

CCA-284

547.495.2:542.945.07

Preliminary Communication

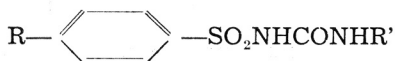
New Method for the Preparation of Arylsulphonylureas*

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Received January 4, 1963

The discovery of the potent hypoglycemic action of *N*-butyl-*N'*-sulphonylurea (Carbutamide, I)¹ stimulated wide investigations of the chemically related compounds², but most of them were toxic for human use. However, *N*-butyl-*N'*-*p*-toluenesulphonylurea (Tolbutamide, II) and *N*-propyl-*N'*-*p*-chlorobenzenesulphonylurea (Chlorpropamide, III) have been widely used without toxic side effects in the treatment of mild diabetes mellitus of the adult type.



I	R = NH ₂ ; R' = C ₄ H ₉	VII	R = Cl; R' = C ₆ H ₅
II	R = CH ₃ ; R' = C ₄ H ₉	VIII	R = CH ₃ ; R' = C ₆ H ₅
III	R = Cl; R' = C ₃ H ₇	IX	R = AcNH; R' = C ₆ H ₅
IV	R = CH ₃ ; R' = C ₃ H ₇	X	R = AcNH; R' = C ₃ H ₇
V	R = Cl; R' = C ₄ H ₉	XI	R = AcNH; R' = C ₄ H ₉
VI	R = Cl; R' = CH ₃		

In the past few years numerous syntheses of *N*-alkyl-*N'*-arylsulphonylureas have been described.³ In the present paper we report a direct synthesis of *N*-alkyl and *N*-phenyl-*N'*-arylsulphonylureas by condensing the sodium salts of arylsulphonylamides with the appropriate *N*-substituted carbamic acid esters. Arylsulphonylamides and the corresponding sodium salts were prepared according to the standard procedure.⁴ *N*-Substituted carbamic acid esters were obtained from ethyl chloroformate and the appropriate alkyl or arylamine.¹⁰ The reaction between the sodium salts of arylsulphonylamides and *N*-substituted carbamates was performed in dimethylformamide as solvent, and the arylsulphonylureas were isolated in yields ranging from 50–70%, and showed no depression of melting point when mixed with authentic samples prepared according to the standard methods.

The following arylsulphonylureas were prepared (Table I): *N*-butyl-*N'*-*p*-toluenesulphonylurea (II); *N*-propyl-*N'*-*p*-chlorobenzenesulphonylurea (III); *N*-propyl-*N'*-*p*-toluenesulphonylurea (IV); *N*-butyl-*N'*-*p*-chlorobenzenesulpho-

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nylurea (V); *N*-methyl-*N'*-*p*-chlorobenzenesulphonylurea (VI); *N*-phenyl-*N'*-*p*-chlorobenzenesulphonylurea (VII); *N*-phenyl-*N'*-*p*-toluenesulphonylurea (VIII); *N*-phenyl-*N'*-*p*-acetamidobenzenesulphonylurea (IX); *N*-propyl-*N'*-*p*-acetamidobenzenesulphonylurea (X); *N*-butyl-*N'*-*p*-acetamidobenzenesulphonylurea (XI).

TABLE I

	R	R'	Yield %	M. p. °C	Reported M. p. °C
II	CH ₃	C ₄ H ₉	70	128	127-9 ⁵
III	Cl	C ₃ H ₇	71	127	126-8 ³
IV	CH ₃	C ₃ H ₇	68	151	151-2 ³
V	Cl	C ₄ H ₉	69	116-7	115-6 ³
VI	Cl	CH ₃	52	189	188-9 ⁵
VII	Cl	C ₆ H ₅	55	180	179-81 ⁶
VIII	CH ₃	C ₆ H ₅	52	172	170-2 ⁷
IX	AcNH	C ₆ H ₅	56	189	188-9 ⁸
X	AcNH	C ₃ H ₇	59	198	—
XI	AcNH	C ₄ H ₉	51	194	193-5 ⁹

EXPERIMENTAL

Sodium salts of arylsulphonylamide (1 part), *N*-substituted carbamic acid ester (3 part) and *N,N*-dimethylformamide (10 parts) were refluxed for eight hours. Dimethylformamide was evaporated *in vacuo*, the semicrystalline residue dissolved in a saturated sodium bicarbonate solution and left to stand in a refrigerator for several hours. The insoluble arylsulphonylamide was removed by filtration and the bicarbonate solution extracted with benzene to remove the unreacted carbamate. Hydrochloric acid was added to the bicarbonate solution (pH 4), and the crude arylsulphonylurea filtered off. The product was recrystallized from diluted ethanol.

Acknowledgment. The authors are grateful to Mr. Eugen Guštak for his continued interest in this work. Thanks are due to Mrs. Ljubica Loborec-Stanić for her technical assistance.

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IZVOD

Nova metoda priprave arilsulfonilurea

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Reakcijom natrijskih soli arilsulfonamida sa *N*-supstituiranim esterima karbaminske kiseline priređene su slijedeće arilsulfoniluree: *N*-butil-*N'*-*p*-toluensulfonilurea (II); *N*-propil-*N'*-*p*-klorbenzensulfonilurea (III); *N*-propil-*N'*-*p*-toluensulfonilurea (IV); *N*-butil-*N'*-*p*-klorbenzensulfonilurea (V); *N*-metil-*N'*-*p*-klorbenzensulfonilurea (VI); *N*-fenil-*N'*-*p*-klorbenzensulfonilurea (VII); *N*-fenil-*N'*-*p*-toluensulfonilurea (VIII); *N*-fenil-*N'*-*p*-acetamidobenzensulfonilurea (IX); *N*-propil-*N'*-*p*-acetamidobenzensulfonilurea (X); *N*-butil-*N'*-*p*-acetamidobenzensulfonilurea (XI).

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Primljeno 4. siječnja 1963.