THE ENOLISATION OF CARBONYL COMPOUNDS UNDER THE INFLUENCE OF GRIGNARD'S REAGENTS.

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I. Introduction.

The enolisation of beta-diketones and of esters of beta-ketonic acids is a well known phenomenon and such compounds are usually selected as some of the best examples for illustrating the characteristics of tautomeric substances. Within recent years various chemical methods of estimating the percentage of the enolic form present in any one of these compounds have been recommended. One of the most interesting of these is that due to K. H. Meyer (*Annalen*, 1911, *380*, 212; *Ber.*, 1911, *44*, 2718) who states that the enolic form reacts instantaneously with an alcoholic bromine solution yielding an unstable dibromide which loses hydrogen bromide forming a bromo-ketone :—

$$\text{-C(OH):CH-} \rightarrow \text{-CBr(OH)·CHBr-} \rightarrow \text{-CO·CHBr-}$$

The amount of bromo-ketone formed can be estimated by adding potassium iodide solution and titrating the liberated iodine by means of standard thiosulphate :—

$$\text{-CO·CHBr-} \rightarrow \text{-CI(OH)· CHBr-} \rightarrow \text{-CI(OH)· CHI-}$$
$$\rightarrow \text{-C(OH) : CH} + \text{I}_2.$$

Knorr and Schubert make use of the colour which the enolic form gives with ferric chloride (*Ber.*, 1911, *44*, 2772) and Scheiber and Herold (Ber., 1913, *46*, 135) recommend the use of ozone, as the enolic form readily yields an ozonide which can be decomposed by water and the products determined quantitatively.

It is clear that these chemical methods are only of use if it is certain that the reagents employed, e. g., bromine solution, ferric chloride solution and ozone, do not affect the keto-enolic equillibrium, and in each of the above mentioned cases the authors claim that the reagent used has no effect.

Other chemical reagents have a pronounced enolising effect and probably the commonest of these are alkalis which tend to produce the alkali derivatives of the enolic form e. g., $CH_3\cdot C(ONa) : CH\cdot CO_2Et$. Magnesium methyl iodide also has an enolising effect. Although ethyl aceto-acetate contains only about 7 per cent. of the enolic form, it reacts with an amyl ether solution of magnesium methyl iodide yielding a volume of methane corresponding with 90 per cent. of enol (Hibbert and Sudborough, J. C. S., 1904, *85*, 936). The production of the large volume of methane is undoubtedly to be attributed to the presence of an active hydrogen atom due to the rapid transformation of the ketonic into the enolic form under the influence of the Grignard reagent.

There are numerous reactions which point to the conclusion that ordinary aldehydes and ketones can also undergo a change into the enolic forms :—

$$R\cdot CH_2\cdot CH : O \rightarrow R\cdot CH : CH\cdot OH$$

and

$$R\cdot CH_2\cdot CO\cdot R \rightarrow R\cdot CH{:}C\cdot(OH)R$$

The probable enolisation of ketones during the process of chlorination was first clearly pointed out by Lapworth (J. C. S., 1904, *85*, 30) in his study of the action of halogens on acetone.

He represents the reaction as taking place in the following stages :—

$$CH_3\cdot CO\cdot CH_3 \rightarrow CH_3\cdot C(OH) : CH_2 \rightarrow CH_3\cdot CCl\ (OH)\cdot CH_2Cl \rightarrow CH_3\cdot CO\cdot CH_2Cl + HCl.$$

. Dawson and his co-workers conclude that a similar series of changes occurs during the chlorination of aldehydes (J. C. S. 1909, *95*, 1860; 1914, *105*, 387, 532) and they show that mineral acids accelerate halogenation, presumably by accelerating the enolisation of the aldehyde.

