

Heterocyclic Syntheses with β -Ketosulfoxides. III. New Syntheses of Coumarins and Carbostryls.

M. von Strandtmann, D. Connor and J. Shavel, Jr.

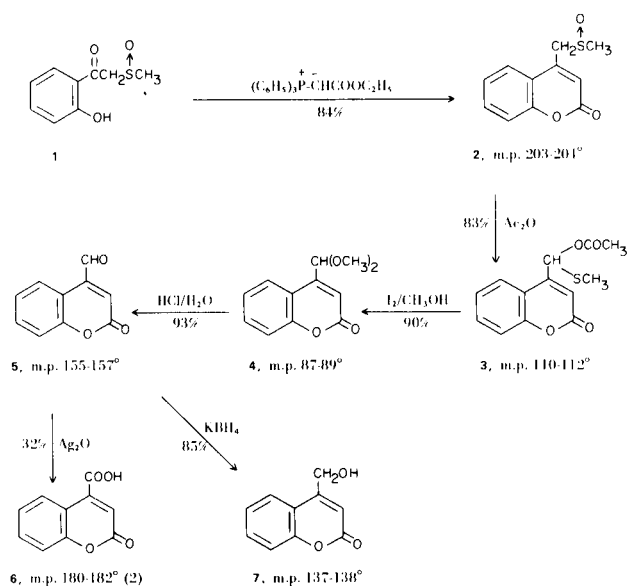
Department of Organic Chemistry, Warner-Lambert Research Institute,
Morris Plains, New Jersey 07950

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Sir:

In the previous communications (1), we described the condensation of *o*-hydroxy-, *o*-mercapto-, and *o*-amino-benzoates with sodium methylsulfinylmethide followed by cyclization reactions to give chromones, flavones, thioflavones, thioindigo, quinolones and cinnolinones. We now report additional synthetic applications of the intermediate *o*-amino- and *o*-hydroxy- ω -(methylsulfinyl)acetophenones.

Reaction of *o*-hydroxy- ω -(methylsulfinyl)acetophenone (1) with carbethoxymethylenetriphenylphosphorane, in dioxane at reflux temperature for 20 hours, yielded 4-(methylsulfinylmethyl)coumarin (2).

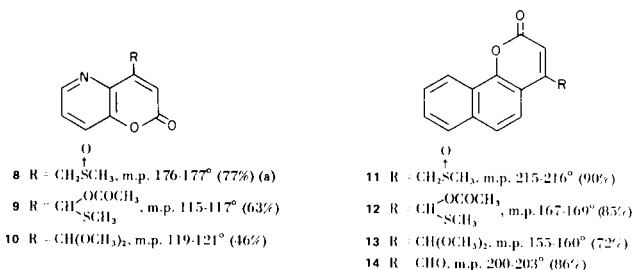


Pummerer reaction of 2 with refluxing acetic anhydride led to the formation of 4-[hydroxy(methylthio)methyl]-coumarin acetate (3) which was converted to the acetal 4 by refluxing in methanol in the presence of 0.1 mole of iodine. Hydrolysis of the acetal with 20% hydrochloric acid yielded 4-formylcoumarin (5), a convenient starting material for the synthesis of 4-hydroxymethylcoumarin

(7) and coumarin-4-carboxylic acid (6) (2).

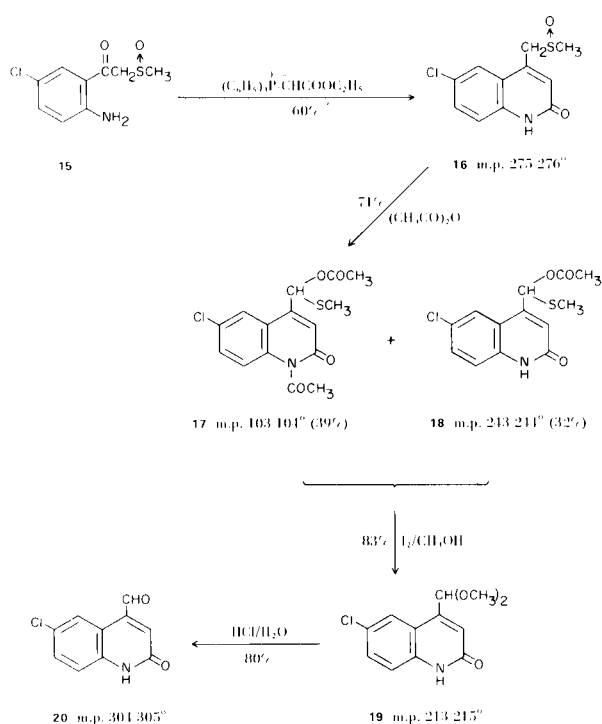
The synthetic utility of the method is attested to by the fact that neither 4-formylcoumarin nor 4-hydroxymethylcoumarin were previously described (3).

The method is general and applicable to other *o*-hydroxy- ω -(methylsulfinyl)acetophenones as illustrated by the following examples:



(a) The starting β -ketosulfoxide, 3-hydroxy-2-pyridyl(methylsulfinyl)methyl ketone, was obtained in 50% yield and had a m.p. of 97-99°.

o-Amino- ω -(methylsulfinyl)acetophenone (15) underwent an analogous reaction to give 4-substituted carbostryls:



The Pummerer reaction, in this series, resulted in a mixture of **17** and **18** due to partial *N*-acetylation. The separation, although facile, is not required since both **17** and **18** give the same acetal **19**.

Satisfactory spectral data and elemental analyses within $\pm 0.3\%$ of calculated values were obtained for all compounds described (4).

REFERENCES

- (1) M. von Strandtmann, S. Klutchno, M. P. Cohen and J. Shavel, Jr., *J. Heterocyclic Chem.*, **9**, 173 (1972).
- (2) Lit., m.p. $179-180^\circ$, H. von Pechmann and F. von Krafft, *Ber.*, **34**, 421 (1901).
- (3) The preparation of a 5-benzyloxy-7-methoxy-4-formylcoumarin by selenium dioxide oxidation of the corresponding 4-methylcoumarin was reported by G. Buchi, D. M. Foulkes, M. Kurono, G. F. Mitchell, and R. S. Schneider, *J. Am. Chem. Soc.*, **89**, 6745 (1967).

According to the originators of this method, A. Schiavello and E. Cingolani [*Gazz. Chim. Ital.*, **81**, 717 (1951)], the oxidation of 4-methylcoumarin with selenium dioxide is successful only in the presence of an electron releasing group at C-7.

(4) The authors are indebted to the Analytical and Physical Chemistry Department under the supervision of Mr. A. D. Lewis. In particular, we wish to thank Dr. C. Greenough for the spectral data and Mrs. U. Zeek for analytical determinations. We also wish to thank the Chemical Development Department under the supervision of Dr. A. W. Ruddy for the large-scale preparation of intermediates.