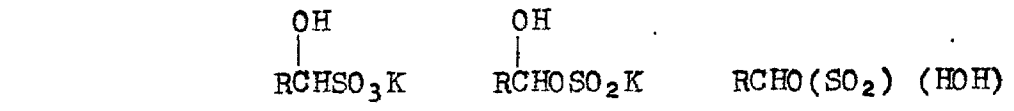
PART III

Formation of methylene bis-derivatives of acetoacet arylamides by means of sodium hydroxy methane sulphonate.

PART III

Theoretical

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 and experimentation. Various workers have, from time to time, favoured either the hydroxysulphonate structure I (Schiff, Ann., 1881, 210, 123 ; Eibner, Ann., 1901, 318, 89) ; the hydroxy sulphite ester formula II (Mendelejef, Ann., 1859, 110, 242 ; Knoevenagel and Lange, Ber., 1904, 37, 4059) ; or a ' polymolecule ' formula III (Schroeter and Sulzbacher, Ber., 1929, 61, 1616 ; Benrath, z.angew. Chem., 1922, 35, 41) as under:

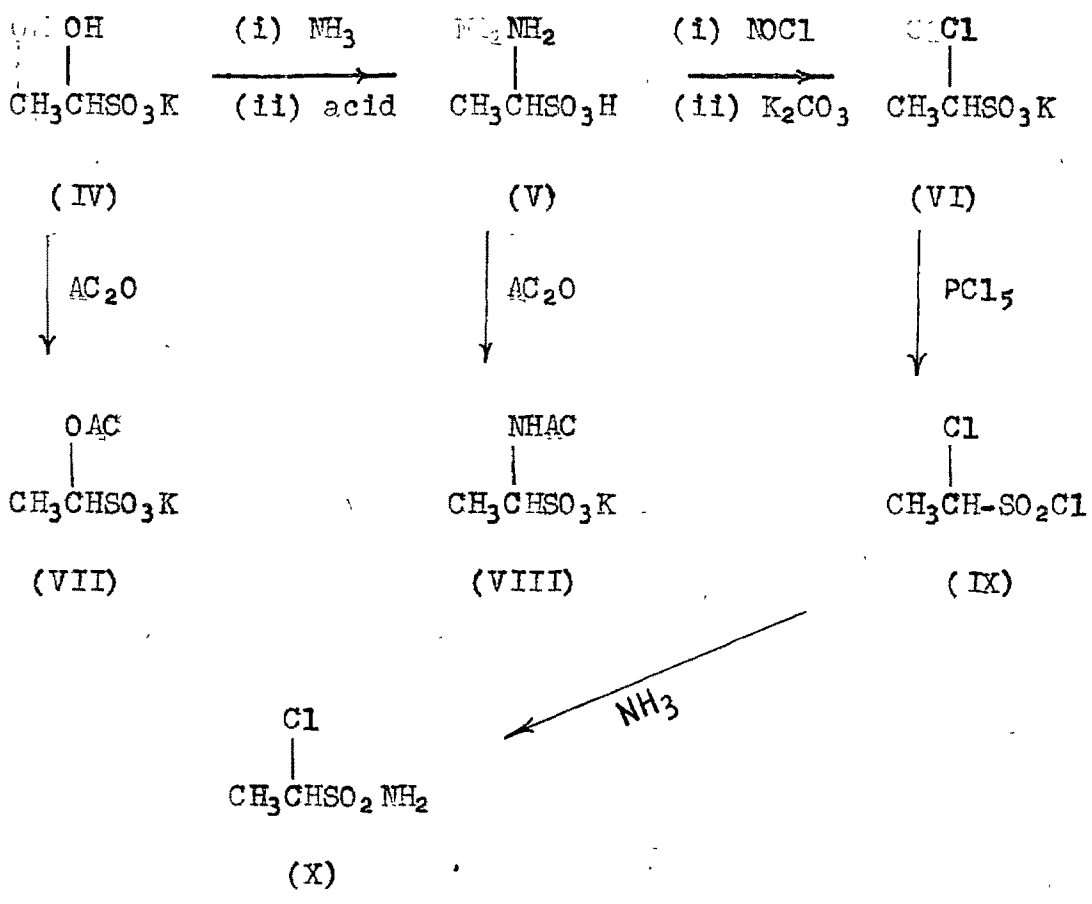


I II III

The experiments of Raschig and Prahl (loc.cit.; Chem.Abst., 1926, 20, 3156), Backer and Mulder (Rec. trav. Chim., 1932, 51, 769) and the recent work of Lauer and Langkammerer (J. Amer. Chem. Soc., 1935, 57, 2360) leave no doubt that the bisulphite compound of formaldehyde is best represented by the hydroxysulphonate structure (I). Sodium hydroxy methane sulphonate was here, condensed with acetoacet arylamides, resulting in the formation of their methylene bis-derivatives.

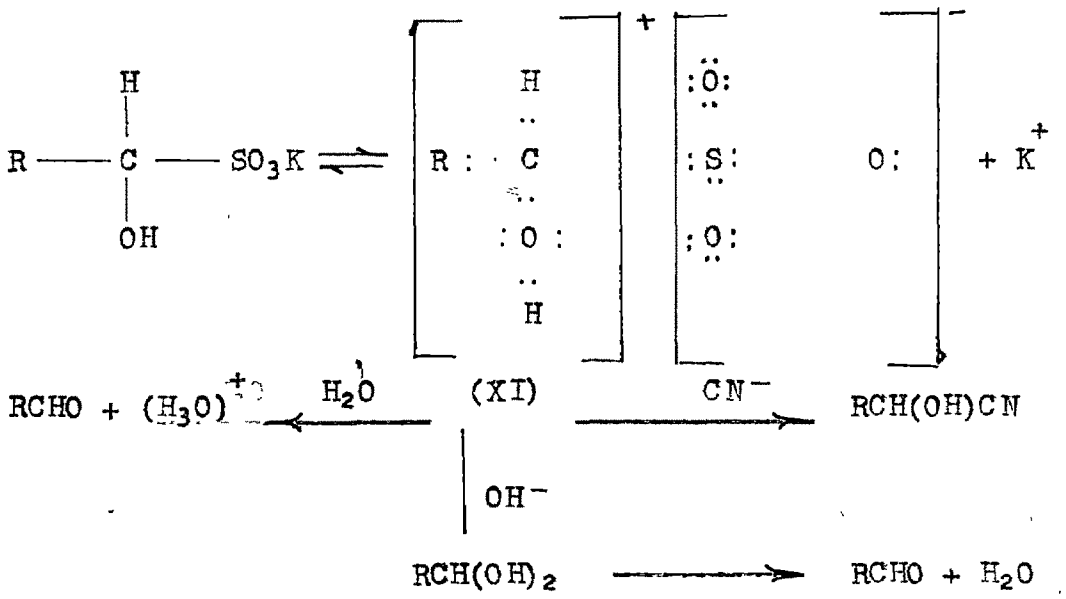
Shriner and Land (J.Org.Chem., 1941, VI,888) for

the above purpose to show the structure of type I, treated either sodium or potassium bisulphite compound (IV) of acetaldehyde with concentrated ammonia and subsequent acidification yielded α-aminoethanesulphonic acid (V). Nitrosyl chloride at 0°C converted this aminosulphonic acid into the α-chloroethanesulphonic acid, which was neutralised with potassium carbonate and isolated as the potassium salt (VI). The compounds (IV) and (V) have been acetylated and their acetyl derivatives (VII) and (VIII) are far more stable than the original hydroxy and amino compounds. The compound (VI), on treatment with phosphorus pentachloride, gave α-chloroethane sulphonyl chloride (IX), which with ammonia gave α-chloroethane sulphonamide (X)



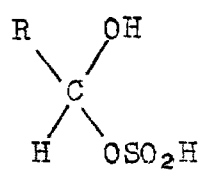
The chief point in connection with the chemistry of bisulphite compounds is their instability, i.e., the reaction, which leads to their formation, is readily reversible and markedly affected by the presence of acids or alkalies. In these α-hydroxysulphonates, the carbon-sulphur linkage is far more labile than in a simple alkyl-sulphonic acid.

