CCA-312 615.778.07

Original Scientific Paper

Synthetic Studies in the Sulphonamide Series. II.* Application of the Wolff Rearrangement to the Preparation of *N*-Acylsulphonamides

A. Markovac-Prpić and N. Tipić

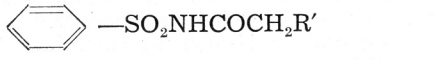
Research Department, »Pliva« Pharmaceutical and Chemical Works, Zagreb, Croatia, Yugoslavia

Received October 11, 1963

The Wolff rearrangement of α-diazoketones was performed in the presence of sodium sulphonamides and the corresponding *N*-acylsulphonamides were obtained. When tested on rats, these compounds showed a very strong diuretic activity.

It has been shown by Wolff, and later by Arndt and Eistert, that α-diazoketones readily lose nitrogen and in the presence of silver oxide rearrange to ketenes[1]. The reaction is usually carried out in the presence of water, alcohols or other protonic reagents, which convert the ketenes to the corresponding derivatives of homologous carboxylic acids.[2]

In as far as we know Wolff rearrangement of α-diazoketones has not been carried out in the presence of sulphonamides or their sodium salts. Therefore, in the course of our experiments in the sulphonamide series a systematic study of this reaction was undertaken. It was found that *N*-acylsulphonamides of the general formula



can be obtained if the Wolff rearrangement of α-diazoketones was performed in the presence of sodium sulphonamides using silver oxide as a catalyst. The free suphonamides, however, did not react under these conditions. The reaction was carried out in dioxane or dimethylformamide to give *N*-acylsulphonamides in a yield ranging from 50—70%.

Using this reaction the following *N*-acylsulphonamides were prepared: *N*-phenylacetyl-benzenesulphonamide (I), *N*-phenylacetyl-*p*-chlorobenzenesulphonamide (II), *N*-phenylpropionyl-*p*-chlorobenzenesulphonamide (III), *N*-*p*-nitrophenylacetyl-*p*-chlorobenzenesulphonamide (IV), *N*-phenylacetyl-*p*-toluenesulphonamide (V), *N*-phenylpropionyl-*p*-toluenesuphonamide (VI), *N*-*p*-nitrophenylacetyl-*p*-toluenesulphonamide (VII) and *N*-phenylacetyl-*p*-acetamidobenzenesulphonamide (VIII) (Table I)**.

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* Part I, A. Markovac-Prpić and N. Tipić, *Croat Chem. Acta* **35** (1963) 73.

** Further examples for this reaction will be found in the thesis of N. Tipić (in preparation).

Preliminary pharmacological tests show that these compounds posses a remarkable diuretic activity when tested on rats. The results of these experiments will be published elsewhere.

TABLE I

Compound	R	R'	M. p. °C	Formula	Analyses					
					Calculated			Found		
					%C	%H	%N	%C	%H	%N
I	H	C_6H_5	102[a]	$C_{14}H_{13}NO_3S$	61.08	4.76	5.09	60.81	4.50	5.32
II	Cl	C_6H_5	151[b]	$C_{14}H_{12}ClNO_3S$	54.28	3.92	4.54	54.50	3.70	4.81
III	Cl	$CH_2C_6H_5$	100[c]	$C_{15}H_{14}ClNO_3S$	55.65	4.36	4.33	55.48	4.09	4.24
IV	Cl	$C_6H_4NO_2$	208[a]	$C_{14}H_{11}ClN_2O_5S$	47.41	3.13	7.90	47.58	3.36	8.19
V	CH_3	C_6H_5	149[c]	$C_{15}H_{15}NO_3S$	62.28	5.23	4.84	62.04	5.45	4.84
VI	CH_3	$CH_2C_6H_5$	118[b]	$C_{16}H_{17}NO_3S$	63.36	5.65	4.62	63.09	5.70	4.69
VII	CH_3	$C_6H_4NO_2$	219[a]	$C_{15}H_{14}N_2O_5S$	53.89	4.22	8.38	53.82	4.53	—
VIII	AcNH	C_6H_5	239[a]	$C_{16}H_{16}N_2O_4S$	57.83	4.85	8.43	58.03	5.04	8.22

[a]Crystallized from 96% ethanol; [b]crystallized from a mixture of ethanol-petroleum ether; [c]crystallized from 80% ethanol.

EXPERIMENTAL

General procedure

A mixture of 0.01 mole of sodium sulphonamide[3], 0.01 mole α-diazoketone[4,5] and 30 ml. of purified dioxane was heated in a bath at 100° and the freshly prepared suspension of silver oxide in dioxane was added gradually. A vigorous evolution of nitrogen occurred at cca 100° and the reaction was complete in about thirty minutes. Silver oxide was removed by filtration and the dark solution evaporated to dryness *in vacuo*. The crystalline residue was dissolved in 20 ml. of hot water, treated with charcoal and acidified with diluted hydrochloric acid, to give the crude crystalline *N*-acylsulphonamide. After two recrystallizations a pure product was obtained

Acknowledgments. The autors are grateful to Mr. Eugen Guštak for his continued interest in this work. Thanks are due to Mr. J. Hranilović and Mrs. N. Škoda for performing the microanalyses.

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IZVOD

Sintetske studije u redu sulfonamida. II. Primjena Wolffova pregrađivanja na pripravu *N*-acilsulfonamida

A. Markovac-Prpić i N. Tipić

Wolffovo pregrađivanje α-diazoketona provedeno je u prisutnosti natrijskih soli sulfonamida uz dodatak srebrnog oksida kao katalizatora, i dobiveni su odgovarajući *N*-acilsulfonamidi. Preliminarna ispitivanja na štakorima pokazala su da ovi spojevi imaju jako diuretsko djelovanje.

ISTRAŽIVAČKI INSTITUT
»PLIVA« TVORNICA FARMACEUTSKIH
I KEMIJSKIH PROIZVODA
ZAGREB

Primljeno 11. listopada 1963.