

- Grol, C. J., Rollema, H. (1977) J. Pharm. Pharmacol. 29: 153-156
- Horn, A. S., de Kaste, D., Dijkstra, D., Rollema, H., Feenstra, M., Westerink, B. H. C., Grol, C., Westerbrink, A. (1978a) Nature (London) 276: 405-407
- Horn, A. S., Grol, C. J., Dijkstra, D., Mulder, A. H. (1978b) J. Med. Chem. 21: 825-828
- Horn, A. S., Rodgers, J. R. (1977) J. Pharm. Pharmacol. 29: 257-265
- Horn, A. S., Dijkstra, D., Rollema, H., Westerink, B. (1980) J. Med. Chem. in the press
- Katz, R., Heller, S. R., Jacobson, A. E. (1973) Mol. Pharmacol. 9: 486-494
- Kier, L. B. (1973) J. Theor. Biol. 40: 211-217
- Komiskey, H. L., Bossart, J. F., Miller, D. D., Patil, P. N. (1978) Proc. Natl. Acad. Sci. U.S.A. 75: 2641-2643
- McDermed, J. D., McKenzie, G. M., Phillips, A. P. (1975) J. Med. Chem. 18: 362-367
- Miller, D. D. (1978) Fed. Proc. Fed. Am. Soc. Exp. Biol. 37: 2392-2395
- Miller, R. J., Horn, A. S., Iversen, L. L., Pinder, R. (1974) Nature (London) 250: 238-241
- Portoghesi, P. S. (1970) Annu. Rev. Pharmacol. 10: 51-76
- Pullman, B., Berthod, H., Courrière, Ph. (1974) Int. J. Quant. Chem. 1: 93-108
- Pullman, B., Coubeils, J. L., Courrière, Ph., Gervois, J. P. (1972) J. Med. Chem. 15: 17-23
- Rekker, R. F., Engel, D. J. C., Nijs, G. S. (1972) J. Pharm. Pharmacol. 24: 589-591
- Richards, W. G. (1977) Quantum Pharmacology. Butterworths, London
- Rick, J., Szabo, M., Payne, P., Kovathana, N., Cannon, J. G., Frohman, L. A. (1979) Endocrinology 104: 1234-1242
- Rollema, H., Westerink, B., Mulder, T., Dijkstra, D., Feenstra, M., Horn, A. S. (1980) Eur. J. Pharmacol. in the press
- Schorderet, M., McDermed, J., Magistretti, P. (1978) J. Physiol. (Paris) 74: 509-513
- Seeman, P., Titeler, M., Tedesco, J., Weinrich, P., Sinclair, D. (1978) in: P. Roberts, G. Woodruff, L. Iversen (eds) Dopamine (Advances in Biochemical Pharmacology) vol. 19,
- Sheppard, H., Burghardt, C. R., Long, J. P. (1978) Res. Commun. Chem. Pathol. Pharmacol. 19: 213-224
- Watling, K. J., Woodruff, G. N., Poat, J. A. (1979) Eur. J. Pharmacol. 56: 45-49
- Westerink, B. H. C., Dijkstra, D., Feenstra, M. G. P., Grol, C. J., Horn, A. S., Rollema, H., Wirix, E. (1979) Ibid. 61: 7-15
- Williams, R. J. P. (1977) Angew. Chem. Int. Ed. Engl. 16: 766-777
- Woodruff, G. N., Elkhwad, A. O., Pinder, R. M. (1974) Eur. J. Pharmacol. 25: 80-86
- Woodruff, G. N., Watling, C. C., Andrews, C. D., Poat, J. A., McDermed, J. D. (1977) J. Pharm. Pharmacol. 29: 422-427

Oxidation of chlorprothixene with potassium permanganate

S. A. TAMMILEHTO, Department of Pharmaceutical Chemistry, School of Pharmacy, University of Helsinki, SF-00170 Helsinki 17, Finland

Psychotropic thioxanthene derivatives can be analysed fluorimetrically after oxidation with potassium permanganate (Mellinger & Keeler 1964; Mjörndal & Oreland 1971); the structure of the derivative of chlorprothixene thus formed and the influence of pH on the oxidation have been examined.

The oxidation product was prepared as follows: to chlorprothixene hydrochloride (300 mg) in distilled water (10 ml), alkaline potassium permanganate solution (3%, pH 12.4, 30 ml) was added slowly with constant stirring. The precipitated oxidation product, together with manganese dioxide, was filtered off and the reaction product was separated from the MnO₂ by washing the precipitate with acetone. The organic solvent was evaporated and the residue crystallized from ethanol, m.p. 150-151 °C. Found: C, 63.3; H, 2.99; calc. for C₁₈H₁₁ClO₅S: C, 63.3; H, 2.9.

The u.v., i.r. and p.m.r. spectra were identical with an authentic specimen of 2-chloro-10-thioxanthone (Agarwal & Blake 1969). The melting point and the thin layer chromatographic behaviour were likewise identical with this substance.

The pure thioxanthone shows intense fluorescence in aqueous solutions. With excess of potassium perman-

ganate, when oxidation is carried out in solutions of pH < 3, complete disappearance of fluorescence results.

The new reaction product, isolated in a similar way to the thioxanthone above, crystallized from ethanol, m.p. 222-224 °C. Found: C, 56.2; H, 2.7; calc. for C₁₈H₁₁ClO₅S: C, 56.0; H, 2.53.

The appearance in the i.r. spectra of this new compound of intense bands at 1300 cm⁻¹ and 1160-1140 cm⁻¹ suggests that the sulphur atom in the thioxanthone has been further oxidized to a sulphone group. The carbonyl absorption is also shifted to higher frequencies (from 1640 to 1675 cm⁻¹). Since the thioxanthone-sulphone has no fluorescent properties, the importance of controlling the pH of the reaction solution during the oxidation step of the fluorimetric analysis is underlined.

October 23, 1979

REFERENCES

- Agarwal, S. P., Blake, M. I. (1969) J. Pharm. Pharmacol. 21: 556
- Mellinger, T. J., Keeler, C. E. (1964) Anal. Chem. 36: 1840-1847
- Mjörndal, T., Oreland, L. (1971) Acta Pharmacol. Toxicol. 29: 295-302