sodium hydroxide was added. The solution was stirred for 1.5 hr. and then poured into 400 ml. of concentrated hydrochloric acid and 1 kg. of ice. The resulting creamy solid was collected by suction filtration, washed with water, dissolved in 125 ml. of cold 2% sodium hydroxide solution, and extracted with three 50-ml. portions of ether to remove traces of an orange impurity. The solid obtained on acidification of the aqueous solution with 5% hydrochloric acid was collected and crystallized from acetic acid to give 3.15 g. (64%) of light tan crystals, m.p. 209–210° dec.; ultraviolet spectrum: $\lambda_{max}$ 255 m$\mu$ ($\epsilon$ 16,000), shoulder at *ca.* 310 m$\mu$ (EtOH); infrared spectrum: very sharp absorption at 2248 cm.$^{-1}$ (C≡N).

*Anal.* Calcd. for $C_{11}H_9N_3O$: C, 66.32; H, 4.55; N, 21.10. Found: C, 66.41; H, 4.52; N, 20.98.

In a similar fashion, the following aromatic amines were converted to the corresponding 1-aryl 3-cyanopyrazolones: *p*-ethylaniline (58%), m.p. 172–173° dec. (benzene); *p*-aminophenethyl alcohol (47%), m.p. 147–148° dec. (nitromethane); and *m*-aminobenzotrifluoride (64%), m.p. 117–120° (1,2-dichloroethane). Satisfactory analyses were obtained for all compounds.

**Acknowledgment.**—We wish to thank Dr. T. W. Milligan for helpful discussions and suggestions made during the course of this work.

## Reactions of Cupric Bromide in Dioxane. Formation of ω-Bromo-*o*-hydroxyacetophenone

K. B. DOIFODE AND M. G. MARATHEY

*Department of Chemistry, Vidarbha Mahavidyalaya, Amravati, Maharashtra State, India*

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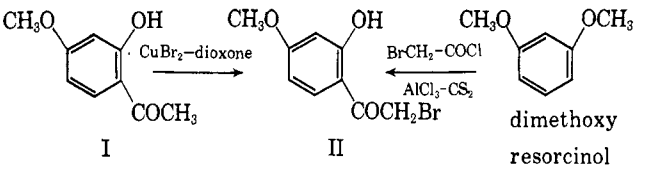
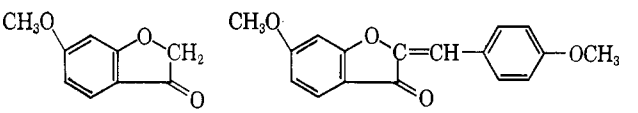
That cupric bromide acts as a brominating agent is not new to the organic chemists. Aliphatic ketones,[1] aliphatic aldehydes,[2] and cyclohexanone[3] have been successfully brominated with cupric bromide in methanol, aqueous methanol, or toluene at the α-carbon atom. Recently, 17-oxoandrostane or its 17-enol acetate has been shown to give 16-α-bromo-17-oxoandrostane[4] with cupric bromide.

The present work deals with the action of cupric bromide in dioxane on *o*-hydroxyacetophenone and on some of its derivatives. When *o*-hydroxyacetophenone is brominated with reagents like bromine in acetic acid, ether, carbon tetrachloride, dioxane,[5] or aqueous acetic acid,[6] or with N-bromosuccinimide (NBS) or pyridine bromine complex,[7] nuclear bromination takes place. 4-Methoxy-2-hydroxyacetophenone (I) with cupric bromide in dioxane under reflux temperature gave a bromo compound (II), m.p. 161°. On analysis, II was found to be $C_9H_9BrO_3$. It was not identical with 5-bromo-4-methoxy-2-hydroxyacetophenone, m.p. 82°.

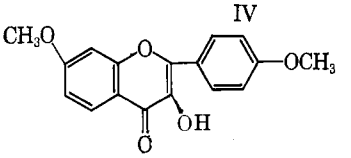
II gave I on treatment with zinc dust in an aqueous medium,[8] an acetoxy derivative *via* an iodo derivative, coumaran-3-one (III) with base,[9] benzal coumaran-3-one (IV) or flavonol V on condensation with an aromatic aldehyde in an alkaline medium,[10] and a rose red color with alcoholic potash. (Rose red coloration with alcoholic potassium hydroxide indicates a labile bromine atom which effects ring closure with an elimination of hydrogen bromide giving a benzofuran-3-one derivative.) These reactions clearly show that bromination has taken place at the ω-position and II is ω-bromo-4-methoxy-2-hydroxyacetophenone. This was further supported by its unambiguous synthesis[11] from dimethoxyresorcinol and bromoacetyl chloride.




