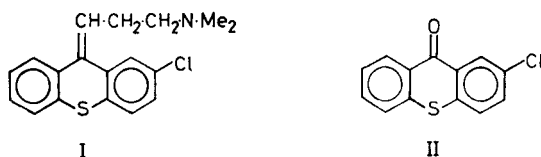


## Oxidation of chlorprothixene with ceric sulphate

Recently, Agarwal & Blake (1969) described a photometric titration procedure for the analysis of a series of therapeutically useful phenothiazine derivatives and their dosage forms. The procedure involved the titration of an acidic solution of the drug with ceric sulphate solution. The equivalence point was determined by following the change in absorbance of the solution at 420 nm. Chlorprothixene (I), *trans*-isomer of 2-chloro-9-(3-dimethylaminopropylidene) thioxanthene which is chemically and pharmacologically related to chlorpromazine, was one compound for which the analysis proved unsuccessful because of the formation of a precipitate during the titration. The composition of the precipitate and the chemical reaction involved in its formation have now been examined.



Chlorprothixene (500 mg) was suspended in 10%  $\text{H}_2\text{SO}_4$  (3 ml). Sufficient ethanol was added to effect solution. Ceric sulphate solution (0.1N) was added slowly until the formation of a heavy yellow precipitate was complete. The reaction mixture was left in an ice bath for 30 min, after which the precipitate was separated by filtration washed with distilled water, dried, and crystallized from ethanol-chloroform, m.p. 51–152°. Found: C, 63.0; H, 3.1.  $\text{C}_{13}\text{H}_7\text{ClOS}$  requires C, 63.3; H, 2.9.

The infrared spectrum indicated strong absorption, characteristic of the carbonyl group, at  $1642\text{ cm}^{-1}$ . The spectrum for chlorprothixene did not show this absorption peak. The nmr spectrum of the reaction product showed peaks in the region of 2.3–2.7 $\delta$ , due to phenyl protons; whereas the spectrum for chlorprothixene, showed peaks at 2.5–2.85 $\delta$  (phenyl protons), 4.1 $\delta$  (=CH–), 7.4–7.6 $\delta$  (–CH<sub>2</sub>–CH<sub>2</sub>–), and 7.8–2 $\delta$  (–NMe<sub>2</sub>). These data indicate that the dimethylaminopropylidene group was removed from the chlorprothixene molecule as a result of the oxidation process producing 2-chloro-10-thioxanthenone (II). The identity of this product was confirmed by synthesis from chlorobenzene and *o*-mercaptobenzoic acid in a concentrated sulphuric acid medium as described by Gilman & Diehl (1959); m.p. 152–153°; mixed melting point with the reaction product obtained by oxidation of chlorprothixene gave no depression. In addition, their infrared and nmr spectra were identical.

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