

Disubstituted Ureas of the 5-R-2-Furylethylene Type

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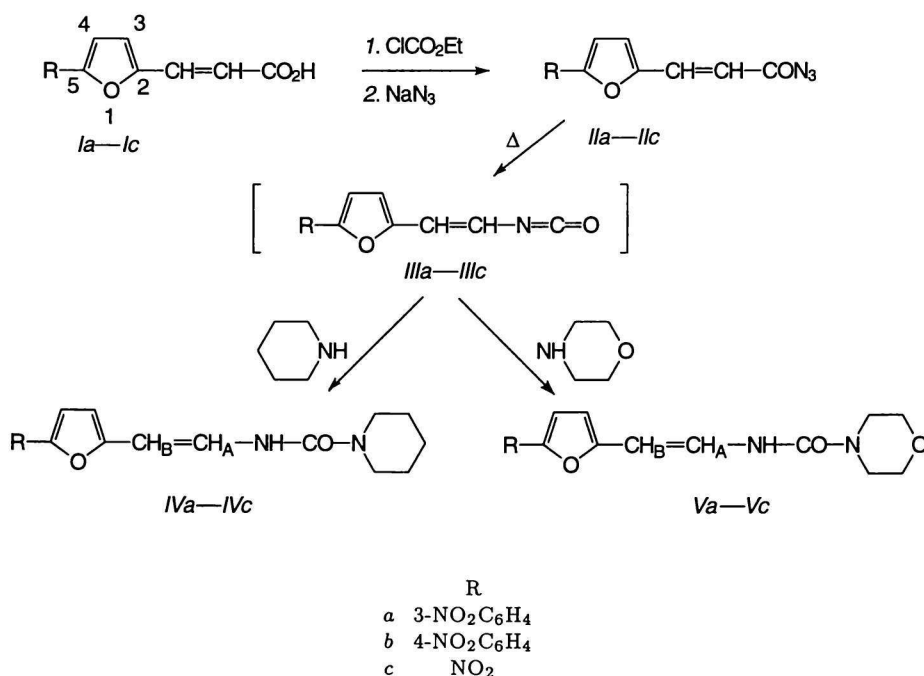
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New disubstituted ureas of furylethylene type were prepared by reaction of secondary amines with appropriate isocyanates available from corresponding acyl azides *via* thermal decomposition. ¹H NMR, IR, and UV spectra are presented.

In our previous papers [1, 2] we described the utilization of 3-[5-(2-nitrophenyl)-2-furyl]propenoic azide in the synthesis of 2-[5-(2-nitrophenyl)]furo[3,2-c]pyridines and their fused derivatives as well as ureas and amides of the 5-(2-nitrophenyl)-2-furyl type. In continuation of this study we present here the synthesis of new disubstituted ureas of the 5-R-2-furylethylene type (R = 3- or 4-NO₂-phenyl and NO₂) *IVa—IVc*, *Va—Vc* from appropriate acyl azides *IIa—IIc*.

Starting 3-(5-nitrophenyl-2-furyl)propenoic acids *Ia*, *Ib* [3] were prepared *via* Doebner condensation from corresponding 5-R-2-furancarbaldehydes. The

acyl azides *IIa—IIc* were synthesized by treatment of the propenoic acids *Ia—Ic* with ethyl chloroformate and sodium azide in a one-pot reaction in excellent yields and transformed *via* thermal decomposition in toluene (Curtius rearrangement) to isocyanates *IIIa—IIIc* (Scheme 1). Obtained isocyanates *IIIa—IIIc* were used without further isolation in an addition reaction with secondary amines (piperidine, morpholine) giving new disubstituted ureas of the furylethylene type *IVa—IVc*, *Va—Vc*. The method described in this paper uses toluene as a solvent for the generation of isocyanates *IIIa—IIIc*. Comparing with our previous study [1, 2] we achieved by this change shortening of



Scheme 1

Table 1. Characterization of Synthesized Compounds

Compound	Formula M_r	$w_i(\text{calc.})/\%$ $w_i(\text{found})/\%$			Yield %	M.p. °C
		C	H	N		
<i>Ia</i>	$C_{13}H_8N_4O_4$	54.94	2.84	19.71	92	118—119 ^a
	284.2	54.87	2.80	19.67		
<i>Ib</i>	$C_{13}H_8N_4O_4$	54.94	2.84	19.71	95	127—128 ^a
	284.2	54.85	2.80	19.63		
<i>Ic</i>	$C_7H_4N_4O_4$	40.40	1.94	26.92	75	103—105 ^b
	208.1	40.30	1.85	26.78		
<i>IVa</i>	$C_{18}H_{19}N_3O_4$	63.33	5.61	12.31	70	169—171 ^a
	341.4	63.35	5.68	12.25		
<i>IVb</i>	$C_{18}H_{19}N_3O_4$	63.33	5.61	12.31	72	187—189 ^a
	341.4	63.28	5.58	12.25		
<i>IVc</i>	$C_{12}H_{15}N_3O_4$	54.33	5.70	15.84	70	132—134 ^a
	265.3	54.30	5.65	15.75		
<i>Va</i>	$C_{17}H_{17}N_3O_5$	59.47	4.99	12.24	65	175—178 ^a
	343.3	59.32	4.85	12.30		
<i>Vb</i>	$C_{17}H_{17}N_3O_5$	59.47	4.99	12.24	60	188—191 ^a
	343.3	59.32	4.85	12.30		
<i>Vc</i>	$C_{11}H_{13}N_3O_5$	49.44	4.90	15.72	70	169—171 ^a
	267.2	49.35	5.03	15.60		

Crystallized from a) toluene, b) isohexane.

