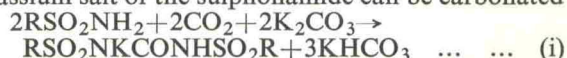


## A New Synthesis of Sulphonylureas by Carbonation of Sulphonamides under Pressure

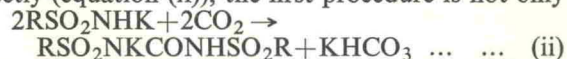
By B. R. Franko-Filipasic and R. Patarcity

High Pressure Laboratory, Central Research Department, FMC Corporation, Princeton, New Jersey, U.S.A.

We report a new synthesis of symmetrical bis(sulphonyl)ureas,  $(\text{RSO}_2\text{NH})_2\text{CO}$ , by pressure carbonation of the sulphonamide in the presence of potassium carbonate (equation (i)). Although the potassium salt of the sulphonamide can be carbonated



directly (equation (ii)), the first procedure is not only



more convenient, avoiding the preparation of the hygroscopic salt, but also gives higher yields. As the bis(sulphonyl)ureas are sufficiently acidic to react with carbonate or bicarbonate in the cold, the mono-potassium salt is isolated from the reaction.

Symmetrical bis(sulphonyl)ureas are difficult to synthesise and are rarely encountered in the literature.

carbon dioxide under pressure for 3-12 hours. The reaction products are rock hard and must be chipped from the autoclave. The solids are ground, suspended in water, and the insoluble sulphonamide is removed by filtration. The filtrate is titrated (pH meter) with cold dilute hydrochloric acid: any soluble potassium sulphonamide reacts with acid at a pH above 7 and the sulphonamide is removed by filtration. The bis(sulphonyl)ureas precipitate in a pH range of 4.3 to 2.7; acidification is continued to 0.5 and stirring continued for 30 minutes to completely free the urea of salt.

Potassium carbonate was the only alkali or alkaline earth carbonate to participate in the reaction; *m*-nitrophenyl- and 2,5-dichlorophenyl sulphonamides failed to react. No side reactions or ring carbonation were observed under these reaction conditions.

Table  
Bis(sulphonyl)ureas by pressure carbonation  
 $(\text{RSO}_2\text{NH})_2\text{CO}$

R	m.p. (°C)	Nitrogen (%)		Yield	Reaction Time (hr)	Temp. (°C)	CO <sub>2</sub> (psig)†
		Found	Theory				
C <sub>6</sub> H <sub>5</sub>	154-5	8.18	8.23	55	3	165	4000
<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	99-101d*	7.18	7.25	85*	3	165	4000
<i>o</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	111-112	7.92	7.61	77	3	165	4000
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	134-136*	6.46	6.56	54*	12	165	4000
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	170-171	7.06	6.85	76	12	165	3900
3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	138-144	5.48	5.64	88	12	200	3700
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	119-120	9.59	9.32	35	12	150	4000

\* Monohydrate.

† Pressure at maximum temperature.

The attempted coupling of the sulphonamide with phosgene<sup>1</sup> usually results in sulphonylisocyanate,  $\text{RSO}_2\text{NCO}$ ;<sup>2</sup> the reaction of the sulphonylisocyanate with sulphonamide has been utilised.<sup>3</sup> Treatment of the sodium salt of sulphonamide with phosgene<sup>4</sup> and treatment of urea with sulphonyl chloride<sup>5</sup> are generally unsuccessful. The reaction of phenyl carbonate with the sodium<sup>6</sup> or potassium<sup>7</sup> salt of the sulphonamide is the only useful method.

Yields of 35-85% (see Table) can be obtained in a pressure autoclave by treating one mole of sulphonamide and two moles of potassium carbonate with

The bis(sulphonyl)ureas exhibit a characteristic carbonyl absorption band in the region of 1700-1750  $\text{cm}^{-1}$ .

Received December 3, 1965

## References

- 1 Tischendorf, J., *J. prakt. Chem.*, 1895, **51**, [2] 350
- 2 British Patent 692,360 (1950)
- 3 Billeter, O. C., *Ber. dt. chem. Ges.*, 1904, **37**, 695
- 4 East Ger. Patent 4255 (1940)
- 5 Kurzer, F., *Chem. Rev.*, 1952, **50**, 13
- 6 Field, L. & Grunwald, F. A., *J. Am. chem. Soc.*, 1953, **75**, 934
- 7 Burmistrov, S. I. & Dubina, V. L., *Chem. Abs.*, 1963, **59**, 13861