JOURNAL OF THE COLLEGE OF SCIENCE, IMPERIAL UNIVERSITY,
TOKYO, JAPAN.
VOL. XXVII., ARTICLE 4.

The Action of the Grignard Reagent on *o*-Phthalic Esters.

By

Y. Shibata, *Rigakushi.*

Research Scholar, Science College, Imperial University of Tokyo.

The action of the Grignard reagent on succinic esters has been thoroughly studied by A. VALEUR,[1] W. DILTHEY and E. LAST[2] and T. URAI[3], all of whom observed that, as the result of the reaction, glycols are produced according to the following scheme:

$$\begin{matrix}CH_2\cdot CO\cdot OR\\ |\\ CH_2\cdot CO\cdot OR\end{matrix} + 2R'MgX = \begin{matrix}CH_2\cdot CR'(OMgX)\,OR\\ |\\ CH_2\cdot CR'(OMgX)\,OR\end{matrix}$$

$$\begin{matrix}CH_2\cdot CR'(OMgX)\,OR\\ |\\ CH_2\cdot CR'(OMgX)\,OR\end{matrix} + 2R'MgX = \begin{matrix}CH_2\cdot CR'R'(OMgX)\\ |\\ CH_2\cdot CR'R'(OMgX)\end{matrix} + 2ROMgX$$

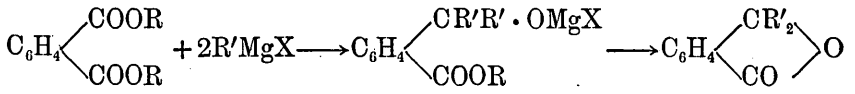
$$\begin{matrix}CH_2\cdot CR'R'(OMgX)\\ |\\ CH_2\cdot CR'R'(OMgX)\end{matrix} + 2H_2O = \begin{matrix}CH_2\cdot CR'R'(OH)\\ |\\ CH_2\cdot CR'R'(OH)\end{matrix} + 2Mg(OH)X.$$

Now, as is well known, a very close analogy exists between succinic acid and *o*-phthalic acid, and I have, therefore, recently studied the action of the Grignard reagent on *o*-phthalic esters, expecting that in this case, also, glycols would be produced. It was found, however, that this is by no means the case, derivatives

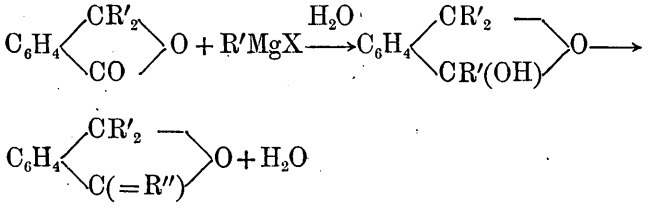
---

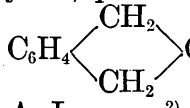
1) Bull., (1903), [3] **29**, 683.
2) Ber., (1904), **37**, 2640.
3) Dissert.

of phthalide being produced instead of the expected glycols. The reaction is to be formulated as follows:



Generally, however, the reaction goes one step further, the ketone group contained in the dialkyl phthalide, formed as above, combining with another molecule of the Grignard reagent and the resulting compound decomposing in contact with water and producing the anhydro-compound, as shown below[1]:



The compound is to be called 1:1-dialkyl(aryl)-3-alkylene (arylene)-phthalane, because it may be considered as a derivative of  , which has been recently named "Phthalan" by A. LUDWIG.[2] The intermediate substance—carbinol—could not, however, be isolated.

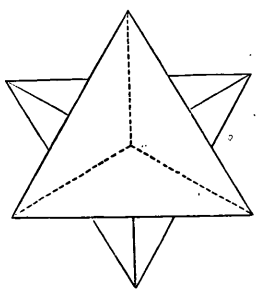
This difference in the action of the Grignard reagent on the esters of succinic and *o*-phthalic acids which, from the study of their derivatives, are regarded as perfectly analogous one to the other, may, however, be easily explained by taking into consideration the position of the carboxyl groups in the molecule of the two acids.

---

1) It appears likely that the dehydration is due to the action of the excess of the Grignard reagent employed. Compare F. W. Kay and W. H. Perkin, jun., Journ. Chem. Soc., (1906), **89**, 848.

