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Note

Sulphonamide Derivatives of Heptamethylenimine. II.* The Preparation of Arylsulphonylureas Containing in their Structure Heptamethylenimine

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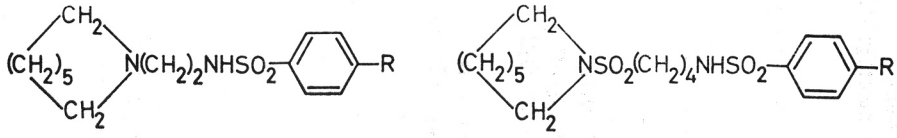
Since the announcement of *N*-*n*-butyl-*N'*-sulphanilylurea (»Carbutamide«)[1,2] as a valuable antidiabetic agent numerous Sulphonylurea derivatives have been widely investigated for their potential hypoglycemic action. Several of these compounds have been successfully used in the treatment of diabetes mellitus.

In our earlier comunications[3] we reported the preparation of sulphonamide derivatives of heptamethylenimine of the general type:



In continuation of our studies we synthesized several analogous arylsulphonylurea compounds, which we tested for their ability to reduce the blood sugar level in mice. The similarly built *N*-[β-(piperidino)ethyl]-*N'*-arylsulphonylurea[4] was reported as completely hypoglycemicaly inactive, but *N*-[ω-(cycloalkylensulphamyl)alkyl]-*N'*-arylsulphonylureas have not been described nor tested until now.

N-[β-(1,1-Heptamethylenimino)ethyl]-*N'*-arylsulphonylureas (Table I) and *N*-[δ-(1,1-heptamethylensulphamyl)butyl]-*N'*-arylsulphonylureas (Table II) were prepared by the reaction of arylsulphonylethylurethanes with β-(1,1-heptamethylenimino)ethylamine and δ-(1,1-heptamethylensulphamyl)butylamine respectively.

N-[β-(1,1-Heptamethylenimino)ethyl]-*N'*-*p*-chlorobenzensulphonylurea reduced the blood sugar level in experimental mice for 18.2% compared to 24.0% for *N*-*n*-propyl-*N'*-*p*-chlorobenzensulphonylurea (»Chlorpropamide«)[5].

EXPERIMENTAL

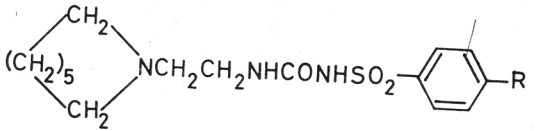
General Procedure

An intimate mixture of β-(1,1-heptamethylenimino)ethyl-amine (15.6 g.; 0.1 mole) respectively δ-(1,1-heptamethylensulphamyl)butylamine (24.8 g.; 0.1 mole) and the corresponding arylsulphonyl-ethylurethane (0.1 mole) was heated (to about 100°) until the dissolution was completed. The resulting clear melt was then heated to 120—130° (melt temperature) under reduced pressure (water aspirator) for 3 hr. The residual

* Part I.: S. Fila-Hromadko, B. Glunčić, and D. Kolbah, *Croat. Chem. Acta* **39** (1967) 207.

TABLE I

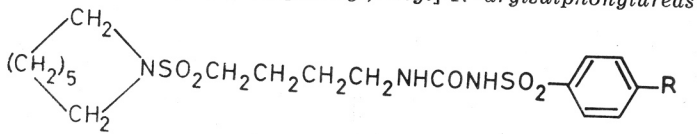
N-[β-*(1,1-Heptamethylenimino)ethyl*]-N′-*arylsulphonylureas*



	R	Yield %	M. p. 0°	Formula	Found (%)				Calc'd. (%)			
					C	H	N	Cl	C	H	N	Cl
I	H	74	165—167	$C_{16}H_{25}N_3O_3S$	56.36	7.47	12.10	—	56.62	7.43	12.38	—
II	CH_3	65	155—156	$C_{17}H_{27}N_3O_3S$	57.59	7.59	11.61	—	57.77	7.70	11.89	—
III	Cl	67	179—181	$C_{16}H_{24}ClN_3O_3S$	51.62	6.43	10.98	9.11	51.41	6.47	11.24	9.48

TABLE II

N-[δ-*(1,1-Heptamethylensulphamyl)butyl*]-N′-*arylsulphonylureas*



	R	Yield %	M. p. 0°	Formula	Found (%)				Calc'd. (%)			
					C	H	N	Cl	C	H	N	Cl
IV	H	67	139—140	$C_{18}H_{29}N_3O_5S_2$	49.85	6.68	9.82	—	50.11	6.78	0.74	—
V	CH_3	75	175	$C_{19}H_{31}N_3O_5S_2$	51.36	7.22	9.72	—	51.23	7.01	9.43	—
VI	Cl	68	138	$C_{18}H_{28}ClN_3O_4S_2$	48.30	6.09	9.50	7.57	48.04	6.27	9.33	7.87

products were crystallised from 96% ethanol and subsequently purified for analysis from the solvents indicated in Table I and II.

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IZVOD

Sulfonamidski derivati heptametilenimina. II. Preparacija arilsulfonilurea koje sadrže u svojoj strukturi heptametilenimin

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Reakcijom β-(1,1-heptametilenimino)etilamina odnosno δ-(1,1-heptametilensulfamil)butilamina s arilsulfoniletiluretanima dobivene su N-[β-(1,1-heptametilenimino) etil]-N′-arilsulfoniluree (Tabela I) odnosno N-[δ-(1,1-heptametilensulfamil)butil]-N′-arilsulfoniluree (Tabela II).

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