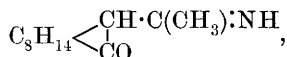


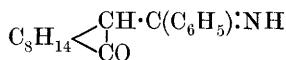
XLV.—*Studies in the Camphane Series. Part XVIII.* *A New Formation of Acetylcamphor.*

By MARTIN ONSLOW FORSTER and HILDA MARY JUDD, B.Sc.

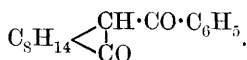
CONCURRENTLY with experiments on the behaviour of hydroxymethylene camphor towards magnesium alkyl halides, we have studied the course of the Grignard reaction on α -cyanocamphor, and find that whilst about 80 per cent. of the latter escapes attack by magnesium methyl iodide, this agent converts the remainder into the compound



which bears to acetylcamphor that relation which the derivative obtained by heating together ammonium formate and benzoylcamphor has to the last-named substance (Forster, *Trans.*, 1903, **83**, 108) :



Phenyliminomethylcamphor.



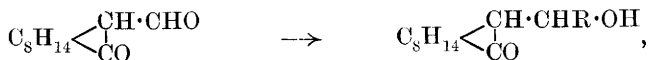
Benzoylcamphor.

Dilute hydrochloric acid resolves the new imino-compound quantitatively into ammonia and acetylcamphor, the properties of which are in complete agreement with those described by Brühl (*Ber.*, 1903, **36**, 4282), who first obtained this β -diketone on hydrolysing methyl *C*-acetylcamphorcarboxylate, and more recently by the action of zinc on α -bromocamphor dissolved in ethyl acetate (*Ber.*, 1904, **37**, 755).

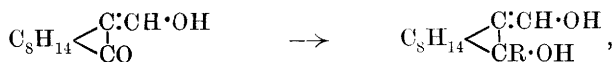
The Grignard reaction has been applied to nitriles already by Blaise (*Compt. rend.*, 1901, **132**, 839, 978, and **133**, 1217), who obtained crystalline magnesium compounds of the type $\text{CRR}' : \text{N} \cdot \text{MgI} \cdot \text{Et}_2\text{O}$, yielding ketones when decomposed with water, but the experimental conditions were not favourable to the isolation of an imino-compound. Moreover, the nitriles examined were simple in structure, and in view of the behaviour of other camphor derivatives towards magnesium methyl iodide (Forster, this vol., p. 232), it was considered desirable to ascertain whether the organo-metallic compound attacked the carbonyl group in preference to the cyanogen.

The conversion of α -cyanocamphor into the imine of acetylcamphor led us to expect that the action of magnesium phenyl bromide would give rise to the phenyliminomethylcamphor already mentioned; although there is no difficulty in isolating this compound from the products of reaction, the yield is inferior to that of the acetylcamphor derivative, which is obtainable in quantities comparing favourably with the return from Brühl's process.

The action of magnesium alkyl iodides on hydroxymethylenecamphor is less easy to interpret, owing to the fact that there is produced in each case a mixture of two liquid substances which are separated with difficulty. Moreover, although the chemical investigations of Claisen (*Annalen*, 1894, **281**, 306) and the physical studies of Brühl (*J. pr. Chem.*, 1894, [ii], **50**, 209; *Zeit. physikal. Chem.*, 1900, **34**, 31) have definitely established the enolic constitution of hydroxymethylenecamphor, it is necessary to keep in view the possibility of that substance behaving towards magnesium alkyl halides in the manner associated with aldehydes :

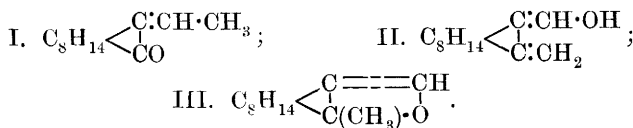


the alternative course,



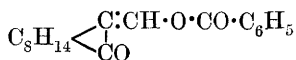
being that followed by isonitrosocamphor.

