PART I

Sulphomethylation of acetoacet arylamides by means of sodium hydroxy methane sulphonate.

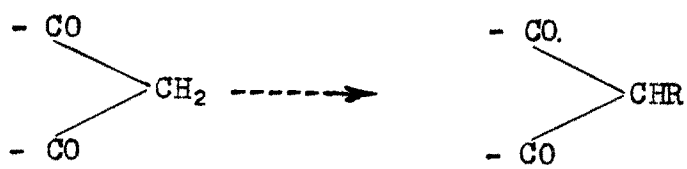
PART I

THEORETICAL

The history of the reactive methylene group goes back to the history of acetoacetic ester and compounds similarly constituted. The reactivity of the two hydrogen atoms, situated between the two carbonyl groups (- CO.CH_2.CO-) of acetoacetic ester and allied compounds, has been advantageously utilised in the synthesis of a large number of organic derivatives (1).

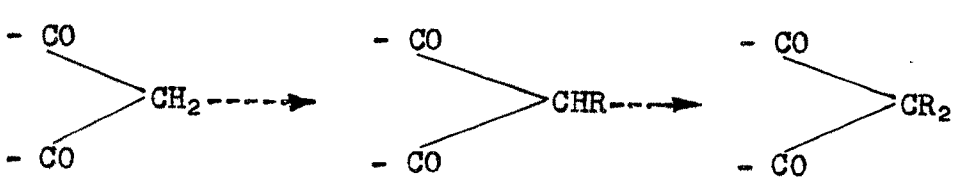
The reaction of compounds containing a reactive methylene group can be conveniently classified as under :-

Class I The reactions in which only one of the two hydrogen atoms of the reactive methylene group is replaced by the substituent,

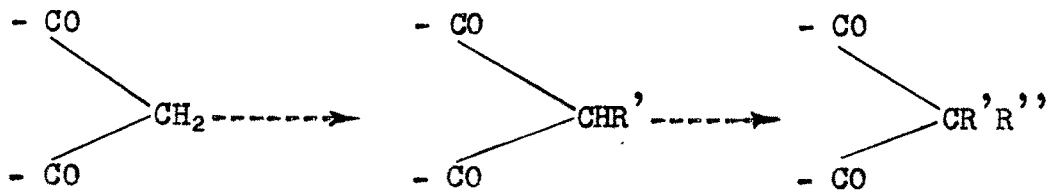


the second hydrogen atom being unaffected even by the excess of the reagent.

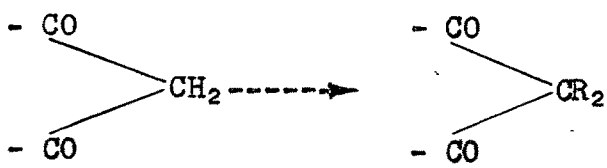
Class II The reactions in which the graduated substitution of the hydrogen atoms of the reactive methylene group is involved,



or



Class III The reactions in which both the hydrogen atoms of the reactive methylene group are simultaneously replaced :-



Examples of class I

The metallic derivatives of acetoacetic ester, though few in number illustrate this class very well. The reaction of acetoacetic ester with metallic sodium results in the formation of a monosodium derivative. Ammonical copper sulphate reacts with acetoacetic ester, giving a compound $Cu\ (C_6H_9O_3)_2$ (2). The same compound is also obtained by the action of aqueous copper acetate on etherial solution of acetoacetic ester (3).

Acid chlorides like sulphur dichloride and thionyl chloride react with acetoacetic ester, giving a monosubstituted product, $S.[CH.(CO.CH_3).COOC_2H_5]_2$ (4) (5).

Malonic ester $CH_2(COOR)_2$, where, R stands for methyl or ethyl groups, forms sodium malonic ester (6) (7).

Ethyl cyanoacetate and cyanoacetamide also give mono-sodium derivatives (8) (9). The mono-sodium derivatives of some cyanacet arylamides have been prepared by Naik and Shah (10).

Naik, Trivedi and Mankad (11) prepared mono chloro acetoacet arylamides and Desai M.N. (12) prepared mono bromo cyanacet arylamides. Mehta, Trivedi and Patel (13) prepared mono bromo acetoacet arylamides. Sodium acetoacet arylamide methane sulphonates have also been prepared by Mehta and Trivedi (14) by the interaction of sodium hydroxy methane sulphonate with acetoacet arylamides. Mehta and Parimoo (15) prepared isonitroso derivatives of malon mono arylamides using nitrosyl chloride as a nitrosating agent.

Examples of class II

On bromination of methyl malonate, monobromo methyl ester is formed (16) ; while on further bromination in presence of diffused daylight in cold dibromo-methyl ester - $CBr_2(COOMe)_2$ is formed (17). Malonic acid forms its mono-chloro derivatives by the action of one molecule of sulphuryl chloride in dry ether, while with two molecules, on heating, dichloromalonic acid is obtained (18).

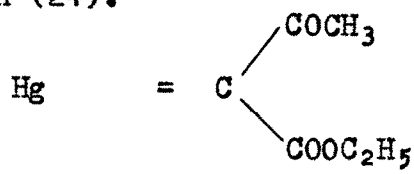
By bromination of malonic acid in acetic acid solution mono-bromo-malonic acid is formed (19) ; while by the action of bromine in chloroform solution dibromo acid results (20).

Dibromomalonamide is formed by the action of two moles of bromine on a hot ($70-80^{\circ}$) aqueous solution of malonamide (21) ; while mono-bromomalonamide is formed by

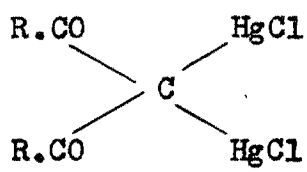
the action of bromine in acetic acid solution (22). Avasare et al. (23) prepared mono iodo and di-iodo derivatives of the substituted amides of malonic, cyanacetic and acetoacetic acids respectively using iodic acid as an oxidising agent.

Examples of class III

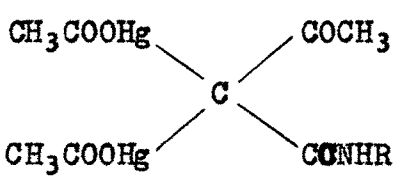
The action of acidified solution of mercuric nitrate (with nitric acid) on acetoacetic ester results in the formation of a compound of the constitution as given by Hofmann (24).



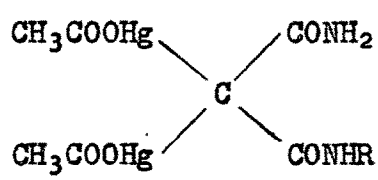
Naik and Shah (25) prepared mercury compounds of substituted amides of malonic acid by means of mercuric chloride in presence of sodium bicarbonate and glycerol and they obtained products having the general formula,



Naik and Patel (26) carried out the reaction of mercuric acetate in methyl alcohol with substituted amides of acetoacetic acid and of malonic acid which resulted in the formula (I) and (II)



(I)



(II)

Alkali nitrites react with acetoacetic ester in presence of mineral acids, giving rise to isonitroso compounds where both the hydrogen atoms of the reactive methylene group simultaneously take part in the reaction and no intermediate compound is separable (27) (28) (29) (30).

