NUCLEAR OXIDATION IN FLAVONES AND RELATED COMPOUNDS

Part XXXVIII. A Transformation of Visnagin to Kellin

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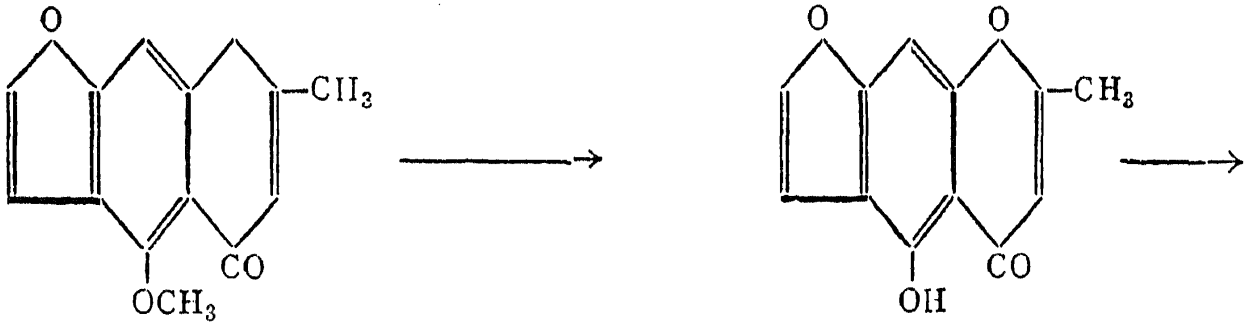
THE main crystalline components of the seeds of *Ammi visnaga* are (*a*) kellin, (*b*) visnagin and (*c*) chellol glucoside; of these, the first is highly valuable therapeutically, the second has much less activity and the third none. But they are related in their chemical structure; consequently methods of conversion of (*b*) and (*c*) into (*a*) will be useful. Already a successful method of conversion of chellol into visnagin has been described by Geissman[1]; a yield of 25% is claimed. Although the next stage (*b* to *a*) has been worked out by Schönberg and Badran,[2] the reported yield of the final product is very poor, being only 3%; further it involves six steps.

It was therefore felt desirable to work out a better method for the conversion of visnagin to kellin. One such is described in this paper. It utilises the nuclear oxidation of nor-visnagin with alkaline persulphate to nor-kellin and subsequent methylation of it. Not only does this reduce the number of the stages to four but it increases the yield of the final product appreciably.



Preparation of nor-visnagin proceeds very satisfactorily by means of hydrochloric acid giving about 80% yield.[2] In the next stage, persulphate oxidation gives somewhat low yields (12%). Methylation of nor-kellin to kellin was originally carried out by Schönberg and Badran,[2] using methyl iodide giving an yield of 50%. When it is done using methyl sulphate the yields are much better (91%). Thus the minimum yield of kellin from visnagin has been raised from about 3% to about 9%.

In the course of experiments described above, it has been possible to effect partial methylation of nor-kellin in the eight position. This substance is identical with the product obtained by partial demethylation of kellin with 50% hydrochloric acid. It is therefore formulated as an 8-methoxy compound and its properties are in accordance with this.

The term nor-kellin was originally used by Murti and Seshadri[3] for the parent dihydroxy compound obtained by the demethylation of kellin without involving isomeric change. Later the term has been used by Schönberg and Sina[4] to designate also the lower homologue of kellin which does not have a methyl group in 2-position. It seems to be desirable to restrict its use to only one compound, that is the parent dihydroxy furano chromone related to kellin. We suggest that the derivatives lacking the 2-methyl group may be called homo-kellin.

EXPERIMENTAL

Oxidation of nor-visnagin to nor-kellin (II→III)

Nor-visnagin[2] (1 g.) was dissolved in pure pyridine (15 c.c.) and to the brown solution was added aqueous sodium hydroxide (0·85 g. in 15 c.c. of water), when the deep yellow sodium salt separated out; some of it dissolved on the addition of more pyridine (10 c.c.). To this suspension which was mechanically stirred and maintained at 15–20°, was added dropwise a saturated aqueous solution of potassium persulphate (2 g. in 35 c.c.) during the course of six hours. The solid gradually went into solution and the colour of the solution which was deep yellow at first changed to deep red in about 3 hours. The stirring was continued for two hours more by which time the whole of the sodium salt dissolved and the solution was left overnight at room temperature. Next day it was made just acidic to congo red when a buff coloured precipitate separated out. This was filtered (it was not unchanged nor-visnagin) and the filtrate was extracted with ether twice to remove impurities. The aqueous solution was then made strongly acidic with concentrated hydrochloric acid (35 c.c.), sodium sulphite (4 g.) was added and the mixture heated in a boiling water-bath for 30 minutes. It was then cooled and thoroughly extracted with ether. On evaporating the ether extract a yellow