In the case of magnesium methyl iodide, the possible isomeric products would have the empirical formula $\text{C}_{12}\text{H}_{20}\text{O}_2$, but in spite of several modifications in the experiments, the liquid obtained has invariably given results on analysis between those required by this formula and by that of its anhydride. Ultimately an individual substance having the composition $\text{C}_{12}\text{H}_{18}\text{O}$ was isolated by treating with zinc dust in alcohol the crystalline dibromide, $\text{C}_{12}\text{H}_{18}\text{OBr}_2$, produced when the liquid mixture is treated with bromine dissolved in light petroleum. Evidently, therefore, the initial product, $\text{C}_{12}\text{H}_{20}\text{O}_2$, becomes transformed to some extent into its anhydride, which might have the constitution represented by any of the formulæ



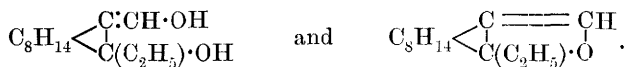
Indifference towards phosphorus pentachloride and the behaviour of the compound towards bromine preclude expression II, whilst the specific rotatory power $[\alpha]_D^{195}$ seems inconsistent with that of ethylenecamphor, Minguin having shown that the latter substance has $[\alpha]_D^{113}$. Moreover, we find that when the α -benzoyl derivative of hydroxymethylenecamphor is treated with magnesium methyl iodide the product is a mixture of the compound $\text{C}_{12}\text{H}_{18}\text{O}$, obtained from hydroxymethylenecamphor itself, with a substance having the empirical formula $\text{C}_{19}\text{H}_{24}\text{O}_3$, from which it doubtless arises by the elimination of benzoic acid; the production of ethylenecamphor can hardly be

reconciled with this observation, as the α -benzoyl derivative of hydroxymethylenecamphor probably has the constitution

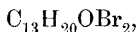


It is more likely, therefore, that the compound $\text{C}_{12}\text{H}_{18}\text{O}$ belongs to the oxide class and has the constitution represented by formula III, an expression which accords with its indifference towards phosphorus pentachloride, phenylcarbimide, hydroxylamine, and ammoniacal silver oxide, whilst agreeing with the behaviour of the dibromide towards zinc dust, and the readiness with which potassium permanganate oxidises it to camphoric acid.

The action of magnesium ethyl iodide on hydroxymethylenecamphor proceeds on similar lines. In this case, also, a mixture is obtained, consisting, we believe, of the normal compound and the unsaturated oxide derived from it by loss of water :



Although fractional distillation fails to separate these two compounds, treatment with bromine gives rise to a crystalline dibromide,

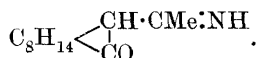


from which the unsaturated oxide, $\text{C}_{13}\text{H}_{20}\text{O}$, may be regenerated by the action of zinc in alcohol. The properties of the substance correspond with those of the lower homologue, $\text{C}_{12}\text{H}_{18}\text{O}$.

EXPERIMENTAL.

Conversion of α -Cyanocamphor into Acetylcamphor and Benzoylcamphor.

Twenty grams of α -cyanocamphor were added to an ice-cold ethereal solution of magnesium methyl iodide prepared from 100 grams of methyl iodide and 14 grams of magnesium powder, the action being very vigorous. On decomposing the product with ice and adding sufficient acetic acid to dissolve the magnesium compounds, a considerable proportion of unchanged cyanocamphor was precipitated, and a further amount was extracted from the ethereal layer by potassium hydroxide. After this treatment, the ether deposited four grams of a crystalline substance on evaporation, and this compound has been identified as the *imine* of acetylcamphor,



The crude material was dissolved in dilute hydrochloric acid, precipitated with potassium hydroxide, dried in the desiccator, and

recrystallised from light petroleum, which deposited striated prisms melting at 126° . A solution containing 0.2659 gram in 25 c.c. of chloroform gave $\alpha_D 5^{\circ}36'$ in a 2-dcm. tube, whence $[\alpha]_D 263.2^{\circ}$.

0.1099 gave 0.2987 CO_2 and 0.0975 H_2O . $\text{C} = 74.12$; $\text{H} = 9.86$.

