Heterocyclic Syntheses with β-Ketosulfoxides. II. New Syntheses of 4-Hydroxyquinolines, Quinolones and Cinnolinones.

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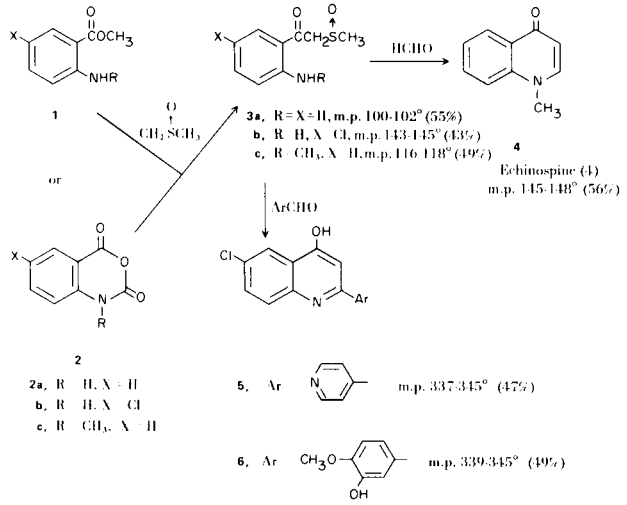
Sir:

In the previous communication (1) we described the condensation of *o*-mercapto- and *o*-hydroxy-ω-(methylsulfinyl)acetophenones with aldehydes to give thioflavones, flavones and chromones. We now report the preparation and synthetic applications of *o*-amino-ω-(methylsulfinyl)-acetophenones.

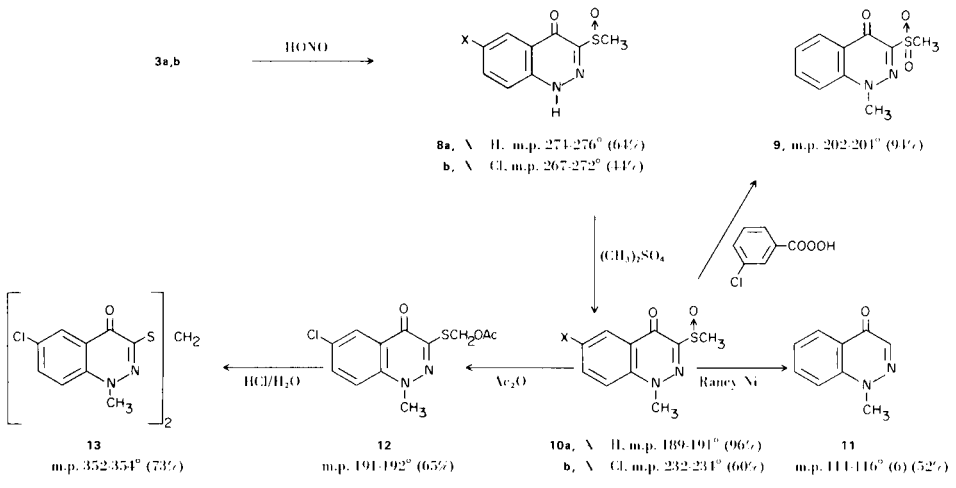


Addition of anthranilic esters (**1**) or isatoic anhydrides (2) (**2**) to a threefold excess of sodium methylsulfinylmethide, in dimethylsulfoxide-benzene solution at 40-45°, resulted in formation of *o*-amino-ω-(methylsulfinyl)acetophenones (**3**) (3).

Condensation of **3c** with formaldehyde in glacial acetic acid at 75-80° for 1 hour yielded the known *N*-methyl-4-quinolone (4) (**4**). Condensation of **3a, b** type compounds with aromatic aldehydes produced a variety of 2-aryl-4-hydroxyquinolines (**5, 6**). These reactions were carried out by refluxing the components in toluene for 1 hour in the presence of catalytic amounts of piperidine.

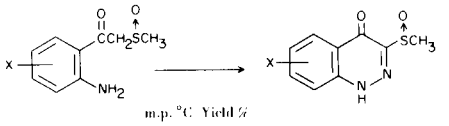
Although quinoline derivatives such as **4**, **5**, and **6** are obtainable by other methods, syntheses involving ring closure by bridging the nitrogen atom and β-carbon are relatively rare (5). The main value of this method, however, lies in the addition of a new building block to quinoline synthesis.

Diazotization of *o*-amino-ω-(methylsulfinyl)acetophenones (**3a, b**) in aqueous medium provided an easy access to 4-cinnolinones having sulfur-containing substituents at C-3 (**8a, b** and **10a, b**).



Various degrees of oxidation states of the sulfur atom were achieved by the Pummerer reaction in acetic anhydride (**12**, **13**) or by the oxidation with *m*-chloroperbenzoic acid (**9**). Desulfurization with Raney-Nickel led to the known 1-methyl-4-cinnoline (6) (**11**).

The method is versatile and applicable to most *N*-unsubstituted *o*-amino-ω-(methylsulfinyl)acetophenones. Several other examples of compounds prepared by this reaction are listed below (**14a**, **b**, **c** and **15a**, **b**, **c**):



	m.p. °C	Yield %		m.p. °C	Yield %
14a, X = 5-CH_3	145-147	47	**15a**, X = 6-CH_3	265-267	77
b, X = 6-Cl	129-132	72	**b**, X = 7-Cl	285-290	87
c, X = 5,6-di-CH_3O	162-164	50	**c**, X = 6,7-di-CH_3O	303-305	81

Satisfactory spectral data and elemental analyses within ± 0.3% of calculated values were obtained for all compounds described (7).

REFERENCES

(1) M. von Strandtmann, S. Klutchko, M. P. Cohen, and J. Shavel, Jr., *J. Heterocyclic Chem.*, **9**, 171 (1972).

(2) After completion of this study, the reaction of *N*-(*p*-methoxyphenyl)isatoic anhydride with sodium methylsulfinylmethide and the subsequent condensation of the product with benzaldehyde to give a quinolone derivative was described by M. R. Bell, A. W. Zalay, R. Oesterlin, P. Schane and G. O. Potts in *J. Med. Chem.*, **13**, 664 (1970).

(3) *o*-Acylamino-ω-(methylsulfinyl)acetophenones can also be prepared by the reaction of sodium methylsulfinylmethide with 1,3-benzoxazine-4-ones. See M. von Strandtmann, S. Klutchko, D. Connor and J. Shavel, Jr., *J. Org. Chem.*, **36**, 1742 (1971).

(4) Echinopsine, "The Merck Index," 8th Ed., p. 402, Merck and Co., Inc., Rahway, N. J., 1968.

(5) See for example, R. C. Elderfield, "Heterocyclic Compounds", Vol. 4, p. 6, John Wiley and Sons, Inc., New York, 1952.

(6) Lit., m.p. 114-116°, D. E. Ames and H. Z. Kucharska, *J. Chem. Soc.*, 4924 (1963).

(7) 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.