[CONTRIBUTION FROM THE NICHOLS CHEMISTRY LABORATORY, NEW YORK UNIVERSITY]

The Use of Selenium Dioxide in the Preparation of Quinoline Aldehydes

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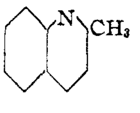
In 1939, Clemo and Hoggarth[2] indicated their inability to duplicate the results reported by Kwartler and Lindwall[3] for the preparation of cinchoninaldehyde from lepidine by direct oxidation with selenium dioxide. The former preferred another method of preparation in which the yield of aldehyde is 38–40%, while the latter reported yields of as much as 61%. At about the same time, and despite the fact that in earlier efforts the oxidative procedure had been highly satisfactory, the writer was experiencing considerable difficulty with the selenium dioxide method.

The procedure as outlined by Kwartler and Lindwall has been significantly modified here. A systematic check on reagents and conditions indicated that the source of the difficulty was probably the selenium dioxide itself. It had been customary in these laboratories to use selenium dioxide prepared in relatively small quantities as needed. Early in the course of the present work it was found practicable to prepare a large quantity; it was from this single preparation that successive samples over a period of months gave at first good results and subsequently preparative runs in which the yield of aldehyde became quite small, often only a trace. The analogous situation was observed in attempt to prepare quinaldehyde from quinaldine.

Normally in the course of these reactions, the quinoline homolog is almost entirely accounted for as either the aldehyde or the corresponding acid. In the instances where the yields of aldehyde became minute, however, there were products that had not been noted previously. These substances were crystalline, relatively insoluble in warm dioxane and most other solvents, and not volatile with steam; they were subsequently identified, one as a new compound and the other as a substance previously described.[4] Accompanying the 2-aldehyde of quinoline, the product proved to be the known quinaldoin[4] (2-hydroxy-1,2-di-2-quinolylethanone); accompanying the 4-aldehyde was 1,2-di-4-quinolylethylene, identified by preparation by another method. No satisfactory explanation can be offered for the formation of these compounds, or for the fact that the two compounds are of different types. It is suggested that there is present at a given time in the respective oxidation systems more of the 2-aldehyde than there is of the 4, since the 2-position in the quinoline series is the more active. Thus, quinaldoin might result from the interaction of two molecules of quinaldaldehyde, while the ethylene type might result from the interaction of one molecule of cinchoninaldehyde with one of lepidine.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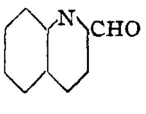
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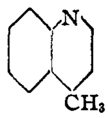
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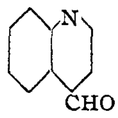
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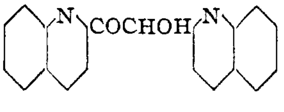
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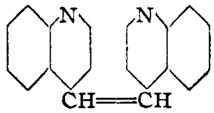
VI

The selenium dioxide employed in these laboratories was in all cases prepared by the oxidation of metallic selenium with hot, concentrated nitric acid; the reaction mixture was evaporated to dryness and the resulting white solid used directly as thus prepared. There are in the literature numerous references to sublimed selenium dioxide, but no satisfactory method for effecting the sublimation has been described until recently.[5] Since early experience in these laboratories indicated that the use of sublimed selenium dioxide offered little, if any, advantage as compared with the unsublimed, the latter was usually employed; the particular preparation to which reference was made above had been stored in the unsublimed state. Fortunately, there was available for comparison a supply of selenium dioxide which had been prepared by the action of nitric acid on metallic selenium, but which had been immediately sublimed, and aged thus in the sublimed state for over a year.

It was found by the writer and corroborated by at least one other worker in these laboratories

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[2] Clemo and Hoggarth, *J. Chem. Soc.*, 1241 (1939).

[3] Kwartler and Lindwall, THIS JOURNAL, **59**, 524 (1937).

[4] Henze, *Ber.*, **67**, 753 (1934).

[5] Hill, Soth and Ricci, THIS JOURNAL, **62**, 2717 (1940).

that selenium dioxide, freshly prepared by the action of nitric acid on metallic selenium, whether used directly or sublimed immediately upon preparation and thus used shortly, gave good yields of the aldehydes consistent with those originally reported by Kwartler and Lindwall. However, selenium dioxide, prepared in the same fashion but allowed to stand for several months prior to use, was found to give poor yields of the aldehydes; these yields were not improved by sublimation of such aged selenium dioxide at the time of use. On the other hand, if the selenium dioxide was sublimed immediately upon preparation and stored in the sublimed form, loss of effectiveness in a given length of time was less marked than in the case of unsublimed material, yields of the aldehydes being only a little diminished even after a year.

