# Oxidations with Selenium Dioxide

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Selenium dioxide has been used as a selective oxidizing agent for activated methyl groups in many different types of compounds (1). Most frequently the oxidation reaction is performed in some inert solvent such as ethyl alcohol or xylene. It has been found that nitrogen heterocyclic compounds of the type 1,4-dimethylcarbostyril and 5-keto-7-methyljuloline were best oxidized to the aldehyde when selenium dioxide was added to the fused substance over a temperature range of 145-175°.

The oxidation of 1,4-dimethylcarbostyril to the 1-methyl-4-carbostyrilcarboxaldehyde has already been reported (2). It has been found that the yield of this preparation can be increased from 70% to 95-98% by increasing the size of the reaction mixture from 0.11 mole of the 1,4-dimethylcarbostyril to 0.22 mole or more of the carbostyril. The increased batch size apparently gives better mixing and the oxidation can be carried almost to completion.

The oxidation of three other compounds, 1-ethyl-4-methyl-carbostyril, 1-benzyl-4-methylcarbostyril and 5-keto-7-methyljuloline by an analogous method gave 1-ethyl-4-formylcarbostyril, 1-benzyl-4-formylcarbostyril and 7-formyl-5-ketojuloline.

## Experimental

1,4-Dimethylcarbostyril, 1-ethyl-4-methylcarbostyril and 1-benzyl-4-methylcarbostyril were prepared by a method described by Kaslow and Cook (3). Reissert has reported the preparation of 5-keto-7-methyljuloline by the action of ethyl acetoacetate on tetrahydroquinoline (4). We have improved this preparation by the use of diketene with tetrahydroquinoline. The selenium dioxide was prepared by the action of nitric acid on selenium and purified by immediate sublimation.

*1-Methyl-4-carbostyrilcarboxaldehyde.*—In a 500 ml., three-necked, round-bottomed flask equipped with an air condenser and mechanical stirrer was placed 38.0 g. (0.22 mole) of 1,4-dimethylcarbostyril. The flask was heated in an oil-bath to 150°. To the fused material 28 g. (0.252 mole) of selenium dioxide was added gradually over a period of thirty minutes. During this time stirring was continuous and the temperature was allowed to rise to 175°. The fused mass was maintained at this temperature with stirring for forty-five minutes or until the mass solidified. When cool, the mixture was ground to a powder and extracted twice with 400 ml. of boiling benzene and thee times with 200 ml. of boiling benzene. The combined extracts were filtered, evaporated to about 600 ml. and cooled in the refrigerator. Yellow needles of 1-methyl-

4-carbostyrilcarboxaldehyde were obtained which melted at 179-180°. Evaporation of the filtrate to about 300 ml. gave a small additional yield. The total weight of product was 40.7 g. (98%). An alternate method of extraction can be used by means of a large Soxhlet extractor with about 600 ml. of benzene used as the solvent.

*1-Ethyl-4-formylcarbostyril.*—In a manner analogous to the preparation of 1-methyl-4-carbostyrilcarboxaldehyde, 19g. (0.10 mole) of 1-ethyl-4-methylcarbostyril was treated with 13.9 g. (0.125 mole) of selenium dioxide. The reaction mass solidified on cooling and was then extracted with two portions of 200 ml. of boiling benzene and four portions of 100 ml. of boiling benzene. The combined extracts were evaporated to 400 ml. and orange-brown needles of the aldehyde crystallized. The weight was 19.8 g. (97%). The product after recrystallization from benzene melted at 117.5-119°.

Anal. Calcd. for $C_{12}H_{13}NO_2$: N, 6.96
Found: N, 7.41

The 2,4-dinitrophenylhydrazone was prepared and found to melt at approx. 315-320° (dec.).

*1-Benzyl-4-formylcarbostyril.*—In a like manner 20.0 g. (0.083 mole) of 1-benzyl-4-methylcarbostyril was oxidized with 10.5 g. (0.094 mole) of selenium dioxide. The reaction mass when extracted with boiling benzene, evaporated and allowed to cool gave yellow needles weighing 11.5 g. (56%). The m.p. of the crude product was 159-160°. A 2 g. sample was recrystallized from 20 ml. of benzene. The m.p. was 161.5-162.5°.

Anal. Calcd. for $C_{17}H_{13}NO_2$: N, 5.32
Found: N, 5.03

The 2,4-dinitrophenylhydrazone was prepared and found to melt at 253-255° (dec.).

*5-Keto-7-methyljuloline.*—In a 250 ml., three-necked flask equipped with a mechanical stirrer, reflux condenser and dropping funnel was placed 20 g. (0.150 mole) of 1,2,3,4-tetrahydroquinoline and 50 ml. of benzene. The solution was heated to reflux on a steam-bath and 12.8 g. (0.188 mole) of diketene was added dropwise. The mixture was then allowed to reflux for four hours. At the end of this time the benzene was drawn off under reduced pressure. The red oil which remained was added in 2 ml. portions to 20 ml. of concentrated sulfuric acid at such a rate that the temperature was held between 100-110°. This mixture was heated on a steam-bath for 10-15 minutes. The sulfuric acid solution was then poured into 150 ml. of ice water and neutralized with 15-16 g. of solid sodium hydroxide. A tan colored, solid, product precipitated which, when dried, weighed 21.2 g. (73%). This material, when recrystallized from benzene-petroleum ether, melted at 130.5-131.5°. Reissert reported a melting point of 129.8°.(4)

Anal. Calcd. for $C_{13}H_{13}NO_2$: N, 7.03
Found: N, 6.79

*7-Formyl-5-ketojuloline.*—In a manner which has been described for the preparation of 1-methyl-4-carbostyrilcarboxaldehyde, 9 g. (0.045 mole) of 5-keto-7-methyljuloline was oxidized with 5.2 g. (0.047 mole) of selenium dioxide. The residual mass was extracted three times with 200 ml. of boiling benzene, filtered and the combined extracts evaporated to about 200 ml. Ten to fifteen milliliters of petroleum ether was added to the benzene solution and, upon cooling, yellow crystals formed. The product weighed 8.2 g. (84%) and when recrystallized from benzene gave a melting point of 149-150°.

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| Anal. Calcd. for $C_{13}H_{11}NO_2$: | N, 6.57 |
| Found: | N, 6.28 |

## Summary

Additional studies of the oxidation of 1,4-dimethylcarbostyril with selenium dioxide have given an increase in the yield of 1-methyl-4-carbostyrilcarboxaldehyde from 70% to 98%.

Several new aldehydes, 1-ethyl-4-formylcarbostyril, 1-benzyl-4-formylcarbostyril and 7-formyl-5-ketojuloline have been prepared.

The preparation of 5-keto-7-methyljuloline has been improved over that of the method of Reissert by the use of diketene with tetrahydroquinoline.

## References

1. Waitkins and Clark, Chem. Rev., **36**, 235 (1945).
2. Cook and Stamper, J. Am. Chem. Soc., **69**, 1467 (1947).
3. Kaslow and Cook, ibid., **67**, 1969 (1945).
4. Reissert, Ber., **24**, 941 (1891).