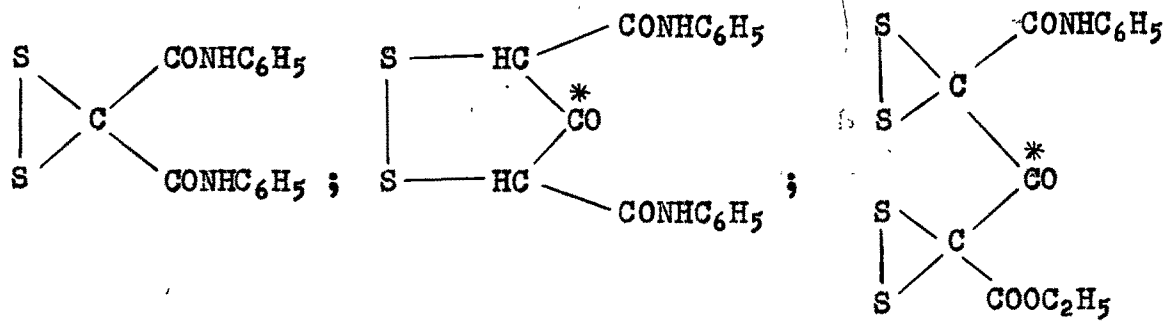
No satisfactory explanation seems to have been given for the factors which govern the reactivity of the hydrogen atoms of the reactive methylene group. It is not known as to why, the second hydrogen atom of the compounds of class (I) cannot be replaced by the same group, though it can be substituted by other radicals (31) (32). The factors, governing the successive replacement as in class (II), as well as the simultaneous replacement of the two hydrogen atoms of the reactive methylene group as in class (III) above, are also unknown.

From time to time three main views have been advanced to account for the reactivity of the hydrogen atoms of the reactive methylene ($-CH_2-$) group. Macbeth and his collaborators have based their explanation on the polarity of the oxygen atoms (33) (34).

According to one view, the reactivity depends upon the keto-enol transformation, which is still the subject of discussion. Here the hydrogen atom of the methylene group is required to enolise before the reaction can take place, and if the tendency of the second hydrogen atom to tautomerise is supressed by the basic nature of the groups attached to the carbonyl group, then, in that case, only one, out of the two atoms of hydrogen, is brought into activity (35) (36) (37) (38).

Another view is yet put forward, that the reactivity of the hydrogen atoms of the reactive methylene group depends upon the combined effect of polarity, steric hindrance and structural characteristics, as would give rise to tautomerism (39) (40) (41).

In 1921 Naik (42) examined the reactivity of a number of substances containing a reactive methylene group with sulphur monochloride etc., and he showed that the total negativity of the adjoining carbonyl groups (-CO.CH_2.CO-) was one of the principal factors, which governed the reactivity of the hydrogen atoms of the reactive methylene group situated between them. It has also been noted that the reactivity of these hydrogen atoms of the reactive methylene group could be modified, either by increasing or decreasing the total negativity of the adjoining carbonyl groups. For example sulphur monochloride reacts with malonanilide and the compound (III) is obtained. But, a compound like acetonedicarboxydianilide, where the negative effect of the central carbonyl group (*) is divided between two adjacent methylene groups, is made to react with sulphur monochloride, it was shown that, only one of the two hydrogen atoms of the methylene group reacted, giving the compound (IV). Again, on increasing the total negativity of the carbonyl groups by replacing one of the aniline groups by the ester group, it was shown that both the hydrogen atoms of the reactive methylene group became reactive and the compound (V) was obtained.



(III) (IV) (V)

Since then a large amount of work has been done by Naik et al. to support this view with the help of various reagents, such as, sulphur monochloride, sulphur dichloride, sulphuryl chloride, chlorosulphonic acid, thionyl chloride, selenium tetrachloride, iodinemonochloride, mercuric chloride, mercuric acetate, sodium and nitrosyl chloride (42 to 59).

Naik and his collaborators have prepared sodium, mercury, sulphur, selenium, halogen derivatives and they have, thus, shown that the hydrogen atoms of the methylene group, situated between the two carbonyl or negative groups (-CO.CH_2.CO- ; -CO.CH_2.CN), which are characterised by multiple bonds, are active and only these hydrogen atoms of the reactive methylene groups take part in the reactions, and not the hydrogen atoms of the amido group or of the nucleus.

They have also 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 further noted that in a number of compounds of the following types (1) $CH_2(CONH_2)_2$, (2) $NH_2CO.CH_2CONHR$, (3) $CH_2(CONHR)_2$, (4) $C_2H_5O.CO.CH_2CONHR$, (5) $CH_3CO.CH_2.CONHR$, (6) $CH_2(COOC_2H_5)_2$, (7) $C_2H_5O.CO.CH_2.CN$.,

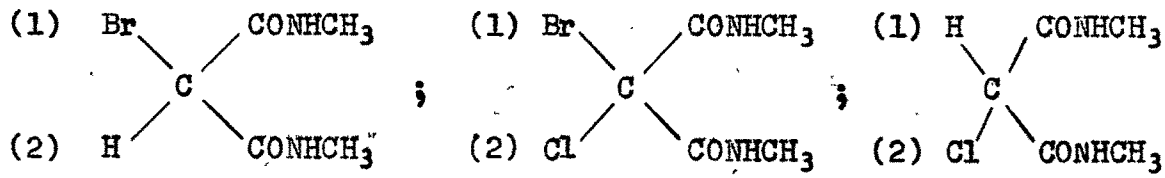
the reactivity of the hydrogen atoms, which is less pronounced in (1) becomes more and more manifest with increasing negative character of the adjoining groups upto (7) in the series.

Kotaro Shimo, Shigeru Wakamatsu and Tadao Inoue (60) have carried out the alkylation of malononitrile, cyanoacetamide and substituted cyanoacetamide in liquid ammonia using alkyl halide, where the reactive methylene group hydrogen is involved in these reactions.

While studying the preparation and the relative stability of the halogenated derivatives of the compounds, containing the reactive methylene group, it was observed that the avidity of the two hydrogen atoms for entering into reactions was not equal, a fact further substantiated by a study of the reduction of these compounds. It was actually found that under a certain set of conditions, only one of the two substituted halogen atoms could be replaced by a hydrogen atom ; while under another set of conditions, both the halogen atoms could be simultaneously replaced by hydrogen (61).