If the initial step in the dissociation of this bisulphite compound results in the following ions,

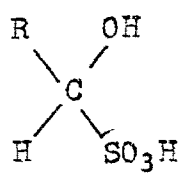


then the carbonium ion (XI) may easily stabilize itself by loss of a proton to the solvent-water, and thus regenarate the aldehyde. It could also combine with a hydroxyl ion, forming an aldehyde hydrate which could then lose water. Both of these reactions would be sensitive to the pH of the solution. In the presence of sodium cyanide, the cyanide anion would combine with the cation (XI) to produce the cyanohydrin.

Lauer and Langkammerer (loc.cit.) studied the constitution of the bisulphite addition of aldehyde and ketone. Since the discovery of the first aldehyde and ketone bisulphite compounds, many difficulties have been encountered in attempting to decide between the α-hydroxy-sulphite ester formula (a) and α-hydroxysulphonic acid formula (b) for these compounds.

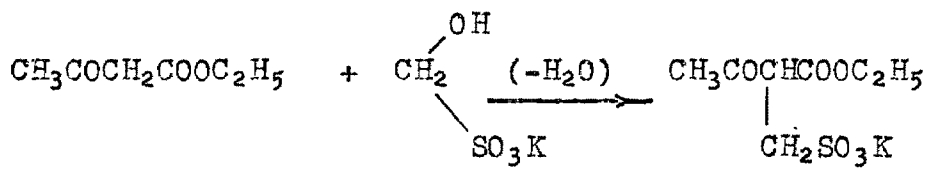


(a)

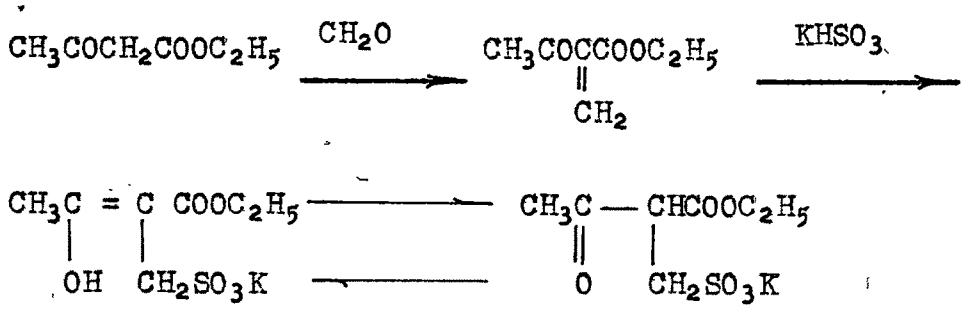


(b)

But for proving α-hydroxysulphonic acid structure (b), Raschig and Prahl (loc.cit.) submitted the reaction,



as indicative of structure (b), since, the cleavage products were definitely sulphonic acids. However, these investigators were not unmindful of the possibility of intermediate formation of methyleneaceto-acetic ester with subsequent 1,4-addition of potassium bisulphite.



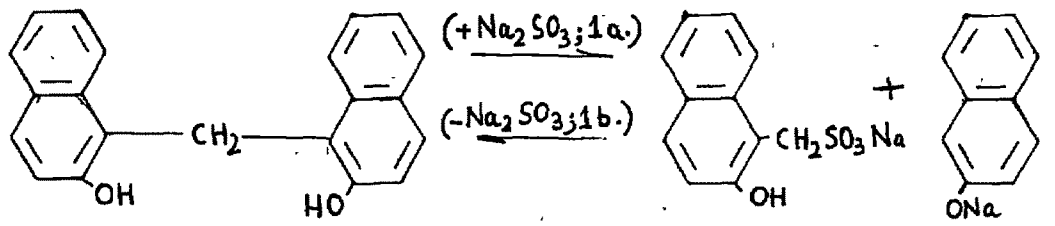
Backer and Mulder (Rec.trav.chim., 1933,52,454) have introduced independent evidence for the hydroxy sulphonic acid structure, for α-amino methane sulphonic acid ($NH_2CH_2SO_3H$ or $NH_3^+CH_2SO_3^-$), obtained by treating formaldehyde bisulphite with ammonia contains a carbon-sulphur linkage. Raschig and Prahl (loc.cit.) have reported that the action of potassium hydroxy-methane sulphonate (formaldehyde potassium bisulphite) with compounds containing reactive methylene groups and few phenols gave their sulphomethylated products. This type of sulphomethylation reaction consists of the replacement of a hydrogen atom by an alkali sulphomethyl group $-(-CH_2SO_3M)$.

Suter, Bair and Bordwell (J.Org.Chem., 1945,X,470) carried out the sulphomethylation reaction of compounds containing active methylene groups, e.g. ethyl acetoacetate, ethyl malonate, ethyl-n-butylacetoacetate and phenyl-acetonitrile with an aqueous solution of formaldehyde sodium bisulphite. The condensation of ethyl acetoacetate with an equivalent quantity of potassium hydroxymethane sulphonate in the presence of one-tenth as much alkali gave monosulphomethylated ester. But attempts to prepare the

disulphomethylated compound, using excess of formaldehyde and sodium bisulphite were unsuccessful. However, when formaldehyde and sodium sulphite were used, a good yield of disulphomethylated ester was obtained. On the other hand, substances such as alkyl or aryl ethers, 2-nitropropane, α-picoline and benzamide were not sulphomethylated under the reaction conditions ; but the reaction with some phenols, viz.,2-naphthol with formaldehyde and sodium sulphite gave sodium 2-hydroxy-1-naphthylmethanesulphonate. Further, they have observed that in the sulphomethylation reaction, it was not likely that the hydroxymethyl compound was ordinarily formed as an intermediate. Since, it has been found that 2-hydroxy-1-naphthylmethanol does not react with sodium sulphite under the conditions employed in the sulphomethylation reaction. Again, they attempted to condense malonic ester with equal amounts of formaldehyde and sodium bisulphite, with one-tenth and one-half the molar ratio of alkali and with even an equivalent amount of sodium sulphite, but no reaction took place in any run even after stirring long periods at room temperature,but by using two moles of sodium sulphite with one mole of 40 % formaldehyde and one mole of malonic ester, its disulphomethylated product was obtained.

Shearing and Smiles (loc.cit.) carried out the above experiment, however, the occurrence of this alcohol along with the product has not been confirmed. Instead, di-2-hydroxynaphthyl-1-methane has always been met with, in fact a relatively large amount of this substance

evidently arising from the condensation of 2-naphthol with formaldehyde (Manasse, Ber., 1894, 27, 2412) is liberating at early stage but this diminishes as the reaction proceeds. Further experiment has established the fact that di-2-hydroxy-naphthyl-1-methane is resolved by hot aqueous sodium sulphite into sodium 2-naphthoxide and sodium 2-naphthol-1-methane-sulphonate according to reaction (Ia) ; moreover, the process is reversible and according to reaction (Ib), the methane derivative being readily formed from the sulphonate with excess of naphthoxide as under:



