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NEW SYNTHESIS OF 2-NITROARYLDIFURYLMETHANES

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A new approach has been developed for the synthesis of 2-nitroaryldifurylmethanes based on the condensation of derivatives of 2-nitrobenzaldehyde and 2-alkylfurans in methylene chloride in the presence of polyphosphoric acid (PPA) silyl ester. The use of such reaction conditions reduces resin formation, which enables the final products to be isolated in higher yields.

Keywords: 2-alkylfuran, 2-nitrobenzaldehyde, condensation reaction.

Derivatives of 2-nitroaryldifurylmethane are good starting materials for the synthesis of such heterocyclic systems as carbazoles [1, 2], indoles [3], and furoquinolines [4]. In addition, 2-nitroaryldifurylmethanes may readily be reduced to the corresponding 2-aminoaryldifurylmethanes, the synthetic potential of which has not been widely exhausted by far. These compounds have been used in the synthesis of derivatives of benzothiazine [5], cinnoline [6], and indole [7]. Consequently the development of an optimal method for synthesizing derivatives of 2-nitroaryldifurylmethanes is an urgent problem.

We showed previously that the condensation of 2-nitrobenzaldehyde derivatives **1** with 2-alkylfurans in dioxane in the presence of perchloric acid at room temperature leads to a fairly high yield of 2-nitroaryldifurylmethane **3** [6, 8], however the duration of the reaction was greater than 1 day. According to our data an increase in temperature accelerates the reaction, but resinification increases and hinders isolation of the product. At present we have found that carrying out this reaction in methylene chloride in the presence of PPA silyl ester reduces the reaction time significantly even at room temperature and reduces resinification during the reaction, which in the end leads to an increase in the yield of 2-nitroaryldifurylmethanes (Table 1).

The proposed conditions for the synthesis of 2-nitroaryldifurylmethanes may also be used for other aryldifurylmethane derivatives.

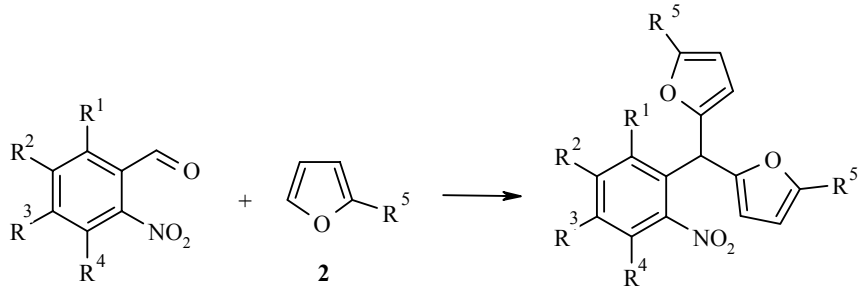

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TABLE 1. Reaction Conditions and Yields of Compounds **3a-l**

Com-pound	R^1	R^2	R^3	R^4	R^5	Time, min	T, °C*	Yield, %
3a	H	H	H	H	Me	30		84 (74 [6, 8])
3b	H	OMe	OMe	H	Me	25		87 (69 [6, 8])
3c	OMe	H	H	OMe	Me	25	35	79
3d	OMe	Me	H	OMe	Me	20		75
3e	OMe	OMe	H	Me	Me	15-20		73
3f	OMe	OMe	H	Cl	Me	40-45	35	84
3g	OMe	OMe	H	Br	Me	30-35		80
3h	H	OH	OMe	H	Me	40	35	70
3i	OMe	OH	OMe	H	Me	50	35	62
3j	H	OCH_2O		H	Me	20-25		83 (64 [6])
3k	H	OCH_2O		H	Et	30-35	35	85 (86 [6])
3l	H	OCH_2O		H	*t*-Bu	35-40	35	82

