SUMMARY

A considerable light has been thrown on the reactivity of hydrogen atoms of the reactive methylene group between the two carbonyl or negative groups, as is observed in the case of acetoacetic ester and allied compounds. Many explanations have been offered to account for the reactivity of such hydrogen atoms of the reactive methylene group. According to Macbeth and his collaborators, the reactivity of hydrogen atoms depends upon the polarity of oxygen atoms (1) (2). Thorpe et al. held the view that the reactivity depends upon the keto-enol transformations, where the hydrogen atom of the reactive methylene group is required to enolise before the reaction can take place, and if the tendency of the second hydrogen atom to tautomerise is suppressed by the basic nature of the groups attached to the carbonyl groups, then, in that case, only one out of the two atoms of hydrogen is brought into activity (3) (4) (5). According to West, Robinson and Kenner, the reactivity depends upon the combined effect of polarity, steric hindrance and structural characteristics as would give rise to tautomerism (6) (7) (8).

Naik and his collaborators (9) have shown that the hydrogen atoms of the reactive methylene group, situated between the two carbonyl or negative groups, characterised by multiple bonds i.e. - $CO.CH_2CO$-, -$CO.CH_2.CN$, are active and these active hydrogen atoms take part into the reactions. They have observed that the reactivity of the hydrogen atoms increases in direct proportion to the increase in the

reactivity of the carbonyl group with its attached groupings and during the course of their investigations, they have noted that in a number of compounds of the following types,

(i) $CH_2(CONH_2)2$, (ii) NH_2COCH_2CONHR , (iii) $CH_2(CONHR)_2$,
(iv) $C_2H_5O.CO.CH_2.CONHR$, (v) $CH_3CO.CH_2.CONHR$,
(vi) $CH_2(COOC_2H_5)_2$, (vii) $C_2H_5O.CO.CH_2.CN$.

the reactivity of the hydrogen atoms, which is less pronounced in (i) becomes more and more manifest with increasing negative characters of the adjoining groups upto (vii) in the above series.

Raschig and Prahl (10) carried out the reactions of potassium hydroxy methane sulphonate with compounds containing reactive methylene group and they obtained the sulphomethylated products. This work gave an impetus to investigate the reactions of sodium hydroxy methane sulphonate with acetoacet arylamides, containing the reactive hydrogen atom, using a trace of potassium cyanide as catalyst, in which case the sulphomethylated products have been obtained by Mehta and Trivedi (11). It may here be pointed out that Mehta and Patel (12) also prepared methylene bis-acetoacet arylamides without using a catalyst by interaction of sodium hydroxy methane sulphonate with acetoacet arylamides. Shearing and Smiles (13) by the interaction of formaldehyde and sodium sulphite with 2-naphthol and 6-bromo-2-naphthol, obtained bis-(2-hydroxynaphthyl) and bis-(6-bromo-2-hydroxynaphthyl)-1-methanes respectively together with the sulphonates of the reactants.

The structure of the compounds resulting from the addition of alkali metal bisulphites to aldehydes and certain ketones has been the subject of much discussion. Schiff (14) and Eibner (15) supported the hydroxysulphonate structure. Mendeleief (16) and Knoevenagel et al. (17) supported the hydroxysulphite ester structure ; Schroeter and Sulzbacher (18) favoured the polymolecule structure ; whereas, the hydroxysulphonate structure was without doubt shown by Lauer and Langkammerer (19) as well as by Shriner and Land (20).

In the present work incorporated in Part I sodium hydroxy methane sulphonate in presence of potassium cyanide as catalyst, is allowed to react with acetoacet arylamides and the following sulphomethylated products have been obtained :

Sodium acetoacet-(-anilide ; -o-, -m-, -p-chloro-anilides ; -o-, -p-toluidides ; -o-anisidide ; -p-phenitidide ; -1:2:4-, -1:3:4-xylidides ; -α-, and β-naphthylamides)-methane sulphonates.

Naik et al. (21) carried out the reactions of thionyl chloride with certain amides containing reactive hydrogen atoms and obtained the corresponding thio-bis derivatives. The condensation of dimethylaniline with formaldehyde has been found to form p-p'-tetramethyldiamino-diphenyl methane (22). Pratt and Green (23) treated n-heptaldehyde with dimethylaniline and obtained 1,1, bis-(p-dimethylaminophenyl)-heptane in presence of p-toluene-sulphonic acid monohydrate as catalyst in sufficient quantity of benzene.

