PH.D. THESIS SUMMARY.

"THE STEREOCHEMISTRY OF 3-COVALENT ARSENIC".

BY

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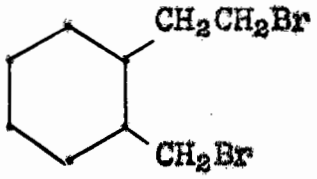
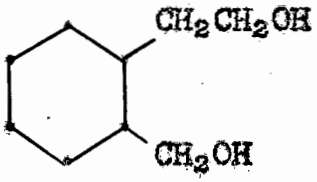
SUMMARY.

In this thesis are described attempts to prepare tertiary arsines of the 2-aryl-1,2,3,4-tetrahydro-iso-arsinoline type in order to demonstrate optical activity arising from an asymmetric arsenic atom.

These iso-arsinolines are synthesised through the use of o-2-bromoethylbenzyl bromide (I), and in the first Section is described an improved synthesis of this dibromide. The starting material was indene which was oxidised to homophthalic acid, the diethyl ester of which on reduction with lithium



I.



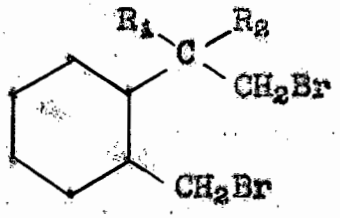
II.

aluminium hydride gave o-2-hydroxyethylbenzyl alcohol (II). This alcohol was easily converted into the dibromide by treatment with hydrobromic acid.

The second section deals with an attempt to extend this synthesis to the preparation of a substituted dibromide of type (III) from the corresponding substituted homophthalic acid (IV). One optical form of the dibromide (III) from the acid (IV) after resolution, was to be converted into the

tetrahydro- /...

tetrahydro-iso-arsinoline (V).



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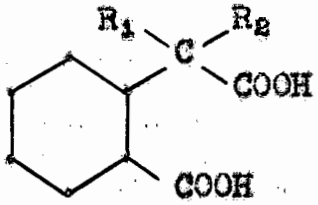

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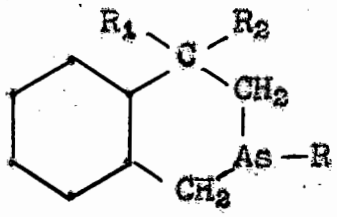
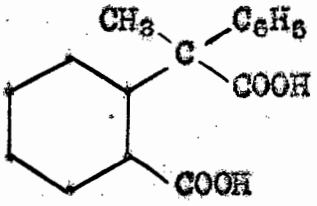


V.

If the arsenic atom exists in two configurations in this compound, this would be manifested by the existence of two diastereo-isomeric forms of (V). It was proposed to separate these two forms by fractional crystallisation as a means of demonstrating optical activity of an asymmetric arsenic atom.

The substituted homophthalic acid chosen was the αα-methylphenyl compound (VI), which was synthesised, being

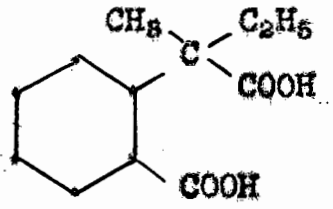


VI.

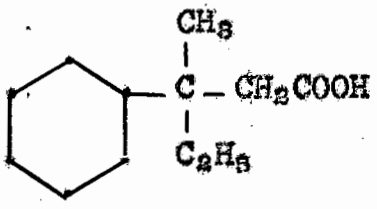
isolated as the anhydride. No success was achieved in its resolution with the alkaloids cinchonine, strychnine and quinidine.

It /...

It was hoped that one optical isomer of a substituted homophthalic acid might be obtained by resolution at an earlier stage in its synthesis. In the synthesis of αα-methylphenyl-homophthalic acid (VI), none of the intermediate acids are asymmetric, but in the case of the synthesis of αα-methyl-ethylhomophthalic acid (VII), the intermediate compound

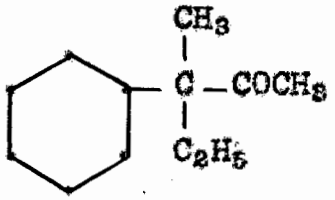


VII.



VIII.

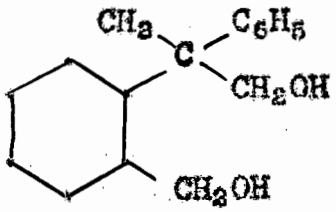
ββ-methylphenylvaleric acid (VIII) is asymmetric and therefore capable of being resolved. Attempts to prepare the acid (VIII) by a Willgerodt reaction on the ketone (IX) were not successful.



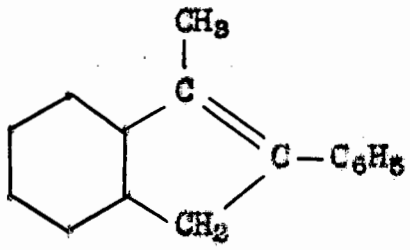
IX.