$\text{C}_{12}\text{H}_{19}\text{ON}$ requires $\text{C} = 74.61$; $\text{H} = 9.84$ per cent.

The imine obtained in this way decolorises a solution of bromine in chloroform, and when the substance dissolved in dilute sulphuric acid is treated with potassium permanganate, the latter is immediately reduced, a transient yellow coloration, suggesting camphorquinone, being followed by a white, crystalline precipitate, probably consisting of camphoric acid. Hot aqueous alkalis have no effect on the substance, which does not reduce ammoniacal silver oxide or Fehling's solution, but ferric chloride develops an intense blue coloration in alcoholic solutions. Phosphorus pentachloride slowly transforms the compound into an oily product, and benzoyl chloride acts in pyridine without yielding a crystalline derivative. If platinic chloride is added to a solution in alcohol, no change occurs at first, but a precipitate of ammonium platinichloride separates slowly.

The *picrate* separates in minute, yellow needles on mixing warm alcoholic solutions of the imine and picric acid. Recrystallisation resolves a portion of the salt into ammonium picrate, which separates in characteristic, transparent prisms, from which the lustrous needles of the imine salt can be sorted mechanically. The latter substance melts at 143° , forming a deep red liquid which does not evolve gas.

0.1296 gave 15.2 c.c. nitrogen at 22° and 760 mm. $\text{N} = 13.65$.

$\text{C}_{12}\text{H}_{19}\text{ON}, \text{C}_6\text{H}_3\text{O}_7\text{N}_3$ requires $\text{N} = 13.27$ per cent.

Hydrolysis to Acetylcamphor and Ammonia.—The substance was dissolved in dilute hydrochloric acid, forming a solution which was clear at first, but gradually became turbid, developing the odour of peppermint. On warming gently, a colourless oil separated, quickly becoming pale yellow; this was collected with ether and dried with calcium chloride, the acid liquid being treated with platinic chloride, which immediately gave an orange-red, crystalline precipitate of ammonium platinichloride. After recrystallisation from boiling water,

0.2849 gave 0.1234 Pt. $\text{Pt} = 43.31$.

$(\text{NH}_4)_2\text{PtCl}_6$ requires $\text{Pt} = 43.91$ per cent.

On evaporating the dried ethereal extract, a pleasant-smelling oil remained, having all the properties ascribed by Brühl to acetylcamphor (*Ber.*, 1903, **36**, 4282), the odour recalling that of peppermint. It dissolves readily in alkali hydroxides, and in alcoholic

solution develops with ferric chloride an intense bluish-violet coloration, which becomes reddish-violet on dilution with water, and yields a beautiful dark red precipitate with sodium acetate. The characteristic copper derivative described by Brühl was obtained also from our product, and crystallised from petroleum in dark olive-green leaflets melting at 200°.

0.2227 gave 0.0377 CuO. Cu = 13.51.

$(C_{12}H_{17}O_2)_2Cu$ requires Cu = 14.14 per cent.

Formation of Phenyliminomethylcamphor.—Ten grams of α -cyanocamphor were added to a solution of magnesium phenyl bromide prepared from 70 grams of bromobenzene and 9.6 grams of magnesium powder; the ethereal layer obtained on decomposing the magnesium derivative with ice and acetic acid was freed from cyanocamphor by 50 per cent. potassium hydroxide, evaporated in boiling water, and distilled in a current of steam in order to remove bromobenzene and diphenyl. The residue formed a sticky solid, which became granular by treatment with a small quantity of cold alcohol. Dilute hydrochloric acid extracted from this material a substance which crystallised from light petroleum in long, tough, lustrous needles melting at 118°, identical with the compound obtained by heating enolic benzoylcamphor with ammonium formate (Forster, Trans., 1903, 83, 108).

Action of Magnesium Methyl Iodide on Hydroxymethylenecamphor.