The formation of mono acetyl derivatives, $R. CH : CH. OAc$, and of diacetyl derivatives, $R\cdot CH_2\cdot CH\ (OAc)_2$ by the action of acetic anhydride and sulphuric acid on aldehydes (Semmler, Ber., 1909, *42*, 584; Wohl and Berthold, ibid., 1910, *43*, 2184; Wegsceider and Sparth, Monats, 1909, *30*, 825; Wohl and Maag, Ber, 1910, *43*, 3291) has been used as an argument in favour of the enolisation of aldehydes during the reaction.

The reaction between phosphorus pentachloride and ketones also indicates enolisation in certain cases (Favorski, J. C. S. Abs. 1913, *1*, 12). With most ketones the reagent yields dichloro-derivatives in which the oxygen atom of the carbonyl group has become replaced by two chlorine atoms $R\cdot CO\cdot R \rightarrow R\cdot CCl_2\cdot R$. In the case of di-isopropyl ketone, however, a chlorinated ketone,

$CClMe_2 \cdot CO \cdot CHMe_2$, is formed. The author accounts for the formation of this product by the following series of reactions :—

$$CHMe_2 \cdot CO \cdot CHMe_2 \rightarrow CMe_2 : C(OH) \cdot CHMe_2 \rightarrow$$
$$CClMe_2 \cdot CCl(OH) \cdot CHMe_2 \rightarrow CClMe_2 \cdot CO \cdot CHMe_2.$$

The sodium derivatives of ketones and aldehydes are derived from the enolic forms of these compounds (Freer, Amer. Chem. J., 1890, *12*, 355 ; 1891, *13*, 319 ; 1898, *18*, 532).

The object of the investigation described in this paper has been to ascertain to what extent ordinary aldehydes and ketones are enolised in the presence of Grignard reagents. The method adopted has been exactly analagous to that used by Hibbert and Sudborough in estimating hydroxyl groups in carbon compounds (loc. cit.) It consists in measuring the volume of gas (methane) produced when a known weight of the substance is brought into contact with an excess of magnesium methyl iodide solution. As slight variations in temperature affect the vapour pressure of ethyl etheral solutions to an appreciable extent, all the experiments were performed in pure amyl ether solutions, and, to obviate the small errors due to the absorption of moisture, carbon dioxide and oxygen, the apparatus was filled with pure dry nitrogen in each case.

The substances used were chloral, propaldehyde, *n*-and *iso*-butaldehyde, *iso*-valeraldehyde, cinnamaldehyde, acetone, benzyl *p*-tolyl ketone, dibenzylideneacetone, and in addition the following beta diketones and beta ketonic esters :—acetylacetone, benzoylacetone, ethyl acetosuccinate, ethyl benzoylacetate and ethyl acetonedicarboxylate.

II EXPERIMENTAL.

(a) *Preparation and purification of materials.* The amyl ether required for the experiments was prepared from commercial *iso*-amyl alcohol (b. p. 128-130°) by Schröter and Sondag's method (Ber , 1908, *41*, 1924) and after fractionation was treated successively with calcium chloride, sodium, a little magnesium methyl iodide, sodium and phosphorus pentoxide and finally redistilled. The treatment with sodium in each case consisted in boiling the ether with sodium wire for 7-8 hours. The Grignard reagent was prepared as described by Hibbert and Sudborough and the nitrogen by the method given by Lupton (Chem. News., 1876, *33*, 90).

The following table (No 1) gives the methods used for preparing the different aldehydes and the constants of the specimens used.

TABLE I.

Aldehyde	*Method of Preparation*	*B. P.*	*D. at 0°C*
Propaldehyde	Lieben (Monats. 1883, *4*, 14)	44·5-45·5 at 683 mm	0·8216
iso-Butaldehyde	Fossek, (ibid., 1881, *2*, 614)	59-60 at 684 mm	0·8140
n-Butaldehyde	Kahlbaum's preparation	70·5 at 682 mm	
iso-Valeraldehyde	Bouveault and Rosset (Bull. Soc. Chim., 1894, [iii], *11*, 301)	88·5-89·5 at 684 mm	0·8259

Bouveault and Rosset (loc. cit.) recommend the use of acetic anhydride for dehydrating aldehydes. This method, however, is not very convenient as it is difficult to remove the last traces of acetic acid by simple distillation, and in most cases calcium chloride has been used for the final drying (compare W. H. Perkin J. C. S., 1884, *45*, 467). When kept for 4-6 hours over calcium chloride no polymerisation occurs and it was found that propaldehyde can be kept for 20 hours in contact with the chloride without undergoing any change.