What the change in the selenium dioxide is has not yet been determined. Tests were made for selenates in the aged material, but these were not detected. Sublimation had no effect upon the aged material, nor did redissolving in hot concentrated nitric acid, followed by evaporation of the excess. It is also believed that the effect is not one of catalysis, since mixtures of the aged unsublimed material with freshly prepared selenium dioxide gave yields of aldehyde commensurate with the amount of fresh material.

It should also be noted that no success attended efforts to oxidize III and VI with fresh selenium dioxide. Likewise impossible was the preparation of III and VI directly from the respective aldehydes, in these attempts the aged, unsublimed selenium dioxide having been used.

Experimental Part

In each of the tabulated runs, the procedure was the same. Selenium dioxide was dissolved in dioxane containing 4% water (13.5 g. in 120 cc. dioxane and 5 cc. water), warmed to 45°. To this was added in the course of fifteen minutes a solution of the quinoline homolog in dioxane (15 g. in 25 cc. of dioxane). During the addition the reaction mixture was brought slowly to reflux and maintained thus one hour further; metallic selenium was thrown down as the reaction proceeded, and the oxidation was assumed to be complete when the mixture became clear. Mechanical stirring was maintained throughout. Selenium was filtered from the hot solution, and dioxane was distilled off under reduced pressure. Both aldehydes (II and V) were recovered by steam distillation; III and VI remained in the residue from the steam distillation, or precipitated directly from the reaction mixture if it was allowed to cool before removal of dioxane. In these runs, the only variant was the aging and/or sublimation of the selenium dioxide. In every case, the yield was calculated upon the basis of the quinoline homolog used.

TABLE I

Run	Selenium dioxide	% Yield II	III	V	VI
1, 2	Freshly prepared, unsublimed	50		58	
3	Freshly prepared, sublimed			55	
4, 5	Unsublimed, aged 4 months	35		42	
6, 7	Unsublimed, aged 12 months	2	84	1	89
8	Sublimed on prepn., aged 12 months			30	
9, 10	Aged 12 months, then sublimed	2	81	2	88
11	Unsublimed, aged 13 months, 1 part Freshly prepared, unsublimed, 3 parts			64	

Identification of III.—To a solution of II in 50% alcohol (1.5 g. in 35 cc.) was added potassium cyanide dissolved in water (0.1 g. in 1 cc.). A brown solid precipitated immediately, the mixture was refluxed one hour and the solid filtered off. From the cooled filtrate a yellow, crystalline solid separated; a further quantity was recovered from the mother liquor. III was recrystallized from dioxane in small, very pale, brown needles; yield 0.9 g. (66%); m. p. 269–271°. *Anal.* Calcd. for $C_{20}H_{14}O_2N_2$: C, 76.4; H, 4.46; N, 8.92. Found: C, 76.7; H, 3.9; N, 9.12.

Identification of VI.—IV and V (0.5 g. each) were sealed into a tube with glacial acetic acid (0.5 cc.) and a few drops of acetic anhydride. The mixture was kept in the oven overnight at 110°, then neutralized with ammonia and extracted with ether. After evaporation of the ether, VI was recrystallized from alcohol: yield 0.6 g. (60%); m. p. 207°. Calcd. for $C_{20}H_{14}N_2$: N, 9.92. Found: N, 10.3.

Summary

In the preparation of quinoline aldehydes from the corresponding homologs by direct oxidation with selenium dioxide, it was found that best yields are obtained when the selenium dioxide has been prepared shortly before use. If the selenium dioxide is to be kept any length of time, it is preferably sublimed immediately upon preparation.

If the selenium dioxide had been stored unsublimed for upward of several months, it was found to convert quinaldine into a benzoin type compound instead of the aldehyde, and lepidine into an ethylenic type compound instead of aldehyde.

The anomalous behavior of selenium dioxide is not due to the presence of selenates, nor is it a catalytic effect.

The anomalous compounds noted are not intermediates in the normal formation of the aldehydes, nor have they been formed from the aldehydes under oxidative conditions.

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RECEIVED JUNE 27, 1941