Ten grams of dry, finely powdered hydroxymethylenecamphor were added in small portions to an ice-cold solution of magnesium methyl iodide prepared from 150 c.c. of absolute ether, 50 grams of methyl iodide, and 7 grams of magnesium powder, a somewhat vigorous action taking place. After 12 hours crushed ice was added, followed by 18 grams of acetic acid diluted with water, the bright pink ethereal layer being washed with water and sodium carbonate; on agitation with aqueous potassium hydroxide, the colour disappeared, and a small quantity of unchanged hydroxymethylenecamphor was removed, the ether being then evaporated and the residue distilled in a current of steam. A colourless oil passed over rapidly, having a pleasant, refreshing odour; it was collected with ether, quickly dried with calcium chloride, freed from ether, and distilled, 7 grams boiling at 234° under 765 mm. pressure being obtained.

0.2186 gave 0.6265 CO_2 and 0.1968 H_2O . C = 78.16; H = 10.00.

0.1983 „ 0.5659 CO_2 „ 0.1790 H_2O . C = 77.83; H = 10.03.

$C_{12}H_{20}O_2$ requires C = 73.47; H = 10.20 per cent.

$C_{12}H_{18}O$ „ C = 80.90; H = 10.11 per cent.

This product had a sp. gr. 0.9639 at 19° and gave n_D 329°20' in a

2-dcm. tube, whence $[\alpha]_D$ 170·8°; a solution containing 0·4647 gram in 20 c.c. of absolute alcohol at 19° gave α_D 7°40', whence $[\alpha]_D$ 165·0°. As the analytical results agreed more closely with the composition of the anhydride, $C_{24}H_{38}O_3$, than with either of the formulæ quoted, determinations of molecular weight were made in benzene, giving as a mean result $M=170$ ($C_{12}H_{18}O$ requires $M=178$; $C_{24}H_{38}O_3$ requires $M=374$). The oil decolorised bromine in chloroform and an acidified solution of permanganate immediately in the cold, but gave no coloration with ferric chloride, and although effervescing with phosphorus pentachloride, the action quickly subsided, and appeared disproportionately slight for the amount of material involved.

These observations indicating a mixture, we prepared 60 grams from 100 grams of hydroxymethylenecamphor, and attempted to isolate an individual by fractional distillation, obtaining 30 grams boiling at 229—231° under 757 mm. pressure, the temperature then rising to 240°; the specific rotatory power of this material in alcohol was $[\alpha]_D$ 173·5°, succeeding fractions having $[\alpha]_D$ 170·4° (b. p. 231—232°) and $[\alpha]_D$ 166·3° (b. p. 232—236°). On redistilling the first fraction, the major portion boiled at 229—230°, but the analytical results still lay between those required by the formulæ $C_{12}H_{20}O_2$ and $C_{12}H_{18}O$.

The Dibromide, $C_{12}H_{18}OBr_2$.

Although treatment with alcoholic potassium hydroxide and with concentrated sulphuric acid failed to hydrolyse the anhydride or to dehydrate the hydroxy-derivative, respectively, and so furnish a single substance, it is possible to isolate the anhydride, $C_{12}H_{18}O$, from the foregoing mixture in the form of the dibromide, $C_{12}H_{18}OBr_2$.

The oily product from hydroxymethylenecamphor and magnesium methyl iodide was mixed with chloroform, cooled in ice, and treated with its own weight of bromine in the same solvent. The colour of the halogen was destroyed, and hydrogen bromide, which did not appear at first, was liberated in some quantity as the liquid evaporated; the residue consisted of a yellow oil, in which crystals were embedded, and these were then drained on earthenware and recrystallised twice from boiling light petroleum.

0·2263 gave 0·3491 CO_2 and 0·1105 H_2O . $C=42·07$; $H=5·43$.

0·3403 „ 0·3803 AgBr. $Br=47·54$.

0·2574 „ 0·2866 AgBr. $Br=47·37$.

$C_{12}H_{18}OBr_2$ requires $C=42·60$; $H=5·32$; $Br=47·34$ per cent.