2) Ber., (1907), **40**, 3062.

As first pointed out by H. G. BETHMANN,[1] certain properties of succinic acid correspond to the following space formula, with its two carboxyl groups in the *trans*-position, and the ease, with which succinic esters react with four molecules of the Grignard reagent and produce glycols, can be readily explained by adopting the same formula, the two carboxyl groups in the *trans*-position having no space influence upon the course of the reaction. But, in the case of *o*-phthalic acid, only one ester group enters into reaction with two molecules of the Grignard reagent, as already pointed out, and phthalide is formed as the intermediate product. This must be considered as due to steric hinderance, or, in other words, to the effect of the *cis*-position of the two carboxyl groups in *o*-phthalic acid.



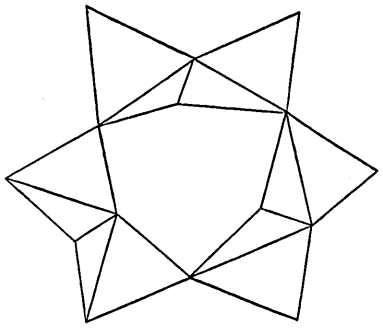
On the other hand, F. ULLMANN and C. SCHAEPFER[2] obtained tetraphenyl-*p*-xylylene glycol $(C_6H_5)_2\,C.\langle\rangle.C\,(C_6H_5)_2$ (OH, OH) by the action of phenyl magnesium bromide upon terephthalic acid dimethyl ester, the reaction being, evidently, quite analogous to that which occurs in the case of succinic esters. It, thus, appears very probable that the two carboxyl groups in terephthalic acid are in the *trans*-position.

These considerations enable us to discuss a little more fully than hitherto the different space formulae of benzene proposed from time to time. The following may be regarded as their representatives :

---

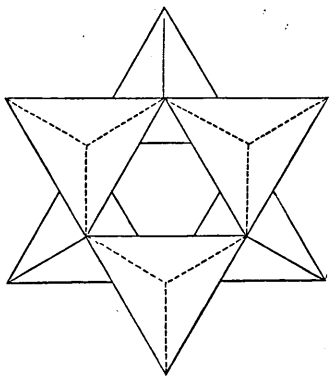
1) Zeitschr. f. physik. Chem., (1890), **5**, 409.
2) Ber., (1904), **37**, 2003.

I



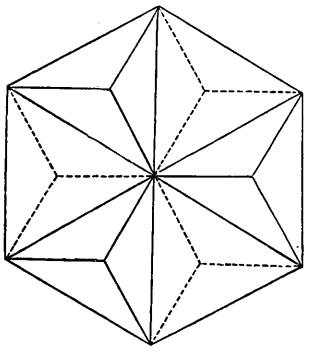
Graebe [Ber., (1902), **35**, 526]

II



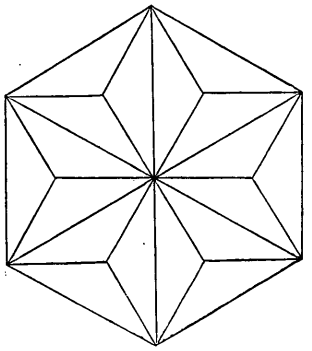
Sachse [Ber., (1888), **21**, 2530]

III



Baubel [J.pr. Chem., (1891), **44**, 137]

IV



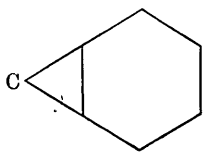
Baeyer [Ann., (1888), **245**, 123]
Erlenmeyer jun. [Ann., (1901), **316**, 57]

Of these, neither III nor IV appears to be in agreement with the facts above mentioned, for according to III (which is constructed by laying six tetrahedra alternately above and below the plane formed by their bases), *o*-phthalic esters, in reacting with the Grignard reagent, should also give the glycols just as terephthalic and succinic esters, which is not found to be the case, while in IV (which is constructed by laying six tetrahedra upon a plane hexagon), though the distance between the *para*-positions is double that between the *ortho*-positions, still the two carboxyl groups

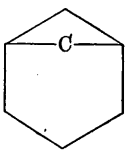
in terephthalic acid lie on the same side in space and must, therefore, to a certain extent, have a hindering influence upon each other on carrying out the Grignard's reaction. This again is not the case.