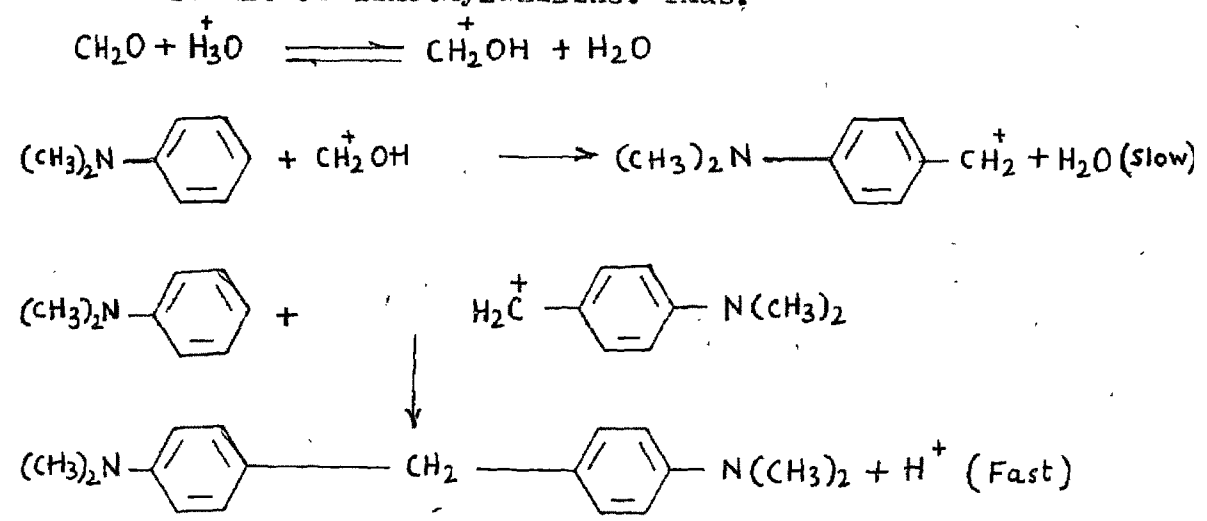
But, not all derivatives of di-2-hydroxynaphthyl-1-methane are so readily resolved by sulphite as the parent substance, viz., the 6,6'-dibromo derivative remains almost unattacked under the same conditions. When 6-bromo-2-naphthol is used instead of 2-naphthol in the reaction with sodium sulphite and formaldehyde, the yields of 6-bromo-2-naphthol-1-methanesulphonate are obtained together with bis-(6-bromo-2-hydroxynaphthyl)-1-methane, which was identical with a sample of bis-(6-bromo-2-hydroxynaphthyl)-1-methane obtained by the method of Fries (Ber., 1906, 39, 439) from formaldehyde and 6-bromo-2-naphthol in presence of sodium acetate. For these reasons it is concluded that

in the original, the source of 2-naphthol-1-methane-sulphonate is at least two-fold ; fission of the methane derivative and condensation of sodium-2-naphthoxide with formaldehyde bisulphite according to reactions (Ia) and (Ib) as shown above.

Here, the support for the process of Cohen and Clutterbuck (J. Chem. Soc., 1923, 123, 2510) has not been found in the isolation of 2-hydroxynaphthyl-1-methanol, but since the conversion of this into the sulphonate by sodium sulphite is without doubt attainable. According to patent literature (D.R.P. 87335), the sodium 2-naphthol-1-methanesulphonate from formaldehyde and sodium sulphite supports the process of Shearing and Smiles in the formation of di-2-hydroxynaphthyl-1-methane. Thus, from the present condensation reaction of acetoacet arylamides (2 moles) with sodium hydroxy methane sulphonate (1 mole) are obtained only the methylene bis-derivatives of acetoacet arylamides, the formation of which supports the process of Suter, Bair and Bordwell (loc.cit.) as well as that of Shearing and Smiles (loc.cit.)

Yoshiro Ogata and Masaya Okano (loc.cit.) studied the condensation of dimethylaniline with formaldehyde and obtained p,p'-tetramethyldiaminodiphenylmethane (XII). The mechanism of the reaction was described as the slow irreversible formation of, $p\text{-}(CH_3)_2N.C_6H_4.\overset{+}{C}H_2$, from dimethylaniline and the conjugate acid of formaldehyde, followed by the rapid condensation of the product with a

second molecule of dimethylaniline. Thus:



(XII)

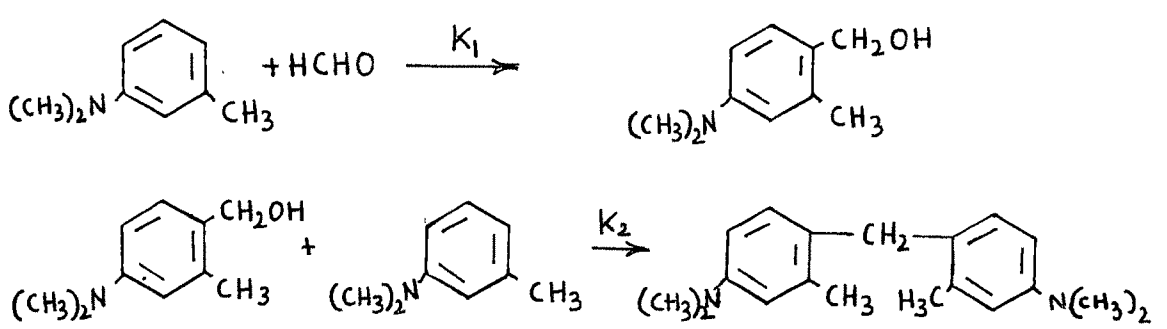
Pratt and Green (J. Amer. Chem. Soc., 1953, 75, 275) treated n-heptaldehyde with dimethylaniline and obtained 1,1-bis-(p-dimethylaminophenyl)-heptane in presence of p-toluenesulphonic acid monohydrate as catalyst in sufficient quantity of benzene.

Smith and Welch (J.Chem.Soc., 1934,1136) prepared methylenebis-o-nitroaniline from p-dimethylaminobenzyl alcohol and o-nitroaniline in the absence of a catalyst at 130°C in one hour. Dimethylaniline and dimethylaminobenzyl-alcohol with one drop of hydrochloric acid gave 4,4'-tetramethyldiaminodiphenylmethane.

Bruson (Chem.Abst., 1946,40,351 ; U.S. 2383444, 1945) studied the reactions of acrylonitrile in presence of alkali with acetoacetic ester, viz., acetoacetic ester and acrylonitrile in dioxane with $Me_3(PhCH_2)NOH$ gave ethyl bis-(2-cyanoethyl)acetoacetate. In a similar manner, reaction of acrylonitrile with acetoacetanilide in dioxane containing $Me_3(PhCH_2)NOH$ yielded bis-(2-cyanoethyl)

acetoacetanilide and reaction with o-chloro acetoacetanilide gave bis-(2-cyanoethyl)acetoacet-o-chloroanilide.

Burnett and Hammett (J.Org.Chem., 1958,23,770) employed the reaction of dimethyl-m-toluidide with formaldehyde in a dioxane-water medium and obtained 4,4'-methylenebis(-dimethyl-m-toluidide) (XIII). It was expected that the reaction would occur in two steps, of which the first would be rate determining under conditions of moderate acidity using perchloric acid.



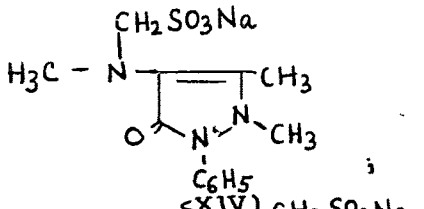
(XIII)

The possibility of isolating the substituted benzyl alcohol (BA) under conditions of high acidity (Smith and Welch, J. Chem.Soc., 1934,730) suggested, however, that there is an inversion of relative specific rates K_1/K_2 as the acidity of the medium is increased. But the conclusion was drawn that the rate of the reaction is markedly accelerated by oxygen, the major product remaining was the above mentioned diphenylmethane derivative.