The tenacity with which each of the reactive hydrogen atom is held by the methylene carbon atom is inversely proportional to the avidity with which that hydrogen atom is thrown into activity. Arguing on these lines, it can be said, that the second halogen atom, which is more difficult to be introduced in the place of the second hydrogen atom of the methylene group, is also more difficult to be removed, when treated with a reducing agent.

If one of these hydrogen atoms is more easily replaced by a halogen, the halogen is capable of being more easily removed during the course of reduction. Further, if the second hydrogen atom is more difficultly removed, - replaced by halogen-, then the halogen atom, which was introduced later on with greater difficulty, should also be removed with more difficulty during the course of reduction. The work of West (62) fully supports this view. Thus, on chlorinating the compound (VI), the compound (VII) was obtained ; which, when reduced with hydriodic acid, the monochloro compound (VIII) was obtained,



(VI) (VII) (VIII)

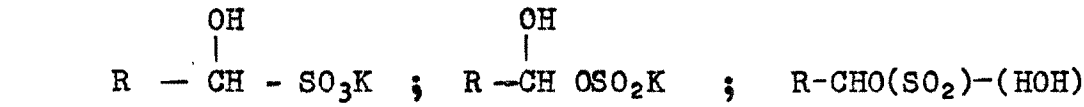
Here, the bromine atom marked (1) in the compound (VI) that came in first and with great ease, could also be reduced with greater ease as represented in (VIII), and the chlorine atom marked (2) in the compound (VII), which entered with greater difficulty, was also removed with more difficulty. Thus, it is evident, that the labile nature, i.e. the activity of the substituted halogen atoms in a reactive methylene group, bears a direct relationship to the hydrogen atoms, which originally occupied that space. Hence, the study of the labile nature of the halogeno-derivatives of the compounds, containing the reactive methylene group, can be shown to throw some light on the reactivity of the hydrogen

atoms of the reactive methylene group present in the original compound.

With a view to throw light on the activity of the hydrogen atoms of the reactive methylene group, situated between two carbonyl or negative groups, the acetoacet arylamides and cyanacet arylamides have been separately selected for study in the interaction of sodium hydroxy methane sulphonate ($OHCH_2SO_3Na$).

Sodium hydroxy-methane sulphonate :

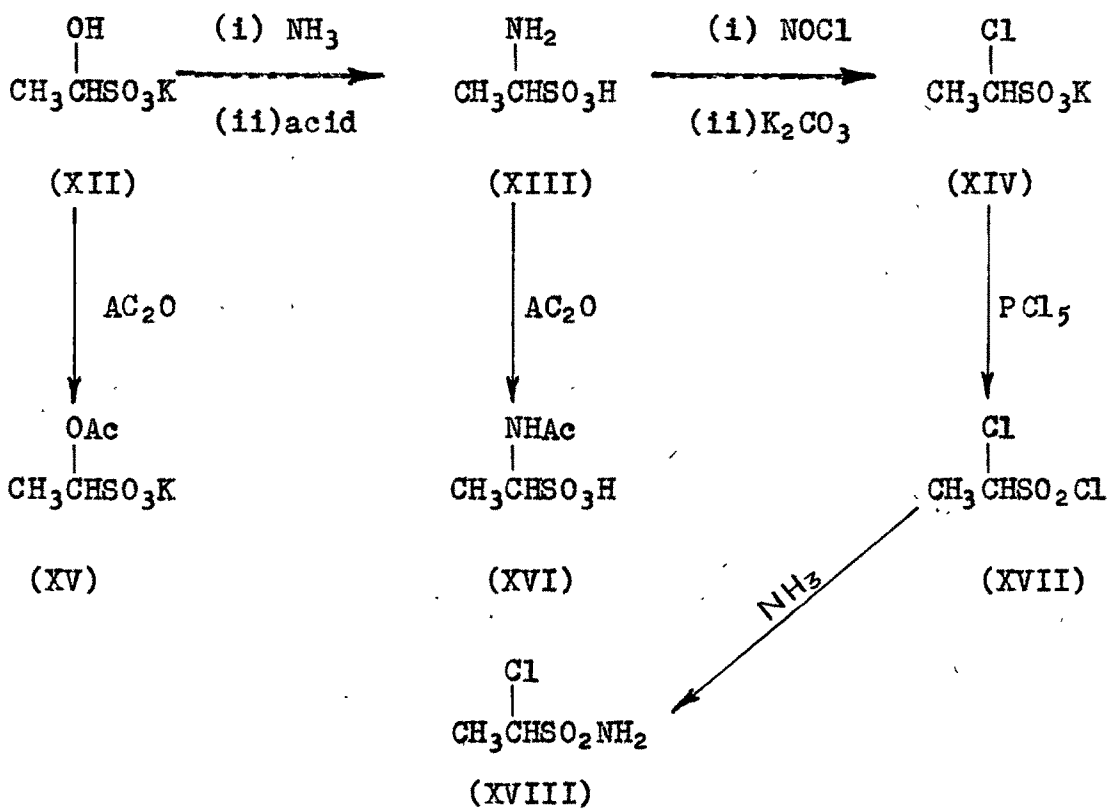
The structure of the compounds resulting from the addition of alkali metal bisulphites to aldehydes and certain ketones has been the subject of much discussion and experimentation. Various workers have, from time to time, favoured either the hydroxysulphonate structure (IX) (63) (64); the hydroxy sulphite ester formula (X) (65) (66) ; or a polymolecule formula (XI) (67) (68) as under :



(IX) ; (X) ; R-CHO(SO_2)-(HOH) (XI)

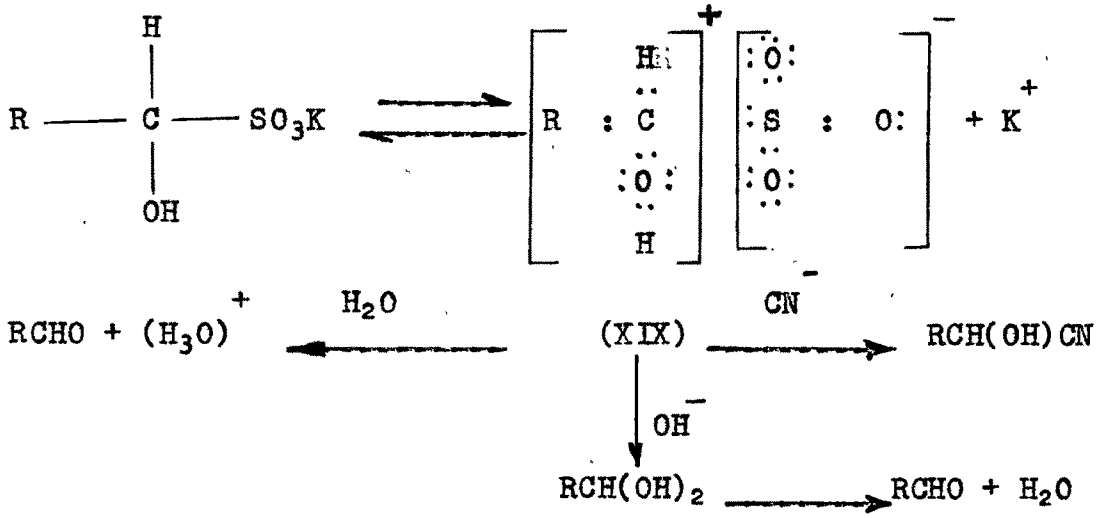
The experiments of Raschig and Prahl (69), Backer and Mulder (70) and the recent work of Lauer and Langkammerer (71) leave no doubt that the potassium bisulphite compound of formaldehyde is best represented by the hydroxysulphonate structure (IX). Sodium hydroxy methane sulphonate was, here, condensed with acetoacet arylamides, using a trace of potassium cyanide as catalyst, resulting in the formation of their sulphomethylated derivatives.

