



Alkaline hydrolysis of these compounds gave the well known sulphonamides VI—VIII in good yields.

When tested *in vitro* only compound V showed a very slight bacteriostatic activity against *Str. haemolyticus*.

#### EXPERIMENTAL

Melting points are not corrected.

#### Carbanilide *p,p'*-disulphonic acid dichloride (II)

Carbanilide (32 g., 0.15 moles) was dissolved in 100 ml. (1.54 mole) of chloro-sulphonic acid by gradual addition under stirring. After subsequent heating to 55–60 for 2 hrs., the reaction mixture was poured onto 600 g. of crushed ice, the separated product filtered off by suction and the filter cake washed with 4 litres of ice-cold water to give 200 g. of a moist product containing 45 g. (0.11 mole) of carbanilide-*p,p'*-disulphonic-acid-dichloride.

#### *p,p'*-bis-(3,4-Dimethyl-iso-öxazolyl-5-sulphamyl) carbanilide (III)

A. A moist cake of II (200 g., 0.11 mole) was added to 150 ml. of methyl-ethyl ketone, the aqueous layer separated and the obtained solution dried with anhydrous sodium sulphate. To the anhydrous solution 15.8 g. (0.14 mole) of 5-amino-3,4-dimethyl-iso-öxazole was added, the resulting mixture cooled to 8–10° and 22 g. (0.28 mole) of dry pyridine dropped in during 3 hrs at the same temperature. After keeping overnight at room temperature the solvent was decanted off, the residue dissolved in a 10% sodium hydroxide solution and the rest of the solvent evaporated *in vacuo* together with pyridine. The resulting alkaline solution was acidified with dilute hydrochloric acid to a pH of 1 to yield 40 g. (theoretical amount) of a crude product with m. p. 190–200°.

For analysis the crude product was extracted with acetone, the undissolved part dissolved in dimethylformamide, filtered and the filtrate precipitated by addition of water to give pure *p,p'*-bis-(3,4-dimethyl-iso-öxazolyl-5-sulphamyl) carbanilide with m. p. 241–243°. The IR-spectra show a characteristic —CONH— band at 1700  $\text{cm}^{-1}$  and —SO<sub>2</sub>N— bands at 1150 resp. 1340  $\text{cm}^{-1}$ .

*Anal.* C<sub>23</sub>H<sub>24</sub>N<sub>6</sub>O<sub>7</sub>S<sub>2</sub> (560.60) calc'd.: C 49.27; H 4.32; N 14.99%  
found: C 49.36; H 4.30; N 14.72%

40 g. of crude III was heated under reflux with 300 ml. of a 12% sodium hydroxide solution during 5 hrs. The separated sodium salt was filtered off after cooling, washed with a 10% sodium chloride solution, dissolved in 200 ml. of water and filtered after addition of some charcoal. Upon acidification with acetic acid 19 g. (49% of the theoretical amount) of pure 5-sulphanilylamido-3,4-dimethyl-iso-öxazole (VI) separated, m. p. 191–193°.

B. The wet cake of II (200 g., 0.11 mole) was suspended in 200 ml. of acetone and this suspension poured into 2000 ml. of cold water. The precipitate was filtered off by suction and dried at room temperature to yield about 50 g. of a crude product (90% pure, 0.11 mole) melting at 195–200° (lit.<sup>2</sup> m. p. 207–211°). This dry product was added in small portions under stirring at a temperature of 25–30° during 2–3 hrs. to a mixture of 25.8 g. (0.23 mole) 5-amino-3,4-dimethyl-iso-öxazole, 22 g. (0.28 mole) pyridine and 22 ml. acetone. Stirring was continued for 8 hrs. and then the reaction mixture diluted with 900 ml. of 1% sodium hydroxide solution and the resulting solution poured into 400 ml. of cold 1 N hydrochloric acid. The separated resinous product was reprecipitated by 1 N hydrochloric acid from a solution in 10% sodium hydroxide to give 40 g. (65% of the theoretical amount) of crude compound VI melting at 194–196°.