***** Compounds **3a,b,d,e,g,j** were obtained at room temperature.

TABLE 2. Physicochemical and Spectral Characteristics of Compounds **3***

Com pound	Empirical formula	Found, % / Calculated, %			mp, °C*[2]	^{1}H NMR spectrum, δ, ppm. (*J*, Hz)
		C	H	N		
1	2	3	4	5	6	7
3c	$C_{19}H_{19}NO_6$	63.67 / 63.86	5.49 / 5.36	26.72 / 26.86	147-148	2.25 (6H, s, CH_3); 3.73 (3H, s, OCH_3); 3.82 (3H, s, OCH_3); 5.76 (1H, s, CH); 5.89 (2H, d, *J* = 3.2, H_{Fur}); 5.97 (2H, d, *J* = 3.2, H_{Fur}); 6.93 (2H, s, H_{Ar})
3d	$C_{20}H_{21}NO_6$	64.83 / 64.68	5.52 / 5.70	4.01 / 3.77	136-137	2.25 (6H, s, CH_3); 2.36 (3H, s, CH_3); 3.50 (3H, s, OCH_3); 3.83 (3H, s, OCH_3); 5.84 (1H, s, CH); 5.90 (2H, d, *J* = 3.2, H_{Fur}); 6.01 (2H, d, *J* = 3.2, H_{Fur}); 6.80 (1H, s, H_{Ar})
3e	$C_{20}H_{21}NO_6$	64.51 / 64.68	5.89 / 5.70	3.92 / 3.77	123-124	2.24 (6H, s, CH_3); 2.26 (3H, s, CH_3); 3.54 (3H, s, OCH_3); 3.89 (3H, s, OCH_3); 5.69 (1H, s, CH); 5.90 (2H, d, *J* = 3.2, H_{Fur}); 6.02 (1H, d, *J* = 3.2, H_{Fur}); 6.73 (2H, s, H_{Ar})
3f	$C_{19}H_{18}ClNO_6$	58.02 / 58.25	4.75 / 4.63	3.49 / 3.57	112-113	2.25 (6H, s, CH_3); 3.58 (3H, s, OCH_3); 3.90 (3H, s, OCH_3); 5.71 (1H, s, CH); 5.91 (2H, d, *J* = 3.2, H_{Fur}); 6.04 (2H, d, *J* = 3.2, H_{Fur}); 6.95 (1H, s, H_{Ar})
3g	$C_{19}H_{18}BrNO_6$	52.39 / 52.31	3.99 / 4.16	3.22 / 3.21	114-115	2.25 (6H, s, CH_3); 3.58 (3H, s, OCH_3); 3.90 (3H, s, OCH_3); 5.69 (1H, s, CH); 5.91 (2H, d, *J* = 3.2, H_{Fur}); 6.03 (2H, d, *J* = 3.2, H_{Fur}); 7.10 (1H, s, H_{Ar})
3h	$C_{18}H_{17}NO_6$	63.07 / 62.97	5.12 / 4.99	4.02 / 4.08	122-123	2.25 (6H, s, CH_3); 3.97 (3H, s, OCH_3); 5.88 (2H, d, *J* = 3.2, H_{Fur}); 5.92 (2H, d, *J* = 3.2, H_{Fur}); 6.04 (1H, br. s, OH); 6.35 (1H, s, CH); 6.89 (1H, s, H_{Ar}); 7.64 (1H, s, H_{Ar})

TABLE 2 (continued)

1	2	3	4	5	6	7
3i	$C_{19}H_{19}NO_7$	61.07 61.12	5.25 5.13	3.86 3.75	118-119	2.23 (6H, s, CH_3); 3.61 (3H, s, OCH_3); 3.97 (3H, s, OCH_3); 5.89 (1H, s, CH); 5.90 (2H, d, J = 3.2, H_{Fur}); 6.05 (2H, d, J = 3.2, H_{Fur}); 6.14 (1H, s, OH); 7.27 (1H, s, H_{Ar})
3l	$C_{24}H_{27}NO_6$	67.65 67.75	6.49 6.40	3.07 3.29	99-100	1.25 (18H, s, $(C(CH_3)_3)_3$); 5.87 (2H, d, J = 3.1, 4-H_{Fur}); 5.93 (2H, d, J = 3.1, 3-H_{Fur}); 6.08 (2H, s, CH_2); 6.29 (1H, s, CH); 6.79 (1H, s, H_{Ar}); 7.49 (1H, s, H_{Ar})

* The physicochemical characteristics of compounds **3a,b,j,k** corresponded to those given in [6].

*[2] Solvents: ethanol (compounds **3c,f-i,l**) and hexane–CH_2Cl_2, 4:1 (compounds **3d,e**).

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker AC 200 (200 MHz) spectrometer in $CDCl_3$ solution, internal standard was TMS.

PPA Silyl Ester. Chloroform was poured onto P_2O_5 (71 g, 0.5 mol) and hexamethyldisiloxane (81 g, 0.5 mol) to a total volume of 0.5 liter. The obtained mixture was boiled under reflux until complete solution of the phosphorus pentoxide and hexamethyldisiloxane. A 1N solution of PPA silyl ester was obtained, which was stored in a completely sealed vessel.

Synthesis of 2-Nitroaryldifurylmethanes 3 (General Procedure). A 0.01 M solution (15 ml) of PPA silyl ester was added with stirring to a solution of *ortho*-nitrobenzaldehyde **1** (0.01 mol) and 2-alkylfuran **2** (0.03 mol) in methylene chloride (15 ml). Stirring was continued until the initial aldehyde was completely used (TLC on Silufol UV 254 plates, eluent was chloroform–petroleum ether, 4:1). At the end of the reaction the reaction mixture was poured into water (200 ml), the excess of acid was neutralized with sodium bicarbonate, and the mixture extracted with methylene chloride (2 × 40 ml). The organic layers were combined, dried with sodium sulfate, passed through a layer of silica gel, and evaporated to dryness. The obtained oil was crystallized.

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