Shriner and Land (72) for the above purpose to show the structure of type (IX) treated either sodium or potassium bisulphite compound of acetaldehyde (XII) with concentrated ammonia and subsequent acidification yielded α-aminoethanesulphonic acid (XIII). Nitrosyl chloride at $0^{0}C$ converted this aminosulphonic acid into α-chloro-ethanesulphonic acid, which was neutralised with potassium carbonate and isolated as the potassium salt (XIV). The compounds (XII) and (XIII) have been acetylated and their acetyl derivatives (XV) and (XVI) are far more stable than the original hydroxy and amino compounds. The compound (XIV), on treatment with phosphorus pentachloride, gave α-chloro-ethane sulphonyl chloride (XVII), which with ammonia gave α-chloroethane sulphonamide (XVIII).



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.

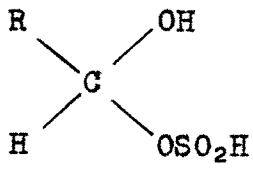
If the initial step in the dissociation of this bisulphite compound results in the following ions,



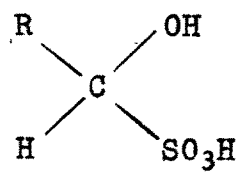
the carbonium ion (XIX) may easily stabilize itself by loss of a proton to the solvent-water, and thus regenerate the aldehyde. It could also combine with a hydroxyl ion forming an aldehyde hydrate which could then lose water. Both of these reactions would be sensitive to the Pʜ of the solution. In the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

Lauer and Langkammerer (71) 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) of these compounds,

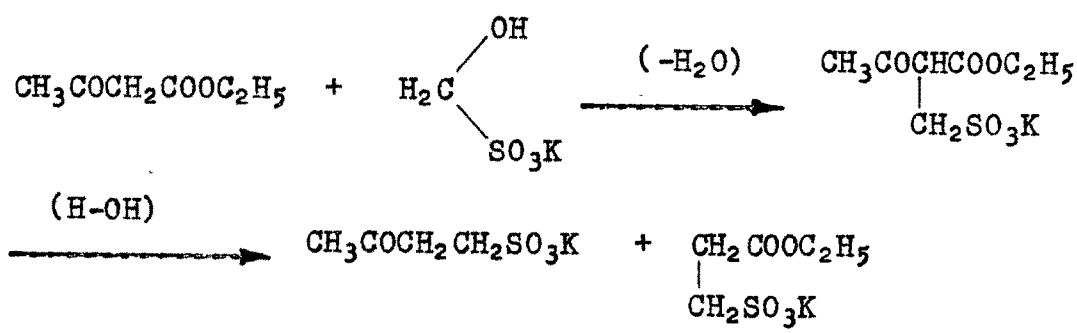


(a)

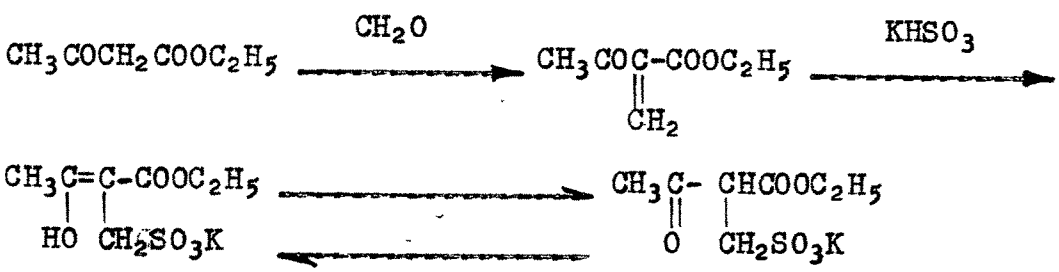


(b)

but for proving α-hydroxysulphonic acid structure (b), Raschig and Prahl (69) 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 (73) 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 (69) 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 reactive hydrogen atom by an alkali sulphomethyl group $-(-CH_2SO_3M)$.

Suter, Bair and Bordwell (74) carried out the sulphomethylation reaction of the 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

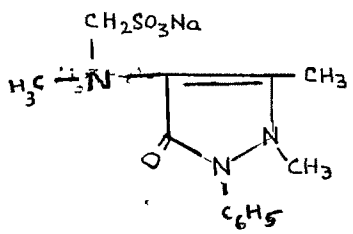
formaldehyde and sodium sulphite gave sodium 2-hydroxy-1-naphthylmethanesulphonate.

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.

Knoll (75) condensed p-(acylamino)benzene sulphonamides with formaldehyde and sodium bisulphite for about 24 hours and obtained, p-$NH_2C_6H_4SO_2NHCH_2SO_3H$, a useful intermediate in the preparation of a number of compounds.

Mehta and Patel (76) carried out the reaction of acetoacet arylamides with sodium hydroxymethane sulphonate without using potassium cyanide as catalyst and got the methylene bis-(acetoacet arylamides), the formation of which supports the process of Suter, Bair and Bordwell(74) as well as that of Shearing and Smiles (77) discussed in Part II.

Schwarz et al. (78) treated a secondary aromatic-aliphatic amine with CH_2O and bisulphite and obtained Na-1-phenyl-2,3-dimethyl-5-pyrazolone-4-methylaminomethyl sulphite (XX) and Na-N-methyl-p-phenitidinemethyl-sulphite (XXI). Methylene bis-1-phenyl-2,3-dimethyl-4-methylamino-5-pyrazolone (XXII) is also obtained by heating with CH_2O, the mixture of amines produced by methylating 1-phenyl-2,3-dimethyl-4-amino-5-pyrazone ; while methylenebis-N-methyl phentidine (XXIII) is obtained by treating with formaldehyde the crude N-methylphenitidine obtained by methylating phenitidine.