The dibromide is readily soluble in cold ether, acetone, chloroform, ethyl acetate, and glacial acetic acid, moderately so in alcohol and light petroleum, crystallising from the last named in long, transparent,

hexagonal prisms, which melt at $152\text{--}153^\circ$ without decomposing. A solution containing 0.2664 gram in 25 c.c. of chloroform gave α_D $3^\circ 21'$ in a 2-dm. tube, whence $[\alpha]_D$ 157.2° .

The Compound $C_{12}H_{18}O$, regenerated from the Dibromide.

Twenty grams of the dibromide (m. p. $152\text{--}153^\circ$) were dissolved in 100 c.c. of absolute alcohol sufficiently warm to keep the substance in solution while 20 grams of zinc dust were added slowly; it is necessary to conduct the treatment with zinc very carefully, as the action is liable to proceed beyond control. After half an hour on the water-bath in a reflux apparatus, the alcohol was distilled off and a current of steam passed through the residue without filtering the excess of zinc. The colourless oil was collected with ether, dried with calcium chloride, and distilled, boiling at $227\text{--}228^\circ$ under 764 mm. pressure. Considerable difficulty was experienced in analysing the compound and its homologue, the percentage of carbon being persistently nearly 1 per cent. too low, but the production from, and conversion into, the dibromide, $C_{12}H_{18}OBr_2$, seem to preclude other empirical formulæ.

0.2361 gave 0.6929 CO_2 and 0.2202 H_2O . C = 80.04; H = 10.36.

$C_{12}H_{18}O$ requires C = 80.89; H = 10.11 per cent.

The liquid has a pleasant, camphor-like odour, and is readily volatile in steam. The solution in chloroform decolorises bromine immediately, and on evaporation yields the dibromide from which the substance arises by the action of zinc. The specific rotatory power corresponds more nearly with the lower fractions of the mixture obtained from magnesium methyl iodide and hydroxymethylenecamphor than with the less volatile portion; a solution containing 0.5257 gram in 20 c.c. of chloroform gave α_D $10^\circ 15'$, whence $[\alpha]_D$ 195.0° .

Oxidation with Potassium Permanganate.—One gram of the oil was shaken with a 2 per cent. solution of potassium permanganate, 100 c.c. of which were required to produce a permanent pink coloration; the filtered liquid was evaporated to small bulk and rendered faintly acid with dilute sulphuric acid. On dissolving the precipitate in sodium carbonate and reprecipitating, camphoric acid was identified; the specimen, when recrystallised from boiling water, did not depress the melting point of the pure substance.

Action of Magnesium Methyl Iodide on the α -Benzoyl Derivative of Hydroxymethylenecamphor.

In their paper on hydroxymethylenecamphor (*Annalen*, 1894, 281, 314), Bishop, Claisen, and Sinclair describe two isomeric benzoyl

derivatives, the relationship of which has not been explained. Of these, the α -compound (m. p. 119—120°) is obtained by the Schotten-Baumann process of benzoylation, and we have studied the action of magnesium methyl iodide on this compound under the conditions prescribed for hydroxymethylenecamphor itself. The action was less vigorous, and the ultimate product, of which 50 grams were obtained from 90 grams of material, was an oil having an odour of peppermint; this product boiled over a somewhat wide range of temperature, the fraction distilling at 230—235° forming the major portion and giving $[\alpha]_D^{20}$ 122.1°.

0.2207 gave 0.6457 CO₂ and 0.1993 H₂O. C = 79.79; H = 10.03.

C₁₉H₂₄O₃ requires C = 76.00; H = 8.00 per cent.

C₁₉H₂₂O₂ „ C = 80.85; H = 7.80 „

C₁₂H₁₈O „ C = 80.90; H = 10.11 „

The substance, therefore, resembles the compound C₁₂H₁₈O, and further decolorises bromine in chloroform and acid potassium permanganate solutions. Its identity with that material was established by converting it into the dibromide, which crystallised from petroleum in lustrous, hexagonal prisms melting at 152°.

0.3183 gave 0.3524 AgBr. Br = 47.12.

C₁₉H₂₂O₂Br₂ requires Br = 36.20 per cent.