On the other hand, both I and II satisfy the main condition that the two carboxyl groups in *o*-phthalic acid are in the *cis*-position, while those in terephthalic acid are in the *trans*-position.

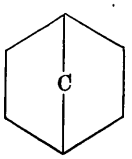
The choice between these two is not so easy. But, as will be shown hereafter (p. 12), I have obtained 1 : 1-diphenyl-3-phenylene-phthalane, $C_6H_4\begin{cases}C(C_6H_5)_2\\C(:C_6H_4)\end{cases}O$, by the action of phenyl magnesium bromide upon *o*-phthalic acid diethyl ester, this compound being, no doubt, produced through the intermediate formation of the alcohol, $C_6H_4\begin{cases}C(C_6H_5)_2\text{——}\\C(C_6H_5)(OH)\end{cases}O$, as already indicated above in a general way, and the alcohol then losing water from the group $>C\begin{cases}C_6H_5\\OH\end{cases}$. Now, there are three possible ways, in which water may be separated from this group, according as the condensation occurs in the *ortho*-, or the *meta*-, or the *para*-position, and producing either one or the other of the following three double rings:



(A)



(B)



(C)

Referring to formulæ I and II which, as already indicated above, are to be preferred to formulæ III and IV, we shall easily find

that formula II proposed by SACHSE, which is constructed in such a way that the six tetrahedra are all rigidly combined with one another and in which the distance between the two free solid angles of any two adjacent tetrahedra is too great for a third tetrahedron of the same size to fit in, can not account for the formation of double ring (A), and still less for the formation of (B) or (C).

In GRAEBE's model, on the other hand, any one of the three pairs of tetrahedra, connected together through two of their solid angles, can be rotated about the points, through which it is connected with the two other pairs and, in this way, any two adjacent free solid angles can be brought closer together until the distance between them is equal to the length of an edge of the tetrahedron, so that the fitting in of the third tetrahedron and, with it, the completion of double ring (A) offers no difficulty.

If, as the limiting case, three pairs of tetrahedra are supposed to be rotated in the manner above described, model I would coincide with model IV and the distance between the two *meta*-positions would become equal to the length of an edge of the tetrahedron, which would render the completion of double ring (B) possible. But, as already explained, formula IV can not be reconciled with certain facts, and the formation of double ring (B) must, therefore, be regarded as improbable.

Again, even in the limiting case above supposed, the distance between the two free solid angles in the *para*-position is too great for the third tetrahedron to fit in between them, so that the formation of double ring (C) is likewise rendered improbable.

It thus appears that of all the space formulæ hitherto proposed, that of GRAEBE, which is nothing but a representation in space of KEKULÉ's well known formula, is in best agreement with

facts and that 1:1-diphenyl-3-phenylene-phthalane to be presently described contains the double ring  .

Experimental Part.

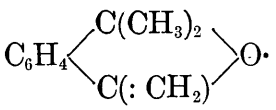
I. *The action of methyl magnesium iodide on o-phthalic acid diethyl ester.*

An ethereal solution of the Grignard reagent was, according to the ordinary method, prepared in a large round bottomed flask (capacity 1.5 litre), having a pretty wide side tube, through which the foot of a dropping funnel passed and was fixed by means of a good cork, and the mouth of the flask was connected with a long reflux condenser, both the dropping funnel and the condenser being, in turn, connected with a U-tube filled with soda-lime and calcium chloride, in order to keep away moisture and carbon dioxide.

When all the methyl iodide had been added through the dropping funnel and nearly the whole of the magnesium powder dissolved, phthalic acid diethyl ester, diluted with four times its volume of absolute ether, was introduced through the dropping funnel in the proportion of one molecule of the ester to four of the Grignard reagent, the whole being well cooled with ice and water. A clearly visible reaction took place, and, as it approached towards the end the contents of the flask were found to be separated into two layers, which, after standing for about twenty hours, were decomposed by adding ice and dilute sulphuric acid. The ethereal layer, which now separated from the aqueous solution, was drawn off and well washed, first, with a dilute solution of sodium carbonate and, then, seveval times with pure water. On distilling off the ether, there remained a very thick

oil of a dark yellow colour and having a faint odour, somewhat resembling that of petroleum. The oil did not solidify even when placed in a vacuum for a month, or when cooled with ice and salt.