The ketones used were all Kahlbaum's preparations and were purified by shaking with hydrated sodium carbonate crystals dehydrating with calcium chloride and then fractionating. Benzoyl-acetone and benzyl p-tolyl ketone were recrystalised from alcohol and dried over sulphuric acid under reduced pressure.

Cinnamic aldehyde, ethyl acetone-dicarboxylate, ethyl aceto-succinate and ethyl benzoylacetate were purified by shaking with sodium carbonate solution and the emulsion extracted with ether, the ethereal solution was dried over calcium chloride for 24 hours, the ether removed and the residue carefully fractionated under a pressure of 5-6 mm.

(b) *General procedure.*

About 0·2 to 0·3 grams of the substance was weighed in a stoppered tube and then dissolved in about 10 c. c. of the dry amyl ether. The tube containing the solution of the aldehyde was lowered vertically into a stout flask of about 250 c. c. capacity, provided with an air tight rubber cork with two holes. Through one of these holes was inserted a stop-cock nearly touching the bottom of the flask and through the other an exit tube consisting of a glass tube bent at right angles. Excess of magnesium methyl iodide solution (about 10—15 c.c.) was put into the flask and the air in the flak was displaced by dry nitrogen (bubbled through concentrated sulphuric acid and passed over phosphorous pentoxide). The exit tube of the flask was attached by a piece of thick-walled rubber tubing about 6″ long to a Lunge's nitrometer filled with dry mercury. The whole apparatus was then left for 1—2 hours to attain room temperature. After that period the temperature, pressure, level of mercury in the nitrometer, &c. were noted and the two solutions were mixed by slightly tilting the flask and shaken vigorously and the apparatus left for 1—2 hours. The volume of gas evolved was then read with usual precautions and corrections for the change of temperature and pressure, during the period was applied. The quantity of the enolic form was then calculated from the amount of methane evolved in the reaction.

Occasionally a blank experiment was made to show that the dry *iso*-amyl ether used as solvent did not give any gas with the Grignard's reagent and to make sure that the ether did not absorb any moisture.

C. *Results.* The reaction studied does not give the relative amounts of keto and enolic form present in each case, as for example does Meyer's bromine method, where only one of the two forms reacts with the reagent and where the reagent has no effect on the equilibrium

The Grignard reagent affects the equilibrium as has already been shown in the case of ethyl acetoacetate and can also react with both keto and enolic forms, with the keto form it reacts to give the compound which on treatment with water produces secondary or tertiary alcohols and with the enolic form to give methane. It is clear that enolisation would have to be rapid, otherwise the whole of the ketonic form would react in the normal way.

The results obtained are given in Table II.

A few experiments were tried in order to determine whether in the presence of the theoretical amount of water the formation of hydrates $R \cdot CH(OH)_2$ was indicated. The results were purely negative as it was found that the amount of methane evolved was only about 30 or 40 per cent. of that required by the water alone (1 mol water=1 mol methane) and this appears to be due to the formation of a protective layer of basic magnesium compound on the outside of the water globules.

TABLE II.