The racemic form of the anhydride of αα-methylphenyl-homophthalic acid (VI), when reduced with lithium aluminium hydride gave the alcohol (X), which however on treatment with hydrobromic acid was found to undergo a neopentyl type of rearrangement resulting in 3-methyl-2-phenylindene (XI) as

the /...



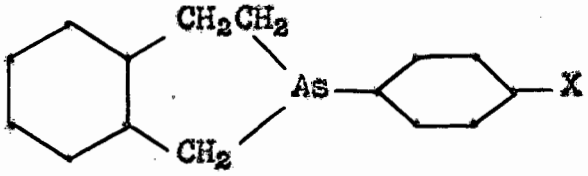
X.



XI.

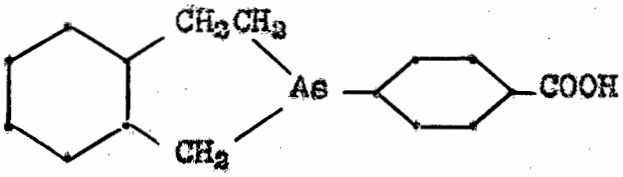
the main product. It was shown therefore that the synthesis of o-2-bromoethylbenzyl bromide described in the first Section cannot be employed for the preparation of substituted dibromides of type (III).

The third Section deals with attempts to prepare a tetrahydro-iso-arsinoline of formula (XII), where X is an acidic or basic group to react with a suitable resolving agent.

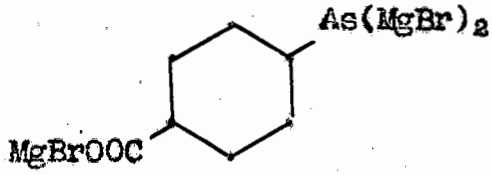


XII.

Unsuccessful attempts were made to prepare 2-p-carboxy-phenyl-1,2,3,4-tetrahydro-iso-arsinoline (XIII) by oxidation



XIII.

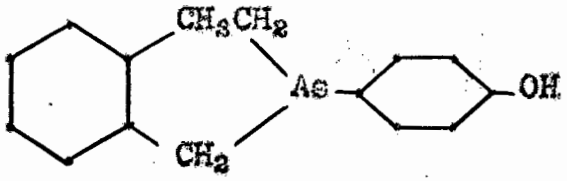


XIV.

of the corresponding p-tolyl compound and by reaction of o-2-bromoethylbenzyl bromide (I) with the tri-Grignard reagent (XIV).

Another /...

Another approach considered was that of preparing 2-p-hydroxyphenyl-1,2,3,4-tetrahydro-iso-arsinoline (XV) from the dibromide (I) and the tri-Grignard reagent (XVI). The



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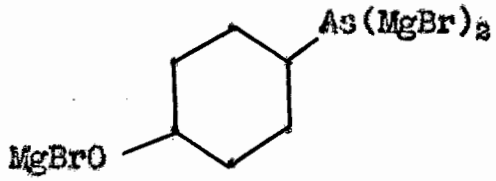
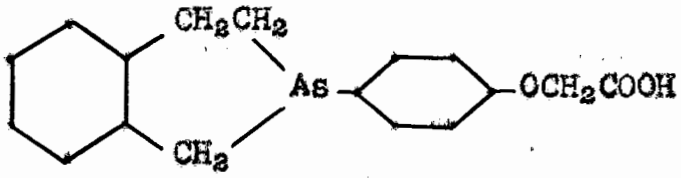


XVI.

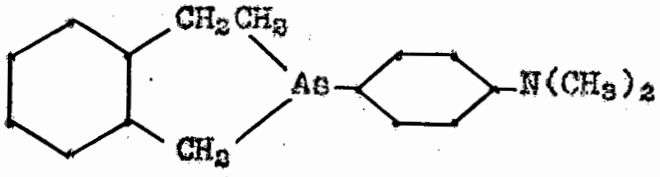
2-p-hydroxy-1,2,3,4-tetrahydro-iso-arsinoline was to be reacted with chloroacetic acid to give the compound (XVII) which



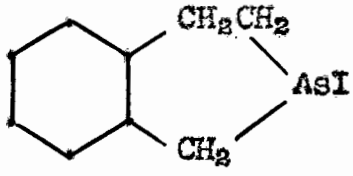
XVII.

could be resolved in the usual way with alkaloids. However, the experimental difficulties involved in the preparation of p-hydroxyphenylarsine and in its isolation in pure form caused this approach to be abandoned.

Success in the preparation of an iso-arsinoline containing a reactive functional group was finally achieved when the compound (XVIII) was prepared by reacting the iodo



XVIII.



XIX.

compound /...

compound (XIX) with p-lithium dimethylaniline. However, the salts of the compound (XVIII) with (+) camphor-10-sulphonic acid and (+)α-bromo-π-sulphonic acid were oils and therefore no separation into the hoped for diastereo-isomeric forms was possible.