The yield of the crude product was almost quantitative when calculated as 1:1-dimethyl-3-methylene-phthalane,



At the ordinary temperature the oil was so viscid that it did not flow out of a vessel even when held up side down, but at about 40° it began to soften and, at about 70°, became sufficiently mobile to be transferred from one vessel into another.

The oil was now subjected to fractional distillation under a reduced pressure of 5 mm., when almost the whole of it distilled between 140° and 155°, the main portion, however, distilling at 145–146°. The distillate, which had a faint yellow colour and the characteristic odour, gave the following results on analysis:

1) 0.1911 g. of the substance gave 0.5805 g. of CO_2 and 0.1249 g. of H_2O.
2) 0.1753 g. of the substance gave 0.5244 g. of CO_2 and 0.1195 g. of H_2O.
3) 0.2083 g. of the substance gave 0.6317 g. of CO_2 and 0.1443 g. of H_2O.
4) 0.1959 g. of the substance gave 0.6018 g. of CO_2 and 0.1318 g. of H_2O.

or

	1	2	3	4		
Carbon	82.85	81.59	82.71	83.78	mean	82.73
Hydrogen	7.31	7.62	7.75	7.52	„	7.56

agreeing well with the numbers required by the formula $C_{11}H_{12}O$, viz.

C=82.50 H=7.50.

The constitution, $C_6H_4\begin{<}C(CH_3)_2\\C(:CH_2)\end{>}O$, given to the substance was proved by the study of its oxidation product.

a) One part of the oil was mixed with 1.5 parts of chromic acid, 2 parts of conc. sulphuric acid, 4 parts of water, and the mixture, contained in a flask provided with reflux condenser, was warmed on a water bath. The original orange yellow colour of the mixture changed into deep green, and large crystals began to adhere to the walls of the flask. After diluting the acid mixture with a large quantity of water, these crystals were removed and recrystallised from alcohol. The substance was thus obtained in the form of large tabular crystals, and its melting point was found to be 69–71°.

b) A benzene solution of the oil was shaken with the mixture of an equal volume of 5% solution of potassium permanganate and dilute sulphuric acid (2%), the permanganate mixture being added in small portions, until it was no longer decolourised. The precipitated manganese dioxide was dissolved by means of sulphurous acid, and the benzene layer separated and distilled. Crystals were thus obtained, which were found to be identical with those above obtained by oxidation with chromic acid mixture.

A determination of carbon and hydrogen gave the following numbers:

0.1769 g. of the substance gave 0.4846 g. of CO_2 and 0.1000 g. of H_2O, therefore

C=74.71 H=6.32.

Dimethyl-phthalide, $C_6H_4\begin{cases}C(CH_3)_2\\CO\end{cases}O$, requires

C=74.03 H=6.23.

Dimethyl-phthalide had been already obtained by R. KOTHE,[1] H. BAUER,[2] and others, BAUER having obtained it synthetically from methyl magnesium iodide and phthalic anhydride, and with a much better yield than the others. The description of the substance given by these authors well coincides with the properties of the sample prepared by me, except its melting point, that given by BAUER (68–69°) being a degree or two lower. A similar difference in the melting point was also observed in the case of dibenzyl-phthalide to be described hereafter.

The existence of a double linking in 1:1-dimethyl-3-methylene-phthalane was easily proved by the action of bromine upon it, a solution of bromine in chloroform, when added drop by drop to one of the substance in the same solvent, being at once decolourised. When allowed to stand for a while, after a slight excess of bromine had been added, the mixture acquired a deep black colour; this, however, has not yet been further investigated.