Table 2. IR and UV Spectral Data of Synthesized Compounds

Compound	$\tilde{\nu}/\text{cm}^{-1}$				λ_{max} nm	$\log(\epsilon/(\text{m}^2 \text{mol}^{-1}))$
	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{C})$	$\nu_{\text{as}}(\text{NO}_2)$	$\nu_{\text{s}}(\text{NO}_2)$		
<i>Ia</i>	1693	1622	1530	1354		
<i>Ib</i>	1678	1626	1510	1327		
<i>Ic</i>	1676	1626	1516	1354		
<i>IVa</i>	1664	1628	1533	1348	349	3.48
					244	3.40
					209	3.32
					425	3.34
					300	3.22
<i>IVb</i>	1664	1628	1508	1329	272	3.02
					232	3.22
					451	3.26
					261	3.25
					422	3.33
<i>IVc</i>	1680	1622	1525	1331	300	3.19
					272	3.00
					412	3.26
					259	3.26
					412	3.26
<i>Va</i>	1676	1632	1522	1350	346	3.37
					243	3.52
					209	3.30
					422	3.33
					300	3.19
<i>Vb</i>	1670	1636	1502	1327	272	3.00
					231	3.20
					412	3.26
					259	3.26
					412	3.26
<i>Vc</i>	1672	1628	1537	1366	412	3.26
					259	3.26

For *Ia*—*Ic* $\tilde{\nu}/\text{cm}^{-1}$: 2147, 2145, and 2143 ($\nu(\text{N}_3)$); for *IVa*—*IVc* $\tilde{\nu}/\text{cm}^{-1}$: 3277, 3264, and 3456 ($\nu(\text{NH})$); for *Va*—*Vc* $\tilde{\nu}/\text{cm}^{-1}$: 3273, 3364, and 3408 ($\nu(\text{NH})$).

the reaction time and simplification of the isolation of the products.

Characteristic data of the synthesized compounds are given in Table 1. Their structure has been confirmed by ^1H NMR, UV, and IR spectroscopy (Tables 2 and 3). ^1H NMR spectra of products *IVa*—*IVc*

and *Va*—*Vc* were taken in $(\text{CD}_3)_2\text{CO}$. The values of the coupling constants $^3J = 14.6$ Hz indicate that the products *IVa*—*IVc* and *Va*—*Vc* were isolated as *E* isomers. In the spectra of *IVc* and *Vc* two values of the coupling constants, $^3J = 14.6$ Hz and $^3J = 9.3$ Hz, appear, *i.e.* the above-mentioned two products exist in

Table 3. ¹H NMR Data of Synthesized Compounds

Compound	δ_i				
	H-3	H-4	H-A	H-B	Other signals, $J_{H,H}$
<i>Ia</i>	6.93 d	6.83 d	6.43 d	7.52 d	7.18—8.55 (m, H _{arom}), $J_{3,4} = 3.5$ Hz, $J_{A,B} = 15.5$ Hz
<i>Ib</i>	6.77 d	6.67 d	6.42 d	7.48 d	7.97 (d, H-2', H-6'), 8.32 (d, H-3', H-5'), $J_{3,4} = 3.5$ Hz, $J_{A,B} = 15.5$ Hz
<i>Ic</i>	7.35 d	6.83 d	6.60 d	7.48 d	$J_{3,4} = 3.7$ Hz, $J_{A,B} = 15.7$ Hz
<i>IVa</i>	7.08 d	6.28 d	6.10 d	7.66 d ^a	1.61 (m, H _{aliph}), 3.48 (m, N—CH ₂), 7.50—8.56 (m, H _{arom}), 8.38 (bs, NH), $J_{3,4} = 3.5$ Hz, $J_{A,B} = 14.6$ Hz
<i>IVb</i>	7.15 d	6.28 d	6.00 d	7.72 d ^a	1.61 (m, H _{aliph}), 3.54 (m, N—CH ₂), 7.91 (d, H-2', H-6'), 8.27 (d, H-3', H-5'), 8.48 (bs, NH), $J_{3,4} = 3.5$ Hz, $J_{2',3'} = 9.1$ Hz, $J_{A,B} = 14.6$ Hz
<i>IVc</i>	7.49 d	6.51 d	6.07 d	7.88 d ^a	8.75 (bs, NH), $J_{3,4} = 3.9$ Hz, $J_{A,B} = 14.6$ Hz
	7.59 d	6.59 d	5.61 d	7.26 d ^a	8.75 (bs, NH), $J_{3,4} = 3.9$ Hz, $J_{A,B} = 9.4$ Hz
<i>IVc</i> ^c	7.61 d	6.59 d	5.97 d	7.68 d ^a	1.48 (m, H _{aliph}), 3.36 (m, N—CH ₂), 9.50 (m, NH), $J_{3,4} = 3.9$ Hz, $J_{A,B} = 14.4$ Hz
<i>Va</i>	7.16 d	6.30 d	6.05 d	^b	3.67 (m, N—CH ₂), 3.70 (m, O—CH ₂), 7.50—8.75 (m, H _{arom}), 8.48 (bs, NH), $J_{3,4} = 3.5$ Hz, $J_{A,B} = 14.4$ Hz
<i>Vb</i>	7.16 d	6.31 d	6.03 d	7.81 d ^a	3.53 (m, N—CH ₂), 3.60 (m, O—CH ₂), 7.92 (d, H-2', H-6'), 8.27 (d, H-3', H-5'), $J_{3,4} = 3.5$ Hz, $J_{2',3'} = 9.1$ Hz, $J_{A,B} = 14.4$ Hz
<i>Vc</i>	7.51 d	6.54 d	6.11 d	7.85 d ^a	8.86 (bs, NH), $J_{3,4} = 3.9$ Hz, $J_{A,B} = 14.6$ Hz
	7.60 d	6.63 d	5.67 d	7.25 d ^a	8.86 (bs, NH), $J_{3,4} = 3.9$ Hz, $J_{A,B} = 9.4$ Hz
<i>Vc</i> ^c	7.62 d	6.62 d	5.99 d	7.67 d ^a	3.43 (m, N—CH ₂), 3.50 (m, O—CH ₂), 9.57 (bs, NH), $J_{3,4} = 3.9$ Hz, $J_{A,B} = 14.4$ Hz

