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

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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 ketenes1. 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

\[ R-\begin{array}{c} \text{SO}_2\text{NHCOC}_2H_5 \end{array} \]

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 sulphonamides, 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-toluenesulphonamide (VI), N-p-nitrophenylacetyl-p-toluenesulphonamide (VII) and N-phenylacetyl-p-acetamidobenzenesulphonamide (VIII) (Table I)**.


** Further examples for this reaction will be found in the thesis of N. Tipić (in preparation).
Preliminary pharmacological tests show that these compounds possess a remarkable diuretic activity when tested on rats. The results of these experiments will be published elsewhere.

**TABLE I**

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>R'</th>
<th>M. D. C</th>
<th>Formula</th>
<th>Analyses</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Calculated</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>%/C</td>
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<tr>
<td>I</td>
<td>H</td>
<td>C₆H₅</td>
<td>102⁵</td>
<td>C₁₄H₁₅NO₂S</td>
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<tr>
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<tr>
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<tr>
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<td>C₂H₅C₆H₅</td>
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<td>C₂H₅NO₂</td>
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<tr>
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<td>AcNH</td>
<td>C₆H₅</td>
<td>239⁵</td>
<td>C₁₃H₁₄N₂O₄S</td>
<td>57.83</td>
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</table>

*Crystallized from 96%/ ethanol; ⁵crystallized from a mixture of ethanol-petroleum ether; ⁶crystallized from 80%/ ethanol.

**EXPERIMENTAL**

**General procedure**

A mixture of 0.01 mole of sodium sulphonamide, 0.01 mole α-diazoketone⁴, and 30 ml. of purified dioxane was heated in a bath at 100⁰ and the freshly prepared suspension of silver oxide in dioxane was added gradually. A vigorous evolution of nitrogen occurred at cca 100⁰ 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.

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**REFERENCES**

IZVOD

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

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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.

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