C. A mixture of 25.8 g. (0.23 mole) of 5-amino-3,4-dimethyl-iso-öxazole, 200 g. (0.11 mole) of the wet cake of II and 500 ml. of acetone was cooled to 6–8° and 45 g. (0.536 mole) of sodium hydrogen carbonate and 10 g. (0.1 mole) calcium carbonate was added gradually under stirring during 2 hrs. After keeping overnight at room temperature the solvent was evaporated and the resinous residue hydrolyzed, as

described before, to yield 8.5 g. (14.45% of the theoretical amount) of crude 5-sulphanilylamido-3,4-dimethyl-*iso*- $\delta$ xazole, m.p. 188—190°.

*p,p'*-(5-Methyl-*iso*- $\delta$ xazolyl-3-sulphamyl) carbanilide (IV)

The preparation was performed according to method A starting with 14.7 g. (0.15 mole) 3-amino-5-methyl-*iso*- $\delta$ xazole. 40 g. of a crude product melting at 220—223° was obtained (theoretical amount).

For analysis it was recrystallized several times from aqueous ethoxyethanol, to yield colourless crystals with m.p. 249—251°. The IR-spectra show the same characteristic bands as for compound VI.

*Anal.* C<sub>21</sub>H<sub>20</sub>N<sub>6</sub>O<sub>7</sub>S<sub>2</sub> (532.55) calc'd.: C 47.36; H 3.79; N 15.78%  
found: C 47.54; H 3.53; N 15.84%

The crude compound IV was hydrolyzed according to the procedure given for compound III. Yield 34 g. (90% of the theoretical amount) of crude 3-sulphanilylamido-5-methyl-*iso*- $\delta$ xazole (VII) with m.p. 165—168°. After several crystallizations from diluted ethanol the m.p. rose to 169—171°.

*p,p'*-bis-(1-Phenylpyrazolyl-5-sulphamyl) carbanilide hydrate (V)

The preparation was performed by a procedure analogous to the one described for compound III starting with 35.3 g. (0.22 mole) of 5-amino-1-phenylpyrazole. The yield was 22.6 g. (30.5% of the theoretical amount) of a crude product with m.p. 165—172°.

For analysis the product was dissolved in 96% ethanol, precipitated with water and then crystallized several times from ethanol. Colourless crystals of pure *p,p'*-bis-(1-phenylpyrazolyl-5-sulphamyl) carbanilide were obtained as a monohydrate melting at 172—175°, solidifying and melting again at 218—220°. The IR-spectra gave the same absorption bands as given for compound III.

*Anal.* C<sub>31</sub>H<sub>26</sub>N<sub>8</sub>O<sub>5</sub>S<sub>2</sub>·H<sub>2</sub>O (672.73) calc'd.: C 55.34; H 4.20; N 16.66%  
found: C 47.54; H 3.53; N 15.84%

The crude product V was hydrolyzed following the procedure given for the preparation of compound IX to yield 15.7 g. (74.8% of the theoretical amount) of crude 5-sulphanilylamido-1-phenyl pyrazole (VIII), m.p. 174—180°. After several crystallizations from alcohol the melting point rose to 180—183°.

REFERENCES

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IZVOD

**Priprava nekih disupstituiranih derivata *p,p'*-bis-(sulfamil) karbanilida i njihova hidroliza u odgovarajuće sulfonamide**

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Kondenzacijom diklorida karbanilid *p,p'*-disulfonske kiseline s 5-amino-3,4-dimetil izooksazolom, 3-amino-5-metil izooksazolom i 5-amino-1-fenil pirazolom dobiveni su *p,p'*-bis-(3,4-dimetilizooksazolil-5-sulfamil) karbanilid (III), *p,p'*-bis-(5-metilizooksazolil-3-sulfamil) karbanilid (IV) i *p,p'*-bis-(1-fenil-pirazolil-5-sulfamil) karbanilid (V). Alkalnom hidrolizom pripremljenih spojeva dobiveni su poznati sulfonamidi (VI—VIII).

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