II. *The action of phenyl magnesium bromide on o-phthalic acid diethyl ester.*

Precisely as in the preceding case, the phthalic ester and phenyl magnesium bromide, both dissolved in ether, were mixed together in the proportion of 1 to 4 molecules, and the reaction product was decomposed by ice and dilute sulphuric acid. After driving off ether from the ethereal layer, separated from the aqueous solution, there remained a yellowish viscous oil, which

1) Ann. d. Chem., (1888), **248**, 56.
2) Ber., (1904), **37**, 735.

had a smell resembling that of phenol and showed a splendid green fluorescence, either by itself or when dissolved in various organic solvents. The crude oil was subjected to steam distillation in order to get rid of diphenyl, which was found to be always formed as a bye-product and which easily distilled off in a current of steam, the main product of the reaction being non-volatile. When brought in contact with air, the oily residue became tenacious and semi-solid, and gradually solidified to a yellow mass.

The yield of the still somewhat impure substance was about 10 gr. from 17 gr. of the ester.

In this state of purity, the solid could not be obtained in a crystalline condition, for if dissolved in any organic solvent and the latter evaporated off, there always remained a viscous residue.

The residue obtained on evaporation of an ethereal solution of the substance was, therefore, now subjected to fractional distillation under a reduced pressure of 8 mm., and it was found that the first portion of the distillate, which solidified in scaly crystals, consisted of diphenyl, which had escaped distillation along with steam. The main portion of the substance distilled between 280° and 295° as a very viscous oil and solidified on cooling in the form of yellowish crystals. These were left on a porous tile, in order to remove the oily matter still adhering to them, then washed with petroleum ether, and finally recrystallised from a mixture of chloroform and ether. Small colourless glittering crystals of melting point 193–194° were thus obtained. The substance is very easily soluble in chloroform, moderately soluble in benzene and ether, and sparingly so in alcohol and petroleum ether.

Its solution decolourises neither bromine nor potassium permanganate.

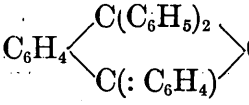
On fusion with potash at 160° the smell of benzophenone was distinctly perceived, but on dissolving in water, the fused mass gave nothing but a small quantity of the original substance.

Analysis of the substance gave the following results:

1) 0.2240 g. of the substance gave 0.7390 g. of CO_2 and 0.1081 g. of H_2O.

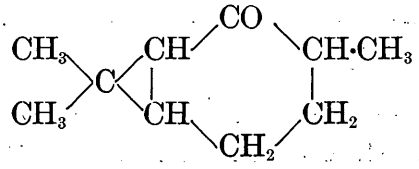
2) 0.2030 g. of the substance gave 0.6674 g. of CO_2 and 0.0972 g. of H_2O, or

	1	2
Carbon	89.97	89.97
Hydrogen	5.39	5.37,

1:1-diphenyl-3-phenylene-phthalane,  , requiring

C=90.14 H=5.24.

As already stated in the introductory part, the substance, doubtless, contains the ring  , and a few other substances, such as carone and its derivatives are known to contain the same ring:



Carone.

III. *The action of benzyl magnesium chloride on o-phthalic acid diethyl ester.*

The proportion of the substances taken and the method of procedure were just the same as before. But it was found that the reaction was much more violent than in the previous cases,

each drop of the ester, in the early stage of the reaction, producing a hissing sound, and causing the Grignard reagent to splash, as it dropped into the latter. The reaction, however, became quite mild as it went on, and ultimately some yellowish substance precipitated out.

The whole was decomposed as before by means of ice and dilute sulphuric acid, when a considerable quantity of a white crystalline substance was obtained. It was found to be insoluble in water, alcohol, ether, or petroleum ether, moderately soluble in benzene and very easily soluble in chloroform, and could, therefore, be conveniently recrystallised from a mixture of chloroform and ether. Thus purified, it was obtained in the form of colourless small needles of melting point 207°, Its properties agreed well with the description given by H. BAUER[1] of dibenzyl-phthalide, except that he gives 204° as its melting point. An analysis of the substance, which gave the following results, has, moreover, left no doubt as to its being dibenzyl-phthalide:

0.1502 g. of the substance gave 0.4634 g. of CO_2 and 0.0795 g. of H_2O, therefore

C=84.14 H=5.92.

Dibenzyl-phthalide, $C_6H_4\begin{cases}C(C_7H_7)_2\\CO\end{cases}O$, requires

C=84.02 H=5.79.