I II

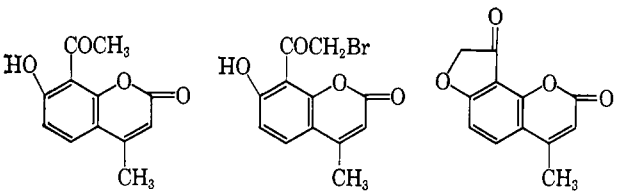



III IV

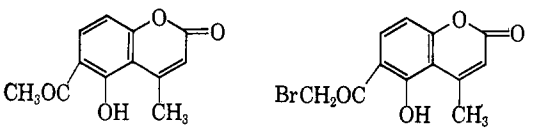



V

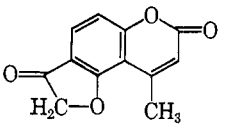
Similarly, 8-acetyl-7-hydroxy-4-methylcoumarin (VI) and 6-acetyl-5-hydroxy-4-methylcoumarin (VII) with cupric bromide in dioxane provided ω-bromo derivatives VIII and IX, respectively. VIII and IX gave the corresponding cyclic derivatives X and XI in alkaline medium.




VI VIII X




VII IX




XI

Bromination of 4-methylhydroxycoumarins with the usual brominating agents (as mentioned earlier) gave nuclear brominated products. The protection of hydroxyl group by acetylation leads to the formation of 4-bromomethyl derivatives with NBS[12] and the pyridine bromine complex.[13] However, cupric bromide in

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(2) C. E. Castro, *J. Org. Chem.*, **26**, 4183 (1961).
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(8) P. N. Wadodkar, *Indian J. Chem.*, **1**, 122 (1963).
(9) (a) P. Friedlander and J. Neudoerfer, *Ber.*, **30**, 1077 (1897); (b) K. Auwers, *ibid.*, **45**, 975 (1912); **47**, 3307 (1914).
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(13) B. J. Ghiya, Ph.D. thesis, Nagpur University, 1962.

dioxane gives the ω-bromo derivative whether the hydroxyl group is protected by acylation or kept as such. This gives cupric bromide–dioxane a decided advantage over other brominating agents. Whether the hydroxyl group is protected or otherwise, bromination proceeds to take place at the carbon atom activated by the >C=O group. In compounds VI and VII, the second >C=O group in the pyrone ring has less activity owing to lactonization with oxygen, and such bromination takes place at the ω-position at the acetyl group in preference to C-3.[14,15]

### Experimental

**Preparation of ω-Bromo-4-methoxy-2-hydroxyacetophenone (II).**—4-Methoxy-2-hydroxyacetophenone (1.7 g., 0.01 mole) and cupric bromide (4.5 g., 0.02 mole) in dioxane (50 ml.) were refluxed for 3 hr. The white cuprous bromide was filtered off at the pump and dioxane was removed under reduced pressure. The gummy greenish product was extracted with ether, the ethereal layer was dried with anhydrous sodium sulfate, and the ether was removed. The residue was crystallized repeatedly from petroleum ether–benzene to obtain shining white, hard crystals (1.1 g.), m.p. 161°.

*Anal.* Calcd. for $C_9H_9BrO_3$: C, 44.08; H, 3.67; Br, 32.65. Found: C, 43.98; H, 3.69; Br, 33.22.

**Preparation of 6-Methoxybenzofuran-3-one (III).**—II (1 g.) was dissolved in ethanol and treated with potassium hydroxide solution (10 ml., 40%). On slight warming the mixture turned rose red. After 2 hr. the mixture was acidified with hydrochloric acid. The rose red solid was filtered off and was crystallized repeatedly from methanol (0.5 g.), m.p. 170–171°. The ethanolic ferric chloride color was violet.

*Anal.* Calcd. for $C_9H_8O_3$: C, 65.86; H, 4.87. Found: C, 65.43; H, 4.92.

**Preparation of 4′,6-Dimethoxybenzylidenecoumaran-3-one. (IV).**—II (3.3 g.) was dissolved in hot ethanol (15 ml.) and anisaldehyde (3 ml.) was added to it. The mixture was heated to boiling and sodium hydroxide solution (10 ml., 40%) was added with stirring. The mixture was brought to boiling again. The yellowish shining solid was filtered off after 1 hr. and was crystallized repeatedly from 60% ethyl alcohol to obtain shining wooly crystals (1.5 g.), m.p. 135–136°. The ethanolic ferric reaction was negative.

*Anal.* Calcd. for $C_{17}H_{14}O_4$: C, 72.35; H, 4.96. Found: C, 72.08; H, 4.99.

The filtrate after removing compound IV, m.p. 135°, was diluted with water and kept overnight. It was acidified with hydrochloric acid, and the gummy yellow solid was fractionally crystallized from ethyl acetate. The first fraction gave 0.3 g. of IV, and the second fraction, m.p. 188° (acetic acid), was found to be 4′,7-dimethoxyflavonol (V).

*Anal.* Calcd. for $C_{17}H_{15}C_5$: C, 68.45; H, 4.7. Found: C, 68.15; H, 4.81.

**Direct Formation of Flavonol V.**—To II (1.5 g.) in hot ethyl alcohol (15 ml.) anisaldehyde (1.5 ml.) was added, and the mixture was boiled. After 15 min. sodium hydroxide solution (25 ml., 5%) was added with stirring and the reaction mixture was kept overnight. It was acidified with hydrochloric acid. The yellow solid was fractionally crystallized to give two fractions: one, m.p. 135° (0.2 g.), was IV; and the second, m.p. 188–189° (0.5 g.), was the flavonol V.

