

A NOTE ON THE OXIDATION OF PAPAVERINE BY SELENIUM DIOXIDE

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DURING the course of recent work, a supply of papaveraldine was required for the purposes of synthesis. The classical preparation of this compound is due to Goldschmiedt¹, who oxidised papaverine by potassium permanganate. Only a 53 per cent. yield of papaveraldine was claimed for this method, and it was therefore decided to investigate other methods of oxidation, selenium dioxide being finally chosen as the oxidising agent.

The most recent review of selenium dioxide oxidation² quotes only one example of the oxidation of papaverine by selenium dioxide, the method of Menon³. This author carried out the reaction in acetic acid solution, and gives no actual yield for the quantities used, although stating in the text that "The quantitative yield of papaveraldine and the absence of other degradation products is specially noteworthy." Postowsky and Lugowkin⁴ carried out the oxidation of diphenylmethane to benzophenone in 87 per cent. yield by heating an intimate mixture of the hydrocarbon and selenium dioxide to 200° to 210°C., in the absence of a solvent, whereas Fisher⁵, who used alcohol as a solvent, claimed only 47 per cent. yield of benzophenone. It seemed probable that the oxidation of papaverine by a modification of the method of Postowsky and Lugowkin would give satisfactory results, and this was therefore carried out.

EXPERIMENTAL

An intimate mixture of papaverine (15 g.) and selenium dioxide (6 g.) contained in a 250 ml. beaker was placed in an oil bath (oil temperature 180° to 190°C.) and thoroughly stirred. The mixture began to darken, soon fused, and a brisk reaction commenced, with the rapid evolution of steam. Steady stirring was required to prevent frothing. The chocolate-brown mixture then resolidified. It was heated for a total time of 30 minutes and allowed to cool; the brittle porous mass was powdered, and extracted with benzene (100 ml.) in a Soxhlet apparatus. When extraction was complete, the extract was cooled, filtered, washed with benzene (2 × 10 ml.) and dried, giving 14.99 g. of almost pure papaveraldine, m.pt. 204° to 206°C. The filtrate and washings, on evaporation, gave a reddish brown residue, m.pt. 192° to 202°C. (0.88 g.).

The main bulk was ground up with hydrochloric acid (30 ml. of concentrated acid in 100 ml. of water), the product made up to approximately 1 l. with water, heated to dissolve all the hydrochloride, filtered hot, and concentrated to small bulk under reduced pressure. On cooling, papaveraldine hydrochloride separated as fine yellow needles, m.pt.

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200°C. (as recorded³). The crude material of m.pt. 192° to 202°C. also yielded a small quantity of papaveraldine hydrochloride. This was added to the main bulk, the whole dissolved in hot water, made alkaline with ammonia, allowed to cool, and the resulting papaveraldine filtered off, washed thoroughly with water, and dried. The product weighed 14.30 g. (91.6 per cent.) and melted at 210°C. (recorded 210°C.¹, 209° to 211°C.³).

SUMMARY

Papaveraldine has been prepared in 91.6 per cent. yield by the oxidation of papaverine with selenium dioxide.

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REFERENCES

1. Goldschmidt, *Mh. Chem.*, 1885, **6**, 956; 1886, **7**, 486.
2. Rabjohn, *Organic Reactions*, John Wiley and Sons, New York.
3. Menon, *Proc. Indian Acad. Sci.*, 1944, **19A**, 21 (*Chem. Abst.* **39**, 390 (1945)).
4. Postowsky and Lugowkin, *Ber. dtsh. chem. Ges.*, 1935, **68**, 855.
5. Fisher, *J. Amer. chem. Soc.*, 1934, **56**, 2056.