A STUDY OF THE
PREPARATION OF SOME TERTIARY
DIMETHYL AMYL CARBINOLS

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R. C. Huston

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A STUDY OF THE PREPARATION OF SOME TERTIARY DIMETHYL AMYL CARBINOLS

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EARL R. ZUEHLKE

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3

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TABLE OF CONTENTS

- INTRODUCTION
- REVIEW OF THE LITERATURE
- EXPERIMENTAL DATA
  - MATERIALS
  - PRELIMINARY PREPARATIONS
  - ALCOHOLS PREPARED
    - 2-METHYL, 3-ETHYL PENTANOL-2
    - 2,3,3-TRIMETHYL PENTANOL-2
    - 2,3,4-TRIMETHYL PENTANOL-2
    - 2,4,4-TRIMETHYL PENTANOL-2
  - TABLE OF RESULTS
- DISCUSSION
- SUMMARY
- BIBLIOGRAPHY

INTRODUCTION

In the past, Dr. Huston and some of his co-workers have worked in this laboratory in the field of Alumimum Chloride condensations. So far, the work with aliphatic alcohols has been completed through the condensation of some of the tertiary dimethyl amyl carbinols with phenol, and with benzene, in the presence of aluminum chloride(1).

The writer has had as his object the preparation of sufficient quantities of some tertiary dimethyl amyl carbinols to make possible the further study of their condensation with phenol, and with benzene, in the presence of aluminum chloride.

REVIEW OF THE LITERATURE

2-METHYL, 3-ETHYL PENTANOL-2

In preparing this Carbinol in 1908, Clark (2) used Conrad's method for the preparation of ethyl diethylacetoacetate which, upon hydrolysis with 10% KOH, gave the ketone 3-ethyl pentanone-2 in a 60% yield (b.p. 138° C. at 760 mm.). This ketone was converted to the carbinol by the use of the methyl iodide Grignard reagent in an approximate 15% yield.

2,3,3-TRIMETHYL PENTANOL-2

Whitmore and Laughlin (3) prepared this carbinol in 1932. Methyl, tertiary amyl ketone (b.p. 129°-131° C.) was prepared from acetyl chloride and tertiary amyl magnesium chloride. This ketone was changed to the carbinol by a Grignard reaction with methyl magnesium chloride in a 65% yield.

The above authors (4) also reported this carbinol in 1933. Ethyl dimethyl ethylacetate (b.p. 140°-140.8° C. at 730 mm.) was prepared in a 37% yield from tertiary amyl magnesium chloride and ethyl chlorocarbonate. This ester was converted to the carbinol by means of a Grignard reaction with methyl magnesium chloride. The reported yield was 78%.

In 1936 Huston and Sculati produced this carbinol from tertiary amyl chloride and acetone by the Grignard reaction. A yield of about 5% was reported.

This carbinol was prepared in 1936, also, by Norton and Haas. It was obtained through the action of diethyl magnesium upon 2,3-dimethyl 2,3-epoxybutane which forms an addition product that upon hydrolysis gives the carbinol. The reported yield was 34.6%.

2,3,4-TRIMETHYL PENTANOL-2

The preparation of this carbinol was reported in 1939 by Huston and Guile (7). The ketone 3,4-dimethyl pentanone (b.p. 135°-140° C. at 744 mm.) was prepared in a 9.3% yield from acetyl chloride and 2-bromo, 3-methyl butane. The carbinol was obtained in a 58.1% yield through the usual methyl iodide Grignard reaction.

2,4,4-TRIMETHYL PENTANOL-2

Butlerow (17) reported the preparation of this carbinol in 1877. Diisobutylene was prepared from tertiary butyl alcohol and sulphuric acid. This, in turn, was converted to the halide 2-iodo, 2,4,4-trimethyl pentane by the addition of dry hydrogen iodide. Treatment of the halide with silver hydroxide (moist silver oxide) yields the carbinol.

EXPERIMENTAL DATA

MATERIALS

Tertiary butyl alcohol was Eastman's "practical", M.P. 23°-25°C., and was used without further purification to prepare diisobutylene.

The bromides of diethyl carbinol, tertiary amyl, and isopropyl were prepared from the corresponding alcohols; Eastman's "technical" without further purification.