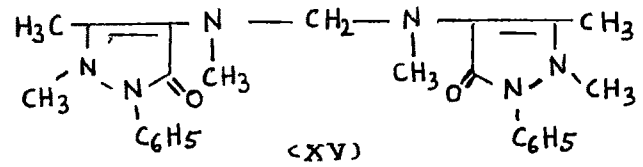
Paul Pastour (Compt.rend., 1953,237,1094 ; Chem. Abst., 1955,49,1614 g.) condensed acetoacetanilide with aliphatic aldehydes and obtained the bis-derivative of the formula $RCH(COCH_3CHCONHC_6H_5)_2$ in pure or alcoholic pyridine.

If traces of piperidine are used, instead, substituted cyclohexanolones are obtained. Thus, acetaldehyde and acetoacetanilide refluxed with alcohol in pyridine gave ethylidenebis-(acetoacetanilide).

Schwarz et al. (Brit.Pat.No. 164002, 1925 ; Chem.Abst., 1927,21,592) treated a secondary aromatic-aliphatic amine with CH_2O and bisulphite and obtained Na-1-phenyl-2,3-dimethyl-5-pyrazolone-4-methylaminomethylsulphite (XIV) and Na-N-methyl-p-phenitidinemethylsulphite (XVI). Methylenebis-1-phenyl-2,3-dimethyl-4-methylamino-5-pyrazolone (XV) is obtained by heating with CH_2O, the mixture of amines produced by methylating 1-phenyl-2,3-dimethyl-4-amino-5-pyrazolone, while methylenebis-N-methyl-phenitidine (XVII) is obtained by treating with CH_2O, the crude N-methyl phenitidine obtained by methylating phenitidine.



(XIV)



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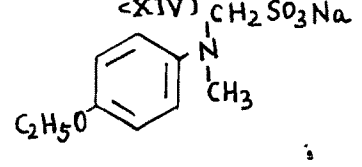
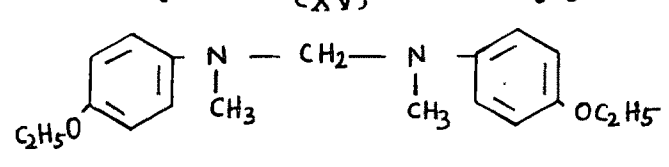


(XVI)

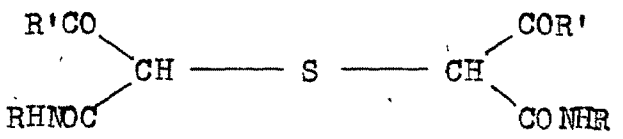


(XVII)

Jean D'ecombe and Monique Pre'tot (Compt.rend., 1954,239, 1502 ; Chem.Abst., 1956,50,207) obtained hydroxymethylacetoacetanilide with equimolecular mixture of alcoholic acetoacetanilide and 30 % formaldehyde without catalyst ; while acetoacetic ester under the same condition

did not react with formaldehyde. But acetoacetanilide and formaldehyde when treated with 0.4 N NaOH solution from which on acidification with acetic acid gave the compound of the type ($PhNHCOCH_2CH_2CHCOCH_3CONHPh$). Further, they stated that three moles of formaldehyde with two moles of acetoacetanilide gave methylenebis-acetoacetanilide, instead of hydroxymethyl acetoacetanilide.

Naik et al. (J.Ind.Chem.Soc., 1932,9,471 ; ibid., 1930,7,145) studied, interalia, the reactions of thionyl chloride with organic compounds containing reactive methylene group and concluded that the course of reaction entirely depended on the conditions of the experiment. The reaction of thionyl chloride with phenols, phenetoles and alcohols in presence of anhydrous aluminium chloride gave rise to sulphides, but sulphoxides are also obtained under changed conditions. Here, thionyl chloride behaves, as if it was a mixture of sulphur dichloride and sulphuryl chloride ($2SOCl_2 \quad SCl_2 + SO_2Cl_2$) and its reaction with acetoacet arylamides and malon diarylamides respectively is found to give thiobis-derivatives of the type (XVIII) as under:



(XVIII)

(Where,R is phenyl,tolyl,xylyl,etc.groups ; and R' is $-CH_3$ or -NHR group.)

The above course of reaction,where only one hydrogen atom of the molecule takes part,is explained on the fact that

the second hydrogen atom becomes sluggish after the first one is replaced by a substituent from the compounds containing reactive methylene group.

Naik and his collaborators (J. Chem. Soc., 1921, 119,379 ; 1922,121,2592, etc.) 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. $-CO.CH_2.CO-$, $-CO.CH_2.CN-$, are active and these active hydrogen atoms take part into the reactions. They have observed that the reactivity of 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 series of compounds of the following types,

(1) $CH_2(CONH_2)_2$ (2) NH_2COCH_2CONHR (3) $CH_2(CONHR)_2$,

(4) $C_2H_5O.CO.CH_2CONHR$ (5) CH_3COCH_2CONHR

(6) $CH_2(COOC_2H_5)_2$ (7) $C_2H_5O.CO.CH_2CN$,

the reactivity of the hydrogen atoms, which is less pronounced in (1) becomes more and more manifest with increasing negative characters of the adjoining groups upto (7). The hydrogen atoms of reactive methylene group $-CH_2-$ of acetoacet arylamides are, thus, involved in the present reaction with sodium hydroxymethane sulphonate, in which case the replacement of hydrogen atoms from the amide molecule is successive and not simultaneous, when one atom of reactive methylene hydrogen is being replaced by a substituent, the other hydrogen atom in the same molecule becomes sluggish ; and this differential activity, as has

been manifested in the above type of compounds, is in complete accord with the hypothesis put forward by Naik and his collaborators.

Robert Lepetit (Atti accad.Lincei., 1917,26, 126 ; Chem.Abst., 1918,12, 366) prepared sodium p-ethoxy phenyl-aminomethanesulphonate (Eto $C_6H_4NHCH_2SO_3Na.H_2O$) from $NaHSO_3$ acting on a molecular mixture of CH_2O and p-phenetidine in water-alcohol at 75-80°C. The work was extended to the sodium aminomethanesulphonate derivatives of aniline,o-toluidine,xylidine,o-anisidine, α-and β-naphthylamine and o-chloroaniline. Knoevenagel and Mercklin (Ber., 1904, 37, 4089) prepared diethylamino-acetonitrile from a mixture of CH_2O and $NaHSO_3$ in the presence of NaCN and $(C_2H_5)_2NH$.

Riesz et al. (Trav.members soc.chim.biol., 1943, 25, 1064 ; Chem. Abst., 1947, 41, 5818) found the method for detecting $CH_2O.NaHSO_3$ in the presence of its condensation products with amino or guanidino compounds consisting in heating with $Ba(OAC)_2$, removal of the liberated CH_2O, formation of $BaSO_3$ and titration of SO_3^{--} iodometrically. The Na-N-methanesulphonic acid derivative of 4-methyl-7-aminocoumarin was obtained from 4-methyl-7-aminocoumarin with a concentrated aqueous solution of $NaHSO_3$ and CH_2O at 95-100°C. The above water soluble sodium salt gave bluish violet fluorescence, which is found to be a more whitening agent for wool and cotton (Chem. Abst., 1950, 44, 6160 ; Ciba ltd.)

Methylene-bis-(acetoacet arylamides) :

Here in this part III acetoacet arylamides, which contain reactive methylene group, have been treated with sodium hydroxyde methane sulphonate. Reactions with potassium hydroxyde methane sulphonate with compounds containing reactive methylene group, have been found to give sulphomethylated products (Raschig and Prahl, (loc.cit.). This work gave an impetus to investigate the interaction between sodium hydroxy methane sulphonate and acetoacet arylamides, where the expected sulphomethylated product, i.e. the sulphonation of the hydrogen atom of the reactive methylene group, was not observed, but instead the products of reaction were found to be methylene bis-(acetoacet arylamides).