product (0·12 g.) was left behind which crystallised from alcohol as yellow rectangular prisms melting at 281–83°. A mixed melting point with an authentic sample of nor-kellin[3] prepared from kellin was undepressed. An alcoholic solution of it gave with ferric chloride a deep green colour which changed to reddish brown with excess. The oxidation was repeated using more pyridine in order to avoid precipitation of solid at any stage and the alkali was added slowly along with the persulphate. But there was no significant increase in yield.

The acetate of nor-kellin was prepared by heating a mixture of nor-kellin (50 mg.), acetic anhydride (2 c.c.) and pyridine (1 drop) at 140–45° for 2 hours. It was then poured into ice-water and the white solid that separated after some time was collected and crystallised from a mixture of ethyl acetate and petrol when it was obtained as colourless rectangular prisms melting at 174–75°. A sample of acetate prepared from an authentic sample of kellin had the same melting point and the mixed melting point of the two samples was undepressed (Found: C, 61·2; H, 3·9; $C_{16}H_{12}O_7$ requires C, 60·8; H, 3·8%).

Methylation of nor-kellin to kellin (III—IV)

Nor-kellin (1 g.) was suspended in dry acetone (100 c.c.) and treated with dimethyl sulphate (1·5 c.c.) and ignited potassium carbonate (6 g.) and the mixture was heated under reflux for 15 hours. The acetone solution was filtered and the potassium salts were washed twice with hot acetone. Acetone was removed from the filtrate and washings and to the residual brownish oily substance, water (100 c.c.) was added to decompose excess of dimethyl sulphate. The crystalline mass which separated on keeping overnight was collected and crystallised twice from dilute alcohol when it separated as colourless rectangular prisms melting at 152–53° alone or when mixed with an authentic sample of kellin. Yield, 0·91 g.

2-Methyl-5-hydroxy-8-methoxy-furano-(3′ : 2′ : 6 : 7) *chromone*

(i) *Partial methylation of nor-kellin.*—Nor-kellin (0·3 g.) was dissolved in dry acetone (50 c.c.), methyl iodide (0·5 c.c.) and ignited potassium carbonate (4 g.) were added and the mixture refluxed in a water-bath for one and a half hours. The acetone solution was then filtered and the potassium salts were washed several times with hot acetone. The inorganic salts did not retain any of the product. The combined filtrate and washings were concentrated when a pale yellow product crystallised out. This was filtered and recrystallised from ethyl acetate when it separated as golden yellow long thick rectangular prisms melting at 200–02°. Yield, 0·21 g. It gave a permanent

deep green colour with ferric chloride and a golden yellow solution in concentrated sulphuric acid (Found: C, 63·8; H, 4·2; $C_{13}H_{10}O_5$ requires C, 63·4; H, 4·1%).

(ii) *Partial demethylation of kellin.*—Kellin (0·5 g.) was dissolved in a hot mixture of concentrated hydrochloric acid (8 c.c.) and water (8 c.c.) and the solution refluxed on a wire-gauze for one and a half hours. A deep red solution was obtained at first and after 15 minutes a yellow precipitate began to form. The mixture was then diluted with water (20 c.c.), cooled and the solid product filtered and washed free from acid. It crystallised from ethyl acetate as golden yellow rectangular prisms melting at 200–02° alone or when mixed with the sample obtained in (i) above. Yield, 0·35 g.

The acetate was prepared by acetic anhydride pyridine method and crystallised from ethyl acetate when it was obtained as colourless stout rectangular prisms melting at 173–75° (Found: C, 63·1; H, 4·3; $C_{15}H_{12}O_6$ requires C, 62·5; H, 4·2%).

SUMMARY

A new method of conversion of visnagin into kellin is described. It involves only three steps and gives much better yields. Nor-visnagin is subjected to nuclear oxidation with alkaline persulphate to yield nor-kellin which is conveniently methylated to kellin by means of dimethyl sulphate and potassium carbonate in acetone solution.

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