PART II
THEORETICAL

Section I: Preparation of 4-halogenated-quinacetophenones and their methyl ethers.

Section II: Synthesis of chalkones and related compounds derived from 4-chloro-quinacetophenone mono and dimethyl ethers.

Section III: Synthesis of chalkones and related compounds derived from 4-bromo-quinacetophenone mono and dimethyl ethers.
The condensation of 4-chloro and 4-bromo-quinacetophenones with various aldehydes particularly benzaldehyde was found to take an abnormal course as discussed before. To simplify the matters the work on the condensation of their methyl ethers was undertaken. The preparation of starting materials viz, 4-chloro and 4-bromo-quinacetophenones presented certain difficulties.

As no satisfactory method for their preparation was available from literature, after several attempts a satisfactory method has been evolved starting from hydroquinone. It was first converted into p-benzoquinone (Underwood and Walch., Org. Syn., Vol., II, 1946, 553), which was transformed into 2-chloro and 2-bromo-quinols (Schultz., Annalar, 1881, 210, 140). The diacetoxy derivatives of the above quinols were prepared by acetic anhydride and sodium acetate method.

Fries rearrangement of the above diacetates gave the corresponding ketones in poor yields. After several attempts it was found that if the flask containing diacetate (1 mol.) thoroughly mixed with anhydrous aluminium chloride (3.3 mols.) was introduced in a pre-heated oil bath at 160-70°C and heating being continued for 5 to 6 hours, optimum yields were obtained. The reaction mixture was worked up as usual and purified by extracting it with cold
dilute alkali. The unreacted diacetate was removed as insoluble portion and the clear alkaline filtrate on acidification gave yellow product in each case in fairly good yields.

Both the ketones are soluble in alkali and give brown colour with ethanolic ferric chloride.

**Methylation of 4-chloro-quinacetophenone:** The method described by Kostanecki and Lampe (Ber., 1903, 37, 773) for methylation of quinacetophenone was applied in this case but it was found to be unsatisfactory as it gave poor yields of a mixture of mono and dimethyl ethers of 4-chloro-quinacetophenone. The yield of the mono variety was very poor. Methylation according to Vyas and Shah (J.I.C.S., 1950, 27, 189) gave a mixture of both mono and dimethyl ethers. If dimethyl sulphate was used as methylating agent mainly the dimethyl ether was obtained; on the other hand if methyl iodide was used, a mixture was obtained from which the mono variety was obtained in better yield. In both the cases the methylated product was steam-distilled and the solid obtained was extracted with cold dilute alkali. The dimethyl ether was obtained as insoluble portion. The clear alkaline filtrate on acidification gave mono methyl ether.

**Methylation of 4-bromo-quinacetophenone:** Methylation using methyl iodide or dimethyl sulphate in presence of dry acetone and anhydrous potassium carbonate gave very poor yields of the methylated product. Mostly unreacted ketone is recovered; longer reaction period also did not improve the yield. After several trials it was
found that higher temperature favours the reaction, hence acetone was replaced by methyl ethyl ketone as solvent. A mixture of mono and dimethyl ethers obtained thus was worked up as above and both the components were isolated.

The mono methyl ether in both the cases is soluble in alkali and gives brown colour with ethanolic ferric chloride.
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\text{OH OH} \xrightarrow{[\text{O}]_2} \text{OH OH} \xrightarrow{\text{HX}} \text{OH OH}
\]

\[
\xrightarrow{(\text{CH}_3\text{CO})_2\text{O}} \quad \xrightarrow{\text{AlCl}_3} \quad \text{OH COCH}_3
\]

\[
\xrightarrow{\text{Methylation}} \quad \text{OH COCH}_3 + \text{OH COCH}_3
\]

\(X = \text{Cl or Br}\)
SECTION I

EXPERIMENTAL

PREPARATION OF 4-CHLORO AND 4-BROMO-QUINACETOPHENONE AND THEIR METHYL ETHERS


1. 2-Chloroquinol: It was prepared according to the method of Schultz (Annalar, 1881, 210, 140) by passing a stream of dry hydrogen chloride into a solution of quinone in dry petrol ether (instead of chloroform used by him) till brown precipitate obtained was completely converted into a white substance. It was collected and crystallised from petrol ether, m.p. 106°C. Literature reports the same melting point.

2. 2-Bromoquinol: It was prepared as above by passing a current of dry hydrogen bromide, which was prepared by action of bromine on naphthalene. The brown black precipitate first obtained was completely converted into a white product. It was crystallised from petrol ether, colourless plates, m.p. 100°C. The same melting point is reported in literature.

3. 2-Chloroquinol-diacetate: 2-Chloroquinol (1 mol.), acetic anhydride (2 mols.) and anhydrous sodium acetate (1 mol.) were heated on water bath for four to five hours. The cooled reaction-mixture was poured into ice water and the product obtained was