**ω-Bromo-4-methoxy-2-hydroxyacetophenone (II). From Dimethoxyresorcinol and Bromoacetyl Chloride.**—A solution of resorcinol dimethyl ether (2 g.) and bromoacetyl chloride (2.5 g., obtained from bromoacetic acid and thionyl chloride) in carbon disulfide (20 ml.) was treated with anhydrous aluminum chloride (5 g.) as described previously[11] to form ω-bromo-4-methoxy-2-hydroxyacetophenone (0.8 g.), m.p. 158–159°, identical with II obtained in the first experiment.

**8-(Bromoacetyl)-7-hydroxy-4-methylcoumarin (VIII).**—8-Acetyl-7-hydroxy-4-methylcoumarin (VI, 3.38 g.) and cupric bromide (9.2 g.) were dissolved in dioxane (100 ml.) in a round-bottom flask (250 ml.), and the contents of the flask were refluxed for 4–5 hr. The white cuprous bromide was filtered off at the pump and the solvent was removed under reduced pressure. A greenish yellow solid was extracted with ethyl acetate and dried over anhydrous sodium sulfate. The solvent was removed and the yellow solid was crystallized from ethyl alcohol to yield 3.0 g. of yellowish white shining crystals, m.p. 135°. It gave a positive test for halogen and a phenolic group. It gave a depression of mixture melting point with 8-acetyl-7-hydroxy-4-methyl-3-bromocoumarin, m.p. 210°.

*Anal.* Calcd. for $C_{12}H_9BrO_4$: C, 48.49; H, 3.03; Br, 26.94. Found: C, 48.25; H, 3.12; Br, 26.98.

**6-(Bromoacetyl)-5-hydroxy-4-methylcoumarin (IX).**—6-Acetyl-5-hydroxy-4-methylcoumarin (VII, 3.38 g.) and cupric bromide (9.2 g.) were dissolved in dioxane (100 ml.) and treated as above. The solid was crystallized fractionally from ethyl alcohol to yield yellowish white crystals (2.5 g.), m.p. 146°. It showed a depression of mixture melting point with 6-acetyl-5-hydroxy-4-methyl-3-bromocoumarin, m.p. 226°, and also with 8-bromo-6-acetyl-5-hydroxy-4-methylcoumarin, m.p. 204°.

*Anal.* Calcd. for $C_{12}H_9BrO_4$: C, 48.49; H, 3.03; Br, 26.94. Found: C, 48.15; H, 3.21; Br, 27.24.

**Action of Alcoholic Alkali on Compounds VIII and IX.**—VIII (1.5 g.) was dissolved in hot ethyl alcohol and potassium hydroxide (10 ml., 40%) was added to it with stirring. The mixture was heated for 5 min. and was kept overnight. The red-colored mixture on acidification with dilute hydrochloric acid gave a red solid. It was crystallized from ethyl alcohol to yield red shining crystals (0.8 g.) of X, m.p. 153–154°.

*Anal.* Calcd. for $C_{12}H_8O_4$: C, 66.67; H, 3.7. Found: C, 66.26; H, 3.75.

IX on similar treatment as above gave a reddish crystalline compound (XI), m.p. 157–159°.

*Anal.* Calcd. for $C_{12}H_8O_4$: C, 66.67; H, 3.7. Found: C, 66.22; H, 3.76.

**Action of Zinc Dust and Water on Compound II.**—A mixture of II (0.5 g.), zinc dust (1 g.), and water (20 ml.) was refluxed for 8 hr. The mixture was extracted with ether and dried over anhydrous sodium sulfate. The ether was removed and a gummy residue obtained on crystallization with 60% ethyl alcohol gave 0.3 g. of shining white crystals, m.p. 50°, which remained undepressed when mixed with 4-methoxy-2-hydroxyacetophenone.

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(15) When this article was under revision a paper by E. R. Glazier was published [*ibid.*, **27**, 4397 (1962)], dealing with bromination of a steroidal ketone in the presence of an olefinic bond using cupric bromide in tetrahydrofuran instead of in dioxane, effecting a similar bromination at the acetyl group.

## The Rate of Oxidation of Alicyclic Ketones with Perbenzoic Acid[1a]

J. L. MATEOS AND H. MENCHACA

*Contribution No. 167 from the Instituto de Quimica de la Universidad Nacional Autónoma de México, México 20, D. F.*

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The oxidation of ketones with peracids to obtain esters or lactones has been thoroughly studied from the preparative[1b] kinetic and mechanistic points of view. The results of Criegee,[3] Friess,[2] and Doering[4,5] on the mechanism were explained on the basis of a slow, rate-controlling addition of the peracid to the ketone group. This is followed by cleavage of the oxygen–oxygen bond leaving an electron-deficient atom to which the more appropiate alkyl group shifts with a concerted release of the proton. In the steroid field the oxidation

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(3) von R. Criegee, *Ann.*, **560**, 127 (1948).

(4) W. von E. Doering and L. Speers, *J. Am. Chem. Soc.*, **72**, 5515 (1950).

(5) W. von E. Doering and E. Dorfman, *ibid.*, **75**, 5595 (1953).