Acetone was the C.P. grade dried over sodium sulfate and twice distilled before using.

Ether used for Grignards was anhydrous dried over metallic sodium.

Acetyl chloride was Baker's C.P., used without further purification.

Magnesium turnings prepared for Grignard reactions were dried over calcium chloride in a desiccator before using.

Acetaldehyde was Eastman's "practical," distilled once through a column and used immediately.

PRELIMINARY PREPARATIONS

3_BROMO PENTANE

Diethyl carbinol was added to an excess of 48% hydrobromic acid and a bromination reaction was carried out by refluxing for 8-10 hours. The reaction mixture was then distilled and the bromide layer was separated, and washed twice with water; then dried over $CaCl_2$. The dried bromide was then distilled, collecting a fraction over a four degree range, 114-118° C.

Iso-propyl bromide (8) was prepared in a similar manner with the one exception that sulfuric acid was also used in the bromination. A fraction from 58.5°-60°C. was collected for this halide.

Tertiary amyl bromide was prepared in a similar manner to 3_bromo pentane, collecting a fraction boiling at 105-108° C.

Tertiary amyl chloride (9) was prepared by slowly adding an excess of C.P. concentrated hydrochloric acid to tertiary amyl alcohol. After shaking, the layers were allowed to separate and the upper layer was drawn off, and washed first with a dilute sodium carbonate solution, then twice with water. The halide was dried with calcium chloride and then distilled, connecting the fraction boiling at 54.5-56° C.

Methyl iso-propyl carbinol (10) was prepared from the Grignard reagent of iso-propyl bromide and acetaldehyde, the reaction being carried out at -5°C. The fraction boiling from 110-112°C. was collected as the product.

The preparation of the bromide of methyl iso-propyl carbinol was carried out as follows: To methyl iso-propyl carbinol, at a -10°C. was added, while stirring, a calculated amount of phosphorous tribromide necessary for a molecular equivalent bromination. After the addition was completed, the reaction mixture was allowed to warm up to 25°C. and remain at that temperature over night. The next day the top layer was separated and washed with water and a dilute sodium carbonate solution. After drying with calcium chloride, the halide was fractionated with the main fraction distilling at 105-108°C. This boiling point did not correspond to that recorded in the literature (11) (114-116° C.), but rather, to the boiling point of tertiary amyl bromide. In order to say more definitely what compound was formed by this bromination, a portion of the product was treated with moist silver oxide in order to convert the halide back to an alcohol. The product obtained had a definite boiling point of 100-102° C., the highest temperature reached being 104°C. This indicated that the bromide formed was that of tertiary amyl and not the expected 2-bromo, 3-methyl butane.

Methyl bromide Grignard reagent. A modification of the methyl chloride preparation (12) was used. A methyl bromide generator (five-liter, round bottom flask) was charged with a cooled solution of 67 ml. of water, 400 ml. of concentrated sulfuric acid, 587 ml. of methyl alcohol, and 1410 grams of sodium bromide (a theoretical 15 moles). The generator flask was fitted with a reflux condenser, on the top of which was placed a delivery tube. Generation of the gas was started by warming a sand bath under the flask. The methyl bromide was passed through a nine bottle washing train consisting of three safety flasks (1,5,9), three bottles of reagent sodium hydroxide solution (2,3, & 4) to remove any free acid formed, and three bottles (6,7 & 8) of sulfuric acid for drying. After drying, the gas was passed into the Grignard reaction flask containing magnesium turnings and ether. It is advisable to initially start the reaction with a small quantity of some reactive halide, such as ethyl bromide. It was necessary to add anhydrous ether to the flask throughout the reaction to keep the temperature down. Addition of methyl bromide was stopped when most of the magnesium disappeared.

Phosphorous tribromide (13) was prepared by adding bromine to a stirred suspension of red phosphorous in carbon tetrachloride. After all the bromine was added, the carbon tetrachloride was removed by distillation and the phosphorous tribromide was fractionated, collecting the portion boiling 169-173°C.

