

## A Convenient Preparation of 3-Cinnolinol

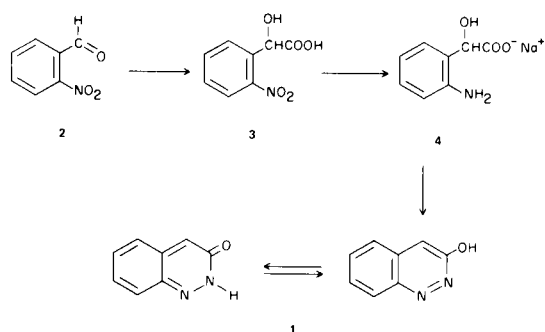
Robert L. Zey

Department of Chemistry, Central Missouri State College,  
Warrensburg, Missouri 64093

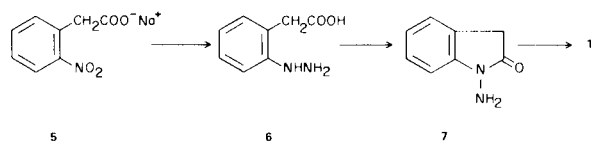
Received May 10, 1972

In 1925, the preparation of 3-cinnolinol (3-hydroxycinnoline, 3(2*H*)-cinnolinone) (**1**) was reported in a Dissertation by Neber's student, Bössel (1). In 1952, Alford and Schofield (2) reinvestigated the preparation.

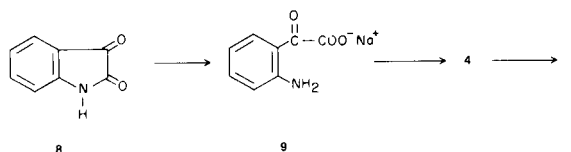
The preparation as described by Alford and Schofield begins with *o*-nitrobenzaldehyde (**2**), an expensive intermediate which is difficult to prepare. The addition of hydrogen cyanide to *o*-nitrobenzaldehyde followed by acid hydrolysis yielded *o*-nitromandelic acid (**3**). Catalytic reduction of sodium *o*-nitromandelate, diazotization of the intermediate sodium *o*-aminomandelate (**4**), and reduction with stannous chloride provided *o*-hydrazinomandelic acid as the tin salt. Removal of the tin with hydrogen sulfide and heating in aqueous hydrochloric acid resulted in cyclization to 3-cinnolinol (**1**).



A second synthetic route to **1** was reported (3) in 1960. Catalytic reduction of sodium *o*-nitrophenylacetate (**5**), diazotization of the intermediate sodium *o*-aminophenylacetate, and reduction with stannous chloride provided *o*-hydrazinophenylacetic acid (**6**) as the tin salt. Removal of the tin with hydrogen sulfide and heating in aqueous hydrochloric acid resulted in cyclization to 1-aminooxindole (**7**). Oxidation of **7** with lead tetraacetate provided **1**. In 1969, it was reported (4) that oxidation with an equimolar amount of *t*-butyl hypochlorite provides a more convenient route from **7** to **1**.



This communication describes the preparation of 3-cinnolinol (**1**) by a modification of the Neber-Bössel Synthesis as described by Alford and Schofield. The basic hydrolysis of isatin (**8**) and the catalytic reduction of the resulting sodium *o*-aminophenylglyoxylate (**9**) provided the intermediate sodium *o*-aminomandelate (**4**) *via* a more convenient method from a readily available and economical starting material. The intermediate **4** was converted to **1** by the previously described method. This modified method now becomes the method of choice for the preparation of 3-cinnolinol. The general applicability of the reaction has not been studied.



## EXPERIMENTAL

3-Cinnolinol (**1**).

To a solution of 11 g. (0.275 mole) of sodium hydroxide in 165 ml. of water was added 37 g. (0.25 mole) of isatin at a temperature below 10°. The light-yellow solution was adjusted to pH 7 and together with 2 g. of 10% palladium-on-charcoal catalyst was hydrogenated at room temperature under a hydrogen pressure of 45 p.s.i.g. The theoretical amount of hydrogen was absorbed within 2-3 hours. The reduction of more basic solutions was not significantly slower. The sodium *o*-aminomandelate solution was treated in the manner described by Alford and Schofield (2) to produce 21.5 g. of 3-cinnolinol (58%), m.p. 199-202°.

## REFERENCES

- (1) G. Bössel, Inaug. Diss. Tübingen, 1925; *Chem. Zentr.*, 100, II, 3015 (1929).
- (2) E. J. Alford and K. Schofield, *J. Chem. Soc.*, 2102, (1952).
- (3) H. E. Baumgarten, P. L. Creger, and R. L. Zey, *J. Am. Chem. Soc.*, 82, 3977 (1960).
- (4) H. E. Baumgarten, W. F. Wittman, and G. J. Lehmann, *J. Heterocyclic Chem.*, 6, 333 (1969).