a) Identified after addition of D₂O; b) overlapped by multiplet of H_{arom}; c) measured in DMSO-*d*₆.

(CD₃)₂CO in both *E* and *Z* isomeric forms. The spectra of *IVc* and *Vc* taken in DMSO-*d*₆ show again only the coupling constant for *E* isomer $^3J = 14.4$ Hz.

EXPERIMENTAL

Melting points were determined on a Kofler hot plate apparatus. ¹H NMR spectra of the compounds were recorded on a Tesla BS 587C (80 MHz) instrument, *Ia*—*Ic* measured in CDCl₃, *IVa*—*IVc* and *Va*—*Vc* in (CD₃)₂CO. Compounds *IVc* and *Vc* were measured also in DMSO-*d*₆. Chemical shifts δ are relative to TMS as internal standard. The UV spectra were measured on a Specord M-40 (Zeiss, Jena) spectrophotometer in methanol, $c = 10^{-4}$ mol dm⁻³. IR spectra were recorded on a FTIR PU 9802/25 (Philips) spectrophotometer using KBr pellets (0.5 mg/300 mg KBr).

The following starting compounds were prepared: 3-[5-(3-nitrophenyl)-2-furyl]propenoic acid (*Ia*) [3], 3-[5-(4-nitrophenyl)-2-furyl]propenoic acid (*Ib*) [3], 3-(5-nitro-2-furyl)propenoic acid (*Ic*) [4].

3-(5-R-2-Furyl)propenoyl Azide *Ia*—*Ic*

Propenoic acids *Ia*—*Ic* (10 mmol) suspended in dry acetone (10 cm³) were cooled to -10°C. Triethylamine (1.6 cm³, 11.6 mmol) and ethyl chloroformate (1.2 cm³, 13 mmol) in dry acetone (1 cm³) were successively added dropwise under stirring at a temperature lower than 0°C. The reaction mixture was stirred for 30 min at the same temperature. A solution of sodium azide (1.0 g; 15.3 mmol) in water (5 cm³) was added. The temperature was not allowed to increase to 0°C.

The yellow suspension was stirred for an additional hour and allowed to warm to room temperature. The mixture was poured on crushed ice, the yellow precipitate was filtered off, washed with water and crystallized.

1-[2-(5-R-2-Furyl)vinyl]-3,3-pentamethyleneurea *IVa*—*IVc* and -(3-oxapentamethylene)urea *Va*—*Vc*

Ia—*Ic* (10 mmol) were refluxed in toluene (100 cm³) for 2 h. To the reaction mixture piperidine (1.0 cm³, 10 mmol) resp. morpholine (0.9 cm³, 10 mmol) were dropwise added and the reflux was kept for 2 h. After cooling the product was precipitated, filtered off and crystallized.

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REFERENCES

- Koreňová, A., Krutošiková, A., Kováč, J., and Celec, S., *Collect. Czech. Chem. Commun.* 52, 192 (1987).
- Koreňová, A., Krutošiková, A., and Kováč, J., *Chem. Papers* 42, 795 (1988).
- Krutošiková, A., Surá, J., Kováč, J., and Juhás, S., *Collect. Czech. Chem. Commun.* 40, 3362 (1975).
- Gilman, H. and Wright, G. F., *J. Am. Chem. Soc.* 52, 2550 (1930).

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