ALCOHOLS PREPARED

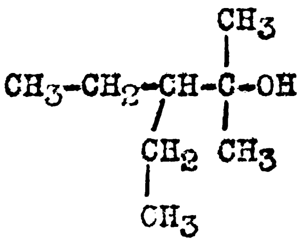
I 2-methyl, 3-ethyl pentanol-2

II 2,3,3-trimethyl pentanol-2

III 2,3,4-trimethyl pentanol-2 *

IV 2,4,4-trimethyl pentanol-2

I 2-methyl, 3-ethyl pentanol-2



This octanol was prepared by two methods: (1) the treatment of the Grignard reagent of 3-bromo pentane with acetone, forming the octanol directly. (2) the treatment of acetyl chloride with the Grignard reagent of 3-bromo pentane giving the ketone, 3-ethyl pentanone-2, and then the reaction of this ketone with a methyl bromide Grignard to give the octanol.

(1) In the first preparation a modification of both the following methods was used: the Whitmore (14) procedure for preparing the Grignard reagent, and the Edgar (15) procedure for the reaction of the reagent

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* Preparation reaction completed, but the alcohol was not obtained because of a rearrangement that took place in the preparation of the bromide, 2-bromo, 3-methyl butane.

with a ketone and subsequent hydrolysis of the resulting compound. Because of these modifications, the procedure used will be given in detail.

A dry* two-liter, three-neck, round bottom flask was fitted with a reflux condenser (with drying tube), an efficient glycerine seal stirrer, and a 500 ml. dropping funnel (with drying tube). A small crystal of iodine was placed in the flask; the flask was then heated until the iodine began to vaporize. When the vapor had condensed, 48.5 grams (2 moles) of fresh, dry magnesium turnings were placed in the flask. 60 ml. of anhydrous ether, sufficient to contact all the magnesium turnings present, were added. 300 ml. of anhydrous ether were added to 332 grams (2.2 moles) of 3-bromo pentane. (.2 mole excess was used to insure complete reaction with all the magnesium turnings present.) 15 ml. of this solution were added directly to the magnesium turnings and the stirrer was started as soon as there was definite evidence of reaction; (external cooling was applied when necessary). The remainder of the halide-ether solution was placed in the dropping funnel and added at such a rate (dropwise) that the reflux did not exceed one drop per second. After approximately one-half the halide-ether

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* It is essential that all apparatus and chemicals used be dry, and that the reaction be protected from moisture throughout.

solution was added an additional 50 ml. of anhydrous ether were placed in the separatory funnel. After the halide-ether addition was completed, the reaction mixture was stirred at least five hours before continuing. At this point the Grignard reagent was black in color.

To complete the reaction a mixture of 116 grams (2 moles) of purified acetone and 100 ml. of anhydrous ether was added, drop-wise, to the Grignard reagent, at such a rate that the reflux did not exceed one drop per second. The Grignard complex was stirred a few hours and let stand overnight before decomposing. The Grignard complex at this point should be white in color, and mostly in the precipitated form.

The next day the decomposition was carried out by slowly pouring the complex on ice and water while stirring. The ether layer was decanted off into a separatory funnel and the remaining precipitated magnesium compounds were dissolved by slowly adding, while stirring, concentrated hydrochloric acid (kept cool with sufficient ice during the addition). The ether layer was separated and added to the first ether portion. The water layer was twice extracted with 60 ml. of ether. The combined ether portion was washed with a small volume of dilute sodium carbonate solution, followed by a washing with a small volume of distilled water. The ether solution was then dried over anhydrous sodium sulfate. The ether was removed by distillation at atmospheric pressure until the temperature reached 45°C. The remainder of the fractionation was carried out at a reduced pressure. Three, two mole runs under these conditions gave an average yield of 13.5% carbinol b.p. 46-47.5° C. at 6 mm.

The other fractions were:

28 grams b.p. 35 - 58° C. at 13 mm.

5 grams b.p. 48 - 59.5° C. at 6 mm.

When the same quantities were used in a similar preparation with increased rate of addition of the halide-ether solution and of the acetone-ether solution, to maintain a gentle reflux throughout, the yield was decreased to 10% carbinol. With the increased temperature there was an increase in the amount of low boiling fraction.

(2) In the second preparation of the octanol, through the ketone synthesis, a modification of the method of Whitmore and Badertscher (14) was used. Because this method for preparing the carbinols was found to be the most satisfactory, it will be given here in detail.