C₁₂H₁₈OBr₂ „ Br = 47.34 „

A solution containing 0.4196 gram in 25 c.c. of chloroform gave α_D^{20} 5°15', whence $[\alpha]_D^{20}$ 156.4°. Thus the principal result of treating the α -benzoyl derivative of hydroxymethylenecamphor with magnesium methyl iodide is to produce the oxide, C₁₂H₁₈O, identical with that obtained from hydroxymethylenecamphor itself. Nevertheless, a benzoyl compound is present also, because on passing a current of steam through the oil which was drained from the crystalline dibromide, C₁₂H₁₈OBr₂, a heavy oil came over having the irritating effect on the eyes produced by benzyl bromide; on heating this liquid with alcoholic potash during several hours and distilling the product in steam, a colourless, heavy, unsaturated oil was obtained, still rich in bromine. Although this compound decolorised bromine in chloroform without losing hydrogen bromide, no crystalline derivative was obtained from it.

Action of Magnesium Ethyl Iodide on Hydroxymethylenecamphor.

Proceeding in the manner described, we obtained from 20 grams of hydroxymethylenecamphor, 14 grams of magnesium, and 100 grams of ethyl iodide dissolved in 400 c.c. of absolute ether, 16 grams of a

pleasant-smelling, colourless oil, the major portion of which distilled at 249—251° under 770 mm. pressure. A solution containing 0.4484 gram in 20 c.c. of chloroform gave α_D 6°46' in a 2-dcm. tube, whence $[\alpha]_D$ 150.9°.

0.1964 gave 0.5614 CO₂ and 0.1815 H₂O. C = 77.96 ; H = 10.27.

C₁₃H₂₀O requires C = 81.24 ; H = 10.41 per cent.

C₁₃H₂₂O₂ „ C = 74.28 ; H = 10.48 „

As in the cases already described, the normal product of action appears to undergo conversion into the anhydride, which we have isolated by the process indicated for the compound C₁₂H₁₈O. The oil was mixed with light petroleum and treated with its own weight of bromine in the same medium ; the first portions of the halogen were decolorised, the liquid afterwards remaining red, and yielding on evaporation crystals embedded in oil. The solid product, the weight of which was roughly the same as that of the material employed, after drainage on earthenware was recrystallised first from light petroleum and afterwards from hot alcohol, which deposited long, colourless prisms melting at 88°.

0.2458 gave 0.3925 CO₂ and 0.1255 H₂O. C = 43.55 ; H = 5.67.

0.3347 „ 0.3561 AgBr. Br = 45.27.

C₁₃H₂₀OBr₂ requires C = 44.32 ; H = 5.68 ; Br = 45.45 per cent.

The dibromide is moderately soluble in petroleum and in alcohol, dissolving freely in chloroform, benzene, acetone, and glacial acetic acid, crystallising from the last named in long, flat, striated needles on diluting with water. A solution containing 0.5108 gram in 25 c.c. of chloroform gave α_D 5°20', whence $[\alpha]_D$ 130.5°.

On dissolving the dibromide in warm absolute alcohol and adding zinc dust in small quantities, a very vigorous action took place, and when this had ceased a current of steam was passed through the liquid, the receiver being changed as soon as the alcohol had been removed. A colourless, limpid oil was thus obtained, lighter than water, and having an agreeable, refreshing odour ; it boiled at 236—238° under 745 mm. pressure, and in spite of the difficulty experienced in the combustion of this substance we have no doubt that it is the unsaturated constituent C₁₃H₂₀O, forming the major portion of the product from hydroxymethylenecamphor and magnesium ethyl iodide.

0.1240 gave 0.3649 CO₂ and 0.1148 H₂O. C = 80.26 ; H = 10.28.

C₁₃H₂₀O requires C = 81.24 ; H = 10.41 per cent.

A solution containing 0.3834 gram in 20 c.c. of chloroform gave

α_D $6^{\circ}27'$ in a 2-dcm. tube, whence $[\alpha]_D$ 168.2° . Potassium permanganate is immediately reduced by the oil, which decolorises bromine in chloroform, regenerating the dibromide, $C_{18}H_{20}OBr_2$, which melts at 88° .

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