Smith and Welch (24) prepared methylene bis-o-nitroaniline from p-dimethylaminobenzyl alcohol and o-nitroaniline in the absence of a catalyst. Bruson (25) studied the reactions of acrylonitrile in presence of alkali with acetoacetic ester and obtained ethyl bis-(2-cyanoethyl)-acetoacetate. Paul Pastour (26) condensed acetoacetanilide with aliphatic aldehydes and obtained the bis-derivative of the formula $RCH(COCH_3.CHCONHC_6H_5)_2$ in pure or alcoholic pyridine.

In the present work incorporated in Part II, sodium hydroxy methane sulphonate was made to react with cyanacet arylamides without the use of catalyst in the reaction. The following methylene bis-(cyanacet arylamides) have, thus, been prepared :

Methylene bis-[cyanacet-(anilide ; -o-, -p-chloro-anilides ; -o-, -m-, -p-toluidides ; -o-anisidide ; -1:2:4--1:3:4-xylidides ; -α-, and -β-naphthylamides].

Schuller (27) prepared 5,5'-methylene bis-8-hydroxyquinoline by treatment of 8-hydroxyquinoline with formaldehyde in con.sulphuric acid. Monti and Verona (28) obtained methylene bis-6-hydroxyquinoline.

Kaslow and Reck (29) reported on the synthesis of several 6,6'-methylene-bis-lepidine derivatives from corresponding 6,6'-methylene-bis-acetoacetanilides through the carbostyrils and chlorolepidine derivatives. Price et al. (30) obtained 1,1-bis-(7-chloro-4-hydroxy-3-quinolyl)-ethane from β-m-chloroaniline acrylates in high dilution of boiling diphenyl ether. A number of 3,3'-methylene bis-(4-hydroxy carbostyrils) have been obtained by the

interaction of 1-substituted carbostyrils with carbonyl compounds at high temperatures (31). 3,3'-methylene bis-(4-hydroxycarbostyril) obtained by the action of formaldehyde on 4-hydroxycarbostyril has been reported as one of the anticoagulant substances (32).

4-Hydroxyquinolines have been prepared on thermal cyclisation of several ethyl β-arylamino-α-β-unsaturated esters obtained from ethyl acetoacetate and primary arylamines (33), (34), (35). Ewins and King (36) synthesised 2-hydroxy-quinolines using concentrated sulphuric acid as a cyclising agent. Bangdiwala and Desai (37) obtained 4-hydroxyquinolines on cyclisation of crotonates and acrylates, using a mixture of acetic anhydride and concentrated sulphuric acid. Mehta and Patel (38) synthesised 2,4-dihydroxyquinolines from cyanacet arylamides as well as from malon-mono arylamides using polyphosphoric acid as a cyclising agent. Further 3,3'-methylene bis-(2-hydroxy-4-methyl)quinolines have also been obtained on cyclisation of methylene bis-(acetoacet-arylamides) by means of a mixture of acetic anhydride and concentrated sulphuric acid. (39).

In the present work incorporated in Part III, the methylene-bis-cyanacetarylamides which are described in part II, have been cyclised using polyphosphoric acid and 3,3'-methylene-bis-(2,4-dihydroxyquinolines) are obtained. The following diquinolyl methanes are, thus, prepared :

3,3'-Methylene bis-(-2,4-dihydroxy-) ; -(8-chloro-2,4-dihydroxy-) ; -(6-chloro-2,4-dihydroxy-) ; -(7-methyl-2,4-dihydroxy-) ; -(6-methyl-2,4-dihydroxy-) ;

-(-6,8-dimethyl-2,4-dihydroxy-) ; -(6,7-dimethyl-2,4-dihydroxy)quinolines)] ; 3,3'-methylene bis-(-2,4-dihydroxy-7,8-benzoquinoline) and 3,3'-methylene bis-(-2,4-dihydroxy-5,6-benzoquinoline).