On distilling off ether from the ethereal solution separated from the aqueous layer and the crystals of dibenzyl-phthalide, a brownish oil was left behind, which solidified to a colourless crystalline mass, when left for some time in a vacuum. It was dried on a porous porcelain plate and then recrystallised from a

1) Ber., (1905), **38**, 240

mixture of chloroform and alcohol. Brilliant minute crystals of melting point 150.5° were thus obtained. A determination of carbon and hydrogen gave the following results:

1) 0.1957 g. of the substance gave 0.6412 g. of CO_2 and 0.1071 g. of H_2O.

2) 0.1559 g. of the substance gave 0.5095 g. of CO_2 and 0.0881 g. of H_2O.

	1	2
Carbon	89.36	89.13
Hydrogen	6.12	6.32.

1:1-Dibenzyl-3-benzal-phthalane, $C_6H_4\begin{cases}C(C_7H_7)_2\\ \\ C(:CH\cdot C_6H_5)\end{cases}O$, requires

C=89.64 H=6.23.

The substance is very easily soluble in chloroform, moderately so in benzene and ether, and almost insoluble in alcohol and petroleum ether.

When oxidised with potassium permanganate, 1:1-dibenzyl-3-benzal-phthalane is readily converted into dibenzyl-phthalide.

The action of bromine upon 1:1-dibenzyl-3-benzal-phthalane in chloroform or carbon bisulphide solution is exactly the same as that upon 1:1-dimethyl-3-methylene-phthalane and takes place very easily at ordinary temperatures.

Potash fusion gave benzoic acid together with a brownish oily matter, which has not yet been further examined.

IV. *The action of ethyl magnesium halide on o-phthalic esters.*

The action of ethyl magnesium bromide and of ethyl magnesium iodide upon *o*-phthalic acid diethyl ester and also the action of ethyl magnesium iodide upon *o*-phthalic acid dimethyl ester

were studied, but, in these cases, no phthalane derivatives were obtained, the only definite product, which has been isolated, being diethyl-phthalide.

On usual treatment, a brownish yellow oil, having a disagreeable odour resembling that of onions, was obtained in each case, but, on fractional distillation under a reduced pressure of 12 mm., it gave no constant boiling portion, until the thermometer rose to 165°, when nearly the whole of the remaining portion distilled over.

This portion, after refractionation, was analysed with the following results, and it proved to consist of diethyl-phthalide:

0.2444 g. of the substance gave 0.6754 g. of CO_2 and 0.1653 g. of H_2O, therefore

C=75.37 H=7.56.

Diethyl-phthalide, $C_6H_4\begin{cases}C(C_2H_5)_2\\CO\end{cases}O$, requires

C=75.75 H=7.43.

Diethyl-phthalide had likewise been already obtained by R. KOTHE[1] and H. BAUER[2]; the former got it as an oil of a boiling point of 210-214° at 210 mm., while the latter obtained it in the form of crystals melting at 54°.

In order to further identify the above product, I prepared its mono-nitro derivative, according to the method described by H. BAUER. The crystals obtained had a melting point of 104° and agreed, in this and other respects, with the description given by BAUER of mononitro-diethyl-phthalide.

The lower boiling portions were carefully refractionated, but no definite product could be isolated.

1) Ann. d. Chem. (1888), **248**, 67.
2) Ber., (1904), **37**, 735.

Summary.

1° In spite of the great analogy existing between *o*-phthalic acid and succinic acid, the action of the Grignard reagent upon *o*-phthalic esters differs from that upon succinic esters in producing derivatives of phthalide, instead of producing glycols.

2° More frequently, the reaction between the Grignard reagent and *o*-phthalic esters goes even one step further, with production of the derivatives of phthalane. 1:1-Dimethyl-3-methylene-phthalane, 1:1-diphenyl-3-phenylene-phthalane and 1:1-dibenzyl-3-benzal-phthalane have thus been obtained and described.

3° Various space formulæ proposed for benzene are discussed from the point of view of the experimental results obtained in this investigation, and it is shown that GRAEBE'S model, which represents KEKULÉ'S well known formula in space, accounts for the facts in the most satisfactory manner.

In conclusion, I desire to express my best thanks to Professor MATSUBARA for his kind guidance and suggestions.

The Chemical Institute of the College of Science,
Imperial University of Tokyo.