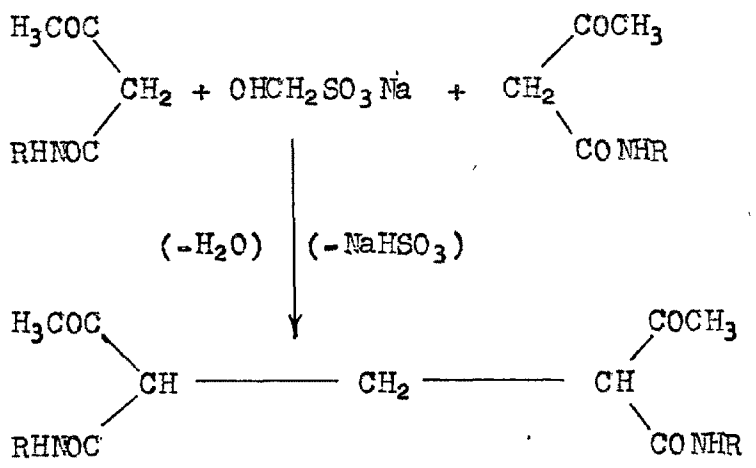
The required acetoacet arylamides were prepared by the method of Ewins and King (loc.cit.) by refluxing the primary amines and ethyl acetoacetate for one and a half minutes, as modified by Naik et al. (J.Ind.Chem.Soc., 1932, 9, 127 ; 1943, 20, 384).

Thus, acetoacetic ester (0.01 mole) was mixed with aromatic amine (0.01 mole) in a conical flask with an air-condenser, and the mixture was heated quickly to boiling for one and a half minutes. On cooling, the acetoacet arylamide crystallised out, which was filtered and washed with a mixture of benzene and petrol (1:1), till it was free from the ester and amine. It was then, crystallised from benzene as white needles. In the same way by slightly varying the time of boiling, the other members of acetoacet

arylamides have been obtained.

Preparation of methylene bis-(acetoacet arylamide)

Two moles of acetoacet arylamide and one mole of sodium hydroxy methane sulphonate were refluxed in 90 % methyl alcohol for 3 hours on a sand bath. It was then diluted with water and a white product appeared on cooling. The crude product, after filtering, was crystallised from acetic acid. A number of other methylene bis-(acetoacet arylamides) were similarly prepared (Mehta and Patel, Current Science, 1960, 29,95). The reaction may be expressed as under:

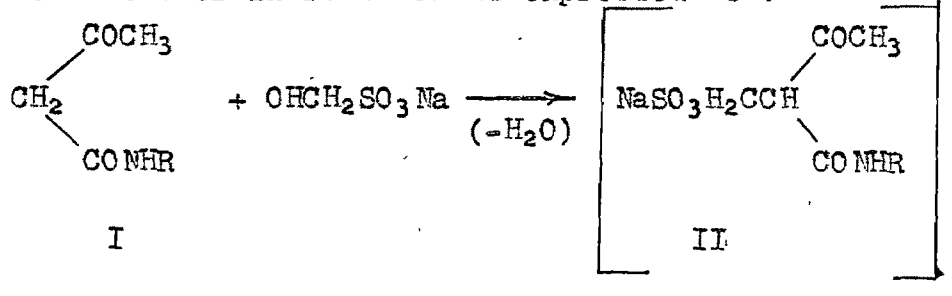


(Where, R is phenyl, tolyl, xylyl and naphthyl groups.)

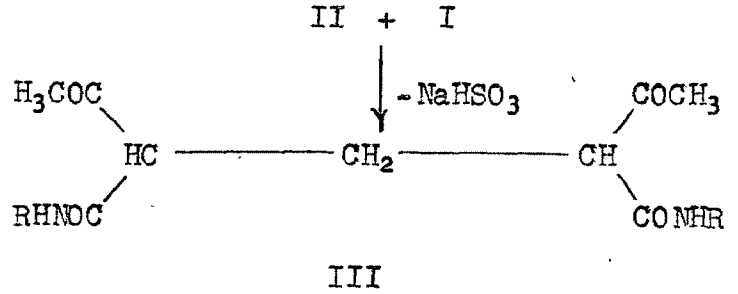
The above reaction is believed to have taken place according to the following two courses:

First course may be visualized through the elimation of water by the intermediate formation of sulphonate (II), with which the reactive hydrogen atom of the methylene group $-CH_2-$ of unreacted molecule of the amide (I) simultaneously interacts, yielding only the corresponding methylene bis-

derivatives (III), with the elimination of sodium bisulphite, and then the overall reaction is expressed as :

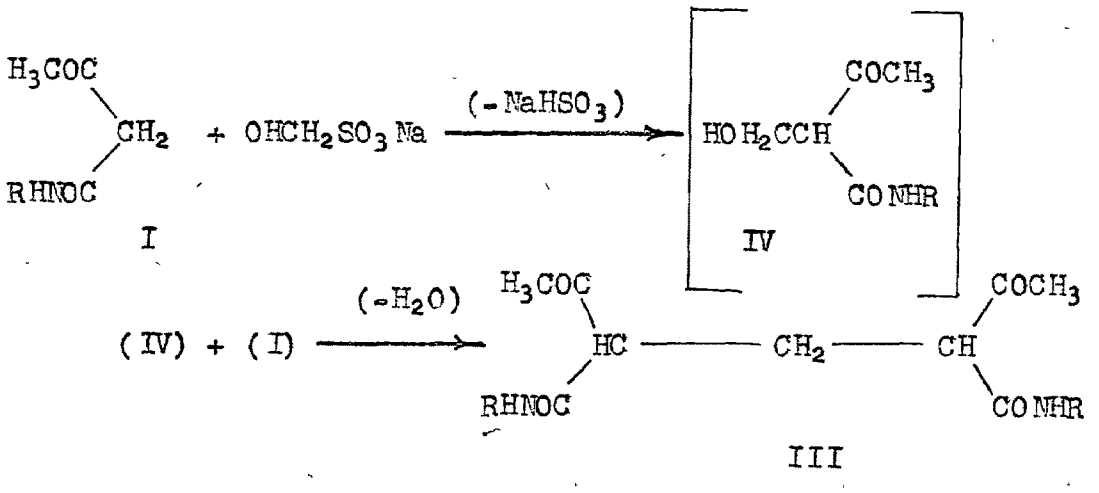


I II



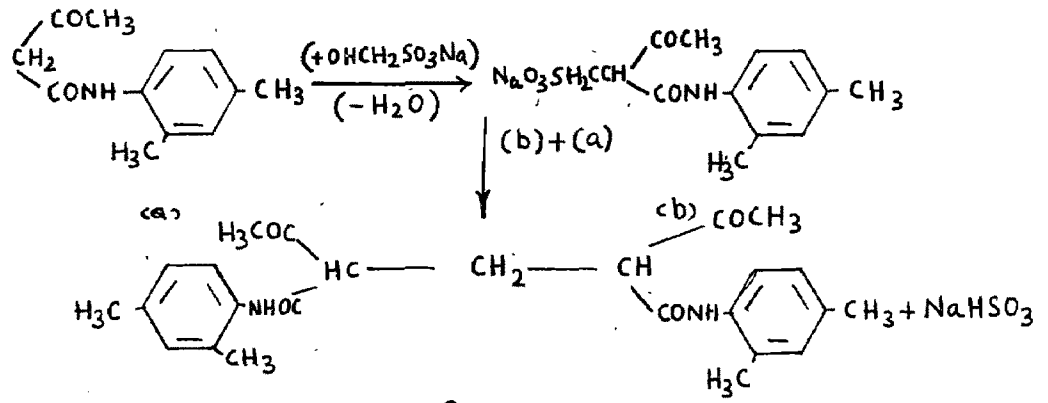
III

The second course may be through the elimination first of sodium bisulphite by the intermediate formation of hydroxy methyl derivative of acetoacet arylamide (IV), with which the reactive hydrogen atom of the unreacted molecule of the amide (I) simultaneously interacts with the elimination of water, yielding only the corresponding methylene bis-derivative: (III) as under:



