(2,3-dioxo-2,3-dihydro-1H-2-isoindolylmethyl)-2-furyl]methyl}-1,3-isoindolinediones 2a-d, f, g. To a suspension of (10 mmol) of compound **1** in 5 ml of dioxane we added (5.5 mmol) of the respective benzaldehyde and (0.7 ml) of 70% perchloric acid. The reaction mixture was stirred at 40-50°C. After 20-40 min the initial substances had completely dissolved. The reaction mixture was stirred until the product had separated as a precipitate and was left at room temperature for 3-4 h. The precipitate was separated by filtration, washed with cold dioxane, dried, and crystallized from a mixture of methylene chloride and petroleum ether.

Synthesis of 2-(5-{4-N,N-Dimethylaminophenyl[5-(1,3-dioxo-2,3-dihydro-1H-2-isoindolylmethyl)-2-furyl]methyl}-2-furylmethyl)-1,3-isoindolinedione 2e. The reaction was carried out by the general procedure for the synthesis of compounds **2** with a 4-ml excess of perchloric acid. The crystalline precipitate was washed with dioxane and was then washed thoroughly with a solution of $NaHCO_3$. The subsequent treatment was similar to the previous method.

Hydrazinolysis of Compounds 2a-d (General Procedure). Synthesis of Aryldi(5-aminomethyl-2-furyl)methanes 3a-d. To a solution of (5 mmol) of the compound **2a-d** in 40 ml of ethanol we added (1 ml) of hydrazine hydrate. The mixture was boiled until the initial imide had completely disappeared (TLC). The reaction mixture was poured into water, the precipitated hydrazide was filtered off, and the amines **3a-d** were extracted from the filtrate with hot ethyl acetate. Evaporation of the solvent at reduced pressure gave the diamines (**3a-d**) in the form of oils.

5-(1,3-Dioxo-2,3-dihydro-1H-2-isoindolylmethyl)-2-furaldehyde (4). To a suspension of compound **1** (2.27 g, 10 mmol) in (3 ml) of DMFA while stirring and cooling with iced water we added dropwise (10 ml) (100 mmol) of phosphorus oxychloride. At the end of the addition the mixture was kept at room temperature for 10 min and then at 50°C until the imide (**1**) had been completely consumed (TLC). The cooled reaction mixture was poured onto crushed ice and neutralized to pH 8 by the successive addition of a solution of sodium hydroxide and solid sodium bicarbonate. The crystalline precipitate was filtered off, washed with water, and dried. After recrystallization from ethanol with active carbon we obtained 2.11 g (83%) of the aldehyde **4** in the form of cream-colored crystals; mp 136-138°C (from ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.96 (2H, s, CH_2); 6.17 (1H, d, *J* = 3.2, H_{Fur}-4); 7.22 (1H, d, *J* = 3.2, H_{Fur}-3); 7.88-8.05 (4H, m, H_{Phth}); 9.40 (1H, s, CHO). Found, %: C 65.91; H 3.52; N 5.53. $C_{14}H_9NO_4$. Calculated, %: C 65.88; H 3.55; N 5.49.

Tris[(1,3-dioxo-2,3-dihydro-1H-2-isoindolylmethyl)-2-furyl]methane (5). A mixture of (1.27 g, 5 mmol) of furfural **4**, (0.33 ml) (6 mmol) of ethylene glycol, and 0.64 g of ion-exchange resin Amberlyst 15 (50% on the weight of the furfural) in 70 ml of benzene was boiled with azeotropic distillation of the water until the furfural had been completely converted. The resin was filtered off, (20 ml) of petroleum ether was added, and the hot solution was filtered through a thin layer of silica gel. After crystallization the trifurylmethane **5** (0.94 g, 80%) was obtained in the form of a white powder; mp 168-169°C (from petroleum ether). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.68 (6H, s, CH_2), 5.56 (1H, s, CH), 5.99 (3H, d, *J* = 3.1, H_{Fur}-3); 6.21 (3H, d, *J* = 3.1, H_{Fur}-4); 7.79-7.89 (12H, m, H_{Phth}). Found, %: C 69.43; H 3.67; N 6.12. $C_{40}H_{25}N_3O_9$. Calculated, %: C 69.46; H 3.64; N 6.08.

Tris(5-aminomethyl-2-furyl)methane (6). The hydrazinolysis of compound **5** was conducted by the method described for compounds **2a-e**, and the triamine **6** was obtained in the form of a yellow oil with a yield of 54%. The oxalate of the amine **6** is a white powder; mp 156-157°C (from ethyl acetate). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.42 (6H, s, CH_2); 5.56 (1H, s, CH); 6.17 (3H, d, *J* = 3.1, H_{Fur}-3); 6.44 (3H, d, *J* = 3.1, H_{Fur}-4); 7.22 (12H, br. s, NH_3^+ + $HOOCCOO^-$). Found, %: C 63.83; H 6.30; N 13.99. $C_{16}H_{19}N_3O_3$. Calculated, %: C 63.77; H 6.36; N 13.94.

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