Here in part IV the absorption spectra of compounds in pairs of series (a) cyanacet arylamides and their corresponding methylene bis derivatives, and (b) 2,4-dihydroxy-quinolines and their corresponding methylene bis-quinolines, have been studied with a view to relatively throw light on the confirmation of their structures. Mme. Ramart, Naik and Trivedi (40) studied the relationship between chemical activity and absorption in the ultra-violet of malon diarylamides and some acetoacet arylamides. Naik et al. (41) extended this work to malon mono arylamides, acetoacet arylamides and dichloro malon diaryl amides. T.N.Ghosh et al. (42) studied the spectrum of 1,1'-methylene bis-3,4-dihydroisoquinolines and observed that it resembles that of -1-methyl-3,4-dihydroisoquinoline.

It is found that if two or more chromophores or auxochromes exist in the same molecule, but are separated from each other by insulating groups ; there is no effective conjugation between them, and their spectral characteristic will be the same as if they were in separate molecules (43).

The general characteristic or the spectral behaviour of bis-derivatives discussed in series (a) and (b) should correspond to mono-derivatives. This expectation has been realised from the study of absorption in the ultra-violet, which is found useful in confirming the structures of mono-and bis-derivatives. Further, the

hyperchromic effect with respect to mono-and bis-derivatives discussed in series (a) and (b) has also been calculated. It has been observed that the hyperchromic effect is here visible by the rise in the intensity of absorption.

Be'champ first isolated p-arsanilic acid by the interaction of aniline and arsenic acid (44). Joseph Kennedy (45) has prepared some p-arsanilic acid derivatives of N-substituted malon amides and studied their physiological activity. The sodium salt of p-arsanilic acid (atoxyl) possesses trypanosomicidal activity, but it is found too toxic. Prof. Ehrlich et al. (46) prepared 3,3'-diamino-4,4'-dihydroxyarsenobenzene (salvarsan), which is used in the treatment of syphilis. Lewis and Bent (47) synthesised sodium formaldehyde sulphoxylate derivative of 3,3'-diamino-4,4'-di-N-glycylamide arsenobenzene. Kaushiva (48) studied the amoebicidal activity of arsenic derivatives of thiazole and thiazolidone. G.M.Borodina (49) reported the condensation of 8-(chloromethyl) caffeine with p-arsanilic acid.

Morgan and Walton (50) condensed p-arsanilic acid with carbethoxyacetylchloride and obtained p-arsenomalon anilate. Pathak and Ghosh (51) prepared organo-arsenicals by condensing p-arsanilic acid and acetanilide in presence of phosphorous trichloride and oxychloride. Naik,Trivedi and Mehta (52) have prepared some organo-arsenicals by condensing atoxyl with monobromo malon-arylamides.

In the present work incorporated in Part V, the chloro,bromo and iodo derivatives of the substituted arylamides of acetoacetic acid are condensed with atoxyl

giving p-arsenoanilino derivatives of the corresponding amides. Similarly, the bromo and iodo derivatives of cyanacet arylamides are allowed to react with atoxyl. The halogen atom of the amide in each case reacted with the hydrogen atom of the amino group of atoxyl to give p-arsonoanilino derivatives (53).

The following halogeno arylamides are condensed with atoxyl :

Monochloro acetoacet-(-anilide; -p-toluidide ; -1:3:4-xylidide ; -α-and -β-naphthylamides) ; monobromo acetoacet-(-anilide;-o-;-p-toluidides ; -p-phenitidide ; -1:2:4-xylidide ; -p-chloroanilide) ; monoiodo acetoacet-(-anilide ; -o-; -p-toluidides and -1:3:4-xylidide).

Monobromo cyanacet-(-o-; -p-toluidides ; -benzylamide ; -o-anisidide ; -p-phenitidide ; -1:3:4-xylidide) ; mono-iodo cyanacet-(-anilide ; -m-; -p-toluidides ; -1:3:4-xylidide ; and -α-naphthylamide).

Thus, from the interaction of atoxyl with mono halogeno acetoacet and cyanacet arylamides, the corresponding p-arsonoanilino derivatives have been prepared as follows :

p-Arsonoanilino acetoacet-(-anilide ; -p-chloro-anilide ; -o-toluidide ; -p-toluidide ; -1:2:4-xylidide ; -1:3:4-xylidide ; p-phenetidide ; -α-naphthylamide and β-naphthylamide).

p-Arsonoanilino cyanacet-(-anilide ; -o-toluidide ; m-toluidide ; -p-toluidide ; -benzylamide ; -o-anisidide ; -phenetidide ; -1:3:4-xylidide and -α-naphthylamide).

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