I IV III

As has been observed by Suter et al. (loc.cit.) in the sulphomethylation reaction of 2-naphthol with formaldehyde and sodium bisulphite, the intermediate formation of 2-hydroxy-1-naphthyl methanol is unlikely ; and in the formation of di-2-hydroxy-naphthyl-1-methane by Shearing and Smiles (loc.cit.), the occurrence of hydroxy methyl compound was not confirmed. Hence the support is given to the first course of reaction, which takes place through the intermediate formation of a sulphonate. Moreover, it became possible only in the case of the interaction of acetoacet-1:2:4-xylidide (a) with sodium hydroxy methane sulphonate, when taken in equimolecular proportion, to isolate the intermediate sulphonate as under:



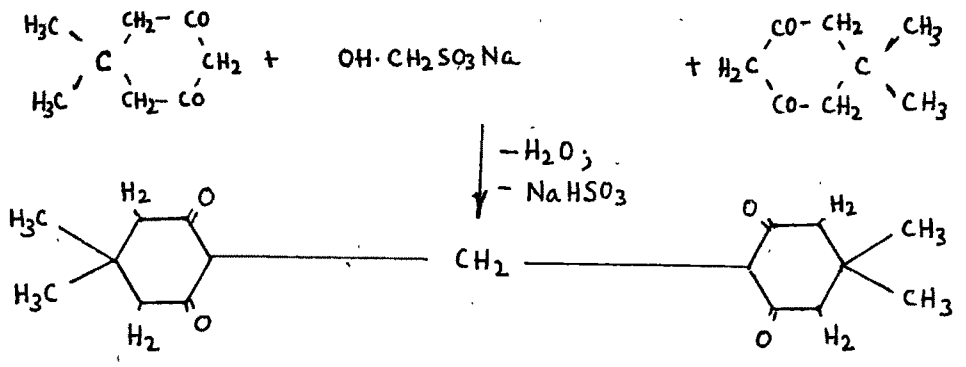
(C)

The above sodium salt of hydroxymethane sulphonate of acetoacet-1:2:4-xylidide (b) was separated, which on analysis, gave the following results.

Required % N = 4.36 % ; found % N = 4.45 % , whose molecular formula is, $C_{13}H_{16}O_5NSNa$, and m.p. is 205°C.

But the above compound (b) when further refluxed with compound (a) in 90 % methanol gave methylene bis-(acetoacet-1:2:4-xylidide) (c), melting at 230°C, which, as usual, was also directly obtained, on refluxing, the reaction mixture of acetoacet-1:2:4-xylidide (2 mols) with sodium hydroxy methane sulphonate (1 mol.) for a longer time. Mixed melting point with methylene bis-(acetoacet-1:2:4-xylidide),described above, was not depressed.

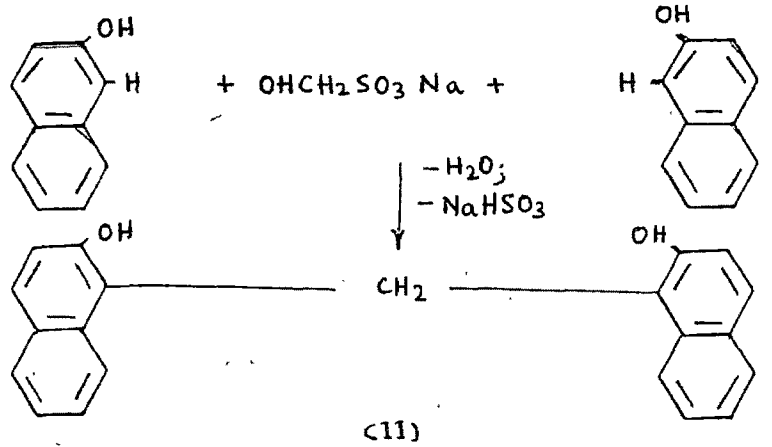
Again, dimedone (5,5-dimethylcyclohexanedione-1,3), which contains reactive methylene group, when treated with formaldehyde, gave a known bis-(dimedon)methane, which gave a melting point 188°C (Ber. VII,888). This very bis-(dimedon)methane (I) melting at 188°C, was prepared from dimedonee (2 mols) and sodium hydroxy methane sulphonate (1 mol) by refluxing in 90 % methanol. Thus,



(c)

Similarly, two molecules of 2-naphthol and sodium hydroxy methane sulphonate (1 mole) in 90 % methanol, gave di-2-hydroxynaphthyl-1-methane (II), which melted at 199°C. Shearing and Smiles (loc.cit.) obtained the same

di-2-hydroxynaphthyl-1-methane (m.p. 199°C) by condensing 2-naphthol, formaldehyde and sodium sulphite. Thus,



(11)

The above reactions indicated that the hydrogen atom of the reactive methylene group in case of dimedone and the α-hydrogen atom in case of 2-naphthol interacted with sodium hydroxymethane sulphonate with the formation of the respective methylene bis-derivatives.

Molecular weight by Rast method :

0.0088 gm. of methylene bis-(acetoacetanilide) was intimately mixed with 0.1 gm. purely sublimed camphor in a glass tube. The other end of the tube was sealed, and heated in a paraffin bath till the contents of the tube were completely dissolved. In order to prepare a homogenous mass of the mixture the tube is cooled and the mass is redissolved by heating. The freezing point of the mixture was found to be 166°C and that of the camphor was 175.8°C. The molecular weight of the bis-compound is thus calculated as 359.08, while its theoretical molecular weight of the formula, $C_{21}H_{22}O_4N_2$, is 354.0

$$\text{Mol.Wt.} = \frac{1000\ gK}{\Delta F}$$ where, g = wt.of compound taken.

K = F.P.constant for camphor

Δ = observed depression in F.P.

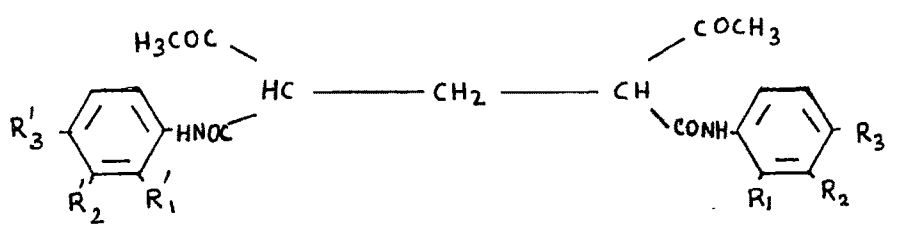
F = wt.of camphor taken.

$$\therefore \text{Mol.wt.} = \frac{(1000 \times 0.0088 \times 40)}{(9.8 \times 0.1)} = 359.08$$

The following acetoacet arylamides, accordingly, are prepared :

(1) Acetoacetanilide (2) Acetoacet-o-toluidide (3) Acetoacet-p-toluidide (4) Acetoacet-o-chloroanilide (5) Acetoacet-m-chloroanilide (6) Acetoacet-p-chloroanilide (7) Acetoacet-o-anisidide (8) Acetoacet-p-phenitidide (9) Acetoacet-1:2:4-xylidide (10) Acetoacet-1:3:4-xylidide (11) Acetoacet-α-naphthylamide and (12) Acetoacet-β-naphthylamide.