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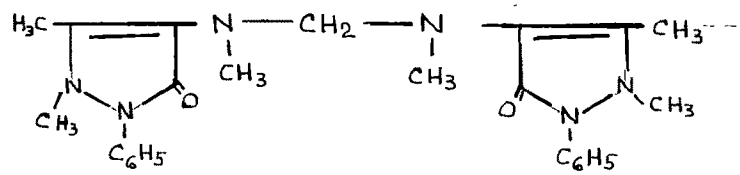

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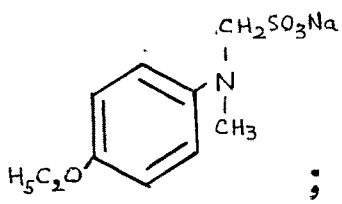

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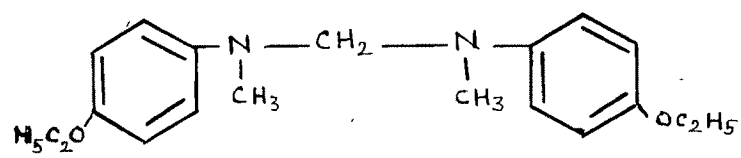
(XXI)



(XXIII)

Robert Lepetit (79) prepared sodium-p-ethoxy phenylaminomethane sulphonate ($EtO.C_6H_4NHCH_2SO_3Na.H_2O$) from $NaHSO_3$ acting on a molecular mixture of formaldehyde and p-phentidine in water-alcohol at 75-80^{0}C. The work was extended to the sodium aminomethane sulphonate derivatives

of aniline,o-toluidine,xylidine,o-anisidine, α- and β - naphthlamine and o-chloroaniline. Knoevenagel and Mercklin (80) prepared di-ethylamino acetonitrile from a mixture of CH_2O and $NaHSO_3$ in the presence of NaCN and $(C_2H_5)_2NH$.

Riesz et al. (81) 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 sodium-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 (82).

Sulphomethylation of acetoacetarylamides

Here, in part I acetoacet arylamides, which contain the reactive methylene group, have been treated with sodium hydroxy methane sulphonate. Reactions with potassium hydroxy methane sulphonate with compounds containing reactive methylene group have been found to give sulphomethylated products (69). This work gave an impetus to investigate the interaction between sodium hydroxy methane sulphonate and acetoacet arylamides, in presence of a trace of potassium cyanide as catalyst, where the expected sulphomethylated product was obtained.

The required acetoacet arylamides were prepared by the method of Ewins and King (83) by refluxing the primary

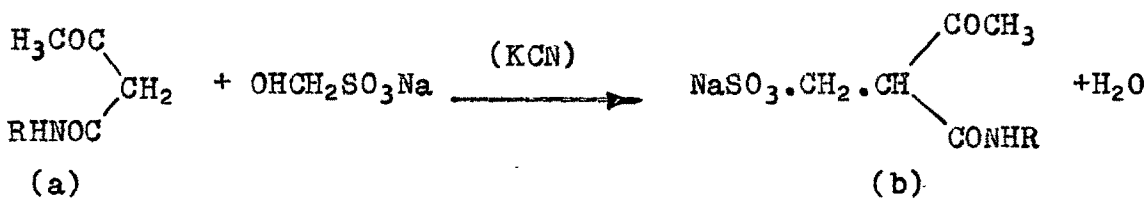
amines and ethyl acetoacetate for one and half minutes, as modified by Naik et al. (56) (59).

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 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 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 sodium acetoacet arylamides methane sulphonate.

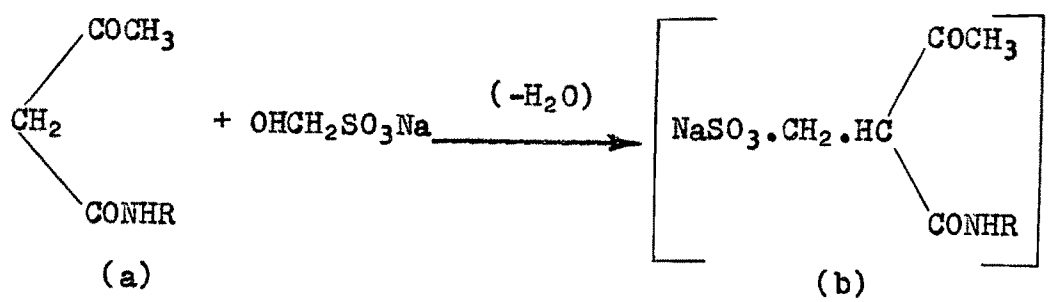
One mole of acetoacet arylamide (a) dissolved in alcohol and one mole of sodium hydroxy methane sulphonate in presence of small amount of aqueous solution containing a trace of potassium cyanide as catalyst were refluxed in ethyl alcohol for half an hour on a sand-bath. A white product (b), which appeared on cooling, was filtered and crystallised from water in white needles. A number of other sulphomethylated products of acetoacet arylamides were similarly prepared (14).

The reaction may be expressed as under :-



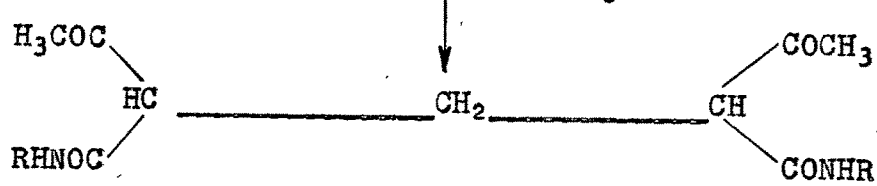
(Where, R is phenyl,tolyl,xylyl and naphthyl groups).

The above sulphomethylated acetoacet arylamides (b) are the intermediate products formed during the preparation of methylene bis-(acetoacet arylamides), which are prepared by Mehta and Patel (76) without using potassium cyanide as catalyst. They have shown that when acetoacet arylamide (a) reacts with sodium hydroxy-methane sulphonate, there will be, in the first course of reaction, the elimination of water, giving the product (b), which simultaneously interacts with (a), yielding the corresponding methylene bis-derivative (XXIV) with the elimination of sodium bisulphite, and the overall reaction is expressed as:



(a) + (b)

