

University of Colorado

The Conversion of Thioxanth-10-one 5,5-Dioxide Oxime Acetates to Amines by Means of Diborane Reduction

P. Catsoulacos (1)

It was shown in a previous communication (2) that reduction of ketoxime acetates with diborane results in the formation of amines.

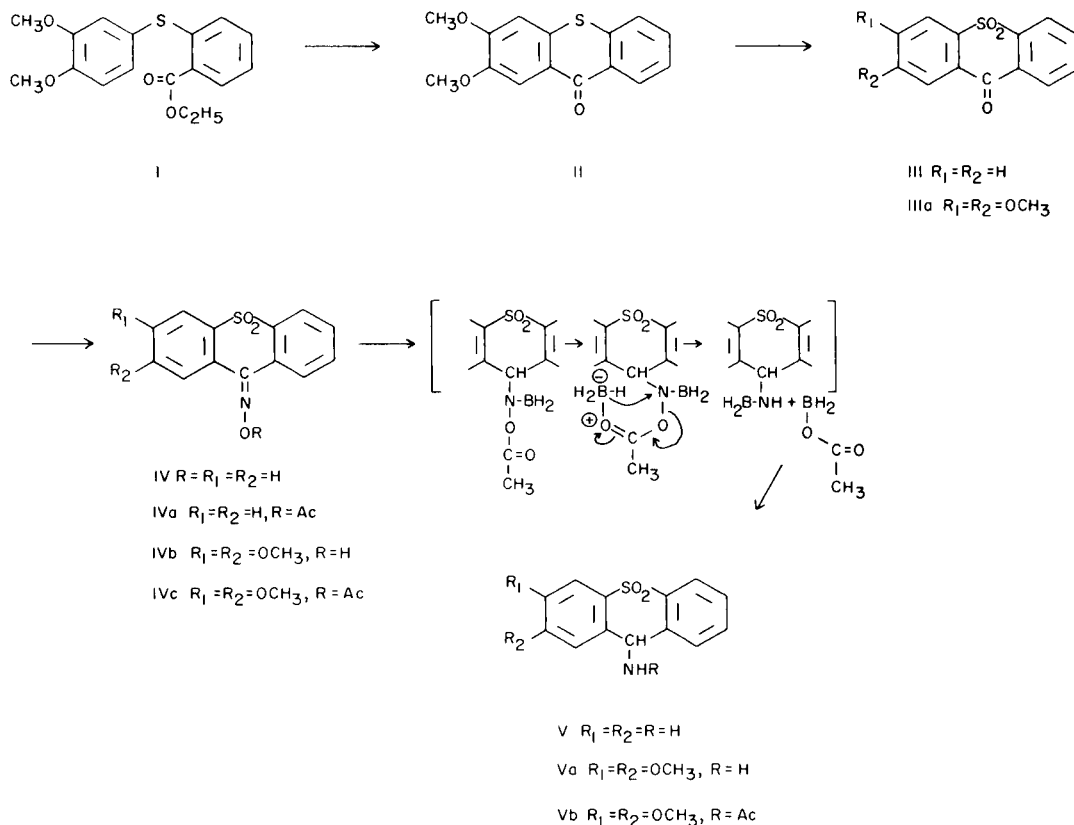
In connection with our study of heterocyclic compounds containing nitrogen and sulfur (3,4), it was found of interest to effect the reduction of a thioxanthone oxime to the corresponding amino compound. It has recently been reported (5) that the reduction of xanthone oxime and thioxanthone oxime with lithium aluminum hydride leads to deaminated products.

I was likewise unable to reduce thioxanthone 5,5-dioxide oxime using a variety of reducing agents until the acetylation and reduction with diborane was applied.

Evidently, the coordination of borane with the carbonyl oxygen provides a good leaving group and, in addition, has

the capability of forming a six membered ring transition state for hydride transfer.

The ethyl ester (I) was prepared in 70% yield according to a similar procedure (6). The thioxanthone (II) was formed by heating compound I or its acid in an excess of polyphosphoric acid. By the well-known oxidation with hydrogen peroxide the thioxanthone 5,5-dioxide (IIIa) was prepared in excellent yield. When the compounds III and IIIa were heated in a mixture of pyridine-ethanol containing an excess of hydroxylamine hydrochloride, the corresponding ketoximes (IV) and (IVb) were produced in 90% yield. The ketoximes were acetylated with excess of acetic anhydride and pyridine to give the corresponding oxime acetates, (IVa) and (IVc), which were converted into the amines V and Va by reduction with excess of diborane at room temperature in an overall yield of 70%.



EXPERIMENTAL

2-Carboethoxy-3',4'-dimethoxyphenylthiobenzene (I).

The cuprous salt of thiosalicylic ethylester (35 g.) was added to a solution prepared by dissolving 25 g. of bromoveratrole in 75 ml. of quinoline and 5 ml. of anhydrous pyridine. The solution was refluxed for 2.5 hours. The reaction mixture was then poured into ice-water containing 85 ml. of concentrated hydrochloric acid. The precipitate was collected by filtration and extracted with hot dichloromethane. The organic layer was washed with dilute hydrochloric acid, then with water and dried over magnesium sulfate. Removal of the solvent produced a semisolid that was crystallized from ethanol in 72% yield, m.p. 87-88°; ν max, 1705 cm^{-1} (C=O).

Anal. Calcd. for $\text{C}_{17}\text{H}_{18}\text{O}_4\text{S}$: C, 64.15; H, 5.71. Found: C, 64.01; H, 5.63.

2,3-Dimethoxythioxanthone (II).