Preparation of 3-ethyl pentanone-2. Using the same apparatus and procedure just described, a 3 mole Grignard reagent was prepared from: 73 grams (3 moles) of magnesium turnings, 100 ml. of anhydrous ether (added to the turnings), a solution of 500 grams (3.3 moles) of 3-bromo pentane and 500 ml. of anhydrous ether, plus an additional 100 ml. of anhydrous ether as the reaction progressed. The yield of Grignard as determined by the

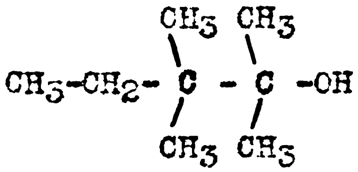
Gilman method (16) was found to be approximately 50%.

An apparatus similar to that just described for the preparation of the Grignard reagent, was next used; the two-liter flask being replaced by a three-liter, three-neck flask. Into this three-liter flask was placed 157 grams (1.5 moles) of acetyl chloride and 200 ml. of anhydrous ether. The stirrer was started and the Grignard reagent was added through the separatory funnel at such a rate that a reflux of two to three drops a second was maintained. When all but approximately 200 ml. of the reagent solution was added, an additional 25 ml. of acetyl chloride was slowly added to the reaction flask through the condenser, to insure an excess. During the reaction a white precipitate was formed which turned light orange on completion. The reaction mixture was allowed to stir at least five hours before decomposing. The decomposing was carried out in the same manner as that of the previous method except that an addition of hydrochloric acid was unnecessary because of the acetic acid formed when the excess acetyl chloride was hydrolyzed. The ether solution in this case can be dried with either anhydrous potassium carbonate or sodium sulfate before distilling at atmospheric pressure. After the ether was removed, the residue was placed in a one-liter distilling flask with 300 ml. of water and a small quantity of sodium or potassium carbonate, and distilled. In this way the ketone was steam distilled away from the higher boiling impurities. It was found unnecessary to salt out the ketone. Therefore, it was separated from the water and dried with anhydrous sodium sulfate. After drying, the ketone was vacuum distilled, collecting a small first and last fraction which were discarded. Next, the middle fraction was distilled, at atmospheric pressure, three times until a main fraction was collected. A 30% yield of ketone was obtained with a boiling range of 135-140°C at 742 mm.

Preparation of 2-methyl, 3-ethyl pentanol. An 8 mole quantity of methyl bromide Grignard (preliminary preparations) was prepared and the ketone in a 1:1.5 dilution with ether (anhydrous) was added to it not faster than one drop every two seconds. The Grignard reaction mixture was stirred at least five hours before decomposing in the usual manner. In this case, the precipitated magnesium compounds were dissolved with dilute hydrochloric acid rather than the concentrated. When the carbinol was fractionated at reduced pressure 78% yield of product b.p. 46 - 47.6° C. at 6 mm. was obtained from the ketone.

This second preparation of the carbinol was by far the better of the two methods. The final product was quite pure, as shown by its easy separation during the distillation.

II 2,3,3-trimethyl pentanol-2



$$CH_3-CH_2-\overset{CH_3}{\underset{CH_3}{C}}-\overset{CH_3}{\underset{CH_3}{C}}-OH$$

Several attempts were made to prepare this octanol following the methods given by Whitmore and Laughlin (3 & 4), but the preparations met with very little success. Trouble was encountered, in the preparation of the Grignard reagent, by the precipitation of magnesium chloride which hindered the formation of the magnesium Grignard complex. Varying the conditions of the reaction gave no appearance of improvement. Seven attempts to prepare the Grignard reagent were made. Of these, all but one solidified before the calculated amount of halide could be added and this contained much precipitate. The reaction mixture was divided into two portions, one was used to prepare the octanol directly by the reaction with acetone, the other used to prepare the ketone 3,3-dimethyl pentanone-2 by the methods already described. Upon fractionation no trace of product could be found; only lower boiling products were recovered, indicating that no Grignard reagent had been formed in the original preparation.

The writer carried out a trial (.25 mole) Grignard on the bromide of tertiary amyl instead of the Chloride as described by Whitmore and Badertscher (14).

This yielded a black Grignard reagent that was without the presence of a precipitate. The Grignard reaction was completed using acetone to prepare the carbinol directly. Upon fractionation a small amount (4 grams), of product was collected in the boiling range of the carbinol.