The following methylene bis-(acetoacet arylamides), thus, prepared from the above mentioned acetoacet arylamides, using sodium hydroxy methane sulphonate:



(VI)

(1) Methylene bis-(acetoacetanilide)
(VI, $R_1=R'_1 = R_2 =R'_2 = R_3 = R'_3 = H$)

(2) Methylene bis-(acetoacet-o-toluidide)
(VI, $R_1=R'_1 = CH_3$; $R_2=R'_2=R_3=R'_3 = H$)

(3) Methylene bis-(acetoacet-p-toluidide)
(VI, $R_3=R'_3 = CH_3$; $R_1=R'_1 = R_2 = R'_2 = H$)

(4) Methylene bis-(acetoacet-o-chloroanilide)
(VI, $R_1=R'_1 = Cl$; $R_2 = R'_2 = R_3 = R'_3 = H$)

(5) Methylene bis-(acetoacet-m-chloroanilide)
(VI, $R_2=R'_2 = Cl$; $R_1 = R'_1 = R_3 = R'_3 = H$)

(6) Methylene bis-(acetoacet-p-chloroanilide)
(VI, $R_3 = R'_3 = Cl$; $R_1 = R'_1 = R_2 = R'_2 = H$)

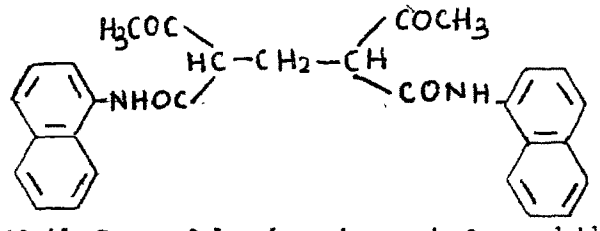
(7) Methylene bis-(acetoacet-o-anisidide)
(VI, $R_1 = R'_1 = OCH_3$; $R_2 = R'_2 = R_3 = R'_3 = H$)

(8) Methylene bis-(acetoacet-p-phenitidide)
(VI, $R_3 = R'_3 = OC_2H_5$; $R_1 = R'_1 = R_2 = R'_2 = H$)

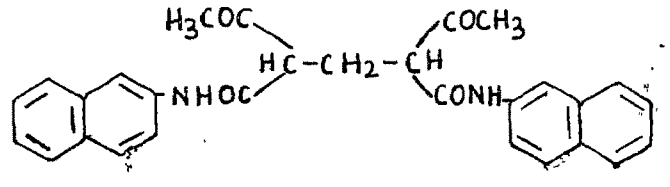
(9) Methylene bis-(acetoacet-1:2:4-xylidide)
(VI, $R_1 = R'_1 = R_3 = R'_3 = CH_3$; $R_2 = R'_2 = H$)

(10) Methylene bis-(acetoacet-1:3:4-xylidide)
(VI, $R_2 = R'_2 = R_3 = R'_3 = CH_3$; $R_1 = R'_1 = H$)

(11) Methylene bis-(acetoacet-α-naphthylamide)



(12) Methylene bis-(acetoacet-β-naphthylamide)



EXPERIMENTAL

Methylenebis-(acetoacetanilide) :

Acetoacetanilide (3.5 g. ; 0.02 M) was dissolved in 20 ml. methyl alcohol to which was added solution of sodium hydroxymethane sulphonate in 5 ml. water (1.34 g.; 0.01 M) and the reaction mixture was refluxed on a sand-bath for 3 hours. 50 ml. of water were added to it at room temperature, the resulting product was then filtered and crystallised from acetic acid, m.p. 212°C. Yield 1.9 g.

Analysis :

4.318 mg. of the substance gave 10.846 mg. of carbon dioxide and 2.362 mg. of water.

9.64 mg. of the same substance gave 0.654 ml. of nitrogen at 33°C and 758 mm. pressure.

Found : C = 68.54 % ; H = 6.12 % ; N = 7.54 %.

$C_{21}H_{22}O_4N_2$ requires : C = 68.83 % ; H = 6.05 % ; N = 7.60 %.

Methylenebis-(acetoacet-o-toluidide):

Acetoacet-o-toluidide (3.8 g.) was dissolved in 25 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml.water(1.34 g.) and the reaction mixture was refluxed on a sand bath for 3 hours. 50 ml. of water were added to it at room temperature, the resulting product was then filtered and crystallised as above, m.p. 179-80°. Yield 1.9 g.

Analysis :

4.112 mg. of the substance gave 10.580 mg. of carbon dioxide and 2.434 mg. of water.

9.10 mg. of the same substance gave 0.585 ml. of nitrogen at 33°C and 758 mm. pressure.

Found : C = 70.22 % ; H = 6.62 % ; N = 7.15 %.

$C_{23}H_{26}O_4N_2$ requires : C = 70.03 % ; H = 6.64 % ; N = 7.10 %.

Methylenebis-(acetoacet-p-toluidide):

Acetoacet-p-toluidide (3.8 g.) was dissolved in 25 ml. methyl alcohol to which was added solution of sodium hydroxymethane sulphonate in 5 ml. water (1.34 g.) and the reaction mixture was refluxed on a sand bath for 3 hours. 60 ml. of water were added to it at room temperature, the resulting product was then filtered and crystallised as above, m.p. 187°C. Yield 2.0 g.

Analysis :

6.36 mg. of the substance gave 0.332 ml. of nitrogen at 31°C and 761 mm. pressure.

Found : N = 6.87 %.

$C_{23}H_{26}O_4N_2$ requires : N = 7.10 %.

Methylenebis-(acetoacet-o-chloroanilide) :

Acetoacet-o-chloroanilide (4.20 g.) was dissolved in 25 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml. water (1.34 g.) and the reaction mixture was refluxed on a sand-bath for 3 hours. 60 ml. of water were added to it at room temperature, the resulting products was then filtered and crystallised as above, m.p. 165°C. Yield 2.6 g.

Analysis :

6.66 mg. of the substance gave 0.357 ml. of nitrogen at 30°C and 761 mm. pressure.

Found : N = 6.04 %.

$C_{21}H_{20}O_4N_2Cl_2$ requires : N = 6.43 %.

Methylenebis-(acetoacet-m-chloroanilide) :

Acetoacet-m-chloroanilide (4.20 g.) was dissolved in 25 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml. water (1.34 g.) and the reaction mixture was refluxed on a sand-bath for 3 hours. 60 ml. of water were added to it at room temperature, the resulting product was then filtered and crystallised from acetic acid, m.p. 172°C. Yield 2.4 g.

Analysis :

4.628 mg. of the substance gave 9.704 mg. of carbon dioxide and 1.920 mg. of water.

5.606 mg. of the same substance gave 0.342 ml. of nitrogen at 32°C and 756 mm. pressure.

Found : C = 57.62 % ; H = 4.64 % ; N = 6.79 %.

$C_{21}H_{20}O_4N_2Cl_2$ requires : C = 57.93 % ; H = 4.60 % ; N = 6.43 %.

Methylenebis-(acetoacet-p-chloroanilide) :

Acetoacet-p-chloroanilide (4.20 g.) was dissolved in 25 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml. water (1.34 g.) and the reaction mixture was refluxed on a sand-bath for 3 hours. 60 ml. of water were added to it at room temperature, the resulting product was then filtered and crystallised as above, m.p. 152°C. Yield 2.3 g.

Analysis :

9.14 mg. of the substance gave 0.510 ml. of nitrogen at 33°C and 758 mm. pressure.

9.48 mg. of the same substance gave 6.10 mg. of silver chloride.

Found : N = 6.20 % ; Cl = 15.92 %,

$C_{21}H_{20}O_4N_2Cl_2$ requires : N = 6.43 % ; Cl = 16.32 %.

Methylenebis-(acetoacet-o-anisidide) :

Acetoacet-o-anisidide (4.0 g.) was dissolved in 15 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml. water (1.34 g.) and the reaction mixture was refluxed on a sand-bath for 3 hours. 50 ml. of water were added to it at room temperature, the resulting product was then filtered and crystallised from acetic acid, m.p. 148°C. Yield 2.4 g.

Analysis :

4.394 mg. of the substance gave 10.372 mg. of carbon dioxide and 2.436 mg. of water.

6.64 mg. of the same substance gave 0.386 ml. of nitrogen at 28°C and 761 mm. pressure.

Found : C = 64.42 % ; H = 6.20 % ; N = 6.60 %.