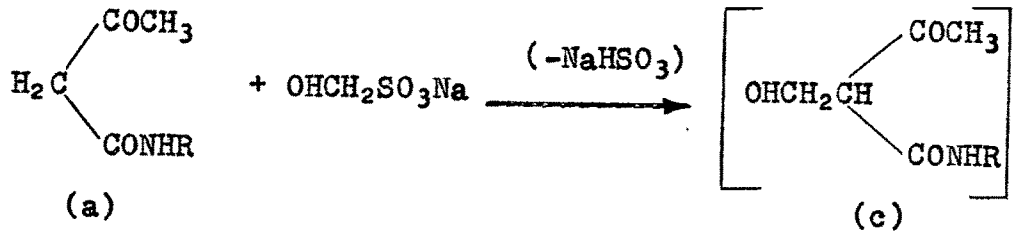
$-NaHSO_3$

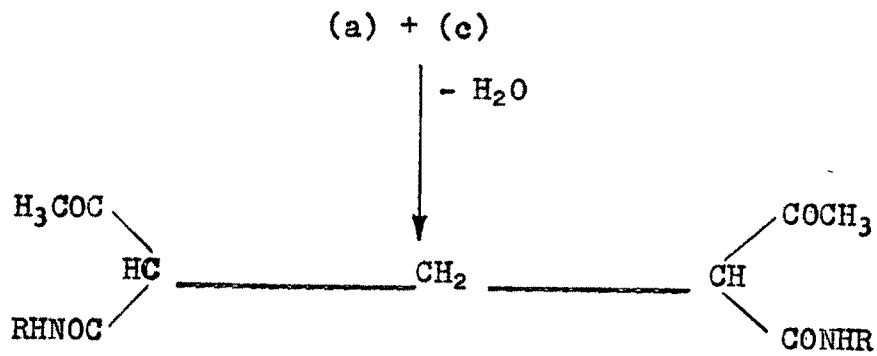


(XXIV)

The second course of reaction is explained by the elimination first of sodium bisulphite by the intermediate formation of hydroxy methyl derivative of acetoacet arylamide (c) with which the reactive hydrogen atom of the unreacted molecule of the amide (a),

simultaneously, interacts with the elimination of water yielding only the corresponding methylene-bis-derivatives as under :-

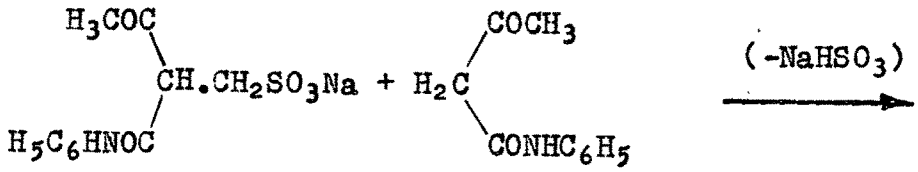




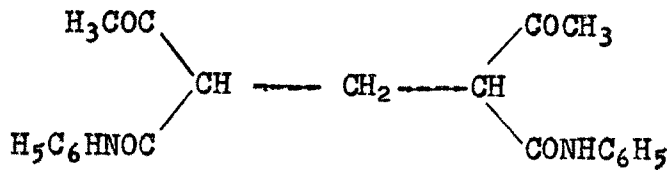
(XXIV)

But, a number of sulphomethylated acetoacet arylamides, which are found to be the intermediate products of the above first course of reaction (b), have been isolated. This proves clearly that the formation of hydroxy methyl derivative of acetoacet arylamides through which the bis-derivatives (XXIV) are also obtained, is not possible. Moreover, in order to varify the above fact incorporated in the present work, one mole of sodium acetoacet anilide methane sulphonate (e) was condensed here with one mole of acetoacet anilide (d) and the product,thus, prepared was found to be identical when compared with methylene bis-(acetoacetanilide) (XXV) obtained by Mehta and Patel (76) by condensing two moles of acetoacetanilide with one mole

of sodium hydroxy methane sulphonate without using potassium cyanide as catalyst.

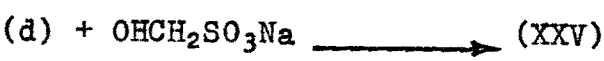


(e) (d)



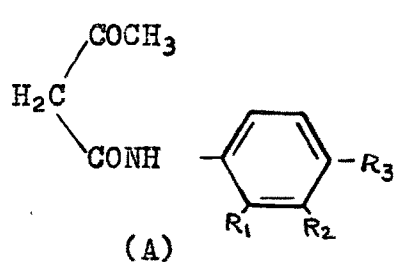
(XXV)

It may,here, be pointed out that one mole of acetoacet anilide (d), without using potassium cyanide as catalyst, when condensed with one mole of sodium hydroxy methane sulphonate, gave the same methylene bis-(-acetoacet anilide) (XXV).



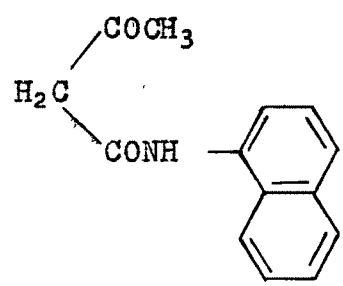
Thus, in part I the formation of sulphonates of acetoacet arylamides and in part II that of bis-derivatives of cyanacet arylamides have been described.

The following acetoacetarylamides required for sulphomethylation are prepared :

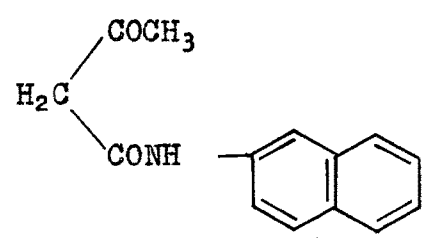


(A)

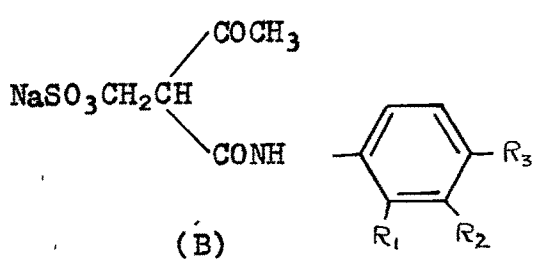
1. Acetoacetanilide (A, $R_1=R_2=R_3=H$)
2. Acetoacet-o-chloroanilide (A, $R_1=Cl$; $R_2=R_3=H$)
3. Acetoacet-m-chloroanilide (A, $R_2=Cl$; $R_1=R_3=H$)
4. Acetoacet-p-chloroanilide (A, $R_3=Cl$; $R_1=R_2=H$)
5. Acetoacet-o-toluidide (A, $R_1=CH_3$; $R_2=R_3=H$)
6. Acetoacet-p-toluidide (A, $R_3=CH_3$; $R_1=R_2=H$)
7. Acetoacet-o-anisidide (A, $R_1=OCH_3$; $R_2=R_3=H$)
8. Acetoacet-p-phenitidide (A, $R_3=OC_2H_5$; $R_1=R_2=H$)
9. Acetoacet-1:2:4-xylidide (A, $R_1=R_3=CH_3$; $R_2=H$)
10. Acetoacet-1:3:4-xylidide (A, $R_2=R_3=CH_3$; $R_1=H$)
11. Acetoacet-α-naphthylamide



12. Acetoacet-β-naphthylamide



The following sulphomethylated derivatives from acetoacet arylamides are prepared from the above mentioned acetoacet arylamides :