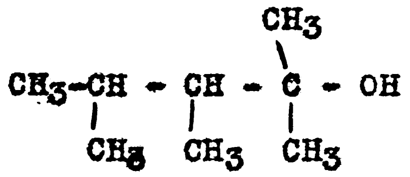
A 2 mole Grignard was carried out using 332 grams (2.2 moles) of halide and 87 grams (1.5 moles)of acetone which yielded upon fractionation a 12 percent yield of the carbinol, boiling at 45° - 47° C. at 6 mm.

A similar Grignard reagent (2 moles) was also made and was used to prepare the ketone 3,3-dimethyl pentanone-2. This gave a 30 percent yield of the ketone, boiling at 46-49° C. at 30 mm.

This .6 mole of ketone was added to a one mole methyl bromide Grignard which, in turn, gave a 50 percent yield of the carbinol boiling at 45.5-47° C. at 6 mm.

A six mole run carried out under similar conditions gave a 38% yield of the ketone from tertiary amyl bromide, which, in turn, gave a 59 percent yield of the carbinol from the ketone.

III 2,3,4-trimethyl pentanol-$_2$

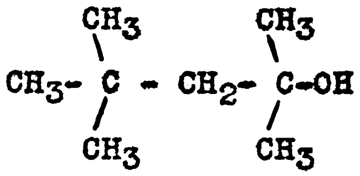


$$CH_3-\underset{CH_3}{CH}-\underset{CH_3}{CH}-\overset{CH_3}{\underset{CH_3}{C}}-OH$$

In this preparation the bromide prepared from methyl iso propyl carbinol and phosphorous tribromide did not have the correct boiling point for 2-bromo, 3-methyl butane as stated in the preliminary preparations.

A ketone-alcohol synthesis was carried out starting with this bromide and following the above outlined procedure. The yield of ketone obtained was 32%. From this an 81% yield of the alcohol (believed to be 2,3,3-trimethyl pentanol-$_2$) was obtained, boiling at 45 - 46.5° C. at 6 mm.

IV 2,4,4-trimethyl pentanol-2



$$CH_3-C(CH_3)_2-CH_2-C(CH_3)_2-OH$$

The method originally described by Butlerow (17) was used with some modifications for the preparation of this carbinol. The procedure consisted essentially of forming the iodide, 2-Iodo, 2,4,4-trimethyl pentane from diisobutylene and then changing the iodide to the alcohol by means of silver hydroxide (moist silver oxide).

The best method for preparing diisobutylene which is a modification of the procedure by Fenske and co-workers (19) was described by Whitmore(18). In a one-liter round bottom flask a cooled mixture of 500 ml. of c.p. sulfuric acid and 500 ml. of water was slowly added to 700 ml. of tertiary butyl alcohol while stirring. This solution was heated on the steam bath for three hours, then allowed to cool. When cool, the two layers were separated and the top layer washed with a dilute solution of sodium carbonate until neutral, then it was very slowly and carefully separated and placed in a distilling flask with a very small quantity of metallic sodium. Suction was then applied to remove a considerable quantity of dissolved isobutylene. The rest of the solution was vacuum distilled, keeping the temperature near

60°C., the first small fraction and the last high fraction being discarded. A second fractionation was carried out at ordinary pressure which gave a 34.5 percent yield of diisobutylene collected, at 100-105° C.

The iodide, 2-iodo,2,4,4-trimethyl pentane, was prepared by passing dry gaseous hydrogen iodide (preliminary preparations) into the diisobutylene until it was completely saturated. In order to have the addition of HI start, an initial temperature of 10°C was used. As soon as there was evidence of adsorption, the temperature was decreased to below o°C. by means of an ice salt bath. This crude iodide (at o°C.) was then washed with 200 ml. of distilled water (at 2°C.), which contained one crystal of sodium thiosulfate, to remove any dissolved hydrogen iodide or any free iodine present. (This iodide is quite unstable at room temperature; therefore it is advisable to keep it at least below 5°C.) After a careful separation, the top layer was drawn off and dried over calcium chloride in the refrigerator. To the dried iodide was added (at o°C.) the moist silver oxide in small quantities, while vigorously stirring. (Sufficient silver oxide has been added when the black silver oxide no longer changes to the yellow iodide upon addition). The resulting mixture was then allowed to come to room temperature and all the liquid was removed from the precipitated silver iodide by filtering with vacuum. The filtrate was separated and dried while the water from the filtrate was extracted twice with ether, dried and distilled. The precipitate was placed in a flask and the adsorbed carbinol was removed by vacuum distillation. The distillate consisted of two layers which were separated and treated in a manner similar to the filtrate. Upon the final distillation 12 percent of the diisobutylene was recovered, while a 44 percent yield of the carbinol was obtained.