$C_{23}H_{26}O_6N_2$ requires : C = 64.77 % ; H = 6.15 % ; N = 6.57 %.

Methylenebis-(acetoacet-p-phenitidide) :

Acetoacet-p-phenitidide (4.40 g.) was dissolved in 25 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml. water(1.34 g.) and the reaction mixture was refluxed on a sand-bath for 3 hours. 60 ml. of water were added to it at room temperature,

the resulting product was then filtered and crystallised as above, m.p. 188°C. Yield 2.6 g.

Analysis :

6.76 mg. of the substance gave 0.337 ml.of nitrogen at 30°C and 761 mm. pressure.

Found : N = 5.82 %.

$C_{25}H_{30}O_6N_2$ requires : N = 6.16 %.

Methylenebis-(acetoacet-1:2:4-xylidide) :

Acetoacet-1:2:4-xylidide (4.10 g.) was dissolved in 25 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml. water(1.34 g.) and the reaction mixture was refluxed on a sand-bath for 3 hours. 60 ml. of water were added to it at room temperature, the resulting product was then filtered and crystallised from acetic acid, m.p. 230°C. Yield 2.8 g.

Analysis :

6.52 mg. of the substance gave 0.366 ml. of nitrogen at 31°C and 760 mm. pressure.

Found : N = 6.30 %.

$C_{25}H_{30}O_4N_2$ requires : N = 6.63 %.

Methylenebis-(acetoacet-1:3:4-xylidide) :

Acetoacet-1:3:4-xylidide (4.10 g.) was dissolved in 25 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml. water(1.34 g.) and the reaction mixture was refluxed on a sand-bath for 3 hours. 60 ml. of water wereadded to it at room temperature, the resulting product was then filtered and crystallised as above, m.p. 202°C. Yield 2.6 g.

Analysis :

4.244 mg. of the substance gave 11.064 mg. of carbon dioxide and 2.710 mg. of water.

6.92 mg. of the same substance gave 0.406 ml. of nitrogen at 31°C and 761 mm. pressure.

Found : C = 71.14 % ; H = 7.14 % ; N = 6.59 %.

$C_{25}H_{30}O_4N_2$ requires : C = 71.06 % ; H = 7.16 % ; N = 6.63 %.

Methylenebis-(acetoacet-α-naphthylamide) :

Acetoacet-α-naphthylamide (4.54 g.) was dissolved in 30 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml. water(1.34 g.) and the reaction mixture was refluxed on a sand-bath for 3 hours. 75 ml. of water were added to it at room temperature, the resulting product was then filtered and crystallised from acetic acid, m.p. 214°C. Yield 2.8 g.

Analysis :

6.28 mg. of the substance gave 0.327 ml. of nitrogen at 30°C and 760 mm. pressure.

Found : N = 5.86 %.

$C_{29}H_{26}O_4N_2$ requires : N = 6.00 %.

Methylenebis-(acetoacet-β-naphthylamide) :

Acetoacet-β-naphthylamide (4.54 g.) was dissolved in 30 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml. water(1.34 g.) and the reaction mixture was refluxed on a sand-bath for 3 hours. 75 ml. of water were added to it at room temperature, the resulting product was then filtered and crystallised as above, m.p. 208°C. Yield 2.5 g.

Analysis :

4.354 mg. of the substance gave 11.902 mg. of carbon dioxide and 2.366 mg. of water.

8.860 mg. of the same substance gave 0.481 ml. of nitrogen at 34°C and 751 mm. pressure.

Found : C = 74.60 % ; H = 6.08 % ; N = 6.01 %.

$C_{29}H_{26}O_4N_2$ requires : C = 74.66 % ; H = 5.62 % ; N = 6.00 %.

Bis-(-dimedone)methane :

Dimedone (5,5-dimethylcyclohexanedione-1,3; 2.80 g.) was dissolved in 20 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml. water (1.34 g.) and the reaction mixture was refluxed on a sand-bath for 3 hours. 50 ml. of water were added to it at room temperature, the resulting product was then filtered and crystallised from alcohol, m.p. 188°C.

The identity of bis-(-dimedon)methane was established by comparing its melting point and mixed melting point with that of the authentic sample.

Di-2-hydroxynaphthyl-1-methane :

2-Naphthol (2.88 g. ; 0.02 M) was dissolved in 20 ml. methyl alcohol to which was added solution of sodium hydroxy methane sulphonate in 5 ml. water (1.34 g. ; 0.01 M) and the reaction mixture was refluxed on a sand-bath for 3 hours. 50 ml. of water were added to it at room temperature, the resulting product was then filtered and crystallised from acetic acid, m.p. 199°C.

The identity of di-2-hydroxy-naphthyl-1-methane

was established by comparing its melting point, and mixed melting point with that of the authentic sample.

Table 4

Methylene bis-(acetoacet arylamides)

S.No.	Compound	Molecular formula	M.P. °C	Yield %	Nitrogen Found %	Nitrogen Reqd. %	Carbon Found %	Carbon Reqd. %	Hydrogen Found %	Hydrogen Reqd. %
1.	Methylene bis-(acetoacet-anilide)	$C_{21}H_{22}O_4N_2$	212	54.0	7.54	7.60	68.54	68.83	6.12	6.05
2.	Methylene bis-(acetoacet-o-toluidide)	$C_{23}H_{26}O_4N_2$	180	50.0	7.15	7.10	70.22	70.03	6.62	6.64
3.	Methylene bis-(acetoacet-p-toluidide)	$C_{23}H_{26}O_4N_2$	187	52.0	6.87	7.10	-	-	-	-
4.	Methylene bis-(acetoacet-o-chloroanilide)	$C_{21}H_{20}O_4N_2Cl_2$	165	61.9	6.04	6.43	-	-	-	-
5.	Methylene bis-(acetoacet-m-chloroanilide)	$C_{21}H_{20}O_4N_2Cl_2$	172	57.0	6.79	6.43	57.62	57.93	4.64	4.60
*6.	Methylene bis-(acetoacet-p-chloroanilide)	$C_{21}H_{20}O_4N_2Cl_2$	152	54.0	6.20	6.43	-	-	-	-
7.	Methylene bis-(acetoacet-o-anisidide)	$C_{23}H_{26}O_6N_2$	148	60.0	6.60	6.57	64.42	64.77	6.20	6.15

Table 4 (Contd)

S.No.	Compound	Molecular formula	M.P. °C	Yield %	Nitrogen Found %	Nitrogen reqd. %	Carbon Found %	Carbon Reqd. %	Hydrogen Found %	Hydrogen Reqd. %
8.	Methylene bis-(acetoacet-p-phenitidide)	$C_{25}H_{30}O_6N_2$	188	59.0	5.82	6.16	-	-	-	-
9.	Methylene bis-(acetoacet-1:2:4-xylidide)	$C_{25}H_{30}O_4N_2$	230	68.0	6.30	6.63	-	-	-	-
10.	Methylene bis-(acetoacet-1:3:4-xylidide)	$C_{25}H_{30}O_4N_2$	202	63.3	6.59	6.63	71.14	71.06	7.14	7.16
11.	Methylene bis-(acetoacet-α-naphthylamide)	$C_{29}H_{26}O_4N_2$	214	61.6	5.86	6.00	-	-	-	-
12.	Methylene bis-(acetoacet-β-naphthylamide)	$C_{29}H_{26}O_4N_2$	208	55.0	6.01	6.00	74.60	74.66	6.08	5.62
13.	Bis-(dimedone)methane	$C_{17}H_{24}O_4$	188	-	-	-	-	-	-	-
14.	Di-2-hydroxynaphthyl-1-methane	$C_{21}H_{16}O_2$	199	-	-	-	-	-	-	-

* In (6) Found Cl = 15.92 % ; requires Cl = 16.32 %.