(B)

1. Sodium acetoacetanilide methane sulphonate .

   (B, $R_1=R_2=R_3=H$)

2. Sodium acetoacet-o-chloroanilide methane sulphonate.

   (B, $R_1=Cl$; $R_2=R_3=H$)

3. Sodium acetoacet-m-chloroanilide methane sulphonate.

   (B, $R_2=Cl$; $R_1=R_3=H$)

4. Sodium acetoacet-p-chloroanilide methane sulphonate.

   (B, $R_3=Cl$; $R_1=R_2=H$)

5. Sodium acetoacet-o-toluidide methane sulphonate.

   (B, $R_1=CH_3$; $R_2=R_3=H$)

6. Sodium acetoacet-p-toluidide methane sulphonate.

   (B, $R_3=CH_3$; $R_1=R_2=H$)

7. Sodium acetoacet-o-anisidide methane sulphonate.

   (B, $R_1=OCH_3$; $R_2=R_3=H$)

8. Sodium acetoacet-p-phenitidide methane sulphonate.

   (B, $R_3=OC_2H_5$; $R_1=R_2=H$)

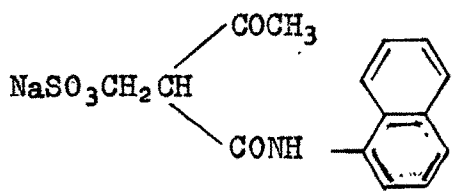
9. Sodium acetoacet-1:2:4-xylidide methane sulphonate.

   (B, $R_1=R_3=CH_3$; $R_2=H$)

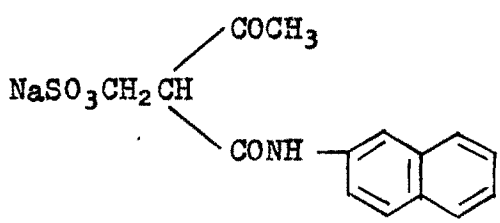
10. Sodium acetoacet-1:3:4-xylidide methane sulphonate.

    (B, $R_2=R_3=CH_3$; $R_1=H$)

11. Sodium acetoacet-α-naphthylamide methane sulphonate.



12. Sodium acetoacet-β-naphthylamide methane sulphonate



EXPERIMENTAL

Sodium acetoacetanilide methane sulphonate

Acetoacetanilide (1.77 g. ; 0.01 M) was dissolved in ethyl alcohol (10 ml.) to which an aqueous solution (2 ml.) of sodium hydroxy methane sulphonate (1.34 g. ; 0.01 M), in presence of a trace of potassium cyanide as catalyst, was added ; and the reaction mixture was refluxed on a sand-bath for half an hour during which time voluminous precipitates from the reaction mixture were obtained. The reaction mixture was then filtered and the product was crystallised from water in white shining needles. M.P.> 300°C.
Yield 1.56 g.

Analysis :

9.162 mg. of the substance gave 0.367 c.c. of nitrogen at 33°C and 754 mm. pressure.

Found : N = 4.43 %.

$C_{11}H_{12}O_5NSNa$ requires : N = 4.74 %.

Sodium acetoacet-o-chloroanilide methane sulphonate

Acetoacet-o-chloroanilide (2.11 g.) dissolved in ethyl alcohol and aqueous solution of sodium hydroxy methane sulphonate (1.34 g.) in presence of a trace of potassium cyanide, were treated as above. The product was crystallised from water in white shining crystals. M.P. 195°C (decomp.).
Yield 1.45 g.

Analysis :

7.202 mg. of the substance gave 0.286 c.c. of nitrogen at 39°C and 751 mm. pressure.

Found : N = 4.29 %.

$C_{11}H_{11}O_5NSClNa$ requires : N = 4.28 %.

Sodium acetoacet-m-chloroanilide methane sulphonate

Acetoacet-m-chloroanilide (2.11 g.) dissolved in ethyl alcohol and aqueous solution of sodium hydroxy methane sulphonate (1.34 g.) with a trace of potassium cyanide as catalyst were treated as before. The product was crystallised from water in white shining crystals. M.P. > 300°C. Yield 1.7 g.

Analysis :

8.596 mg. of the substance gave 0.316 c.c. of nitrogen at 28°C and 747 mm. pressure.

Found : N = 4.10 %.

$C_{11}H_{11}O_5NSClNa$ requires : N = 4.28 %.

Sodium acetoacet-p-chloroanilide methane sulphonate

Acetoacet-p-chloroanilide (2.11 g.) dissolved in ethyl alcohol and aqueous solution of sodium hydroxy methane sulphonate (1.34 g.), in presence of a trace of potassium cyanide as catalyst, were treated as above. White shining crystals were obtained when crystallised from water. M.P. >300°C. Yield 1.5 g.

Analysis :

8.500 mg. of the substance gave 0.336 c.c. of nitrogen at 30°C and 746 mm. pressure.

Found : N = 4.37 %.

$C_{11}H_{11}O_5NSClNa$ requires : N = 4.28 %.

Sodium acetoacet-o-toluidide methane sulphonate

Acetoacet-o-toluidide (1.91 g.) dissolved in ethyl alcohol and aqueous solution of sodium hydroxy methane

sulphonate (1.34 g.) with a trace of potassium cyanide as catalyst, were treated as above. The product was crystallised from water in white shining crystals. M.P. 235°C (decomp.). Yield 1.7 g.

Analysis :

7.436 mg. of the substance gave 0.316 c.c. of nitrogen at 38°C and 752 mm. pressure.

Found : N = 4.61 %.

$C_{12}H_{14}O_5NSNa$ requires : N = 4.56 %.

Sodium acetoacet-p-toluidide methane sulphonate

Acetoacet-p-toluidide (1.91 g.) dissolved in ethyl alcohol and aqueous solution of sodium hydroxy methane sulphonate (1.34 g.) with a trace of potassium cyanide as catalyst, were treated as above. The pure product was obtained when crystallised from water in white shining crystals. M.P. > 300°C. Yield 1.65 g.

Analysis :

10.240 mg. of the substance gave 0.395 c.c. of nitrogen at 32°C and 754 mm. pressure.

15.094 mg. of the same substance gave 11.790 mg. of barium sulphate.

Found : N = 4.28 % ; S = 10.73 %.

$C_{12}H_{14}O_5NSNa$ requires : N = 4.56 % ; S = 10.42 %.

Sodium acetoacet-o-anisidide methane sulphonate

Acetoacet-o-anisidide (2.07 g.) dissolved in ethyl alcohol and aqueous solution of sodium hydroxy methane sulphonate (1.34 g.) in presence of a trace of potassium cyanide as catalyst, were treated as above. The product was crystallised from water in shining crystals. M.P.270°C(decomp.). Yield 1.55 g.