TABLE OF RESULTS

ALCOHOL	BOILING POINT Temp. 0°C.	Press. mm.	REFRACTIVE INDEX n^D	SPECIFIC GRAVITY	SURFACE* TENSION
I	151.2	742	1.4308^{20°	$.8268^{26^\circ}$	22.121^{28°
II	155.5	740	1.4407^{20°	$.8395^{26^\circ}$	22.453^{28°
III	155.5	740	1.4406^{20°	$.8363^{26^\circ}$	22.387^{28°
IV	146	740	1.4290^{20°	$.8190^{26^\circ}$	20.911^{28°

* Du Nouy Tensiometer

ALCOHOLS

I 2_METHYL, 3_ETHYL PENTANOL-$_2$

II 2,3,3_TRIMETHYL PENTANOL-$_2$

III 2,3,4_TRIMETHYL PENTANOL-$_2$

IV 2,4,4_TRIMETHYL PENTANOL-$_2$

DISCUSSION

In the study of the preparation of these tertiary dimethyl amyl carbinols, the best synthesis was through the initial preparation of the corresponding heptanone. This ketone, when allowed to react with a methyl bromide Grignard reagent, gave a good yield in every instance.

The methyl bromide Grignard reagent was found more suitable than the methyl iodide reagent, because an excess of the bromide reagent could be used without the loss of product by dehydration, as would be the case if an excess of the iodide were used.

3-methyl butanol-2, the preliminary compound in the preparation of 2,3,4-trimethyl pentanol-2, did not yield 2-bromo,3-methyl butane, as expected, when brominated with phosphorous tribromide. A rearrangement, which gave tertiary amyl bromide, took place during the bromination.

SUMMARY

The three tertiary dimethyl amyl carbinols: 2-methyl,3-ethyl pentanol-$_2$;2,3,3-trimethyl pentanol-$_2$; and 2,4,4-trimethyl pentanol-$_2$ were prepared. These products will be used, in this laboratory, for the study of their condensation with benzene in the presence of aluminim chloride.

Preliminary work on the preparation of 2,3,4-trimethyl pentanol-$_2$ indicated that a method for brominating 3-methyl butanol-$_2$ must be found before the ketone synthesis can be used to obtain this carbinol.

BIBLIOGRAPHY

1. Huston and Hsieh J.A.C.S. 58 439 1936

Huston and Anderson Master's Thesis,
Michigan State College 1936

Huston and Hedrick J.A.C.S. 59 2001 1937

Huston and Guile J.A.C.S. 61 69 1939

2. Clark J.A.C.S. 39 574 1917

(or) Chemisches Zentralblatt 2 31 1908

3. Whitmore and Laughlin J.A.C.S. 54 4013 1932

4. Whitmore and Laughlin J.A.C.S. 55 3733 1933

5. Huston and Soulati Master's Thesis
Michigan State College 1936

6. Norton and Haas J.A.C.S. 58 2148 1936

7. Huston and Guile J.A.C.S. 61 69 1939

8. Gilman, Organic Synthesis Coll. Vol. Pg. 25

9. Gilman, Organic Synthesis Coll. Vol. Pg. 138

10. Drake and Cook, Organic Synthesis Vol. 12 Pg. 48

11. Mulliken Vol. IV # 4605 Pg. 88

12. Organic Synthesis Vol. 10 Pg.32

13. Gilman, Organic Synthesis Coll. Vol. I Pg. 419

14. Whitmore and Badertscher J.A.C.S. 55 1561 1933

15. Edgar J.A.C.S. 51 1485 1929

16. Gilman J.A.C.S. 45 150 1923

17. Butlerow Annalen 189 53 1877

18. Tongberg, Fenske
Pickens, Whitmore J.A.C.S. 54 3707 1932

19. Fenske & co-workers Ind. & Chem.
Eng. 24 408 1932