To 15 g. of ester (I) was added 100 g. of polyphosphoric acid and the mixture was stirred at 100° for one hour. The brown solution was then poured into ice-water. The precipitate that formed was filtered and washed well with water. The dry thioxanthone was crystallized from ethanol to yield compound II in 93% yield, m.p. 172-173° (lit. (7) m.p. 172°); ν max, 1625 (C=O).

Anal. Calcd. for $\text{C}_{15}\text{H}_{12}\text{O}_3\text{S}$: C, 66.17; H, 4.41. Found: C, 66.04; H, 4.61.

2,3-Dimethoxythioxanthone 5,5-Dioxide (IIIa).

To a solution containing 5 g. of II in 30 ml. of acetic acid was added 15 ml. of 35% hydrogen peroxide and the mixture was heated on a steam bath for 2 hours. The crystalline material was collected by filtration after pouring into water. Crystallization from acetic acid gave compound IIIa in 90% yield, m.p. 148-148.5°; ν max, 1660 cm^{-1} (C=O).

Anal. Calcd. for $\text{C}_{15}\text{H}_{12}\text{O}_5\text{S}$: C, 59.21; H, 3.94. Found: C, 59.12; H, 4.12.

Thioxanthone 5,5-Dioxide Oxime (IV).

This compound was obtained in 90% yield, following the method of Truce and Simms (8), m.p. 234-235° (lit. (8) 213-214°).

Anal. Calcd. for $\text{C}_{13}\text{H}_9\text{NO}_3\text{S}$: C, 60.23; H, 3.50; N, 5.40. Found: C, 60.27; H, 3.40; N, 5.55.

2,3-Dimethoxythioxanthone 5,5-Dioxide Oxime (IVb).

Following the above procedure, ketoxime (IVb) was obtained in 88% yield, after recrystallization from ethanol, m.p. 226-227°; ν max, 3400 cm^{-1} (OH).

Anal. Calcd. for $\text{C}_{15}\text{H}_{13}\text{NO}_5\text{S}$: C, 56.42; H, 4.07. Found: C, 56.59; H, 4.22.

Thioxanthone 5,5-Dioxide Oxime Acetate (IVa).

Compound IV was acetylated with an excess of acetic anhydride and pyridine at room temperature for 10 hours. Then the solution was poured into ice water and the precipitate was collected by filtration, washed well with water and recrystallized from methanol to afford white crystals in 85% yield, m.p. 167-168°; ν max, 1775 cm^{-1} .

Anal. Calcd. for $\text{C}_{15}\text{H}_{11}\text{NO}_4\text{S}$: C, 59.80; H, 3.65; N, 4.65. Found: C, 59.63; H, 3.67; N, 4.77.

2,3-Dimethoxythioxanthone 5,5-Dioxide Oxime Acetate (IVc).

This compound was obtained in 92% yield, m.p. 242-243°; ν max, 1775 cm^{-1} .

Anal. Calcd. for $\text{C}_{17}\text{H}_{15}\text{NSO}_6$: C, 56.50; H, 4.15. Found: C, 56.09; H, 4.33.

10-Aminothioxanthone 5,5-Dioxide (V).

Ten g. of thioxanthone 5,5-dioxide oxime acetate (IVa) was placed in a 500 ml. round bottom flask. To this was added 120 ml. of a 1 M solution of borane in THF, within 30 minutes. The reaction mixture was allowed to stand at room temperature for 12 hours. The solvent was removed under reduced pressure at room temperature. Water was added slowly to the residue, which was then extracted several times with chloroform. The solvent was removed *in vacuo* after washing with water and drying over magnesium sulfate. The residue was crystallized from ethanol to yield 5.6 g. (69%) of V. Recrystallization from ethyl acetate-dichloromethane gave m.p. 171-173°; ν max, 3400 cm^{-1} (NH).

Anal. Calcd. for $\text{C}_{13}\text{H}_{11}\text{NO}_2\text{S}$: C, 63.66; H, 4.49. Found: C, 63.48; H, 4.37.

Picrate, m.p. 213-215°.

Anal. Calcd. for $\text{C}_{19}\text{H}_{14}\text{N}_4\text{O}_9\text{S}$: N, 11.81. Found: 11.93.

10-Acetamido-2,3-dimethoxythioxanthone 5,5-Dioxide (Vb).

The amine (Va) was obtained from 6 g. of 2,3-dimethoxythioxanthone 5,5-dioxide oxime acetate, as described for V, to yield, after acetylation, 10-acetamido-2,3-dimethoxythioxanthone 5,5-dioxide (Vb), 4.75 g. (82%). Recrystallization from chloroform-methanol gave m.p. 243-244°; ν max, 1680 cm^{-1} (C=O).

Anal. Calcd. for $\text{C}_{17}\text{H}_{17}\text{NSO}_5$: C, 58.78; H, 4.89; N, 4.03. Found: C, 58.91; H, 5.07; N, 3.89.

REFERENCES

- (1) Present address: Department of Chemistry, The University of British Columbia, Vancouver 8, Canada.
- (2) A. Hassner and P. Catsoulacos, *Chem. Commun.*, 590 (1967).
- (3) R. Quelet and P. Catsoulacos, *Compt. Rend.*, 258, 1251 (1964).
- (4) R. Quelet, C. Broquet and P. Catsoulacos, *ibid.*, 258, 3504 (1964).
- (5) N. V. Dudykina and V. A. Zagorevskii, *Chem. Abstr.*, 65, 683d (1966).
- (6) R. Quelet, E. Matarasso and P. Catsoulacos, *Compt. Rend.*, 257, 169 (1963).
- (7) K. C. Roberts and S. Smiles, *J. Chem. Soc.*, 863 (1929).
- (8) W. E. Truce and J. A. Simms, *J. Org. Chem.*, 22, 617 (1957).

Received July 7, 1967

Boulder, Colorado 80302