Expt.	Name of substance.	Weight in grams	Vol. of gas evolved in c. c.	*Pressure in m. m	Temperature in degree centigrade	Vol of gas at N. T. P. in c. c.	Theretical Vol. in c. c.	Enolization %
1.	Propaldehyde	0·3010	3·17	673	28·75	2·54	116·20	2·19
2.	n-Butaldehyde	0·2788	3·27	665	27·0	2.60	86·74	3·00
3.	iso-Butylaldehyde	0·2408	2·27	682	27·0	1·85	74·90	2·48
4.	iso-Valeraldehyde	0·2098	6·77	680	31·5	5 43	54 64	9·94
5.	Acetone	0·2328	2.37	681	28·0	1·93	89.89	2·14
6.	Chloral	0·1940	nil	680	26·75	...	...	nil
7.	Cinnamic aldehyde	0·3014	7·72	682	25·0	6·35	51.15	12·41
8.	Methyl propyl ketone	0·2164	7·67	683	24·5	6·33	56·37	11·22
9.	Methyl *iso*-propyl ketone.	0·1886	6·47	683	24·0	5·35	49·12	10.88
10.	Methyl butyl ketone	0·2408	4·17	683	25·75	3·42	53·93	6·35
11.	Allylacetone	0·2784	3·47	684	24·25	2·87	63·62	4·51
12.	Benzoylacetone	0·1758	26·77	680	28·25	21.70	24·30	89·30
13.	Acetylacetone	0 1446	34·67	704	25·0	29·44	32·39	90 87
14.	*Benzylp-tolyl ketone.	0·2100	nil	681	21·5	...	...	nil
15.	Ethyl acetone-dicarboxylate.	0·1798	21·57	683	24·25	17·80	19·94	89·27
16.	Ethyl acetosuccinate	0·1584	19·97	680	24·5	16·40	16·43	99·85
17.	Ethyl benzoylacetate	0·2612	30·97	699	25·5	26·06	30·46	85·54
18.	†Di-benzilidene-acetone.	0·1132	nil	684	24·5	...	...	nil

*Vapour pressure of iso-amyl ether has been neglected in these experiments.

†These Ketones were insoluble in cold iso-amylether. Before mixing the two liquids in the flask, the latter was heated up to about 60°c and then the liquids were mixed. In these experiments the final readings were taken 2—3 hours after mixing the liquids.

TABLE III.

Expt. No.	Amount of substance in grams.	Per cent. of acid (Isovaleric) †	Real weight of aldehyde	Vol of gas evolved c. c.	Pressure m.m	Temp. in °C	Vol. N. T. P.	Vol. corresponding to acid * at N. T. P.	Vol. for the Aldehyde at N. T. P.	Theoretical vol. for 100% enolisation	Percentage enolised
1	0·2138	4·60	0·2040	26·75	683	26	21·95	2·16	19·79	53·13	37·26
2	0·2824	2·92	0·2741	23·00	682	26	18·84	1·81	17·03	71·40	23·85
3	0·1830	4·30	0·1751	22·30	683	25·25	18·34	1·73	16·61	45·59	36·43

*It is assumed that one molecule of acid gives one molecule of methane.

†The amount of acid is determined by titration of the substance with decinormal Caustic soda in the atmosphere of dry Nitrogen and using phenolpthalein as indicator.

In one experiment with *iso*-valeraldehyde which was slightly acidic (some of it being oxidised to valeric acid) the amount of gas obtained was much greater than what was obtained previously. It was thought that the high results were due to the presence of free acid in the aldehyde. A few experiments, therefore, were made at intervals, allowing the aldehyde to be oxidised and again treating this product with calcium chloride. In these experiments it was found that the percentage of enolization in the aldehyde increased with the amount of free acid in the aldehyde. The amount of free acid in the aldehyde was obtained by titrating a known amount of aldehyde with decinormal caustic soda solution using ph enolpthalein as indicator. The titrations were made in the atmosphere of nitrogen. The results of these experiments are given in Table III

III. *Summary and conclusion.*

(1) Generally the carbonyl group in aldehydes and ketones is enolised to a small extent only, the maximum enolization being 11 per cent. Similar results have been obtained by Hibbert and Sudborough (loc. cit) in the case of benzoin and deoxybenzoin, Enolization in the former case being about 3 per cent and in the latter about 13 per cent.

(2) In the case of beta-diketones and of esters of beta-ketonic acids, however, the carbonyl group has a very great tendency to undergo enolization. The results in the case of benzoyl acetone and acetyl acetone show that the enolization is as much as 90 per cent.

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