Analysis :

7.114 mg. of the substance gave 0.267 c.c. of nitrogen at 32°C and 752 mm. pressure.

Found : N = 4.16 %.

$C_{12}H_{14}O_6NSNa$ requires : N = 4.33 %.

Sodium acetoacet-p-phenitidide methane sulphonate

Acetoacet-p-phenitidide (2.21 g.) dissolved in ethyl alcohol and aqueous solution of sodium hydroxy methane sulphonate (1.34 g.) with a trace of potassium cyanide as catalyst, were treated as above. The product was crystallised from water in white shining crystals. M.P. > 300°C. Yield 1.86 g.

Analysis :

6.442 mg. of the substance gave 0.222 c.c. of nitrogen at 31°C and 752 mm. pressure.

11.876 mg. of the same substance gave 8.578 mg. of barium sulphate.

Found : N = 3.83 % ; S = 9.92 %.

$C_{13}H_{16}O_6NSNa$ requires : N = 4.12 % ; S = 9.50 %.

Sodium acetoacet-1:2:4-xylidide methane sulphonate

Acetoacet-1:2:4-xylidide (2.05 g.) dissolved in ethyl alcohol and aqueous solution of sodium hydroxy methane sulphonate (1.34 g.) with a trace of potassium cyanide as catalyst, were treated as above. The product was crystallised from water in shining white crystals. M.P. 205°C (decomp.). Yield 1.8 g.

Analysis :

8.26 mg. of the substance gave 0.481 c.c. of nitrogen at 33°C and 755 mm. pressure.

Found : N = 4.45 %.

$C_{13}H_{16}O_5NSNa$ requires : N = 4.36 %.

Sodium acetoacet-1:3:4-xylidide methane sulphonate

Acetoacet-1:3:4-xylidide (2.05 g.) dissolved in ethyl alcohol and aqueous solution of sodium hydroxy methane sulphonate (1.34 g.) in presence of a trace of potassium cyanide as catalyst, were treated as above. The product was crystallised from water in bright white crystals. M.P. 196°C (decomp.). Yield 1.75 g.

Analysis :

6.930 mg. of the substance gave 0.266 c.c. of nitrogen at 38°C and 753 mm. pressure.

Found : N = 4.17 %.

$C_{13}H_{16}O_5NSNa$ requires : N = 4.36 %.

Sodium acetoacet-α-naphthylamide methane sulphonate

Acetoacet-α-naphthylamide (2.27 g.) dissolved in ethyl alcohol and aqueous solution of sodium hydroxy methane sulphonate (1.34 g.) in presence of a trace of potassium cyanide as catalyst, were treated as above. The product was crystallised from water in bright shining crystals. M.P. 230°C (decomp.). Yield 2.0 g.

Analysis :

8.850 mg. of the substance gave 0.316 c.c. of nitrogen at 31°C and 747 mm. pressure.

Found : N = 3.94 %.

$C_{15}H_{14}O_5NSNa$ requires : N = 4.08 %.

Sodium acetoacet-β-naphthylamide methane sulphonate

Acetoacet-β-naphthylamide (2.27 g.) dissolved in ethyl alcohol and aqueous solution of sodium hydroxy methane sulphonate (1.34 g.) with a trace of potassium cyanide as catalyst, were treated as above. The product was crystallised from water in bright white crystals. M.P. > 300°C. Yield 1.95 g.

Analysis :

9.570 mg. of the substance gave 0.346 c.c. of nitrogen at 30°C and 746 mm. pressure.

13.702 mg. of the same substance gave 9.780 mg. of barium sulphate.

Found : N = 4.00 % ; S = 9.80 %.

$C_{15}H_{14}O_5NSNa$ requires : N = 4.08 % ; S = 9.33 %.

Methylene bis-(acetoacetanilide)

Acetoacetanilide (1.7 g. ; 0.01 M) dissolved in 20 ml. methyl alcohol, was added to a solution of sodium acetoacetanilide methane sulphonate in 5 ml. of water (2.9 g. ; 0.01 M). The reaction mixture was then refluxed on a sand-bath for three hours. 50 ml. of water were added to it at room temperature, and the resulting product was filtered and crystallised from acetic acid. M.P. 212°C.

The identity of methylene bis-(acetoacetanilide) was established by comparing its melting point with that of the authentic sample.

Table 1

Sodium acetoacetarylamide methane sulphonates

S.No.	Compound	Molecular formula	M.P. °C	Yield %	Nitrogen Found %	Nitrogen reqd. %	Sulphur Found %	Sulphur reqd. %
1.	Sodium acetoacetanilide-methane sulphonate	$C_{11}H_{12}O_5NSNa$	> 300	53.23	4.43	4.74	-	-
2.	Sodium acetoacet-o-chloroanilide-methane sulphonate	$C_{11}H_{11}O_5NSClNa$	195	44.35	4.29	4.28	-	-
3.	Sodium acetoacet-m-chloroanilide - methane sulphonate	$C_{11}H_{11}O_5NSClNa$	> 300	51.99	4.10	4.28	-	-
4.	Sodium acetoacet-p-chloroanilide-methane sulphonate	$C_{11}H_{11}O_5NSClNa$	> 300	45.87	4.37	4.28	-	-
5.	Sodium acetoacet-o-toluidide-methane sulphonate	$C_{12}H_{14}O_5NSNa$	235	55.38	4.61	4.56	-	-
6.	Sodium acetoacet-p-toluidide-methane sulphonate	$C_{12}H_{14}O_5NSNa$	> 300	53.75	4.28	4.56	10.73	10.42

Table 1 (Contd.)

S.No.	Compound	Molecular formula	M.P. °C	Yield %	Nitrogen Found %	Nitrogen reqd. %	Sulphur Found %	Sulphur reqd. %
7.	Sodium acetoacet-o-anisidide - methane sulphonate	$C_{12}H_{14}O_6NSNa$	270	47.98	4.16	4.33	-	-
8.	Sodium acetoacet-p-phenitidide - methane sulphonate	$C_{13}H_{16}O_6NSNa$	>300	55.20	3.83	4.12	9.92	9.50
9.	Sodium acetoacet-1:2:4-xylidide- methane sulphonate	$C_{13}H_{16}O_5NSNa$	205	56.08	4.45	4.36	-	-
10.	Sodium acetoacet-1:3:4-xylidide- methane sulphonate	$C_{13}H_{16}O_5NSNa$	196	54.50	4.17	4.36	-	-
11.	Sodium acetoacet-α-naphthylamide- methane sulphonate	$C_{15}H_{14}O_5NSNa$	230	58.30	3.94	4.08	-	-
12.	Sodium acetoacet-β-naphthylamide methane sulphonate	$C_{15}H_{14}O_5NSNa$	>300	56.71	4.00	4.08	9.80	9.33

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